Available online at www.sciencedirect.com
SCIENCE DIRECT®
Inorganic Chemistry Communications 6 (2003) 1113–1116
INORGANIC CHEMISTRY COMMUNICATIONS
www.elsevier.com/locate/inoche

Clear Ag–Ag bonds in three silver(I) carboxylate complexes with high cytotoxicity properties

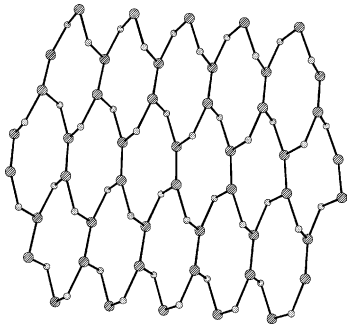
Hai-Liang Zhu [a,*], Xian-Ming Zhang [b], Xiu-Ying Liu [a], Xian-Jiang Wang [a], Gao-Feng Liu [a], Anwar Usman [c], Hoong-Kun Fun [c]

[a] *Department of Environmental and Chemical Engineering, Wuhan Institute of Science and Technology, Textile Road 1, Hongshan District, Wuhan 430073, PR China*
[b] *Department of Chemistry, Shanxi Normal University, Linfen, Shanxi 041004, PR China*
[c] *X-ray Crystallography Unit, School of Physics, Universiti Sains Malaysia, 11800 USM, Penang, Malaysia*

Received 1 March 2003; accepted 31 May 2003
Published online: 5 July 2003

Abstract

The reaction of Ag_2O and carboxylate ligands in ammonium solution results in three coordination polymers, $[Ag(fbc)]_n$ **1**, $[Ag_2(cpd)]_n$ **2** and $[Ag_2(idc)]_n$ **3**, where fbcH is 4-fluorobenzoic acid, $cpdH_2$ is cyclopentane-1,1-dicarboxylic acid and $idcH_2$ is iminodiacetic acid. The X-ray crystal structural analysis indicates that compounds **1** and **2** are two-dimensional frameworks and **3** is a three-dimensional framework. All the three complexes show clear Ag–Ag bonds and high cytotoxicity properties to normal cells and carcinoma cells.



Keywords: Silver coordination complex; Ag–Ag bonds; Cytotoxicity; Supramolecular chemistry

1. Introduction

One of the recently hot topics in the coordination chemistry of coinage metal(I) is the d^{10}–d^{10} interactions between two closed-shell cations, many examples of which have been reported and reviewed in silver(I) complexes [1]. We have been investigating on cytotoxicity of silver(I) complexes [2] and, as an extensive work, here report the syntheses, structures and cytotoxicities of three silver(I) complexes with carboxylate ligands. The three complexes show high cytotoxicity properties and clear Ag–Ag bonds in their structures.

2. Experimental

The complex was prepared by dissolving Ag_2O and bi-equimolar carboxylic acid (or equimolar carboxylic

* Corresponding author. Tel.: +86-27-87804252-377; fax: +86-27-87800795.
E-mail address: hlzhu@wist.edu.cn (H.-L. Zhu).

1387-7003/$ - see front matter © 2003 Elsevier Science B.V. All rights reserved.
doi:10.1016/S1387-7003(03)00205-3

Table 1
Crystallographic and experimental data for complexes **1**, **2** and **3**

Compound	**1**	**2**	**3**
Formula	$C_7H_4O_2FAg$	$C_7H_8O_4Ag_2$	$C_4H_5NO_4Ag_2$
FW	246.97	371.87	346.83
Crystal shape	Long rod	Cube	Long rod
Crystal size/mm	$0.29 \times 0.13 \times 0.08$	$0.40 \times 0.40 \times 0.40$	$0.19 \times 0.12 \times 0.06$
Crystal system	Monoclinic	Orthorhombic	Orthorhombic
Space group	$P2_1/c$	*Pbcn*	*Pbca*
a/Å	15.619(17)	6.447(2)	6.955(4)
b/Å	3.699(4)	10.893(3)	9.527(5)
c/Å	11.178(12)	23.536(10)	19.384(11)
α/°	90	90	90
β/°	98.951(15)	90	90
γ/°	90	90	90
U/Å^3	638.0(12)	1652.9(10)	1284.4(12)
Z	4	8	8
T/K	298(2)	293(2)	298(2)
μ/mm^{-1} (Mo-Kα)	3.102	4.712	6.053
D_c/g cm^{-3}	2.446	2.989	3.587
Reflections	1311	1305	1263
Independent reflections	972	991	1000
$F(000)$	448	1408	1296
T_{max}	0.7894	1.0082	0.7128
T_{min}	0.4665	0.9860	0.3926
Goodness of fit on F^2	1.025	1.079	0.879
R_1, $wR[I \geqslant 2\sigma(I)]$[a]	0.0407, 0.1029	0.0388, 0.0879	0.0211, 0.0368
R_1, wR (all data)[a]	0.0564, 0.1092	0.0602, 0.0979	0.0317, 0.0389

