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Microchemical identification of Amidone.

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UNIVERSITY OF LOUISVILLE

MICROCHEMICAL IDENTIFICATION OF AMIDONE

A Dissertation

Submitted to the Faculty

Of the Graduate School of the University of Louisville

In Partial Fulfillment of the

Requirements for the Degree

Of Master of Science

Department of Chemistry

By

Robert C. Watson

Year

1948

NAME OF STUDENT: Robert C. Watson

TITLE OF THESIS: Microchemical

Identification of Amisone

APPROVED BY READING COMMITTEE COMPOSED OF THE
FOLLOWING MEMBERS:

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DATE: Oct. 9 1948

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Purpose

The purpose of the experimental work dealt with in this paper was to develop microchemical methods and tests to be used in the identification of Amidone.

At the present time there is in the literature little or no reference to suitable methods of identification of this new drug. Since Amidone is classed as a dangerous drug and placed under the Harrison Narcotic Act, it is highly desirable to have identifying tests to detect the presence of Amidone in seizures of illicit drugs by the Bureau of Narcotics.

Historical

In the 1930's the chemists in Germany were looking for an antispasmodic as a substitute for atropine and developed a compound which they called Dolantin. It was discovered that this drug was a better analgesic than antispasmodic and they introduced it to medicine as such in 1939. Subsequently Dolantin (known in this country as the drug Demerol) was shown to possess many morphine-like properties including those of tolerance and addiction liability, but its analgesic potency was more nearly like codeine than morphine.

The Germans made many Demerol derivatives, but apparently none showed more than minor improvement. At the same time they were developing a series of diphenyl derivatives and some of these showed remarkable activity. The outstanding example of the series the Germans called "10820" or "Amidon". Accounts of this substance have appeared in American literature under these designations and as "Dolophine" and "AN-148". Methadon is the name recommended for it by the Council on Pharmacy and Chemistry of the American Medical Association. Amidone is the name

which has been most commonly employed in investigative work.

It should be emphasized, however, that all of the names mentioned refer to the same chemical entity. Amidone then is 6-dimethylamino-4,4-diphenyl-3-heptanone. Chemically it is not at all related to morphine nor directly to Demerol. It is somewhat related to a diphenyl ethanolamine which has been described as mildly analgesic, but which is not at all morphine-like. The structural formulas for these compounds are shown below.

MORPHINE

DEMEROL

B-HYDROXY- α,β -DIPHENYL
ETHYLAMINE

AMIDONE

The hydrochloride of Amidone is a white crystalline substance, having a melting point of 236° C. It is soluble in water to about 5%, has a bitter taste, and is somewhat irritating when injected subcutaneously. Amidone is a racemate and has been resolved into its levo- and dextrorotatory isomers.

The racemate and the isomers have about the same toxicity in laboratory animals, but the analgesic effect and other morphine-like properties are exhibited chiefly by the l-form. In animals Amidone is three to ten times more toxic than morphine, according to the species, and two to three times more toxic than Demerol, but its analgesic effect is twice that of morphine and ten times greater than that of Demerol so it still has a very wide margin of safety.(1)

Using the German procedure in preparing Amidone, the Medical Research Division of Sharp and Dohme, Inc., led to the finding that the reaction between diphenylacetonitrile and 1-dimethylamino-2-chloropropane results in a mixture containing equal amounts of two isomeric aminonitriles, III (m.p. $66-67^{\circ}$) and IV (m.p. $90-91^{\circ}$). The high-melting nitrile (IV) reacted with ethylmagnesium bromide to

yield a product that possessed all of the properties reported for Amidone.

From these data, it appears that Amidone possesses the structure I although the structure II should result if the reaction followed a normal course. It seems probable that the reaction proceeds through the ethyleneimmonium ion (IX) in a manner similar to that demonstrated for other reactions of the halogenated alkylamines.(3)

The toxic doses of the optical isomers of Amidone upon intravenous injection in mice all lie between 15 and 18 mg./Kg. for LD50 value; for iso-Amidone nitrate the comparative figure is approximately 40 mg./Kg. (6)

The Approach to the Problem

1. All available compounds and reagents known to give crystalline precipitates with plant alkaloids, synthetic drugs, etc., were first tested with a 1/50 solution of Amidone for crystals.

