

STABILITY AND TOXICITY OF A COMPLEX SALT OF SILVER  
CHLORIDE AND THIOUREA.\*

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During an investigation covering double-compounds of Silver Chloride with Thiourea, it was noted that it was impossible to obtain stable solutions of a complex compound of 1 mol Ag Cl and 5 mols Thiourea.

This compound has been described previously (1) as a stable compound in water.

Ag Cl·CH<sub>4</sub>N<sub>2</sub>S (2) is only sparsely soluble in water and easily decomposed.

The compound Ag Cl·5CH<sub>4</sub>N<sub>2</sub>S was prepared as described in German Patent No. 193,661. The preparation was evaporated *in vacuo* in a water-bath of 45° C.-50° C.

Six Gm. Ag Cl·5CH<sub>4</sub>N<sub>2</sub>S were dissolved in 120 cc. H<sub>2</sub>O. A clear solution was obtained which in a few minutes deposited a fine crystalline precipitate. This was filtered, washed with 120 cc. H<sub>2</sub>O, followed by 40 cc. of alcohol and by 15 cc. of ether. A residue of 0.76 Gm. remained.

0.4 Gm. was analyzed.—0.1932 Gm. Ag Cl was obtained. Found: 48.3% Ag Cl.  
Calculated for Ag Cl·2CH<sub>4</sub>N<sub>2</sub>S: 48.7% Ag Cl.

The solubility of this salt seemed to be about 0.1% in water. It was found that an addition of a small amount of Thiourea caused immediate solution in a small amount of water.

One mol Ag Cl·5CH<sub>4</sub>N<sub>2</sub>S was mixed with 1 mol and with 2 mols Thiourea, respectively, and the resultant mixtures dissolved in 10 parts of water. The Ag Cl·6CH<sub>4</sub>N<sub>2</sub>S compound deposited crystals in a few hours, while the Ag Cl·7C-H<sub>4</sub>N<sub>2</sub>S remained clear.

The toxicity of Thiourea is known to be low, but definite (3). In order to be certain that none of the results of this investigation should be influenced by toxic actions of free Thiourea, a 5% aqueous Thiourea solution was fed to 5 rats by way of a stomach tube.

CHART I.

Rat No.	Weight of Rat in Gm.	Dosage in mg.	5% Thiourea Solution, Cc.	Results.
21	214	107	2.14	Alive, no toxic symptoms
22	152	76	1.52	Alive, no toxic symptoms
23	146	73	1.46	Alive, no toxic symptoms
24	152	76	1.52	Alive, no toxic symptoms
25	102	51	1.02	Alive, no toxic symptoms

This chart shows that 0.5 mg. Thiourea was given per one Gm. of rat weight. This dosage represents a slight excess over the amount of Thiourea contained in the largest dose of Ag Cl·5CH<sub>4</sub>N<sub>2</sub>S + 2CH<sub>4</sub>N<sub>2</sub>S employed. This shows that the small additional amount of 2CH<sub>4</sub>N<sub>2</sub>S is of little influence upon the toxicity of the salt.

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## CHART II.

Rat No.	Weight in Gm.	Dosage of Ag Cl·5CH <sub>4</sub> N <sub>2</sub> S + 2C H <sub>4</sub> N <sub>2</sub> S per 1 Gm. Rat Weight.	Equivalent to Dosage of Ag Cl·5CH <sub>4</sub> N <sub>2</sub> S per 1 Gm. Rat Weight.	Amount of "Free" 2 mols CH <sub>4</sub> N <sub>2</sub> S per 1 Gm. Rat Wt.	Given as an Aqueous Solution of	Results.
1	140	0.26	0.20	0.06	2%	Alive, but severe toxic symptoms
2	108	0.26	0.20	0.06	2%	Alive, but severe toxic symptoms
3	156	0.26	0.20	0.06	2%	Alive, but severe toxic symptoms
4	166	0.26	0.20	0.06	2%	Alive, but severe toxic symptoms
5	140	0.26	0.20	0.06	2%	Alive, but severe toxic symptoms
6	142	0.325	0.25	0.075	2½%	Dead after 4 hours
7	178	0.325	0.25	0.075	2½%	Dead after 12 hours
8	150	0.325	0.25	0.075	2½%	Dead after 12 hours
9	200	0.325	0.25	0.075	2½%	Dead after 12 hours
10	175	0.325	0.25	0.075	2½%	Alive, but severe toxic symptoms
11	178	0.39	0.30	0.09	3%	Alive, but severe toxic symptoms
12	136	0.39	0.30	0.09	3%	Dead after 3 hours
13	132	0.39	0.30	0.09	3%	Dead after 1 hour
14	150	0.39	0.30	0.09	3%	Dead after 3 hours
15	142	0.39	0.30	0.09	3%	Dead after 3 hours

