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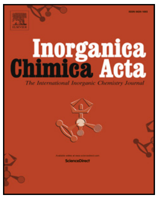

Research paper

Synthesis, structures and urease inhibitory activities of three silver(I) complexes derived from 2,6-dichlorophenylacetic acid

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ABSTRACT

Three new silver complexes based on 2,6-dichlorophenylacetate (dcpa), namely $[Ag_2(dcpa)_2]_n$ (**1**), $[Ag(NH_3)_2]$(dcpa) (**2**), and $[Ag_3(N,N\text{-eten})(dcpa)_3]_2$ (**3**) (*N,N*-eten = *N,N*-diethylethylenediamine), were synthesized and structurally characterized. The dcpa ligand adopts a μ_2-η^1:η^1 bridging coordination mode in silver complexes **1** and **3**, whereas it is a non-coordinating counter anion in silver complex **2**. Complex **1** shows a two-dimensional sheet polymer in which the dimeric $[Ag(dcpa)]_2$ units with a short Ag···Ag separation of 2.783 Å are linked to each other by weak Ag···O and Ag···Cl interactions. Complex **2** contains a linear $[Ag(NH_3)_2]^+$ cation and a dcpa anion, which constructs a two-dimensional sheet structure *via* intermolecular N–H···O interactions. Complex **3** features an unusual discrete hexanuclear silver(I) dimer, $[Ag_3(N,N\text{-eten})(dcpa)_3]_2$, formed by Ag···O and argentophilic interactions (Ag3···Ag3$^\#$ = 3.335 Å), which are further connected by intermolecular N–H···O interactions to offer a one-dimensional ladder-like chain. The urease inhibitory activities of the obtained silver complexes **1**, **2** and **3** were investigated and complex **3** was proven to be a potent inhibitor against jack bean urease.

1. Introduction

The self-assembly of silver(I) complexes containing carboxylate groups and ancillary ligands has become the focus of intense interest in coordination chemistry in recent years [1–3]. The inherent properties of the metal ion and ligands as well as the non-covalent interactions involving counterions and/or solvent molecules are the most important factors that affect the supramolecular assembly of silver(I) complexes into extended structures. The silver ion is the soft acceptor characteristic and has relatively flexible coordination sphere, which allows the ion to adopt coordination numbers ranging from two to six and to possess flexible coordination geometries varying from linear to trigonal planar, tetrahedral, square pyramidal, and octahedral. Silver(I) has been widely used to construct an extensive array of networks and topologies in the literature [4–6]. Besides, the closed d^{10} shell electronic configuration of silver(I) ions can result in argentophilic interactions involving ligand-supported or ligand-unsupported by the ancillary ligands. Such argentophilic interactions between d^{10} Ag(I) ions have been proved to play an important role in many supramolecular assemblies [7,8].

The ligands choice plays a critical role in the construction of argentophilic interactions. Multifunctional carboxylate ligands with the diversity bridging capacity have been utilized to promote the synthesis of various structures with Ag···Ag interactions. It is well known that silver(I) complexes with carboxylate groups tend to form a dimeric $(RCO_2)_2Ag_2$ eight-membered ring structure with the Ag···Ag interactions typically found in the range of 2.8–3.0 Å [9,10]. Furthermore, the supramolecular contacts such as H-bonding, Ag···π, π···π stacking, and host-guest interactions may link discrete subunits or low dimensional entities into generating multidimensional arrays or high-dimensional networks [11–15]. So far it was found that chloride-substituted phthalate ligands with versatile binding capability could form the Cl···Cl noncovalent interactions to generate the supramolecular architecture [16,17]. The various chloride-substituted phenylacetic acids such as 2,3-dichlorophenylacetic acid and 2,4-dichlorophenylacetic acid have also been used for supramolecular building blocks [18,19]. Our group recently described the ligand-unsupported and ligand-supported Ag···Ag interactions of silver complexes with chloride-substituted *trans*-cinnamates and their biological evaluations [20]. As a continuation of previous work on silver carboxylate complexes containing variable Ag…Ag

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argentophilic contacts, in this work we report the synthesis and structures of three silver(I) complexes derived from 2,6-dichlorophenylacetic acid, with formulas $[Ag_2(dcpa)_2]_n$ (**1**), $[Ag(NH_3)_2]$(dcpa) (**2**) and $[Ag_3$(*N,N*-eten)$(dcpa)_3]_2$ (**3**) (*N,N*-eten = *N,N*-diethylethylenediamine), and investigate their urease inhibitory activity properties.