2. From an inspection of the chemical formula of Amidone it was predicted that the ketone group would be most active. Therefore reactions with sodium bisulfite, hydroxylamine, phenylhydrazine, semicarbazide were tried. None of these reagents gave crystals with Amidone under the conditions of the experiment.

3. Screening tests were made on all other available elements and compounds and those not giving crystalline precipitates with Amidone were eliminated.

4. Substances giving crystals with Amidone were then further screened and selected by applying four principles of good crystal-forming reagents. (see page 12)

5. Ten substances were finally selected as reagents under step four and the best concentrations were arrived at by experiment.

6. The salts of all available alkaloids and synthetic

drugs were tested with each of the ten reagents to determine if similar crystals were formed with Amidone and to select the reagents giving the fewest crystalline precipitates with the common alkaloids.

7. Photomicrographs were made of the characteristic crystal formation with Amidone and the various reagents. Photographs were also made of the crystals formed by the selected reagents and the common alkaloids.

Experimental

Neutral aqueous solutions were made of all substances tested. For the most part 1% solutions were prepared, however, saturated solutions were made of compounds having low water solubility. Mild heat was applied when necessary to effect a clear solution. All solutions were filtered before testing. Water insoluble compounds were tested for solubility in dilute HCl and NH_4OH .

In general the same procedure was followed in making all of the preliminary screening tests. Three separate drops of the test solution were placed on a clean glass slide. One drop was acidified with dilute HCl, another made basic with dilute NH_4OH while the third was left neutral. If a precipitate formed after the addition of the acid or base the drop was removed from the slide and not further tested. Next a drop of Amidone solution (1/50) was placed on the slide adjacent to each test drop and allowed to flow into it. Microscopic examination of the slide was made at once, using the low power objective. If there was no immediate crystal formation the slide was allowed to stand for fifteen minutes and examined again. If no crystals had formed on standing the

material on the slide was discarded. Although all slides were examined under ultra-violet light, none showed fluorescent activity.

Substances Giving Crystals With Amidone

Of 197 substances tested only 42 gave crystalline precipitates with Amidone under the conditions of the experiment. These are shown in the following table. Unless otherwise indicated the concentration of the Amidone solution was 1:50 and the test solutions 5%.

<u>Test Solution</u>	<u>Crystal Formation</u>				
	<u>Class*</u>	<u>Class</u>	<u>Class</u>	<u>Class</u>	<u>Class</u>
	<u>A</u>	<u>B</u>	<u>C</u>	<u>D</u>	<u>E</u>
Ammonium Acetate		x	x		
Ammonium Carbonate	x	x			
Ammonium Hydroxide	x	x			
Ammonium Iodide				x	x
Ammonical Nickel Acetate (2)		x	x		
Ammonium Oxalate		x	x		
Ammonium Sulfide	x			x	
Ammonical Silver Nitrate (2)		x	x		
Barium Acetate	x		x	x	
Barium Chloride		x	x		
Barium Hydroxide (sat.soln.)		x	x		x
Bromine Water (sat.soln.)				x	x
Cadmium Iodide		x			x
Calcium Chloride	x	x	x		
Hydrobromic Acid (conc.)	x	x			
Hydriodic Acid (47%)	x			x	
Iodine (sat. soln.)				x	x

(Continued to next page)

Substances Giving Crystals With Amidone (Concluded)

