

Synthesis Of Some Novel Silver-Cysteamine Complexes

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Abstract: The aim of this research was to synthesize some new silver-cysteamine complexes of potential biological interest. Reactions were carried out between silver nitrate and cysteamine (2-aminoethanethiol hydrochloride) under different conditions of pH and mole ratios of the metal (silver) to the ligand (cysteamine). Some novel silver-cysteamine complexes were made, and after characterization of the complexes by cyclic voltammetry, pH measurements, and microanalysis, it is now obvious that the mole ratio of the metal to the ligand in complexes is about four to three.

Keywords: Silver-cysteamine complexes, cyclic voltammetry, pH measurements, microanalysis

Introduction

Cysteamine itself and some of its metal complexes have been used in chemistry and the pharmaceutical industry for many years [1-2]. For example, cysteamine has been used in treatment of cystinosis for several years. Cystinosis is a metabolic disease characterized by an abnormal accumulation of the amino acid cystine in various organs of the body such as kidney, eye, muscle, pancreas, and brain. Without specific treatment, children with cystinosis develop end-stage renal failure, i.e., lose their kidney function at approximately nine years of age.

The aim of specific treatments for cystinosis is to reduce cystine accumulation within the cells. This goal is achieved by cysteamine treatment, which has proven effective in delaying or preventing renal failure. The US Food and Drug Administration (FDA) has approved a capsule form of cysteamine called "CYSTAGON".

Cysteamine has been also used as a ligand in preparation of copper complexes by Parish and coworkers [3-5]. They investigated the structure of the complexes, as well as their biological properties. Because of the similarity of the chemistry of silver to copper (I), we decided to make some complexes of cysteamine with silver. Several experiments under different conditions (eg: pH, and the mole ratio of the ligand to the metal) were carried out and the structure of the complexes were investigated by analytical means.

Results and Discussion

1) Microanalysis results for 16 different silver-cysteamine complexes

Table 1 shows 16 different complexes with different calculated (taken) mole ratio of silver nitrate to cysteamine hydrochloride with different pHs. The table indicates that the mole ratio of the metal to the ligand is approximately four to three in all cases.

Table 1. Microanalysis data for the complexes prepared with different mole ratios of silver nitrate to cysteamine, at different pHs.

No.	Mole ratio of AgNO ₃ to cysteamine (taken)	pH	Microanalytical data (experimental)						Metal to ligand ratio (observed)
			%C	%H	%N	%S	%Ag	empirical formulas	
1	1 : 1	7	9.1	2.6	5.2	12.0	52	(C ₂ H ₇ NS), Ag _{1.3}	4 : 3
2	1 : 1	8	9.1	2.7	5.5	12.3	53.1	(C _{1.98} H ₇ NS), Ag _{1.28}	4 : 3
3	1 : 1	9	8.5	2.5	5.1	11.7	52.0	(C _{1.95} H _{6.9} NS), Ag _{1.32}	4 : 3
4	1 : 1	10	9.2	2.6	5.2	12.0	51.9	(C ₂ H ₇ NS), Ag _{1.29}	4 : 3
5	1 : 2	7	9.1	2.6	5.2	12.1	52.4	(C ₂ H ₇ NS), Ag _{1.3}	4 : 3
6	1 : 2	8	9.2	2.8	5.6	12.8	54.3	(C _{1.92} H ₇ NS), Ag _{1.25}	4 : 3
7	1 : 2	9	9.4	2.8	5.6	12.7	55.0	(C _{1.97} H ₇ NS), Ag _{1.28}	4 : 3
8	1 : 2	10	9.1	2.6	5.4	12.0	53.2	(C ₂ H _{6.9} NS), Ag _{1.31}	4 : 3
9	1 : 3	7	9.1	2.6	5.2	11.9	53.2	(C ₂ H ₇ NS), Ag _{1.32}	4 : 3
10	1 : 3	8	9.2	2.6	5.2	12.0	52.0	(C ₂ H ₇ NS), Ag _{1.3}	4 : 3
11	1 : 3	9	10.0	2.6	5.2	12.1	52.8	(C _{2.2} H ₇ NS), Ag _{1.31}	4 : 3
12	1 : 3	10	9.2	2.7	5.2	12.0	53.0	(C ₂ H _{7.2} NS), Ag _{1.32}	4 : 3
13	1 : 4	7	10.0	2.8	5.7	13.0	54.0	(C ₂ H ₇ NS), Ag _{1.27}	4 : 3
14	1 : 4	8	9.2	2.7	5.7	13.0	54.0	(C _{1.9} H _{6.8} NS), Ag _{1.25}	4 : 3
15	1 : 4	9	9.1	2.6	5.2	11.9	52.9	(C ₂ H _{7.1} NS), Ag _{1.32}	4 : 3
16	1 : 4	10	9.1	2.6	5.2	12.0	52.7	(C ₂ H ₇ NS), Ag _{1.31}	4 : 3

