

Synthesis, Crystal Structure, and Cytotoxic Property of (5-Chloro-2-nitrobenzoato)bis(3-methyl-2-pyridylamine)-silver(I)

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5-Chloro-2-nitrobenzoic acid reacts with silver oxide and 3-methyl-2-aminopyridine to give a mononuclear silver(I) complex, [Ag(C₇H₃ClNO₄)(C₆H₈N₂)₂]. The complex was characterized by elemental analysis and X-ray diffraction. The Ag atom in the complex is three-coordinated by two pyridine N atoms from two 3-methyl-2-aminopyridine ligands and by one O atom of a 5-chloro-2-nitrobenzoate ligand, forming a distorted T-shaped coordination. In the crystal structure, the molecules are linked through intermolecular N–H···O hydrogen bonds, forming chains running along the *a* axis. The complex shows high cytotoxic property to both normal and carcinoma cells.

Keywords cytotoxic property, crystal structure, hydrogen bonding, silver complex, synthesis

INTRODUCTION

Silver(I) complexes with carboxylate anions as counter-ions or ligands are a group of metal compounds that, because of their wide usage in many fields, have received much attention and have been structurally characterized for many years.^[1–3] Studying the variety of products in the self-assembly processes between labile metal ions and multidentate ligands is an interesting topic in supramolecular chemistry. The balance between the formation of different structures is often subtle. Factors that affect the coordination topology include not only the highly influential factors of metal and ligand coordination preferences but also anion-based influences. The latter factor is particularly notable in silver(I) complexes. Owing to the versatile coordination geometry of silver, coordination numbers from two to six are possible, and because of the relatively weak nature of many Ag–ligand interactions, including some anion–Ag interactions, such

complexes are particularly susceptible to the influence of weaker supramolecular forces. Thus, one can not precisely predict what structure will be formed for the silver(I) complex, and more work needs to be done to understand better the influence effects of such complexes, which has becoming an interesting topic in supramolecular chemistry.^[4–6] Recently, we have reported a few silver(I) complexes.^[7] In this paper, the synthesis, crystal structure and cytotoxic property of a new silver(I) complex with the formula [Ag(C₇H₃ClNO₄)(C₆H₈N₂)₂], is reported.

EXPERIMENTAL

Materials and Measurements

All chemicals and reagents were commercially available and used without further purification. C, H, and N elemental analyses were performed on a Perkin-Elmer 240C elemental analyzer. The X-ray diffraction was carried out on a Bruker SMART 1000 CCD area diffractometer at 298(2) K.

Synthesis of the Complex

Ag₂O (0.1 mmol, 23.2 mg) and 5-chloro-2-nitrobenzoic acid (0.1 mmol, 20.1 mg) were dissolved in an ammonia solution (10 mL, 30%), and the mixture was stirred for 30 min at room temperature in the dark. To the above mixture was added with stirring the solid of 3-methyl-2-aminopyridine (0.2 mmol, 21.6 mg). The final mixture was further stirred for 30 min at room temperature in the dark. The resulting clear colorless solution was kept in the dark for five days, yielding colorless block-shaped crystals. Yield: 72%. Anal. calcd. for C₁₉H₁₉AgClN₅O₄: C, 43.5; H, 3.6; N, 13.3. Found: C, 43.2; H, 3.7; N, 13.5%.

X-ray Crystallography

A suitable single crystal of the complex was mounted on the top of a glass fiber. Graphite-monochromatized Mo-K α radiation ($\lambda = 0.71073 \text{ \AA}$) and the ω scan technique were used to collect the diffraction data. Absorption correction was applied

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TABLE 1
Crystallographic data for the complex

