To what extent the silver ions adsorbed to the nuclei are directly derived from migrant silver ions of the silver halide crystal, or from the contiguous solution, is not yet clear, and must await further researches. Also, the direct determination of silver-ion adsorption to metallic silver and to silver sulfide is under investigation as a further phase of the present work, and also the direct determination of the adsorption of gelatin to silver halide. Incidentally, later experiments have shown that under the conditions studied in the foregoing experiments no adsorption of developer was found on silver sulfide.

Summary

1. A method is described for the determination of the adsorption of organic reducing substances to metallic (colloid) silver in an oxygen-free atmosphere.

2. Under these conditions no adsorption of hydroquinone or of methyl-*p*-aminophenol was observed greater than accountable by the error of experiment, of the order of ~0.3 per cent.

3. It is concluded that the evidence adduced by A. J. Rabinovitch in support of the hypothesis of adsorption to metallic silver is unreliable.

4. Experiments under the same conditions with silver sulfide failed to show any adsorption of these developers.

5. The bearing of the results on the theory of photographic development is discussed.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

The Synthesis of Pyrimidine and Purine Derivatives of Cystamine and of a New Type of Thiazolidinopyrimidine[1]

BY ALAN HART NATHAN AND MARSTON TAYLOR BOGERT

Following up the investigations on the synthesis of some new pyrimidines and uric acids from cystamine, by Mills and Bogert,[2] the classical Traube method[3] was utilized for the preparation of the desired iminobarbituric acid (IX) by condensation of *bis*-(β-ureidoethyl) disulfide (V) with cyanoacetic acid and acetic anhydride to the corresponding cyanoacetyl derivative (VIII), and cyclization of the latter by treatment with aqueous alkali.

Baum[4] has reported that, in the cyclization of cyanoacetylurea and of its derivatives, very small amounts of alkali suffice to bring this about, but that there is apt to be a simultaneous competing hydrolytic action. This hydrolysis occurs most easily with cyanoacetylurea itself, less readily with N-alkyl derivatives, and not to any appreciable extent with N,N′-disubstituted ureas. In our experiments, concentrated sodium hydroxide effected the cyclization of the ureido compound (VIII) to the iminobarbituryl derivative (IX), but weaker alkalies, *e. g.*, sodium bicarbonate and ammonium hydroxide, were found to be equally effective and therefore were used, to diminish the risk of hydrolysis.

By the action of sodium or isoamyl nitrite on (IX), an isonitroso group was introduced in position 5, and the resultant iminovioluric acid (X) was reduced by sodium hydrosulfite in ammoniacal solution, following the procedure of Hepner and Frenkenberg[5] to the corresponding diaminouracil (XI). Fused with urea at 170–180°, by the Gabriel and Colman method,[6] the uric acid derivative (XII) was obtained.

The reduction of this disulfide (XII) to the corresponding mercaptan, with immediate or subsequent cyclization to a thiazolidinouric acid, has not yet been accomplished.

Mills and Bogert[2] synthesized a *bis*-(β-[uric acid ethyl]) disulfide, in which it was not determined whether the —SCH_2CH_2— group was attached to the uric acid nucleus at position 1 or position 3. Since the compound (XII) described in the present paper carries its —SCH_2CH_2— group in position 3, and is not identical with the Mills and Bogert product, it follows that the latter is probably the isomer carrying the substitution in position 1. This conclusion is supported also by the fact that the Mills and Bogert uric acid was prepared

(1) Presented in abstract before the Division of Organic Chemistry, April 10, 1940, at the Cincinnati Meeting of the Am. Chem. Soc.

(2) Mills and Bogert, THIS JOURNAL, **62**, 1173 (1940).

(3) (a) Traube, *Ber.*, **33**, 1371, 3036 (1900); (b) Conrad, *Ann.*, **340**, 310 (1905).

(4) Baum, *Ber.*, **41**, 532 (1908).

(5) Hepner and Frenkenberg, *Helv. Chim. Acta*, **15**, 350, 533 (1932).

(6) Gabriel and Colman, *Ber.*, **34**, 1247 (1901).