[a] $R_1 = \sum ||F_o| - |F_c|| / \sum |F_o|$, $wR_2 = \left[\sum w(F_o^2 - F_c^2)^2 / \sum w(F_o^2)^2\right]^{1/2}$, $w = \left[\sigma^2(F_o)^2 + (0.1(\max(0, F_o^2) + 2F_c^2)/3)^2\right]^{-1}$.

acid for **2** and **3**) for **1** in ammonium solution, which was stood still in the air to vaporize about three quarters of the solvents and filtered, washed three times with water, and dried in a vacuum desiccator over drying $CaCl_2$. The elemental analyses and IR sepectra confirmed the formulae of the complexes $[Ag(fbc)]_n$ **1**, $[Ag_2(cpd)]_n$ **2** and $[Ag_2(idc)]_n$ **3**, where fbcH is 4-fluorobenzoic acid, $cpdH_2$ is cyclopentane-1,1-dicarboxylic acid and $idcH_2$ is iminodiacetic acid.

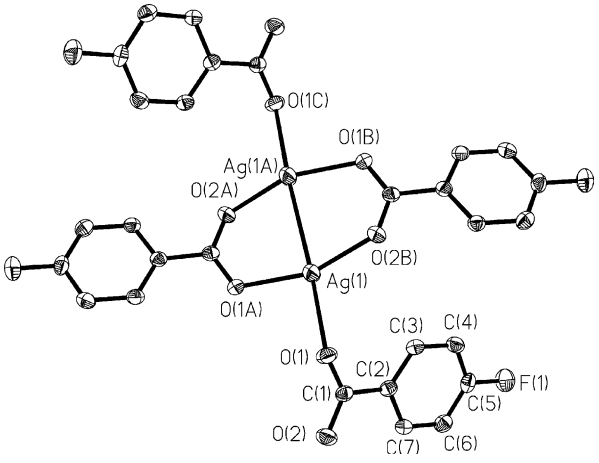


Fig. 1. Perspective view of the coordination environments of Ag in **1**.

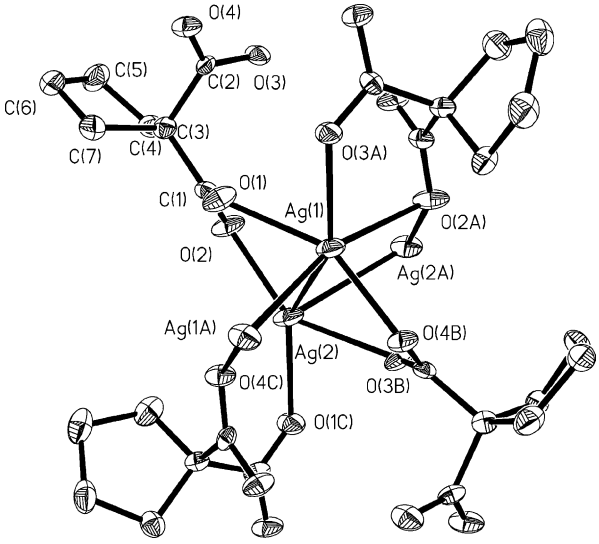


Fig. 2. Perspective view of the coordination environments of Ag in **2**.

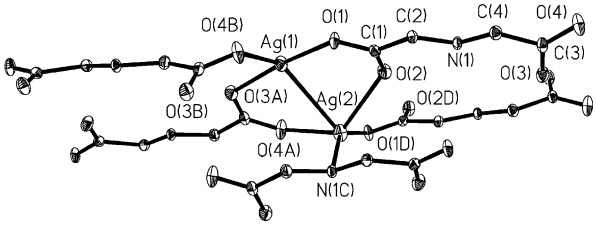


Fig. 3. Perspective view of the coordination environments of Ag in **3**.