<u>Test Solution</u>	<u>Crystal Formation</u>				
	<u>Class*</u>	<u>Class</u>	<u>Class</u>	<u>Class</u>	<u>Class</u>
	<u>A</u>	<u>B</u>	<u>C</u>	<u>D</u>	<u>E</u>
Mercuric Chloride				x	x
Mercuric Nitrate (sat.soln.)				x	x
Magnesia Mixture (2)	x		x	x	
Nickel Acetate		x	x		
Palladium Chloride (in dilute HCl)				x	x
Potassium Acetate		x	x		
Potassium-Bismuth Iodide	x	x	x		
Potassium Bitartrate		x	x		
Potassium Chromate	x			x	
Potassium Ferrocyanide				x	x
Potassium Iodide				x	x
Potassium Nitrate		x	x		
Potassium Oxalate		x	x		
Saccharin	x			x	
Silver Iodide-					
Potassium Iodide (1:15)	x	x			
Sodium Acetate			x	x	
Sodium Bicarbonate	x	x			
Sodium Borate	x	x			
Sodium Carbonate	x	x			
Sodium Fluoride		x	x		
Sodium Iodide			x	x	
Sodium Phosphate (dibasic)	x	x	x		
Sodium Silicate (sat. soln.)	x	x	x		
Sodium Sulfite	x	x	x		
Sodium Tungstate		x	x		

*Class A - Crystal shape not definite or distinct.

Class B - Crystals slow in forming.

Class C - Crystals probably due to reagent being thrown
out of solution.

Class D - Rapid crystal formation.

Class E - Crystals having definite and distinctive shapes.

Selection Of Reagents

Ten substances were selected as having the most possibilities for reagents. This selection was based on their appearance under Class D and Class E of the preceeding table. These compounds were reexamined and arranged below in order of their decreasing desirability.

<u>Test Solution</u>	<u>Qualities Possessed for Good Crystal Formation</u>			
	*			
	<u>Criteria I</u>	<u>Criteria II</u>	<u>Criteria III</u>	<u>Criteria IV</u>
1. <u>1% Palladium Chloride</u> <u>in dilute HCl</u>	x	x	x	x
2. <u>5% Potassium Ferrocyanide</u> <u>(freshly made)</u>	x	x	x	
3. <u>Dilute Bromine Water</u>	x	x	x	
4. <u>Saturated Iodine Water</u>		x		x
5. <u>1% Potassium Iodide</u>		x	x	
6. <u>3% Sodium Iodide</u>		x	x	
7. <u>1% Mercuric Nitrate</u>			x	
8. <u>Iodine-Potassium Iodide</u> <u>(dilute solution)</u>				x
9. <u>5% Cadmium Iodide</u>			x	
10. <u>1% Mercuric Chloride</u>			x	x

*Criteria I. Crystals should form rapidly from widely varying concentrations of sample and reagent, and should have well defined and characteristic shapes.

Criteria II. Slight variations in pH of media should not affect shape, formation time, etc., of crystals, nor should the presence of small amounts of impurities interfere with the test.

The proper concentration of reagents were determined by testing a 1/200 solution of Amidone with 1, 2, 5, 10 and 20% solutions of each reagent. After this was done each reagent was tested with Amidone solutions of the following concentrations: 1/50; 1/200; 1/500; and 1/1000. This was done to establish the optimum concentrations for each reagent and to ascertain the limit of reaction for each test. Photomicrographs were made of characteristic crystals formed with each reagent. (See Plates I to VI.)

The salts of 35 available narcotic alkaloids and synthetic drugs were tested with the selected reagents. (See Chart I.) Photomicrographs were made of the crystals produced with the more common alkaloids. (See Plates I to VI.)

Criteria III. A minimum of crystalline precipitates should be given with other drugs and these crystals should have distinctive shapes.

Criteria IV. The reagent should have a maximum of stability and should not be precipitated itself in a crystalline form resembling the crystals formed with the compound being examined.

Substances Not Giving Crystalline Precipitates With Amidone

Under the conditions of the experiment the following
substances did not yield crystalline precipitates with Amidone:

Acetic Anhydride	Bismuth Nitrate
Acetic Acid	Boric Acid
Aluminum-Potassium Sulfate	Cadmium Chloride
2-Amino-Sulfuric Acid	Cadmium Sulfide
Ammonium Chloride	Chloral Hydrate
Ammonium Molybdate	Calcium Carbonate
Ammonium Thiocyanate	Calcium Hydroxide
Ammonium Vanadate	Calcium Sulfate
Antimony-Potassium-Tartrate	Carbolic Acid
Antimony Sulfide	Citric Acid
Antimony tri-Chloride	Chromic Acid
Arsenic Chloride	Chromium Trichloride
Arsenic Trioxide	Chromium Nitrate
Barium Nitrate	Cobalt Acetate
Benzidine	Cobalt Chloride
Benzoic Acid (reagent crystals)	Cobalt Nitrate
Betanaphthal	Cobalt Sulfate