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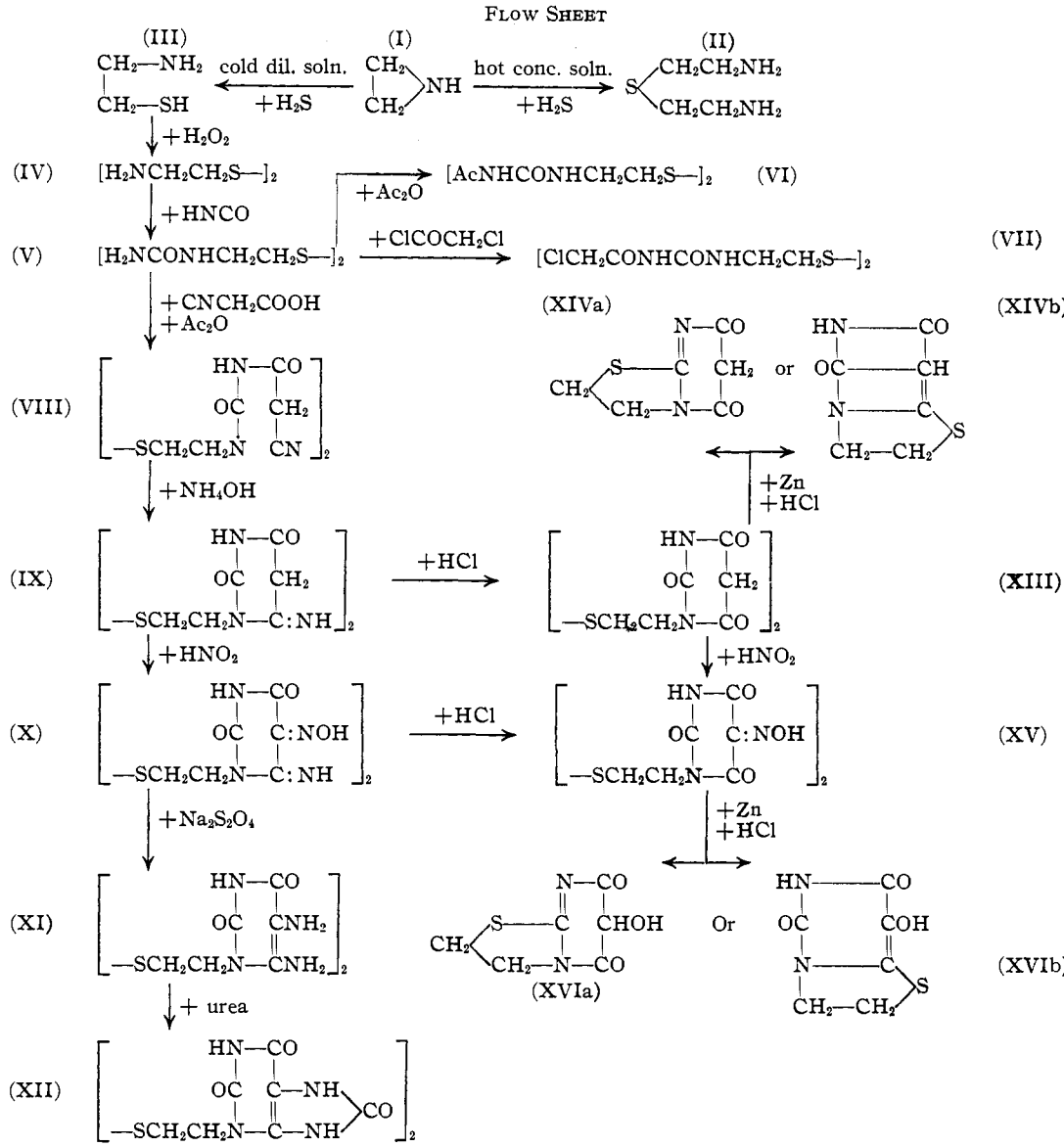

through the pseudouric acid by cyclodehydration, and Fischer and Clemm[7] have shown that, in the conversion of 1-methyluramil into the corresponding methyluric acid, via the pseudouric acid, it is the 1-methyl and not the 3-methyl uric acid which results.