2) Electrochemical behavior of the cation, the ligand, and the complexes by cyclic voltammetry

- a) Electrochemical behavior of the silver cation: According to figure A, the voltammogram has a cathodic peak at 240, and an anodic peak at 500 mv versus SCE. The cathodic peak belongs to the reduction of Ag^+ to metallic silver. The anodic counterpart is related to the oxidation of metallic silver.

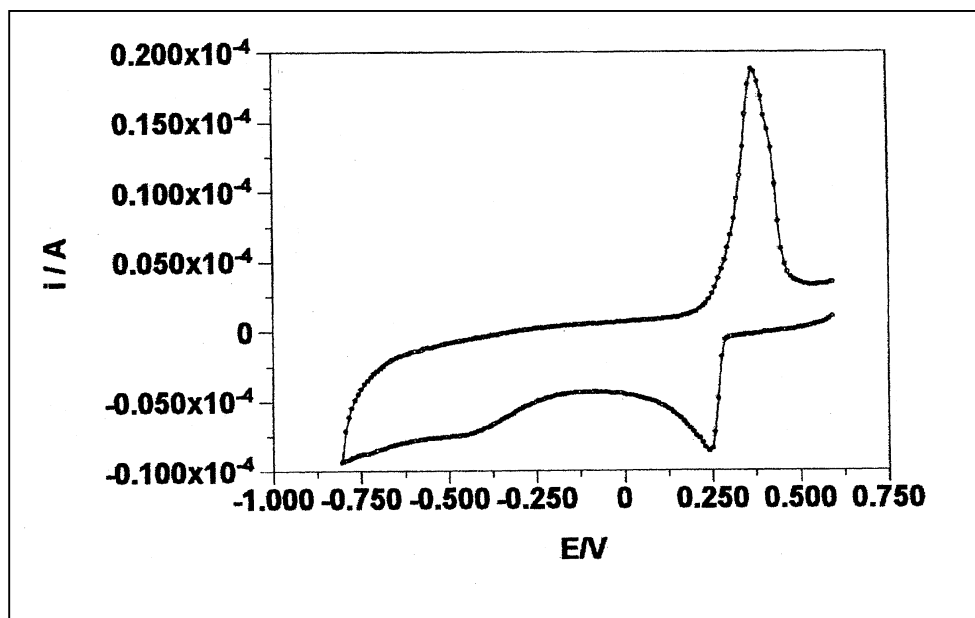


Figure A. Electrochemical behavior of the silver cation.

- b) Electrochemical behavior of the cysteamine ligand: According to figure B, the cysteamine ligand does not participate in any electron transfer in scanned region.