2. Experimental

Urease (from jack beans, type III, activity 22 units/mg solid), (N-[2-hydroxy-ethyl] piperazine-N'-[2-ethanesulfonic acid]) buffer (HEPES), phosphate buffered saline (PBS) and urea (Molecular Biology Reagent) were from Sigma-Aldrich. All other chemicals and solvents were purchased from Alfa Aesar and used without further purification. Distilled water was used for all procedures. Elemental analyses (C, N, and H) were performed using an elementar vario EL *III* elemental analyzer. Infrared spectra were recorded using KBr pellets on a Nexus 870 FT-IR spectrophotometer in the 4000–400 cm^{-1} range. The enzyme inhibitory activity data were obtained with a Bio-Tek Synergy™ HT Enzyme-labeled meter.

2.1. Synthesis of the complexes

$[Ag_2(dcpa)_2]_n$ (**1**). A solution of Ag_2O (0.116 g, 0.5 mmol) in aqueous ammonia solutions (25 mL) was added to a stirred solution of 2,6-dichlorophenylacetic acid (Hdcpa) (0.205 g, 1 mmol) in methanol (25 mL). The resulting mixture was vigorously stirred for 30 min before being filtered. After slow evaporation of the filtrate at ambient temperature for ca. 10 days, colorless block crystals of **1** were obtained. The crystals of **1** were isolated, washed three times with distilled water and dried in a vacuum desiccator containing anhydrous $CaCl_2$. Yield: 0.202 g (65%). Anal. Calc. for $C_8H_5Cl_2AgO_2$: C, 30.81; H, 1.62%. Found: C, 30.68; H, 1.73%. IR (KBr, cm^{-1}): 3399(br), 2978(w), 2936(w), 1714(w), 1580(vs), 1433(m), 1384(vs), 1279(m), 1160(m), 1140(m), 1085(m), 943(m), 923(m), 851(w), 772(s), 683(m), 645(m), 577(m), 509(w), 449(w).

$[Ag(NH_3)_2]$(dcpa) (**2**). A solution of Ag_2O (0.116 g, 0.5 mmol) in aqueous ammonia solutions (25 mL) was added into a stirred solution of Hdcpa (0.205 g, 1 mmol) in aqueous ammonia solutions (25 mL). The resulting mixture was vigorously stirred for 30 min before being filtered. After slow evaporation of the filtrate at ambient temperature for ca. 10 days, colorless block crystals of **2** were obtained. The crystals of **2** were isolated, washed three times with distilled water and dried in a vacuum desiccator containing anhydrous $CaCl_2$. Yield: 0.249 g (72%). Anal. Calc. for $C_8H_{11}Cl_2AgN_2O_2$: C, 27.77; H, 3.20; N, 8.10%. Found: C, 27.61; H, 3.36; N, 8.00%. IR (KBr, cm^{-1}): 3312(br), 3148(w), 2974(w), 2938(w), 1710(w), 1611(m), 1580(vs), 1433(m), 1377(vs), 1267(m), 1162(m), 1138(m), 1081(m), 941(m), 908(m), 848(w), 767(s), 680(m), 640(m), 579(m), 509(w), 475(w), 437(w).

$[Ag_3$(*N,N*-eten)$(dcpa)_3]_2$ (**3**). A solution of Ag_2O (0.116 g, 0.5 mmol) in aqueous ammonia solutions (25 mL) was added into a stirred solution of Hdcpa (0.205 g, 1 mmol) and *N,N*-diethylethylenediamine (*N,N*-eten) (1 mmol) in aqueous ammonia solutions (25 mL). The resulting mixture was vigorously stirred for 30 min before being filtered. After slow evaporation of the filtrate at ambient temperature for ca. 10 days, colorless block crystals of **3** were obtained. The crystals of **3** were isolated, washed three times with distilled water and dried in a vacuum desiccator containing anhydrous $CaCl_2$. Yield: 0.091 g (52%). Anal. Calc. for $C_{30}H_{31}Cl_6Ag_3N_2O_6$: C, 34.25; H, 2.97; N, 2.66%. Found: C, 34.32; H, 3.06; N, 2.80%. IR (KBr, cm^{-1}): 3318(br), 3163(w), 2969(w), 2934(w), 2808(w), 1715(w), 1581(vs), 1436(m), 1383(vs), 1282(m), 1161(m), 1143(m), 1083(m), 1064(m), 940(m), 852(w), 773(s), 678(m), 644(m), 581(m), 514(w), 449(w).