By the action of zinc and hydrochloric acid upon the *bis*-(β[3-barbiturylethyl]) disulfide (XIII), and upon the *bis*-(β[3-violurylethyl]) disulfide (XV), thiazolidinopyrimidines (XIV and XVI) were secured, but whether these possess the (a) or the (b) structure remains to be determined.

Hydantoin has been prepared from bromoacetylurea by elimination of hydrogen bromide with ammonia[8]; and 1-arylhydantoins by the action of alcoholic potassium hydroxide upon arylchloroacetyl ureas[9]; but attempts to obtain hydantoins from the chloroacetylurea derivative of the ethyl disulfide (VII), by the action of ammonia, potassium hydroxide, or pyridine, were uniformly unsuccessful.

In the preparation of *bis*-(β-aminoethyl) sulfide (thioethylamine) by the Gabriel method,[10] Cashmore and McCombie,[11] and later Mann,[12] reported the formation also of 1,4-thiazane (thio-

(7) Fischer and Clemm, *Ber.*, **30**, 3092 (1897).

(8) Baeyer, *Ber.*, **8**, 612 (1875).

(9) Frerichs and Beckurts, *Arch. Pharm.*, **237**, 331 (1899).

(10) Gabriel, *Ber.*, **24**, 1114 (1891).

(11) Cashmore and McCombie, *J. Chem. Soc.*, **123**, 2884 (1923).

(12) Mann, *J. Chem. Soc.*, 1752 (1930).

morpholine). Our efforts to obtain this thiazane from thioethylamine by procedures akin to that used by Ladenburg[13] for the preparation of piperidine from pentamethylenediamine, all proved futile.

If we may regard the sulfide linkage as the spatial equivalent of the ethylene group, it is worth noting that von Braun and Müller[14] were unable to obtain heptamethyleneimine from either heptamethylenediamine or 7-chloro (or bromo) heptylamine.

Benzal and cinnamal derivatives of thioethylamine were prepared, and may prove useful in the characterization of this amine, since they are easily obtained, crystallize well, and have sharp melting points.

Acknowledgments.—Our grateful thanks are due to the Carbide and Carbon Chemicals Corporation of New York, for a generous gift of the ethanolamine required for this investigation. We are indebted also to Mr. Saul Gottlieb of these Laboratories, by whom the analytical work was carried out.

Experimental Part

Unless otherwise stated, all melting points recorded have been corrected for stem exposure.

Ethyleneimine (I).—The ethyleneimine used as initial material in this research was prepared from ethanolamine by Wenker's method[15] and boiled at 55–56°, in agreement with the figures given by Wenker and by Mills and Bogert.[2]

bis-(β-**Aminoethyl**) **Sulfide** (**Thioethylamine**) (II).—As observed by Mills and Bogert,[2] ethyleneimine reacts with hydrogen sulfide, to form either β-mercaptoethylamine (III) or thioethylamine (II), depending upon the conditions. Low concentrations of the imine and low temperatures give mainly the mercaptan (III), while high concentrations and moderate temperatures yield mainly the sulfide.

The thioethylamine prepared from ethyleneimine by Gabriel and Eschenbach,[16] and by Mills and Bogert,[2] was not obtained pure, but was identified in the former case as its picrate, and in the latter as its urea derivative. We have therefore prepared and purified the sulfide by the following modified procedure.

Hydrogen sulfide was passed into 43 g. (one mole) of ethyleneimine contained in a flask equipped with an efficient reflux condenser, while maintaining the temperature of the liquid at about 60° by external cooling. After fifty minutes, the lemon-yellow viscous product showed no further evolution of heat from influx of hydrogen sulfide, so the introduction of the gas was discontinued. The honey-like product was dissolved in 1.25 volumes of absolute ethanol and left overnight in the refrigerator. The separated mercaptoethylamine (5.6 g.) was filtered and the alcohol distilled from the filtrate under diminished pressure. When the liquid residue was heated, 4.9 g. more of mercaptoethylamine sublimed, bringing the total yield to 10.5 g., or 13.6%. It was identified by its m. p. (97–98.5°), its oxidation to the disulfide (IV), and the preparation of the dibenzoyl derivative of the latter.[17] The main fraction of the distillate from the liquid residue was collected at 130–131° (uncor.) at 22 mm. pressure, and amounted to 29.8 g., or a 50% yield. It was characterized as the pure thioethylamine by its dibenzoyl derivative, m. p. 107.5–108° (literature,[10] 107–108°); its picrate, m. p. 221–223° (literature,[10] 212°); and hydrochloride, m. p. 129–131° (literature,[10] 131°).

