sulfur of phenothiazine yielding the diarylamine.[12]

Subsequent attempts at alkylation of I using freshly prepared sodamide by the method of Yale did give the 10-alkyl derivative. Even in this instance some 2-anilinopyridine was recovered from the reaction mixture indicating partial reductive dethionation of I.

Thionation of *N*-phenyl-*N*-(2-pyridyl)-*N'*,*N'*-dimethyl ethylenediamine (IV), in an attempt to achieve ring closure with the 10-alkyl substituent (in this instance diethylaminoethyl) previously attached gave IV as the only isolable product.

As has been noted with phenothiazine, I changes color, developing a reddish crust on standing for a period of three years under normal conditions of light and temperature, with a subsequent lowering of the melting point. Recrystallization restores both color and melting point.

EXPERIMENTAL

Carbon and hydrogen analyses are by Clark Microanalytical Laboratory, Urbana, Ill. Nitrogen and sulfur analyses by Clark or this Laboratory. All melting points were determined using Anschutz, short scale thermometers, totally immersed in the heating bath.

1-Azaphenothiazine (I). A mixture of 12 g. (0.075 mole) of 2-anilinopyridine,[13] 4.8 g. of sulfur (0.15 g. atom) and 0.3 g. of iodine was intimately mixed in a mortar and heated under reflux at 160–180° (pot temperature) for 3 hr. The tarry mass was directly distilled from the reaction flask to give 6.3 g. (42%) of 1-azaphenothiazine (I), b.p. 178–184° at 3 mm., m.p. 109–112°. An analytical sample recrystallized from ethanol melted at 112.5–113.5° (yellow rosettes).

Anal. Calcd. for $C_{11}H_8N_2S$: N, 13.99; S, 16.00; Mol. wt. 200.3. Found: N, 14.07; S, 16.49, 16.20; Mol. wt. 196 (Rast). I gives the same color reactions used for the identification of phenothiazine.[14] A dilute alcoholic solution of I (0.05%) gives a green color with 1% aqueous ferric chloride and a red color with acidified hydrogen peroxide solution.

Reaction of I *with hydrochloric acid.* Mixing equimolar ethereal solutions of I and dry hydrogen chloride caused the precipitation of yellow crystals which, after recrystallization from absolute ethanol-ether, melted at 182–183° dec., and was only partially water soluble.

Anal. Calcd. for $C_{11}H_8N_2S.HCl$: Cl, 15.0; for $C_{11}H_8N_2S.2HCl$: Cl, 26.7. Found: Cl, 16.65.

With concentrated hydrochloric acid I formed a clear yellow solution and gave yellow needles on spontaneous evaporation. Two recrystallizations from absolute ethanol-ether gave yellow needles melting at 167–170°, which also showed incomplete water solubility and inconclusive analytical results.

Oxidation of I. Two grams of I (0.01 mole) in 50 cc. of ethanol at 50° was treated with 10 cc. (0.09 mole) of 30% hydrogen peroxide to give a clear yellow solution which on dilution with 5 volumes of water yielded 2-anilinopyridine, m.p. and mixed m.p. 109–110°.

Reaction of I *with copper.* Freshly precipitated copper was prepared by immersion of aluminum rods into a concentrated solution of copper sulfate with agitation. The precipitated copper was filtered, washed well with water, alcohol, and ether, then dried at 40° for 0.5 hr. and used immediately. An intimate mixture of 1 g. of I and 5 g. of copper powder was heated at 130° for 1 hr. in a nitrogen atmosphere. The powdered residue was extracted with ether, the solvent evaporated, and the pale yellow residue recrystallized from ethanol to give 0.27 g. of II, m.p. and mixed m.p. 108–110°.

1-Azaphenothiazine picrate. Mixing of saturated alcoholic solutions of I and picric acid gives the *mono picrate,* m.p. 198–200° dec.

Anal. Calcd. for $C_{17}H_{11}N_5O_7S$: N, 16.31. Found: N, 16.29.

Alkylation of I. Alkylation with dimethylaminoethyl chloride and sodamide[2] proceeded smoothly using freshly prepared sodamide. After vacuum distillation of the 10-alkyl derivative the residue in the flask solidified. Several recrystallizations from ethanol gave white plates, m.p. 108–109° which did not depress the melting point of an authentic sample of 2-anilinopyridine.