Cobalt Thiocyanate (blue ppt.)	Hydrochloric Acid
Cupric Acetate	Hydroxylamine-HCl
Cupric Ammonium Chloride	Iodic Acid
Cupric Bromide	Iridium Chloride
Cupric Carbonate	Krauts Reagent (<u>4</u>)
Cupric Chloride	Lactic Acid
Cupric Nitrate	Lanthanum Nitrate
Cupric Sulfate	Lead Acetate
p-Dimethyl Aminobenzaldehyde	Lead Iodide
Dimethyl Glyoxime	Lead Subacetate
2-4-Dinitro-phenylhydrazine	Lithium Carbonate
Diphenyl	Lithium Chloride
Diphenylamine	Lithium Nitrate
Ferric Chloride	Magnesium Chloride
Ferric Ammonium Citrate	Marme's Reagent (<u>4</u>)
Ferric Ammonium Sulfate	Mayer's Reagent (<u>4</u>)
Ferric Nitrate	Manganous Chloride
Ferrous Chloride	Mercuric-Potassium-Iodide
Ferrous Sulfate	Millons Reagent (<u>4</u>)
Formic Acid	Molybdic Acid
Froehdes Reagent (<u>4</u>)	Nickel Chloride
Gallic Acid	Nickel Nitrate

Nickel Sulfate	Potassium Chloride
Nitric Acid	Potassium Cyanide
o-Nitrobenzaldehyde	Potassium Dichromate
Oxalic Acid	Potassium Ferricyanide
Picric Acid	Potassium Hydroxide
Picrolonic Acid	Potassium Iodate
m-Phenylene-diamine-HCl	Potassium Permanganate
n-Phenylene-diamine-HCl	Potassium Phosphate
Phenylhydrazine-HCl	Potassium Sulfide
Phloroglucinol	Potassium-Zinc-Iodide
Phosphomolybdic Acid	Pyrogalllic Acid
Phosphoric Acid	Resorcinol
Phospho-Tungstic Acid	Rhodanine
Phthalic Anhydride	Rhodium Chloride
Platinum Chloride	Ruthenium Chloride
Potassium Acid Phthalate	Salicylous Acid
Potassium Arsenate	Selenious Acid
Potassium Bromate	Semi-Carbazide-HCl
Potassium Bromide	Silico-Tungstic Acid
Potassium Bisulfide	Silver Acetate
Potassium Carbonate	Silver Sulfate
Potassium Chlorate	Sodium Benzene-Sulfonate

Sodium Benzoate	Sulfamic Acid
Sodium Bichromate	Sulfuric Acid
Sodium Bisulfite	Sulfurous Acid
Sodium Chloride	Stannous Chloride
Sodium-Cobalt-Nitrate	Strontium Chloride
Sodium Formate	Tannic Acid
Sodium meta-Bisulfite	Tartaric Acid
Sodium Nitrate	Tetrachloro-Phthalic Acid
Sodium Nitrite	Tetrachloro-Phthalic Anhydride
Sodium Nitro Prusside	Uranium Acetate
Sodium Peroxide	Uranium Nitrate
Sodium Phospho-Molybdate	Wagner's Reagent (<u>4</u>)
Sodium Sulfate	Zinc Acetate
Sodium Sulfide	Zinc Chloride
Sodium Thiocyanate	Zinc-Chloro-Iodine
Sodium Tartrate	Zirconium Nitrate
Sodium Thiosulfate	

Detailed Description of Microcrystalline

Tests With Amidone

Palladium Chloride - These crystals form almost at once from an amorphous precipitate in the 1/50 solution and somewhat slower in the 1/200 solution. In greater dilutions the crystals were very slow in forming and resembled double headed flint spearheads. These crystals show brilliantly under polarized light. They grow to considerable size, forming rosettes of brown fern-like plates or fragments. One notable feature is the fact that the rod-like crystal growth occurs on one side only of each arm and at an angle of approximately 30° from the main axis. This was found to be the most satisfactory crystalline test. (Plate I, Figs. 1, 2, 3, 4)