Dibenzal Derivative.—When benzaldehyde (2.1 g.) was added slowly to thioethylamine (1.2 g.), an exothermic reaction occurred with separation of oily drops. The mixture was heated for a minute at 100°, then left for several hours at room temperature, when it solidified completely. The yield of crude product was practically that calculated. For purification, 2.6 g. of the crude product was dissolved at room temperature in 2 cc. of benzene, and 14 cc. of petroleum ether was added while warming gently in a hot water-bath. As the solution cooled, white crystals separated, m. p. 56.4–57.4°.

Anal. Calcd. for $C_{18}H_{20}N_2S$: C, 72.9; H, 6.8. Found: C, 72.8; H, 7.0.

The compound was soluble in most of the usual neutral organic solvents, except water and petroleum ether, and dissolved also in cold 5% hydrochloric acid. Heated with water or dilute alcohol, hydrolysis evidently occurred, for the odor of benzaldehyde immediately was noted.

Dicinnamal Derivative.—Prepared in the same way as the above, using cinnamic instead of benzaldehyde, the yield of crude product was likewise essentially that calculated. For purification, it was dissolved in warm benzene and an equal volume of boiling petroleum ether was added. As the solution cooled, pale yellow crystals separated, m. p. 83.5–84°. The compound could be crystallized also from dilute alcohol.

Anal. Calcd. for $C_{22}H_{24}N_2S$: C, 75.8; H, 6.9. Found: C, 75.6; H, 7.0.

β-**Mercaptoethylamine** (III) was prepared in the same manner as described by Mills and Bogert,[2] except that the alcoholic solution of the ethyleneimine was dropped into about twice as large a volume of alcoholic hydrogen sulfide as they used, and the reaction was cooled by an ice–salt bath. These modifications raised the yield to 96.7%.

bis-(β-**Aminoethyl**) **Disulfide** (**Cystamine, or Dithioethylamine**) (IV).—Instead of oxidizing the mercaptoethylamine with air or oxygen, as reported by Mills and Bogert,[2] it was found more convenient to dissolve 10 g. of the mercaptan in water (30 cc.) and add a 3% solution of hydrogen dioxide gradually, with external cooling, until a drop of the solution, acidified with hydrochloric acid, no longer decolorized an iodine–potassium iodide solution. Hydrochloric acid was added until the solution was acid to Methyl Orange, when it was evaporated to dryness, and the crude *dihydrochloride* crystallized from alcohol until its melting point remained constant at 217° (literature,[2] 212–215°, or[18]

(13) Ladenburg, *Ber.*, **18**, 3100 (1885).
(14) Von Braun and Müller, *ibid.*, **39**, 4110 (1906).
(15) Wenker, THIS JOURNAL, **57**, 2328 (1935).
(16) Gabriel and Eschenbach, *Ber.*, **30**, 2497 (1897).
(17) Coblentz and Gabriel, *ibid.*, **24**, 1123 (1891).
(18) Fruton and Clarke, *J. Biol. Chem.*, **106**, 667 (1934).

214°). The yields of both free base and dihydrochloride were practically those calculated.

The *dibenzoyl derivative*, prepared by the Schotten–Baumann reaction, formed white needles, from alcohol, m. p. 132.5–133.5° (literature,[17] 132–133°).

bis-(β-**Ureidoethyl**) **Disulfide** (V) was prepared from cystamine (IV) by the action of nitrourea, as described by Mills and Bogert;[2] or by the action of potassium cyanate upon an aqueous solution of its dihydrochloride. The yield was about 65% in both cases, and the melting point of the recrystallized product (from water) was 166.5–167.5°, which melting point was not depressed by admixture with an authentic sample of the *bis*-(β-ureidoethyl) disulfide.

Diacetyl Derivative (VI).—Prepared from (V) by the action of acetic anhydride and fused sodium acetate and purified by repeated crystallization from water, this derivative formed a snow-white powder, m. p. 208.5–209.5°; only slightly soluble in cold water, methyl or ethyl alcohol, acetone, or ethyl acetate; soluble in glacial acetic acid, in hot water, or hot alcohol. It decomposed slowly at its melting point with evolution of minute bubbles.