10-Acetyl-1-azaphenothiazine (III). A mixture of 2 g. (0.01 mole) of I, 0.21 g. (0.0025 mole) of anhydrous sodium acetate and 15 cc. of acetic anhydride (16.2 g., 0.16 mole) was refluxed for 0.5 hr. then poured into 50 cc. of ice water with stirring. Recrystallization of the separated solid from ethanol gave 2 g. (83.5%) of 10-acetyl-1-azaphenothiazine melting at 167–8° (pale yellow plates).

Anal. Calcd. for $C_{13}H_{10}N_2OS$: C, 64.43; H, 4.16; N, 11.55. Found: C, 64.53; H, 4.18; N, 11.28.

Infrared spectral data.[15] (KBr pellet, wave length and % transmission).

I[16]; 3.08 (23), 3.12 (36), 3.25 (38), 6.23 (20), 6.36 (33), 6.55 (29), 6.70 (12), 6.90 (1), 7.58 (28), 7.24 (33), 7.33 (41), 8.09 (67), 8.62 (72), 8.85 (41), 9.19 (50), 9.53 (26), 9.63 (58), 10.79 (62), 11.07 (67), 11.81 (63), 12.87 (12), 13.29 (8), 13.50 (1).

III; 3.27 (48), 5.89 (12), 6.30 (22), 6.36 (40), 6.75 (34), 7.01 (4), 7.25 (6), 7.58 (11), 7.64 (1), 7.76 (21), 7.93 (1), 8.27 (10), 8.72 (24), 8.84 (49); 9.19 (34), 9.55 (43), 9.69 (52), 9.87 (19), 10.04 (76), 10.60 (67), 10.18 (79), 11.05 (80), 11.62 (56), 12.45 (1), 13.00 (38), 13.15 (9), 13.30 (12), 13.40 (2), 13.69 (37), 14.20 (63).

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(12) K. H. Shah and K. Venkataraman, *Proc. Indian Acad. Sci.*, **28A**, 142 (1948).

(13) The preparation of substituted anilinopyridines and quinolines for the attempted synthesis of substituted 1-azaphenothiazines and azabenzophenothiazines by the thionation method has led to some interesting observations which will be discussed in a future paper.

(14) *The National Formulary,* 10th edition, J. B. Lippincott Co., Philadelphia, Pa. 1955, p. 442.

(15) The infrared spectra were run on a Beckman IR-4 double beam recording spectrophotometer equipped with sodium chloride optics.

(16) The infrared spectrum of I is identical with that of a sample of 1-azaphenothiazine generously supplied by Dr. H. L. Yale, The Squibb Institute for Medical Research, New Brunswick, N. J.

Preparation of 2-Imino- and 2-Nitrimino-1,3-diazacycloalkanes

L. S. HAFNER AND ROBERT EVANS

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In a previous publication[1] the isolation of 5,5-bis(hydroxymethyl) - 2 - nitrimino - 1,3 - diazacyclohexane and the salts of 5,5-bis(hydroxymethyl)-

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(1) L. S. Hafner and Robert Evans, *J. Am. Chem. Soc.*, **79**, 3783 (1957).

2-imino-1,3-diazacyclohexane and 1-amino-2,2-bis-(hydroxymethyl)-3-guanidinopropane as three of the products of the reactions between 2-methyl-1-nitro-2-thiopseudourea or salts of 2-methyl-2-thiopseudourea and 1,3-diamino-2,2-bis(hydroxymethyl)propane has been described. The conditions for these reactions have been extended and modified so that the reaction of alkyldiamines with the salts of 2-methyl-2-thiopseudourea or with 2-methyl-1-nitro-2-thiopseudourea can be considered as a general method of preparation for 2-nitrimino-1,3-diazacycloheptanes, hexanes, and pentanes as well as for 2-imino-1,3-diazacyclohexanes and pentanes. In Table I the yields of 2-nitrimino-1,3-diazacycloalkanes obtained from the reaction between the corresponding diamine and 2-methyl-1-nitro-2-thiopseudourea are compared with those obtained by McKay and Wright[2] from the reaction between alkyldiamines and nitroguanidine. When 1,3-diaminopropanol was allowed to react with 2-methyl-1-nitro-2-thiopseudourea, the amounts of the products formed were dependent on the reaction medium. In water the yield of 5-hydroxy-2-nitrimino-1,3-diazacyclohexane was 46%, the yield of 2-imino-1,3-diazacyclohexane 20%, and 17% unreacted 1,3-diaminopropanol was recovered. With ethanol as the reaction medium, the yield of the imino compound was 38%, of the nitrimino compound 15%, while 34% unreacted 1,3-diaminopropanol was recovered.