Table 2
Selected bond lengths (Å) and angles (°) for complexes **1**, **2** and **3**

1			
Ag(1)–O(2B)	2.196(4)	Ag(1)–O(1)	2.512(4)
Ag(1)–O(1A)	2.210(4)	Ag(1)···Ag(1A)	2.850(3)
O(2B)–Ag(1)–O(1A)	157.9(2)	O(1)–Ag(1)–O(1A)	93.5(1)
O(2B)–Ag(1)–O(1)	99.0(2)		
2			
Ag(1)–O(4B)	2.213(6)	Ag(1)–O(3A)	2.404(6)
Ag(1)–O(1)	2.342(7)	Ag(1)–O(2A)	2.591(7)
Ag(1)···Ag(1A)	2.789(2)	Ag(1)···Ag(2)	2.850(1)
Ag(2)–O(2)	2.215(6)	Ag(2)–O(1C)	2.353(6)
Ag(2)–O(3B)	2.400(6)	Ag(2)···Ag(2A)	2.996(2)
O(4B)–Ag(1)–O(1)	151.7(2)	O(4B)–Ag(1)–O(2A)	84.1(2)
O(4B)–Ag(1)–O(3A)	128.0(2)	O(1)–Ag(1)–O(2A)	116.8(2)
O(1)–Ag(1)–O(3A)	74.3(2)	O(3A)–Ag(1)–O(2A)	88.4(2)
O(2)–Ag(2)–O(1C)	140.3(3)	O(1C)–Ag(2)–O(3B)	74.2(2)
O(2)–Ag(2)–O(3B)	143.8(2)		
3			
Ag(1)–O(3A)	2.201(2)	Ag(1)–O(4B)	2.488(3)
Ag(1)–O(1)	2.213(3)	Ag(1)···Ag(2)	2.939(1)
Ag(2)-N(1C)	2.284(3)	Ag(2)–O(1D)	2.382(3)
Ag(2)–O(4A)	2.365(3)	Ag(2)–O(2)	2.489(3)
O(3A)–Ag(1)–O(1)	172.5(1)	O(1)–Ag(1)–O(4B)	77.07(9)
O(3A)–Ag(1)–O(4B)	100.3 (1)	N(1C)–Ag(2)–O(4A)	116.6(1)
N(1C)–Ag(2)–O(1D)	146.2(1)	O(4A)–Ag(2)–O(2)	127.8(1)
O(4A)–Ag(2)–O(1D)	76.44(9)	O(1D)–Ag(2)–O(2)	96.82(8)
N(1C)–Ag(2)–O(2)	97.7(1)		

Table 3
Cytotoxicities of complexes **1**–**3**

Complex	IC_{50} (μM)						
	Hela	HepG2	BGC	95-D	CNE	L-02	NIH 3T3
1	8.1	8.7	9.3	8.7	16.2	17.4	41.6
2	4.2	4.2	6.3	4.2	10.8	4.2	4.2
3	20.6	13.4	25.4	26.8	60.1	25.8	11.7

The cytotoxicity properties of **1**–**3** were studied. Five human solid carcinoma cell lines, Hela (cervix adenocarcinoma), HepG2 (hepatocellular carcinoma), BGC (gastric carcinoma), 95-D (lung carcinoma), CNE (rhinocarcinoma) and two normal cell lines, NIH 3T3 (mouse normal fibroblast) and L-02 (human normal liver cell) were obtained from Shanghai Cell Institute of Chinese Science Academy. These cells were subcultured in media RMPI 1640 (GIBCO-BRL product) with 10% fetal bovine serum (Hyclone product), at 37 °C with 5% CO_2. Cells were adjusted to a concentration of 10^5 cells ml^{-1} and were planted in 96-well tissue culture plate, and then were exposed to the test compounds ranging in concentrations from 2.5 to 100 μg ml^{-1} for 48 h. The cells were pigmented by MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide], and the O.D. values were measured by ELX800 (universal microplate reader, BIO-TEK Instruments, Inc.) under 490 nm wavelength. The IC_{50} value (concentration of drug required to inhibit 50% growth) was calculated from linear regression of the percent viable cells versus the log of the drug concentration. As the results, the concentrations required to yield 50% inhibition of the viable cells (IC_{50}) [4] are listed in Table 3.

3. Structure description

The crystallographic data for the three compounds are summarized in Table 1. X-ray crystallographic study reveals that the asymmetric unit of compound **1** consists of one Ag ion and one ligand fbc. The asymmetric unit of both compound **2** and **3** consist of two Ag ions and one ligand, cpd and idc, respectively. The coordination geometries of Ag ion in three complexes are showed in Figs. 1–3, respectively.