Anal. Calcd. for $C_{10}H_{18}O_4N_4S_2$: C, 37.2; H, 5.6. Found: C, 37.6; H, 5.6.

Mills and Bogert[2] obtained this same compound by the elimination of carbon dioxide from its monocarboxylic acid, and reported its m. p. as 209–210°.

Di-(chloroacetyl) Derivative (VII).—A mixture of 1.3 g. of (V) with 5 g. of chloroacetyl chloride was refluxed for fifteen minutes, 20 cc. of glacial acetic acid was added, and the solid dissolved by boiling. As the solution cooled, 2 g. (93.5% of that calculated) of the crude product separated as a white solid, which was washed with cold glacial acetic acid and then crystallized from this same solvent. For analysis, it was recrystallized once from cellosolve and then twice from alcohol–acetone, in which latter mixture its solubility at the boiling point was only about 0.2 g. per 100 cc. The product so purified formed glistening platelets, which melted, with darkening, at 207.5–208.5°. Mixed with the foregoing diacetyl derivative (VI) in the ratio 25:75, 50:50, or 75:25, by weight, the melting point was not depressed, but was in every case raised to 213–214.5°.

Anal. Calcd. for $C_{10}H_{16}O_4N_4Cl_2S_2$: C, 30.7; H, 14.1. Found: C, 31.0; H, 14.2.

The condensation of *bis*-(β-ureidoethyl) disulfide (V) with ethyl cyanoacetate in alcoholic solution, in the presence of sodium ethoxide, could not be realized. When the reaction was continued for six hours, the original compound (V) was recovered unaltered. When the refluxing was more prolonged, either no pure product could be isolated, or the initial compound was broken down, as evidenced in one case by the recovery of some free sulfur.

bis-(β-**Cyanoacetylureidoethyl**) **Disulfide** (VIII).—To 23.8 g. of the urea (V), there was added a solution of 17.1 g. of cyanoacetic acid in 61.3 g. of acetic anhydride, and the mixture was warmed. The initial urea (V) dissolved and almost immediately there ensued a rapid precipitation of a white solid and an exothermic reaction which caused the solution to boil for a short time. Upon subsidence of the ebullition, the mixture was heated for an hour at 100° under a moisture-protected reflux. Excess of acetic anhydride was hydrolyzed, the precipitate removed and washed carefully with a large volume of hot water. A small quantity of the original urea (V), m. p. and mixed m. p. 208.5–209.5°, was recovered from these washings. The yield of crude *bis*-cyanoacetyl derivative (VIII) was 32.8 g., or 88.3%. For analysis it was crystallized from 87% formic acid and then appeared in small glistening white leaflets, melting (with darkening and slight decomposition) at 221–222°. It was difficultly soluble in glacial acetic acid or in boiling water, practically insoluble in boiling 95% alcohol.

Anal. Calcd. for $C_{12}H_{16}O_4N_6S_2$: C, 38.7; H, 4.3. Found: C, 38.7; H, 4.4.

bis-(β-**3**[**4-Iminobarbituryl**]-**ethyl**) **Disulfide** (**IX**).—The foregoing cyanoacetyl derivative (VIII) was easily cyclized by either 30% sodium hydroxide, 5% sodium carbonate, 5% sodium bicarbonate, or 5% ammonium hydroxide solution. The last one was best, because then the product was free from the adsorbed inorganic salts which in the other cases proved exceedingly difficult to remove by washing with hot water, and the need for recrystallization was thus obviated.

When the finely powdered cyanoacetyl derivative (VIII) was heated to boiling with any of the above reagents (except 30% NaOH, which was employed at room temperature), using about 4 g. of (VIII) to 100 cc. of solution, the white opaque mixture rapidly became nearly clear and, either on further boiling or allowing it to cool, the white insoluble iminobarbituryl derivative (IX) precipitated. The yields were 62–70%.