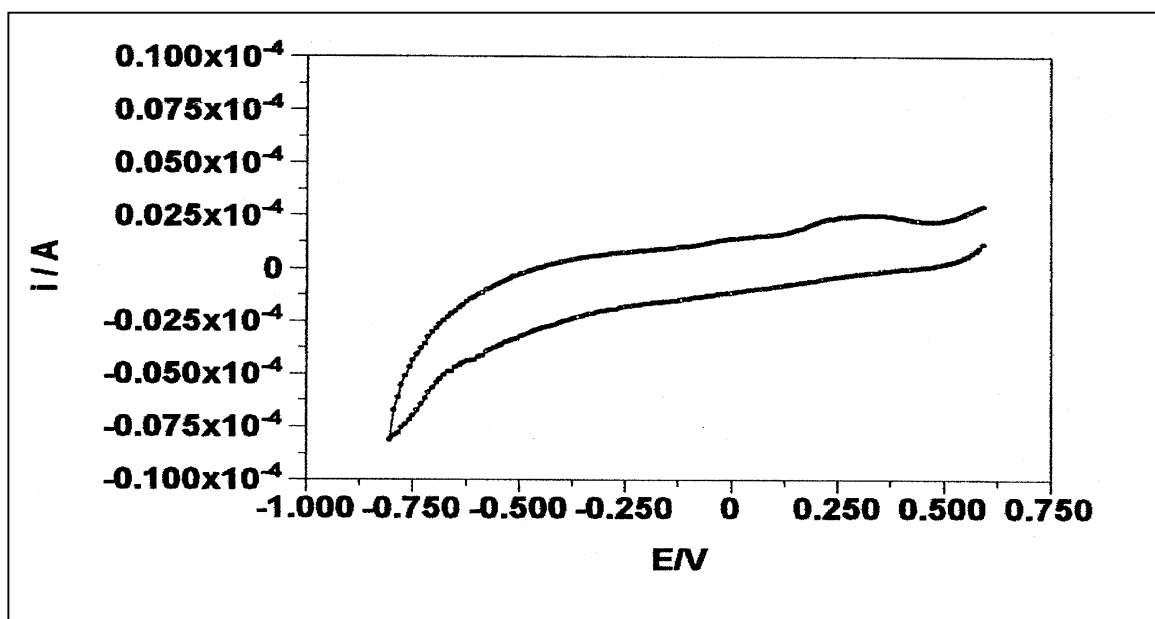


Figure B. Electrochemical behavior of the cysteamine ligand.

- c) Electrochemical behavior of the silver-cysteamine complex: According to figure C, and its comparison with the figure A, it can be seen that the anodic and the cathodic peaks of the complex were shifted to a more negative potential. The cathodic peak belongs to the reduction of the silver ion in the presence of ligand. Due to participation of the silver in formation of the complex, its reduction is more difficult, and thus it is reduced at a more negative potential. The anodic peak in the voltammogram belongs to the oxidation of metallic silver in the presence of the relevant ligand, and thus it is oxidized at a more negative potential in comparison with the simple oxidation of the silver (i.e. oxidation of the silver has been facilitated in the presence of the ligand).