TABLE I

2-NITRIMINO-1,3-DIAZACYCLOALKANES

Compound	M.P.	Yield, %	Lit.[a] M.P.	Lit.[a] Yield
2-Nitrimino-1,3-diazacyclopentane	215–218 dec.	72.1	220–221 dec.	65.4
4-Methyl-2-nitrimino-1,3-diazacyclopentane	170–173	64.3	170.5	64.0
5-Hydroxy-2-nitrimino-1,3-diazacyclohexane	228–235	50.5	233–235	59.0
2-Nitrimino-1,3-diazacyclohexane	255–256 dec.	36.4	251–252 dec.	55.0
2-Nitrimino-1,3-diazacycloheptane	226–227 dec.	14.5	219–220 dec.	64.3

[a] A. F. McKay and G. F. Wright, *J. Am. Chem. Soc.*, 70, 430 (1948).

In order to determine whether or not the imino compound could be formed in the reaction between nitroguanidine and an alkyldiamine,[2] an excess of the dihydrochloride salt of 1,3-diaminopropanol was reacted with an aqueous solution of nitroguanidine (10% excess) and potassium hydroxide. A 12% yield of the imino compound was isolated as the picrate.

There is some indication[1] that when 2-methyl-2-thiopseudourea salts are reacted with alkyldiamines, 1-amino-3-guanidinoalkane may be an intermediate in the formation of 2-imino-1,3-diazacycloalkanes. In order to test this theory, 1-amino-3-guanidinopropanol was prepared as the dihydrochloride salt. This salt, when half neutralized with aqueous sodium hydroxide and heated, gave a 53% yield of the hydrochloride salt of 5-hydroxy-2-imino-1,3-diazacyclohexane. Apparently the salt of 2-methyl-2-thiopseudourea reacts first with one amino group of the alkyldiamine to form the salt of 1-amino-3-guanidinoalkane; then if the reaction conditions are favorable for cyclization, ammonia is eliminated and the cyclic compound is formed instead of the 1,3-bis(guanidino)alkane salt. Table II lists the yields of 2-imino-1,3-diazacycloalkanes, isolated as the picrates, prepared by the reaction between the nitrate salt of 2-methyl-2-thiopseudourea and the corresponding alkyldiamine.

TABLE II

2-IMINO-1,3-DIAZACYCLOALKANES

Picrate	Yield, %	M.P.	M.P.
2-Imino-4-methyl-1,3-diazacyclopentane[a]	65.2	195–196	—
2-Imino-1,3-diazacyclohexane[b]	57.2	185–186	—
5-Hydroxy-2-imino-1,3-diazacyclohexane[c]	62.5	184–186	—
2-Imino-1,3-diazacyclopentane[d]	57.0	223–224	218–220

[a] Calcd. for $C_{10}H_{12}N_6O_7$: C, 36.58; H, 3.69; N, 25.60. Found: C, 37.03; H, 3.86; N, 25.75. [b] Calcd. for $C_{10}H_{12}N_6O_7$: C, 36.58; H, 3.69; N, 25.60. Found: C, 36.77; H, 3.69; N, 25.30. [c] Calcd. for $C_{10}H_{12}N_6O_8$: C, 34.88; H, 3.51; N, 24.41. Found: C, 34.93; H, 3.99; N, 24.44. [d] O. Stefanye and W. Howard, *J. Am. Chem. Soc.*, **77**, 761 (1955).

During this investigation 1-amino-3-guanidinopropane was nitrated to give what was probably 1-amino-3-nitroguanidinopropane which was isolated as the picrate and nitrate salts.