Potassium Ferrocyanide - Crystals form at once from a clear solution in the 1/50 concentration. At first these crystals appear as bundles of needle-like rods curving outward at the ends, having somewhat the appearance of sheaves of grain. Later rosettes of plates were formed. Crystals were not formed in the more dilute solutions. The three dimensional growth of these crystals may best be observed under polarized light. (Plate II, Figs. 3, 4, 5)

Bromine Water - Many small crystals formed at once in all solutions, but those in the 1/500 and 1/1000 solutions were best for identification purposes. This test was improved by adding a drop of dilute HCl to the Amidone solution and stirring before adding the bromine water. The crystals at first appear to be single plates having notched ends in such a manner as to resemble the letter "N", when slightly out of focus. Later they develop into rosettes of rod-like plates. (Plate III, Fig. 1)

Iodine Water - Small plates, having notched ends similar to those produced with bromine water, first appear in the 1/50 solution of Amidone. In the more dilute solutions few crystals were formed. These crystals were slow in forming and small in size. Crystal formation may be improved by the addition of a drop of dilute HCl to the sample drop. (Plate III, Fig. 2)

Potassium Iodide - Heavy rosettes of fern-like crystals formed at once in the 1/50 solution of Amidone. The more dilute solutions on standing gave a few small crystals. In the 1/50 solution the crystals started as dark shapeless masses

which later began to branch. The crystal form was very dense and lacked detail, but had a characteristic shape. (Plate III, Fig. 3)

Sodium Iodide - These crystals have the same general appearance as those formed with potassium iodide. The addition of a drop of dilute HCl to the sample drop causes clearer crystal formation.

Mercuric Nitrate - These crystals form best in a neutral solution. A precipitate was formed in the 1/50 solution of Amidone only, from which crystals formed at once. These crystals sometimes dissolved in the reagent drop upon stirring. The crystals formed as rosettes of needles. This is not a sensitive test. (Plate III, Fig. 5)

Iodine-Potassium Iodide - Crystals formed rapidly in all solutions. The crystalline form was affected greatly by the concentration of the sample. In the 1/50 solution the crystals were rectangular plates while in the 1/500 solution they showed three dimensional growth and frequently resembled the letters "H", "Y", and "X". (Plate IV, Figs. 5, 6)

Cadmium Iodide - Rosettes of root-like crystals formed slowly from the 1/100 solution of Amidone. Their growth was three dimensional and only a portion of the crystal was in focus at one time. Crystals formed in the 1/200 solution were brown in color and not clearly defined. (Plate III, Fig. 6)

Mercuric Chloride - The best crystals occurred in the 1/200 solution of Amidone. They appeared at once from an amorphous precipitate as rosettes and bundles of rods which may be viewed to advantage under polarized light. (Plate VI, Fig. 1)

Amidone, when allowed to crystallize from a saturated aqueous solution, first appears as diamond shaped plates.

Preparation of Reagents For Microcrystalline Tests

1. Palladium Chloride - (Approximately 1% in dilute HCl). Make up 1 gram $\text{PdCl}_2 \cdot 2\text{H}_2\text{O}$ to 100 ml. with dilute HCl (35 ml HCl s.g. 1.19 q.s. 100 ml with distilled water), warm gently until solution is complete.
2. Potassium Ferrocyanide - (Approximately 5% aqueous solution). Make up 5 grams $\text{K}_4\text{Fe}(\text{CN})_6 \cdot 3\text{H}_2\text{O}$ to 100 ml with distilled water. (4) This reagent should be made up fresh each day since it slowly decomposes on standing.
3. Bromine Water - (Dilute solution). Make up 3.5 ml saturated bromine water to 100 ml with distilled water. This reagent should be made up frequently.
4. Iodine Water - (Saturated solution). Place about 1 gram I_2 in a test tube containing about 15 ml distilled water and warm gently over a flame until the I_2 vapors completely saturate the solution, cool and filter. For best results this solution should be completely saturated.