From a sodium bicarbonate cyclization, the white powder, washed carefully with hot water and dried, melted with decomposition at 268–269°, and contained 0.8% less carbon than that calculated. Crystallized from formic acid, it was yellow, melted with decomposition at 276°, and gave the following figures on analysis.

Anal. Calcd. for $C_{12}H_{16}O_4N_6S_2$: C, 38.7; H, 4.3. Found: C, 38.3; H, 4.1.

When dilute ammonia was used for the cyclization, the product was pure white and melted (with decomposition) at 279° without recrystallization.

The stability of this iminobarbituric compound in the presence of alkalies is noteworthy in comparison with the barbituric acids of Mills and Bogert,[2] which were easily split between N_1 and C_6 by alkali. In acid solution, however, the imino group, as is true of most 4-iminopyrimidines, was readily hydrolyzed to the keto group.[19]

bis-(β-[**3-Barbiturylethyl**]) **Disulfide** (**XIII**).—A mixture of 1 g. of the above imino compound (IX) with 30–35% of 5% hydrochloric acid was heated to boiling. Solution ensued rapidly and the boiling was continued until crystals began to precipitate. After cooling the mixture thoroughly in a refrigerator, the crystals were removed, and showed a m. p. of 219–220°; mixed melting point with an authentic sample of different origin showed no depression; yield 88%. Mills and Bogert,[2] who prepared this same compound by other methods, giving lower yields, reported its melting point as 216.8–218.8°. Additional proof of the hydrolysis of the imino group was secured by a positive test for the ammonium ion in the filtrate from the crystals with Nessler's reagent, and the strong odor of ammonia

(19) Johnson and Hahn, *Chem. Rev.*, **13**, 251 (1933).

when a portion of the filtrate was warmed with concentrated sodium hydroxide.

bis-(β-3[4-Imino-5-violuryl]-ethyl) **Disulfide (X).**—This compound was secured by three different procedures.

(1) A solution of 5 g. of the imino derivative (IX) in 60 cc. of 87% formic acid was prepared at room temperature and to this was added all at once a concentrated aqueous solution of 2 g. of sodium nitrite. Effervescence and the production of a deep purple color immediately ensued. After allowing the reaction to proceed for about a minute, the mixture was diluted with about 0.1 its volume of cold water. After standing for a short time, the purple isonitroso derivative (X) precipitated in yields of 87–98%. It was removed and washed with water until the washings were colorless.

(2) To a solution of 1 g. of the imino derivative (IX) in 10 cc. of formic acid, and cooled by running tap water, 0.6 g. (0.8 cc.) of isoamyl nitrite was added, the mixture was warmed, 2–3 cc. of warm 95% alcohol poured in and, as the solution cooled, the purple isonitroso derivative crystallized in yields of 72–79%.

(3) A suspension of 9 g. of (IX) in 320 cc. of 5% acetic acid was heated to 80° and a concentrated aqueous solution of 3.4 g. of sodium nitrite added. Heating and vigorous stirring were continued for an hour, the suspended imino derivative (IX) changing from a white to a purple powder, apparently without going into solution; yield 8.2 g., or 82%.

The insolubility of this product in all the usual solvents tried, except water and formic acid, rendered purification difficult. Boiling water destroyed the product, and formic acid caused some hydrolysis of the imino group to the keto group.

Purification of the products of any of the above procedures was accomplished by dissolving them in dilute ammonium hydroxide, decolorizing the warm solution of the ammonium salt with Norit, filtering and reprecipitating with dilute hydrochloric acid. When an ammoniacal solution of 0.4 g. of the compound per 100 cc. was acidified at 100° and allowed to cool slowly, minute purple crystals were obtained. Such deep colors are characteristic of 4-iminovioluric acids and of their alkali solutions.[20]

Dried either in a desiccator at room temperature, or in an oven at 110°, the crystals developed a kind of stickiness, which caused them to adhere to one another but, on prolonged exposure to the air at room temperature, or dried in an oven at 150°, this stickiness disappeared, and the crystals then decomposed at 197–198°. The analytical figures for the crystals dried at 110° were as follows. *Anal.* Calcd. for $C_{12}H_{14}O_6N_8S_2 \cdot 2H_2O$: C, 30.9; H, 3.9. Found: C, 31.2; H, 4.0.