EXPERIMENTAL[3,4]

2-Nitrimino-1,3-diazacycloalkanes (*Table I*). The diamine (0.05 mole) in 30 ml. of water was placed in a flask and heated to 55° with stirring while 0.0525 mole of 2-methyl-1-nitro-2-thiopseudourea was added in increments over a period of 15 min. The reaction mixture was heated for an additional 30 min. at the same temperature, then cooled, and filtered. The precipitate was washed with cold water and crystallized from hot water.

Reaction of nitroguanidine with 1,3-diaminopropanol. Potassium hydroxide (6.24 g. of 85.3%, 0.095 mole) dissolved in 17 ml. of water was placed in a flask fitted with a stirrer. Nitroguanidine (5.77 g., 0.055 mole) was added and stirred until solution was complete. 1,3-Diaminopropanol dihydrochloride (9.05 g., 0.055 mole) was then added and the mixture stirred and warmed to 60–65° for 30 min. At the end of the reaction period the mixture was cooled in an ice bath and filtered. The precipitate was washed with

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(2) A. F. McKay and G. F. Wright, *J. Am. Chem. Soc.*, 70, 430 (1948).

(3) All melting points were measured on a Kofler micro hot stage.

(4) The yields are based on the total amount of diamine.

ethanol, and this ethanol wash was combined with the original reaction filtrate. An ethanol solution of picric acid was added to these combined solutions and two crystalline picrates were obtained. The first picrate, weighing 12.9 g., was removed and upon examination proved to be a mixture of potassium picrate and the dipicrate of 1,3-diaminopropanol. The second picrate, which weighed 3.16 g., was extracted with ether to remove residual picric acid and recrystallized from ethanol. Three crops were obtained. The second and third crops were combined and recrystallized from ethanol; care was taken not to dissolve all the solid in the ethanol (about 0.2 g.). A picrate was obtained which melted at 179–185° (2.0 g., 10.5% calculated as 5-hydroxy-2-imino-1,3-diazacyclohexane picrate). After recrystallization from ethanol the compound melted at 182–185°. A mixed melting point with an authentic sample of 5-hydroxy-2-imino-1,3-diazacyclohexane picrate was not depressed. The combined first crops and insolubles were processed and an additional 1.5% of the imino compound was isolated.

1-Amino-3-guanidinopropanol dihydrochloride. 1,3-Diaminopropanol (25.1 g., 0.278 mole) was dissolved in 35 ml. of ethanol, heated to 40° and stirred while 56.2 g. (0.368 mole, 32% excess) of 2-methyl-2-thiopseudourea nitrate dissolved in 35 ml. of warm water was added over a period of 40 min. After the addition was complete, the reaction mixture was maintained at 40° for an additional 15 min., then cooled, filtered, and the precipitate washed with ethanol. The filtrate was added to an excess of an aqueous picric acid solution and the picrate formed, after extraction with ether and hot methanol, weighed 39.0 g. These salts, after conversion to hydrochloride salts, weighed 10.2 g. (17.9%) and melted at 145–150°. Recrystallization from ethanol gave a product which melted at 154.5–155.5°.

Anal. Calcd. for $C_4H_{14}Cl_2N_4O$: C, 23.42; H, 6.88; Cl, 34.58; N, 27.32. Found: C, 23.42; H, 6.55; Cl, 34.28; N, 27.37.

1-Amino-3-guanidinopropane dihydrochloride. This salt was prepared in the same manner as 1-amino-3-guanidinopropanol. However, a somewhat smaller excess of 2-methyl-2-thiopseudourea nitrate can be used since the dihydrochloride salt of 1,3-diaminopropane separates readily from the dihydrochloride salt of 1-amino-3-guanidinopropane when the hydrochloric acid solution is allowed to evaporate. After crystallization from absolute ethanol and then from an ethanol-benzene solution, the product melted at 156–157°.

Anal. Calcd. for $C_4H_{14}Cl_2N_4$: C, 25.41; H, 7.46; Cl, 37.50; N, 29.63. Found: C, 25.41; H, 7.68; Cl, 37.90; N, 29.69.