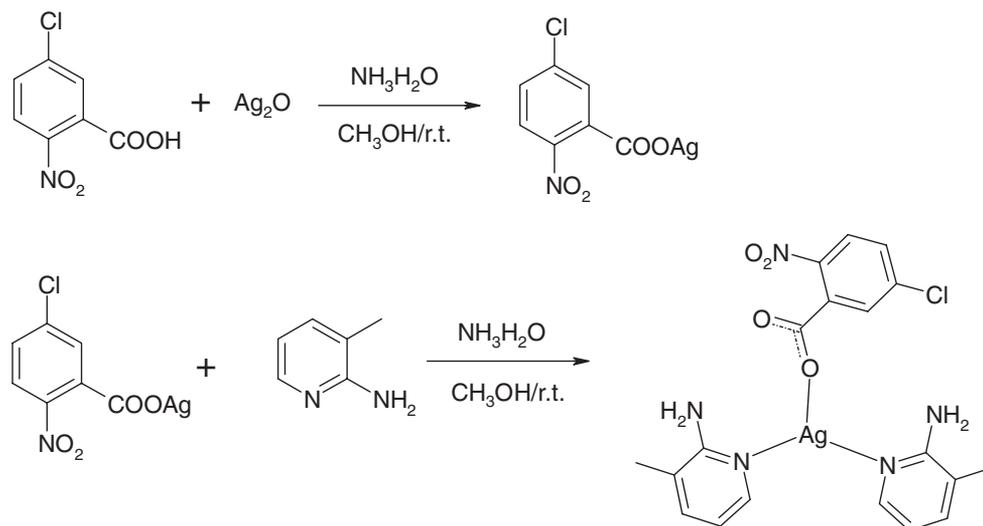
Formula	C ₁₉ H ₁₉ AgClN ₅ O ₄	T/K	298(2)
FW	524.71	μ /mm ⁻¹ (Mo-K α)	1.120
Crystal shape/color	Block/colorless	T_{\min}	0.7445
Crystal size /mm	0.28 × 0.27 × 0.27	T_{\max}	0.7520
Crystal system	orthorhombic	No. of measured reflections	12263
Space group	<i>Pna</i> 2 ₁	No. of unique reflections and R_{int}	3917 and 0.0405
$a/\text{\AA}$	9.589(2)	No. of observed reflections	2913
$b/\text{\AA}$	13.670(3)	data/restraints/parameters	3917/7/285
$c/\text{\AA}$	16.070(3)	$F(000)$	1056
$V/\text{\AA}^3$	2106.5(7)	Goodness of fit on F^2	1.037
Z	4	$R_1, wR_2 [I \geq 2\sigma(I)]$	0.0398, 0.0773
λ (MoK α)/ \AA	0.71073	R_1, wR_2 (all data)	0.0611, 0.0853

using SADABS.^[8] The crystal structure was solved with direct method and refined with a full-matrix least-squares technique using SHELXTL package.^[9] Anisotropic thermal parameters were applied to all non-hydrogen atoms. Amino hydrogen atoms were located from a different Fourier map and refined isotropically, with N–H and H ··· H distances restrained to 0.90(1) and 1.43(2) Å, respectively. Other hydrogen atoms were generated geometrically. The crystallographic data and the details of the data collection and refinement for the complex are listed in Table 1. Selected bond lengths and angles are given in Table 2. Hydrogen bonding information is given in Table 3. Crystallographic data for the complex has been deposited with the Cambridge Crystallographic Data Centre (CCDC 727572).

RESULTS AND DISCUSSION

Synthesis

The synthetic procedure is described as shown in Scheme 1.



SCH. 1.

Structure Description of the Complex

The compound is a mononuclear silver(I) complex, as shown in Figure 1. The Ag atom is three-coordinated by two pyridine N atoms from two 3-methyl-2-aminopyridine ligands and by one O atom of a 5-chloro-2-nitrobenzoate ligand, forming a distorted T-shaped coordination, the distortion being caused by the weak coordination of the carboxylate O atom (Ag1–O1 = 2.492(4) Å). The Ag–N bond lengths are comparable with the values observed in other silver(I) complexes.^[7,10–12] The two amino groups of the 3-methyl-2-aminopyridine ligands lie toward the same direction, due to the intramolecular N3–H3A ··· O1 and N5–H5A ··· O1 hydrogen bonds. The dihedral angle between the two pyridine rings is 18.3(3)°. The C1–C6 benzene ring forms dihedral angles of 23.4(3) and 71.8(3)°, respectively, with the O3–N1–O4 and O1–C7–O2 planes.

In the crystal structure of the complex, molecules are linked through intermolecular N–H ··· O hydrogen bonds, forming chains running along the *a* axis, as shown in Figure 2. There are no obvious short contacts among the chains.

TABLE 2

Selected bond lengths (Å) and angles (°) for the complex

Bond lengths			
Ag1–O1	2.492(4)	Ag1–N2	2.231(4)
Ag1–N4	2.226(3)		
Bond angles			
N2–Ag1–O1	112.43(14)	N4–Ag1–O1	103.05(13)
N4–Ag1–N2	137.31(15)		

TABLE 3

Hydrogen-bonding geometry (Å, °)

D–H···A	D–H	H···A	D···A	D–H···A
N5–H5B···O2 ⁱ	0.893(10)	2.14(2)	2.980(6)	157(4)
N5–H5A···O1	0.896(10)	2.082(13)	2.973(6)	173(5)
N3–H3A···O1	0.895(10)	2.426(18)	3.293(6)	163(5)

Symmetry code: (i) $-1/2 + x, 3/2 - y, z$.