Another sample was dried at 150°, which caused some decomposition, to judge by the slight darkening in color. Its analysis was as follows. *Anal.* Calcd. for $C_{12}H_{14}O_6N_8S_2$: C, 33.5; H, 3.3. Found: C, 34.2; H, 3.4.

bis-(β-[3-Violuryl]-ethyl) **Disulfide (XV).**—When a suspension of 1.52 g. of the iminovioluryl derivative (X) in 55 cc. of 5% hydrochloric acid was heated to boiling, the purple color of (X) disappeared as the solid gradually dissolved, but the amount of solvent present was insufficient to dissolve it all. As the mixture cooled, 1.2 g. (or 80%) of white crystals separated which, after crystallization from water, melted at 230.5–231° (uncor.) with decomposition, after having changed to a pink color above about 200°. In recrystallizing this compound from water, its aqueous solution possessed a bluish tint, and the crystals which separated were pale gray. When a trace of hydrochloric acid was added to the solution, no color appeared either in the solution or the crystals.

Anal. Calcd. for $C_{12}H_{12}O_8N_6S_2$: N, 19.5. Found: N, 19.6.

A sample of *bis*-(β-[3-violuryl]-ethyl) disulfide (XV), prepared by Mills and Bogert[2] by a different method, was recrystallized from water to the constant m. p. of 230–231°. When this was mixed with the product obtained from (X), as described above, no depression of the melting point occurred.

bis-(β-3-[4,5-Diaminouracilyl]-ethyl) **Disulfide (XI).**—To 5 g. of (X) there were added 6–7 cc. of concentrated ammonium hydroxide and 20–25 cc. of water. The solution was heated at 100°, and a solution of 11 g. of $Na_2S_2O_4 \cdot 2H_2O$ in 55 cc. of cold water was poured in all at once. The color of the deep red solution of the ammonium salt changed rapidly, first to a pale green, and then to a faint yellow. On standing overnight, 2.53 g. of pale yellow crystals separated, which melted with decomposition at 261.6°, and were freely soluble in dilute mineral acids. With sulfuric acid, the compound formed a difficultly soluble sulfate, as is the case with 4,5-diaminouracil itself,[21] which could not be crystallized undecomposed from water. This diaminouracil (XI) was quite unstable, decomposing on prolonged exposure to the air, and could not be purified satisfactorily by reprecipitations from acid solution. Its identity, therefore, rests upon its method of preparation, its properties, and its conversion into the compound which follows.

In reducing the isonitroso compound to the diamine, acid reducing agents were unsuitable because of the ease with which the imino group is hydrolyzed by acids. Either ammonium sulfide,[22] or an ammoniacal solution of sodium hydrosulfite,[5] proved effective, but the former does not keep well, and gives a product contaminated with sulfur, so the latter was used.

bis-(β-[3-Uric acid]-ethyl) **Disulfide (XII).**—An intimate mixture of the diamino uracil (XI) with twice its weight of urea was spread evenly over the bottom of a small Erlenmeyer flask, where it was heated at 170–180° under reduced pressure. When the temperature reached 135° the mixture softened, bubbled vigorously at about 150°, and became a clear brown melt at 165°. Soon thereafter it solidified to a yellow cake. After heating for an hour, this cake was removed, washed carefully with water and dried. The yield of crude product was nearly that calculated. The compound was purified by repeated precipitation of its hot dilute ammoniacal solution by dilute hydrochloric acid. It was practically insoluble in boiling water. When precipitated from ammoniacal solutions, it formed minute white crystals, carrying a mole of water of crystallization which was not removed by drying overnight at 110°, as the following analysis indicates.

Anal. Calcd. for $C_{14}H_{14}O_6N_8S_2 \cdot H_2O$: C, 35.6; H, 3.4; N, 23.7. Found: C, 35.6; H, 3.6; N, 23.9.

(20) Lifschitz and Kritzmann, *Ber.*, **50**, 1719 (1917).

(21) Traube, *ibid.*, **33**, 1382 (1900).

(22) Traube, *Ann.*, **351**, 64 (1904).

The compound darkened at higher temperatures, but did not melt below 350°. It did not give a definite murexide test. A sodium salt was prepared by dissolving it in warm dilute caustic soda solution containing two equivalents of sodium hydroxide. It was freely soluble in hot water, and moderately soluble in cold, and separated in small crystals which retained a yellowish tint even after repeated treatments with a decolorizing carbon.