Cyclization of 1-amino-3-guanidinopropanol. A. 1-Amino-3-guanidinopropanol dihydrochloride (0.3 g., 0.00146 mole) was added to 15 ml. of water and refluxed 3 hr. An excess of an aqueous picric acid solution was then added, and the precipitate which formed was collected and extracted with ether. A mixed melting point with an authentic sample of 1-amino-3-guanidinopropanol dipicrate was not depressed.

B. 1-Amino-3-guanidinopropanol dihydrochloride (0.28 g., 0.00139 mole) was added to 15 ml. of water containing 0.00138 mole of sodium hydroxide and refluxed for 2 hr. An excess of an aqueous solution of picric acid was added, and the precipitate after extraction with ether melted at 185–186° and weighed 0.25 g. (52%). A mixed melting point with an authentic sample of 5-hydroxy-2-imino-1,3-diazacyclohexane picrate was not depressed.

2-Imino-1,3-diazacycloalkane salts. The corresponding diamine (0.04 mole) was dissolved in 10 ml. of water in a flask equipped with a reflux condenser and stirrer. The diamine solution was heated to reflux and 0.04 mole of the nitrate salt of 2-methyl-2-thiopseudourea, dissolved in 25 ml. of water, was added over a period of 40 min. After the addition was complete, the reaction mixture was refluxed for 3 hr. The water was then removed under aspirator pressure (30 mm.). The residue was dissolved in ethanol, added to an excess of picric acid dissolved in water, and allowed to stand overnight. The precipitate was removed and purified by crystallization from ethanol. Pertinent data about the picrates formed are given in Table II. Two of the picrates formed were converted to nitrate salts:

(a) 2-Imino-1,3-diazacyclopentane nitrate salt. This compound melted at 112.5–114.0°.

Anal. Calcd. for $C_3H_8N_4O_3$: C, 24.32; H, 5.44; N, 37.83. Found: C, 24.24; H, 5.40; N, 37.57.

(b) 2-Imino-1,3-diazacyclohexane nitrate salt. This compound melted at 160–161°.

Anal. Calcd. for $C_4H_{10}N_4O_3$: C, 29.63; H, 6.22; N, 34.55; Found: C, 29.54; H, 6.38; N, 34.29.

Nitration of 1-amino-3-guanidinopropane. 1-Amino-3-guanidinopropane dihydrochloride (2.0 g.) was added with cooling to 7 ml. of concentrated sulfuric acid. After all the salt had dissolved and the evolution of hydrogen chloride was complete, the solution was cooled to −30° and 4 ml. of 99% nitric acid was added. The nitration mixture was allowed to reach room temperature and held for 1 hr. The mixture was then poured over crushed ice and treated with a barium hydroxide solution until just acid to congo red paper. The barium sulfate was removed and the filtrate evaporated in a current of air. Barium nitrate crystallized and was removed as the solution was concentrated. The final residue weighed 2.08 g. (87%) and melted at 130–138°. After recrystallization from an ethanol-water solution, the salt melted at 140–141°. Considering the conditions used for nitration, this compound was probably the nitrate salt of 1-amino-3-nitroguanidinopropane. The ultraviolet absorption spectrum showed a maximum at 269–270 mμ which corresponded to a maximum obtained by McKay and Sandorfy[5] for the nitroguanidino group.

Anal. Calcd. for $C_4H_{12}N_6O_5$: C, 21.43; H, 5.39; N, 37.49. Found: C, 21.83; H, 5.62; N, 37.08.

The *nitrate* salt was converted to the picrate which melted at 190–192°.

Anal. Calcd. for $C_{10}H_{14}N_8O_9$: C, 30.77; H, 3.61; N, 28.71. Found: C, 30.99; H, 3.38; N, 28.90.

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(5) A. F. McKay and C. Sandorfy, *Can. J. Chem.*, **31**, 42 (1952).

Inhibition of the Nitrostyrene Condensation in Acetic Acid by Traces of Water[1]

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Catalysis by a primary amine in glacial acetic acid is frequently prescribed for the synthesis of β-nitrostyrenes from aromatic aldehydes and nitromethane.[2] In extending our earlier studies of

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(2) W. S. Emerson, *Chem. Revs.*, **45**, 347 (1949).