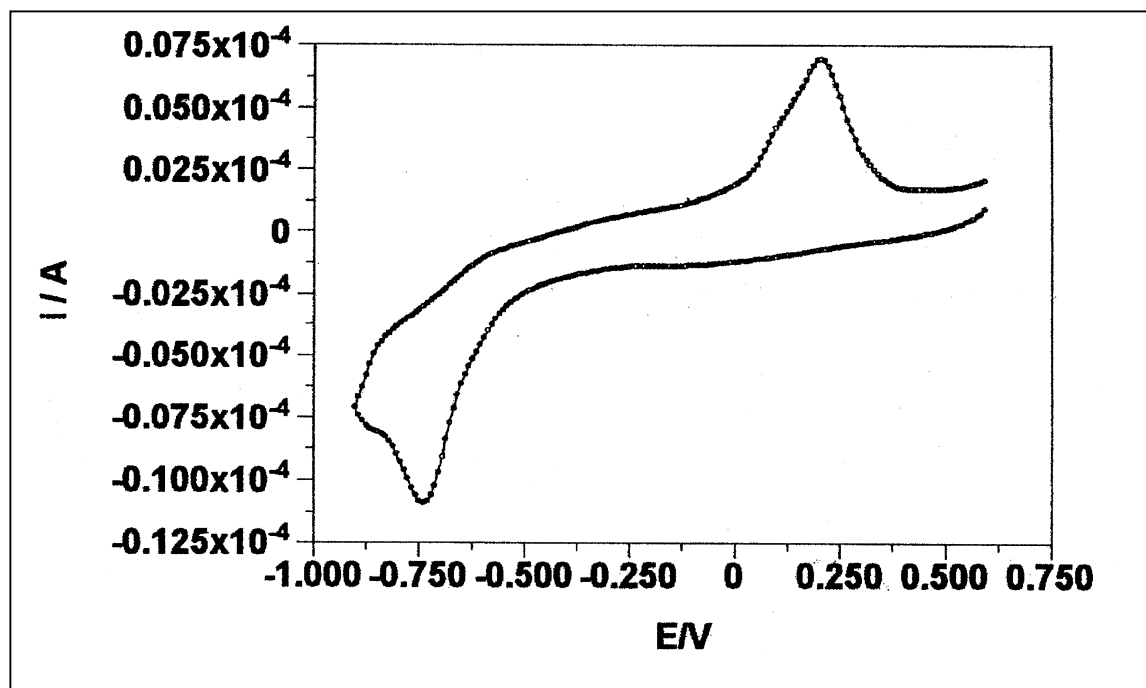


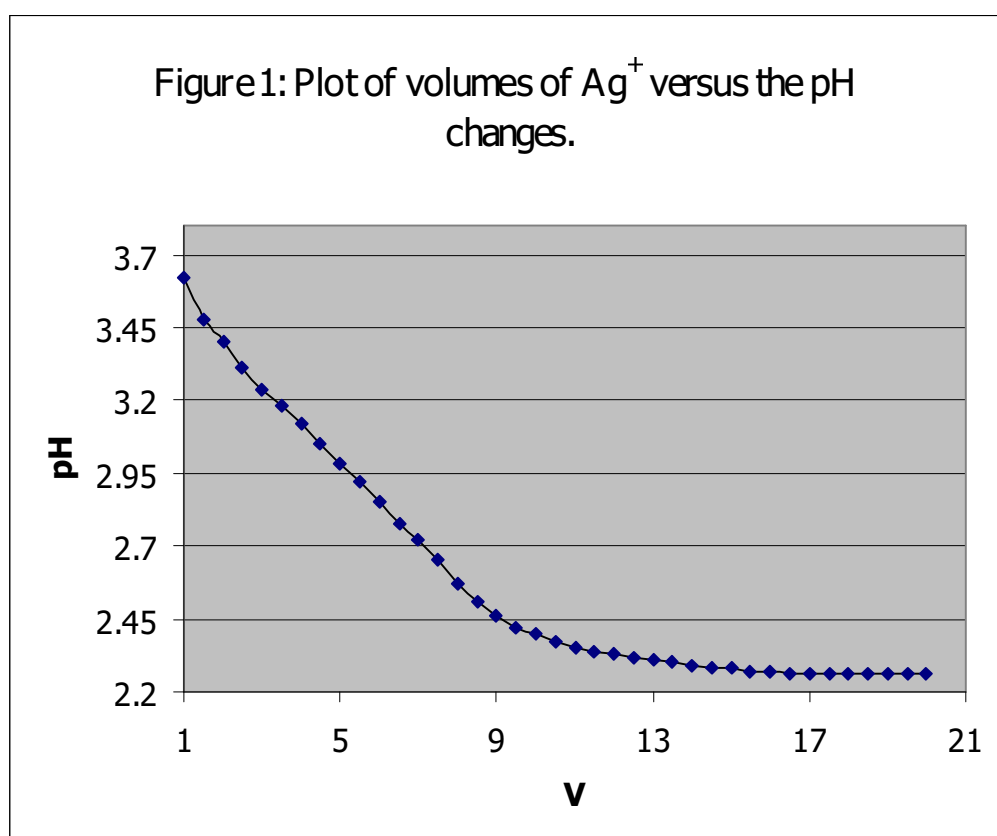
Figure C. Electrochemical behavior of the silver-cysteamine complex.

3) Formation of complexes by pH investigations

The mole ratio of the metal to the ligand can be determined by gradual addition of an aqueous solution of silver nitrate (0.01 M) to an aqueous solution of cysteamine hydrochloride (25 mL, 0.005 M), and the investigation of the resultant pHs.

Table 2. Volumes of silver nitrate (0.01 M), and the relevant pHs.