This uric acid, therefore, differs from the isomer described by Mills and Bogert[2] in being practically insoluble in boiling water, in carrying water of crystallization not removed at 110°, and in not giving a positive murexide test.

Thiazolidinobarbituric Acid (XIVa or b).—4.8 g. of the barbituryl disulfide (XIII) was heated with 120 cc. of 5% hydrochloric acid, about 2 g. of zinc dust added in small portions, and the mixture boiled gently for thirty minutes. During the reduction, a drop of the mixture gave a decided nitroprusside test for the mercaptan group. The solution was filtered hot from undissolved zinc and, as it cooled, the filtrate deposited glistening white crystals, which left a slight ash on ignition, but neither decolorized an iodine-potassium iodide solution, nor gave a nitroprusside reaction in alkali solution. Recrystallized from water, fine white odorless needles were obtained, m. p. 300.5–301°, free from inorganic salts; yield 3.1 g. By concentrating the mother liquors, 0.7 g. more was recovered, bringing the total yield up to 87.1%.

Anal. Calcd. for $C_6H_6O_2N_2S$: C, 42.3; H, 3.6; N, 16.5. Found: C, 42.3; H, 3.6; N, 16.4.

It dissolved in cold concentrated nitric acid to an intense red-violet solution. On evaporation of this solution, under reduced pressure, at ordinary temperature, and over solid sodium hydroxide, there remained a red hygroscopic gum, easily soluble in water, 95% alcohol, or commercial acetone, from which no pure product could be isolated.

When (XIV) was treated with dilute acid and sodium nitrite, no reaction occurred. Boiling with strong aqueous sodium hydroxide resulted in a copious evolution of ammonia, but no other products were identified, except in one instance where the refluxing in alkali had been continued for twenty hours, and acidification of the alkali solution then caused an evolution of hydrogen sulfide.

Thiazolidinodialuric Acid(?) (XVIa or b).—The iminovioluryl disulfide (X) (1 g.) was boiled with about 50 cc. of 5% hydrochloric acid until the purple color was discharged. An excess (>0.75 g.) of zinc dust was added, the mixture heated gently for thirty minutes, and filtered hot. As the filtrate cooled, white crystals separated which, after recrystallization from water, appeared as white needles. These needles darkened but did not melt below 330°, left no ash on ignition, contained no halogen, gave no test for the mercaptan group, but did give a positive murexide test; as well as a faint blue color with 2% phosphotungstic acid in ammonia, a reaction which Johnson and Johns[23] found to be associated always with the presence of an amino or imino group in position 5 on the pyrimidine ring. The compound was insoluble in cold water or cold 5% hydrochloric acid, but dissolved both in cold concentrated hydrochloric acid and cold 5% sodium hydroxide. It was unchanged by either potassium isocyanate in acid solution, or nitrourea in dilute alkali.

Anal. Calcd. for $C_6H_6O_3N_2S$: C, 38.7; H, 3.2; N, 15.0; S, 17.2. Found: C, 38.9; H, 3.7; N, 14.8 (Dumas), 14.6 and 14.7 (Kjeldahl); S, 16.2.

These results are not altogether satisfactory, at least so far as the figures for hydrogen and sulfur are concerned; but further analyses must await the preparation of an additional supply of this compound.

Summary

1. From *bis*-(β-ureidoethyl) disulfide, by standard synthetic procedures, there have been prepared derivatives of cystamine, in which its β-amino nitrogen constitutes one of the members of a pyrimidine or purine cycle.

2. By reduction of certain of these disulfides, thiazolidino derivatives of barbituric and dialuric acids have been obtained.

3. The *bis*-(β[3-uric acid]-ethyl) disulfide thus synthesized is not the same as the isomer described in a previous paper by Mills and Bogert, from which it follows that the Mills and Bogert acid probably carries its —SCH_2CH_2— group in position 1 of the purine nucleus.

NEW YORK, N. Y. RECEIVED JUNE 10, 1941

(23) Johnson and Johns, THIS JOURNAL, **36**, 970 (1914).