5. Potassium Iodide - (Approximately 1% solution). Make up 1 gram KI to 100 ml with distilled water. This solution may become yellow in time due to oxidation and should, therefore, be made up frequently.
6. Sodium Iodide - (Approximately 2% solution). Make up 3 grams NaI to 100 ml with distilled water. This solution may become brown in time due to the liberation of iodine and should be made up frequently.
7. Mercuric Nitrate - (Approximately 1% solution). Add 1 gram $\text{Hg}(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ to 100 ml distilled water. An insoluble basic salt is formed in dilute aqueous solutions or upon heating. Filter the solution, using only the clear filtrate in tests.
8. Iodine-Potassium Iodide - (Dilute solution). Make up 1.25 gram KI and 0.25 gram I_2 to 250 ml with distilled water.
9. Cadmium Iodide - (Approximately 5% solution). Make up 5.0 grams CdI_2 to 100 ml with distilled water. This solution may become yellow on long exposure to light and should be, therefore, made up frequently.

10. Mercuric Chloride - (Approximately 1% solution). Make up
1 gram HgCl_2 to 100 ml with distilled water.

Notes on Making Photomicrographs

In making photomicrographs it was sometimes found advisable to use a cover glass on the sample drop. In other cases this caused the crystals to become distorted in shape, as well as to increase the formation time.

A 16 mm. low power objective and a No. 10 ocular were used throughout. The camera lens was removed and the microscope draw-tube was extended into the camera bellows, allowing the image to be focused on a ground glass screen. Unusually good negatives were obtained in this manner, but some detail was lost in making the final prints.

Summary and Conclusion

Palladium Chloride (1%) in dilute HCl is a satisfactory reagent for the microcrystalline identification of Amidone, and offers several important advantages over other reagents tested.

Not only does it give characteristic crystals from widely varying solutions but it is not affected by slight differences in pH and gives relatively few crystalline precipitates with other common drugs.

Potassium Ferrocyanide (5%) and dilute Bromine Water make valuable collateral reagents when used in conjunction with Palladium Chloride.

CHART NO. 1REAGENTSGIVING CRYSTALLINE PRECIPITATES WITH AMIDONE

<u>Drugs Tested</u>	<u>Palladium Chloride</u>	<u>Potassium Ferrocyanide</u>	<u>Bromine Water</u>	<u>Iodine Water</u>	<u>Potassium Iodide</u>	<u>Sodium Iodide</u>	<u>Mercuric Nitrate</u>	<u>Iodine-Potassium Iodide</u>	<u>Cadmium Iodide</u>	<u>Mercuric Chloride</u>
Dicodid	-	-	-	a	-	-	-	a	a	-
Dilaudid	-	-	-	a	-	-	-	a	a	-
Demerol	-	-	-	a	-	-	-	a	a	-
Cocaine	-*	-	-	a	-	Q*	-	a	a	a
Morphine	-	a	-	-	-*	-	a	c	c	-*
Narcotine	a	-	a	a	a	-	a	a	a	-
Codeine	-	-	a	a	-*	c	a	c	c	-
Narceine	-*	c*	-	a	-*	c	a	c	a	a
Thebaine	a	-	-	a	-	-	a	a	a	a
Papaverine	a	a	a	a	a	a	c	c	c	c
Dionin	-	-	-	a	-	-	-	c	a	-*
Pantopon	-	-	-	a	-	-	-	a	c	-
Heroin	-	-	-	-	-	-	-	a	a	-*
Atropine	-	-	-	c	-	-	a	c	a	-
Caffeine	c	-	-	-	-	-	-	-	-	-*
Brucine	c	-	-	c	-*	c	-	c	a	c
Strychnine	c	-*	-	c	c	c	a	c	c	-*
Saccharin	-	-	-	-	-	-	a	-	a	-
Stovaine	-	-	a	a	-	-	a	a	a	a
Quinine	-	a	a	c	-	-	c	a	a	c*
Novocaine	-	-	-	a	-	-	-	a	a	a
Alpin	-	-	a	a	c	c	-	c	a	c
Phenacetin	-	-	-	-	-	-	c	-	-	-
Sulfon-Methane	-	-	-	-	-	-	-	-	-	-