Volume of Ag^+	pH	Volume of Ag^+	pH	Volume of Ag^+	pH	Volume of Ag^+	pH	Volume of Ag^+	pH
1.0	3.62	5.0	2.98	9.0	2.46	13.0	2.31	17.0	2.26
1.5	3.48	5.5	2.92	9.5	2.42	13.5	2.30	17.5	2.26
2.0	3.40	6.0	2.85	10.0	2.40	14.0	2.29	18.0	2.26
2.5	3.31	6.5	2.78	10.5	2.37	14.5	2.28	18.5	2.26
3.0	3.24	7.0	2.72	11.0	2.35	15.0	2.28	19.0	2.26
3.5	3.18	7.5	2.65	11.5	2.34	15.5	2.27	19.5	2.26
4.0	3.12	8.0	2.57	12.0	2.33	16.0	2.27	20.0	2.26
4.5	3.05	8.5	2.51	12.5	2.32	16.5	2.26		



According to Table 2, as well as Figure 1, after addition of 16.5 mL of silver nitrate, the pH becomes constant. With respect to the consumption of silver nitrate (16.5 mL, 0.01 M), and cysteamine hydrochloride (25 mL, 0.05 M), the mole ratio of the metal to the ligand is approximately 4 to 3 ($16.5 \times 0.01 / 25 \times 0.005$), which is in excellent agreement with the microanalytical results.

Experimental

Preparation of silver-cysteamine complexes

a) Preparation of silver-cysteamine complexes using a 1:1 metal to ligand ratio:

An aqueous solution of silver nitrate (10 mL, 170 mg, 1 mmol) was added to 10 mL of an aqueous solution of cysteamine hydrochloride (113.6 mg, 1 mmol). After adjusting the pH by addition of NaOH (four different pHs, from 7 to 10), solids were filtered off and washed with water, ethanol and ether several times (at some pH values, there were no solids). All solid complexes were then submitted for microanalysis.

b) Preparation of silver-cysteamine complexes by using a 1:2 metal to ligand ratio:

The same procedure and conditions as described in (a) were applied, except that the amount of the ligand (cysteamine) was doubled (227.2 mg, 2 mmol). All solid complexes were then submitted for microanalysis.

c) Preparation of silver-cysteamine complexes using a 1:3 metal to ligand ratio:

The same procedure and conditions as in (a) were applied, except that the amount of the ligand (cysteamine) was tripled (340.8 mg, 3 mmol). All solid complexes were then submitted for microanalysis.

d) Preparation of silver-cysteamine complexes using a 1:4 metal to ligand ratio:

The same procedure and conditions as in (a) were applied, except that the amount of the ligand (cysteamine) was increased four fold (454.4 mg, 4 mmol). All solid complexes were then submitted for microanalysis.

Formation of silver-cysteamine complexes for pH investigations

To the aqueous solution of cysteamine hydrochloride (25 mL, 0.005 M), was gradually added the solution of silver nitrate (0.01 M), and the resulting pH values were measured (Table 2 and Figure 1).

Electrochemical behavior of the cation, the ligand, and the complexes by cyclic voltammetry

All experiments were carried out by Beckman Cyclic Voltammetry. Water was used as the solvent, potassium nitrate as the supporting electrolyte, a glass carbon electrode (5 mm diameter) as the working electrode, potassium wire as the auxiliary electrode, and a saturated calomel electrode (SCE) as the reference electrode.

a) The cation (Ag I): silver nitrate (2.11 mg, 0.0125 mmol) was dissolved in water (25 mL) and potassium nitrate (252.5 g, 2.5 mmol) was then added. The resulting solution was transferred to the voltammetric cell, and the relevant voltammogram (Figure A) was obtained.

b) The ligand (2-aminoethanethiol, cysteamine): 2-aminoethanethiol hydrochloride (1.42 mg, 0.0125 mmol) was dissolved in water (25 mL) and potassium nitrate (252.5 mg, 2.5 mmol) was then added. The resulting solution was transferred to the voltammetric cell, and the relevant voltammogram

(figure B) was obtained.

c) The complex $\text{Ag}(\text{SCH}_2\text{CH}_2\text{NH}_2)$: To the saturated solution of the complex in water (25 mL), was added potassium nitrate (252.5 mg, 2.5 mmol). The resulting solution was transferred to the voltammetric cell, and the relevant voltammogram (figure C) was obtained.

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Sample Availability: Samples are available from the authors.

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