TABLE 4

Cytotoxic results of the complex (IC₅₀, μM)

Hela	HepG2	BGC	95-D	CNE	L-02	NIH 3T3
21.3	15.7	12.3	32.3	8.9	23.2	20.7

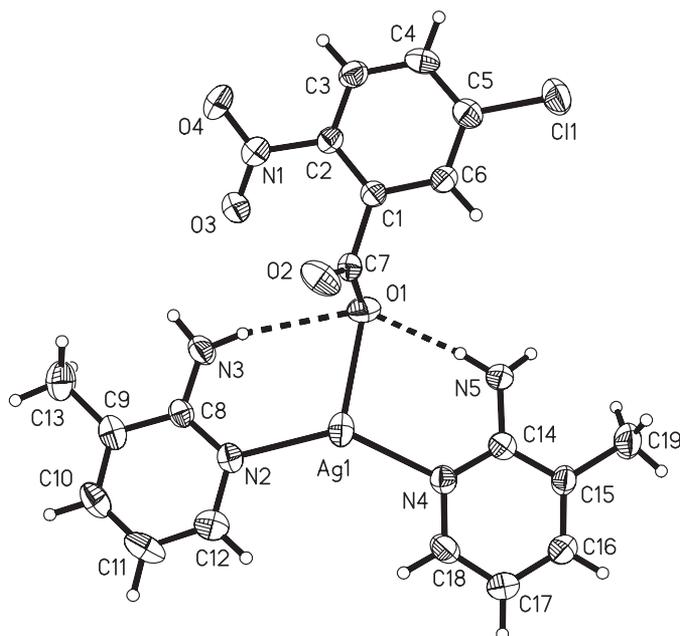
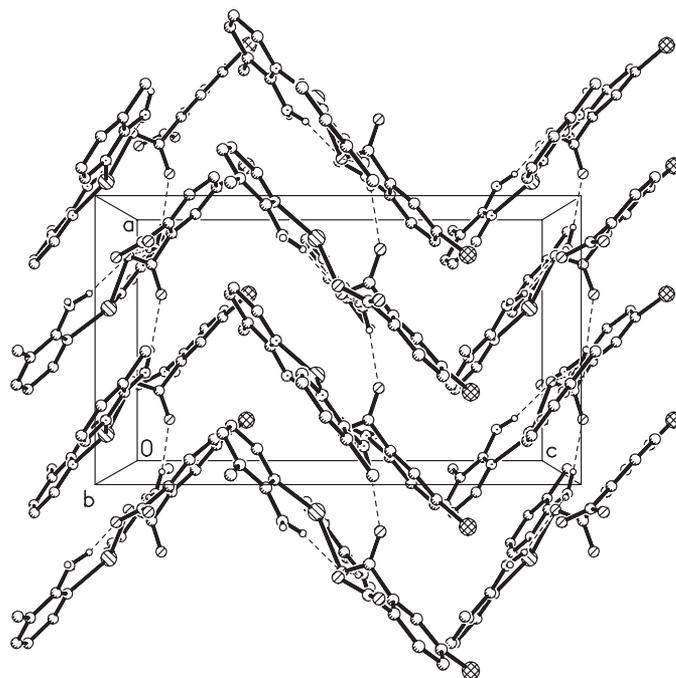


FIG. 1. The structure of the complex with 30% probability level. Intramolecular N–H···O hydrogen bonds are shown as dashed lines.

Cytotoxic Tests

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 Hubei Cancer Hospital. These cells were subcultured in media RMPI 1640 (GIBCO-BRL product) with 10% fetal bovine serum (Hyclone product), at 37°C with 5% cells ml⁻¹ and were planted in a 96-well tissue culture plate, and then were exposed to the test compounds with concentration ranging 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. Each test was performed in triplicate. The IC₅₀ values are listed in Table 4. It can be seen that the complex shows high cytotoxic property to both normal and carcinoma cells, which is in accord with those reported by Zhu and co-workers.^[13] Yet, it is difficult to conclude the structure–activity relationship, since the significant difference among the structures. Further work should be carried out to prepare analogous silver(I) complexes through appropriate chemical modification for higher activity and selectivity, as well as to explore the structure–activity relationship.

FIG. 2. Molecular packing of the complex, viewed along the *b* axis. Inter-molecular N–H···O hydrogen bonds are shown as dashed lines.

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