This chart indicates that the toxicity for Ag Cl·5CH<sub>4</sub>N<sub>2</sub>S + 2CH<sub>4</sub>N<sub>2</sub>S lies between 0.26 and 0.325 mg. per one Gm. rat weight. That would correspond to 0.2 and 0.25 mg. Ag Cl·5CH<sub>4</sub>N<sub>2</sub>S, provided that this compound remained stable in solution. As shown in the foregoing, this is not the case. It was of interest to determine how a freshly prepared solution of Ag Cl·5CH<sub>4</sub>N<sub>2</sub>S would differ from one which had 2 mols CH<sub>4</sub>N<sub>2</sub>S in addition. This was given as a 2½% aqueous solution.

## CHART III.

Rat No.	Weight in Gm.	Dosage of Ag Cl·5CH <sub>4</sub> N <sub>2</sub> S per 1 Gm. Rat Wt.	Results.
16	196	0.25	Alive, but severe toxic symptoms
17	170	0.25	Alive, but severe toxic symptoms
18	152	0.25	Alive, but severe toxic symptoms
19	160	0.25	Dead after 15 hours
20	165	0.25	Alive, but severe toxic symptoms

When compared with rats Nos. 6, 7, 8, 9 and 10 on Chart II, which had received the same dosage plus 2 mols of Thiourea, it is quite possible that the formation of Ag Cl·2 Thiourea might account for the lower toxicity when Ag Cl·5CH<sub>4</sub>N<sub>2</sub>S is given alone.

The additional toxicity of 0.75 mg. Thiourea per one Gm. rat weight does not seem in itself to be the reason, because as Chart I shows 0.5 mg. Thiourea per one Gm. rat weight showed no visible symptoms of toxicity.

## SUMMARY.

The complex salt Ag Cl·5CH<sub>4</sub>N<sub>2</sub>S was found to be unstable in aqueous solutions due to the formation of Ag Cl·2CH<sub>4</sub>N<sub>2</sub>S. Ag Cl·7CH<sub>4</sub>N<sub>2</sub>S was found to be

very stable in aqueous solutions. The toxicity of the latter compound is about 0.3 mg. per one Gm. rat.

## REFERENCES.

- (1) Ger. Patent No. 193,661.
- (2) Reynolds, *J. Chem. Soc.*, 61, 253 (1891).
- (3) Sollman, *Manual of Pharmacology*, 1936, page 743.

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SULFOMORPHID; AND THE PURPLE FLUORESCENCE TEST, A NEW  
DERIVATIVE TEST FOR MORPHINE.\*

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The product resulting from heating morphine in sulfuric acid was known to the early students of morphine chemistry as "sulphomorphid." Perhaps they had noted the loss of amine properties, and assumed that the nitrogen had in some way gone to the amide form. What actually happens (in addition to dehydration) is doubtless sulfonation, with formation of an inner salt (1). Modern texts either say nothing about the specific action of sulfuric acid, or, apparently losing sight of the actual nature of the usual product, say that apomorphine is formed. There probably is partial conversion to apomorphine with *diluted* sulfuric acid (5 plus 3, for example), but with the usual concentrated acid *no* apomorphine is formed under any circumstances.

True enough, the product may be regarded as a derivative of apomorphine, as well as a derivative of morphine. The derivative first formed with concentrated acid, at temperatures below 60° C., is probably identical with apomorphine-sulfonic-acid, as obtained and described by Kitasato and Goto (1, 2). But this is not apomorphine, any more than sulfanilic acid is aniline. Nor is there anything to indicate that apomorphine is formed first and then sulfonated. On the contrary, sulfonation, with formation of an inner salt, probably occurs first, almost coincident with solution; but dehydration begins simultaneously, and it is difficult, if not impossible, to separate these effects. Without any heating, at room temperature or even below, the transformation begins at once in concentrated acid; it is made complete within a few minutes by warming to 40–50° C. (3). As the acid is diluted its power to dehydrate seems to outlast, for a time, and to some extent, its power to sulfonate, so that a partial conversion to apomorphine, as appears from qualitative tests, may be obtained by heating. However, the unqualified assertion of many texts, that apomorphine is the resultant product, is little better than entirely erroneous, particularly as concentrated sulfuric acid seems to be the reagent meant.

## OBTAINING INSOLUBLE CRYSTALLINE SULFOMORPHID.

Place some dry morphine or its salt in a dry test-tube; dissolve in a little pure concentrated sulfuric acid, taking care to get all the morphine in the tube into solution. Stand in a beaker of water at about 40° C. for 7 or 8 minutes. Dilute with 1 cc. water for every 0.1 cc. sulfuric acid.

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