What should be noted about the structures of the three complexes are the Ag–Ag distances (Table 2). The Ag–Ag distances of 2.850(3) Å in **1** and 2.789(2), 2.850(1) and 2.996(2) Å in **2** are all significantly shorter than that (2.89 Å) in metal silver [3], indicating an apparent Ag–Ag bond. In particular, the distance of 2.789(2) Å in **2** is among the shortest Ag–Ag separations ever reported and therefore indicates a more clear evidence of the existence of Ag–Ag bonding interactions. In addition, each Ag ion in **2** has another two Ag ions approaching to it. As to the compound **3**, the Ag–Ag distance of 2.939(1) Å is below the sum of van de Walls radii of two Ag ions (3.44 Å) and is close to the Ag–Ag distance in metal silver (2.89 Å), also indicating a strong interaction of Ag···Ag.

On the other hand, the Ag–O distances in complex **1**, **2** and **3** are all slightly longer than common Ag–O contacts in silver(I) complexes with similar aromatic carboxylic acids. It possibly also due to the existence of Ag–Ag bond.

In summary, there are clear Ag–Ag bonds in all the structures of the three complexes.

4. Cytotoxicity

The low IC_{50} concentrations of the three complexes show that they are strong cytotoxic in vitro [5] to normal cells and carcinoma cells. The high cytotoxicities to cells and good stability both to air and to light of these complexes imply that they are potential candidates for antitumor agents. On the other hand, different kinds of the cells have different sensitivities to these compounds, therefore, further exploration in generating analogous silver(I) complexes through appropriate chemical modification is required for higher selectivity as well as for understanding the structure–activity relation.

Notes

Anal. Calc. for **1**: C, 34.04; H, 1.63. Found: C, 33.83; H, 1.70. IR (KBr, cm^{-1}): 3170w, 1691w, 1604s, 1503s, 1376s, 1300w, 1233s, 1157m, 1097m, 1053w, 1014w, 959w, 852s, 796m, 773s, 689w. Anal. Calc. for **2**: C, 22.61; H, 2.17. Found: C, 22.55; H, 2.25. IR (KBr, cm^{-1}): 2941m, 1529vs, 1439s, 1395s, 1360vs, 1268m, 1203w, 882w, 801m, 775w, 711m. Anal. Calc. for **3**: C, 13.85; H, 1.45; N, 4.04. Found: C, 14.01; H, 1.50; N, 3.95. IR (KBr, cm^{-1}): 3290w, 1603m, 1559-1557vs, 1425m 1411m, 1384s, 1329m, 1292m, 1279m, 1109m, 1106m, 1035m, 966w, 915m, 730m, 700w.

Acknowledgements

H.K.F. thanks the Malaysian Government and Universiti Sains Malaysia for the research grant R&D No. 305/PFIZIK/61961. H.L.Z. thanks the Education Office of Hubei Province for the research grant 2002B29002. A.U. thanks Universiti Sains Malaysia for a Visiting Postdoctoral Fellowship.

References

[1] (a) V.W.-W. Yam, K.K.-W. Lo, Chem. Soc. Rev. 28 (1999) 323;
(b) M.C. Tse, C.M. Che, V.M. Miskowski, J. Am. Chem. Soc. 121 (1999) 4799;
(c) Q.-M. Wang, T.C.W. Mak, J. Am. Chem. Soc. 123 (2001) 1501.
[2] (a) H.-L. Zhu, Q. Chen, W.-L. Peng, S.-J. Qi, A.-L. Xu, X.-M. Chen, Chin. J. Chem. 19 (2001) 263;
(b) Q. Chen, S.-J. Qi, H.-L. Zhu, W.-L. Peng, A.-L. Xu, Chin. J. Med. Chem. 11 (2001) 5;
(c) Q. Chen, H.-L. Zhu, S.-J. Qi, W.-L. Peng, A.-L. Xu, Acta Sci. Natural Uni. Sunyatseni 40 (2001) 65.
[3] J. Emsley, The Elements, Clarendon, Oxford, 1989, p. 174.
[4] J. Carmichael, W.C. DeGrafp, A.F. Gazdar, Cancer Res. 47 (1987) 936.
[5] B. Rosenberg, L. van Camp, J.E. Trosko, V.H. Mansour, Nature 222 (1969) 385.