(Continued on next page)

CHART NO. 1R E A G E N T SGIVING CRYSTALLINE PRECIPITATES WITH AMIDONE (Concluded)

<u>Drugs Tested</u>	<u>Palladium Chloride</u>	<u>Potassium Ferrocyanide</u>	<u>Bromine Water</u>	<u>Iodine Water</u>	<u>Potassium Iodide</u>	<u>Sodium Iodide</u>	<u>Mercuric Nitrate</u>	<u>Iodine-Potassium Iodide</u>	<u>Cadmium Iodide</u>	<u>Mercuric Chloride</u>
Sodium Phenobarbital	c	-	-	-	-	-	a	-	-	a
Nembutal	c	-	-	-	-	-	a	-	a	a
Seconal	a	-	-	-	-	-	a	-	a	a
Ephedrine-Amytal	-	-	-	-	-	-	a	-	-	a
Digitalin	-	-	-	-	-	-	-	-	-	-
Nitroglycerine	-	-	-	-	-	-	-	-	-	-
Scopolamine	-	-	-	-	-	-	-	-	-	-
Strophauthin	-	-	-	-	-	-	-	-	-	-
Ergotrate	-	-	-	-	-	-	-	-	-	-
Nicotine	-	-	-	a	-	-	a	a	a	a*

a = Amorphous precipitate

c = Crystalline precipitate

* Disagreement with the findings of Stephenson (5) previously reported. It should be noted that the reagent concentrations discussed in this paper differ in most cases from those used by Stephenson.

CRYSTALS FORMED WITH PALLADIUM CHLORIDE

PLATE I

Fig. 1.-Amidone 1 : 50

Fig. 2.-Amidone 1 : 200

Fig. 3.-Amidone 1 : 500

Fig. 4.-Amidone 1 : 1000

Fig. 5.-Brucine 1 : 100

Fig. 6.-Caffeine 1 : 100

CRYSTALS FORMED WITH PALLADIUM CHLORIDE

PLATE II

Fig. 1.-Strychnine 1 : 50

Fig. 2.-Strychnine 1 : 1000

CRYSTALS FORMED WITH POTASSIUM FERROCYANIDE

Fig. 3.-Amidone 1 : 50

Fig. 4.-Amidone 1 : 50

Fig. 5.-Amidone 1 : 200

Fig. 6.-Strychnine 1 : 50

CRYSTALS WITH BROMINE WATER

CRYSTALS WITH IODINE WATER

PLATE III

Fig. 1.-Amidone 1:200

Fig. 2.-Amidone 1:50

CRYSTALS FORMED WITH POTASSIUM IODIDE

Fig. 3.-Amidone 1:50

Fig. 4.-Narceine 1:100

CRYSTALS WITH MERCURIC NITRATE

CRYSTALS WITH CADMIUM IODIDE

Fig. 5.- Amidone 1:50

Fig. 6.-Amidone 1:1000

CRYSTALS FORMED WITH SODIUM IODIDE

PLATE IV

Fig. 1.-Amidone 1:50

Fig. 2.-Strychnine 1:50

Fig. 3.-Narceine 1:100

Fig. 4.-Codeine 1:50

CRYSTALS FORMED WITH IODINE-POTASSIUM IODIDE

Fig. 5.-Amidone 1:50

Fig. 6.-Amidone 1:500

CRYSTALS FORMED WITH IODINE-POTASSIUM IODIDE

PLATE V

Fig. 1.-Brucine 1:500

Fig. 2.-Morphine 1:50

Fig. 3.-Narceine 1:100

Fig. 4.-Codeine 1:50

Fig. 5.-Atropine 1:50

CRYSTALS FORMED WITH MERCURIC CHLORIDE

PLATE VI

Fig. 1.-Amidone 1:200

Fig. 2.-Caffeine 1:100

Fig. 3.-Morphine 1:50

Fig. 4.-Papaverine 1:50

Fig. 5.-Quinine 1:50

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