2.2. Crystal structure determinations

A suitable crystal of silver complexes **1**, **2** and **3** was selected and measured on a Bruker Smart Apex CCD diffractometer using graphite-monochromated Mo Kα (λ = 0.71073 Å) radiation, respectively. The crystal was kept at 273–291 K during data collection. The collected data were reduced using the SAINT program, and empirical absorption corrections were performed using the SADABS program. Using Olex2 [21], the structure was solved with the olex2.solve [22] structure solution program using Charge Flipping and refined with the ShelXL [23] refinement package using Least Squares minimisation. All of the non-hydrogen atoms were refined anisotropically. All other hydrogen atoms were placed in geometrically ideal positions and constrained to ride on their parent atoms.

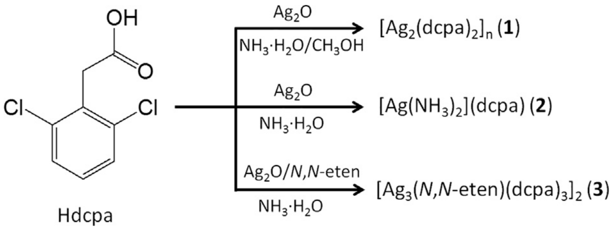
2.3. Measurement of jack bean urease inhibitory activity

The assay mixture containing 25 μL of jack bean urease (12 kU/L) and 25 μL of the test complexes with the concentration range of 0.5–7.5 μM (dissolved in DMSO:H_2O = 1:1 *v/v*) was preincubated for 1 h at 37 °C in a 96-well assay plate. After preincubation, 200 μL of 100 mM HEPES (N-[2-hydroxy-ethyl]piperazine-N′-[2-ethanesulfonic acid]) buffer pH = 6.8 containing 500 mM urea and 0.002% phenol red was added and incubated at 37 °C. The reaction was measured with a micro plate reader (560 nm), where an increase of the pH value from 6.8 to 7.7 for the HEPES buffer is determined by the color change of the Phenol Red indicator.

3. Results and discussion

3.1. Synthesis and characterization

Three silver complexes containing the 2,6-dichlorophenylacetate ligand were prepared in a one-pot reaction at room temperature as shown in Scheme 1. The complex **1** was synthesized in the stoichiometric ratio (1:2) of Ag_2O and 2,6-dichlorophenylacetic acid in a mixture solution of ammonia and methanol (1:1, *v/v*) while complex **2** was obtained in the stoichiometric amounts (1:2) in aqueous ammonia solution. The complex **3** was prepared from aqueous ammonia solution in the stoichiometric ratio (1:2:2) of Ag_2O, 2,6-dichlorophenylacetic acid and *N,N*-diethylethylenediamine (*N,N*-eten). The complexes **1**, **2** and **3** were characterized by single-crystal X-ray diffraction, FT-IR spectra and elemental analysis. The IR spectra results are consistent with the results of the X-ray diffraction analysis. The IR spectra of the three complexes show that the $\nu(C-Cl)$ stretching vibrations of dcpa ligands are at 772 cm^{-1} for **1**, 767 cm^{-1} for **2**, and 773 cm^{-1} for **3**, respectively. The characteristic stretching vibrations of the carboxylate groups of dcpa locate in the region of 1580–1581 cm^{-1} (ν_{asym}) and 1377–1384 cm^{-1} (ν_{sym}), respectively, with a $\Delta\nu$ value of 196–203 cm^{-1}. The IR spectra of **2** and **3** exhibit weak absorption bands at 3148 and 3163 cm^{-1}, respectively, due to the ν(N–H) stretching vibrations. In the spectrum of **2**, there is a characteristic absorption band at 1611 cm^{-1}, which can be assigned to the ammine deformation vibrations [24,25]. Besides, the presence of a weak ν(Ag–N) absorption at 437 cm^{-1} is consistent with silver-ammine coordination. This value represents a shift to higher



Scheme 1. The preparation route of three silver(I) complexes.