ride the sample melted at 104–106°) appears to be due to the fact that the compound is a mixture of the active and racemic acids.[11]

Anal. Calcd. for $C_5H_8O_4$: C, 45.45; H, 6.10. Found: C, 45.30; H, 6.26.

(B).—Oxidation of xanthatin under the above conditions gave an 18% yield of methylsuccinic acid, m.p. 112–114°; mixed with *dl*-methylsuccinic acid the m.p. was 105–114°.

Monoanilide of Methylsuccinic Acid (from Xanthinin).—A solution of 85 mg. of methylsuccinic acid in 0.75 ml. of thionyl chloride was refluxed for 45 minutes. The excess thionyl chloride was removed and to the residue was added a solution of 0.5 g. of aniline in 5 ml. of benzene. After 5 minutes refluxing a precipitate appeared. This was collected, washed with dilute hydrochloric acid, dissolved in 5% sodium hydroxide solution, and reprecipitated with dilute acid. Recrystallized from ethanol–benzene, the anilide melted at 150–151.5°.

Anal. Calcd. for $C_{11}H_{13}O_3N$: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.85; H, 6.59; N, 6.74.

Authentic *dl*-methylsuccinanilic acid was prepared, and had m.p. 147–149° (reported 148–149°,[20] 147°[21]), and a mixture of the two melted at 140–144°. Again, the presence of a mixture of active and racemic forms in the product derived from xanthinin is probably responsible for the differences in melting point.

Quinine Salt of *d*-Methylsuccinic Acid (from Xanthinin).—To a hot aqueous solution of 0.114 g. of the methylsuccinic acid from the oxidation of xanthinin was added an equivalent amount of *l*-quinine. On cooling, the solution deposited the crystalline salt, m.p. 168–169.5°. The quinine salt derived from authentic *dl*-methylsuccinic acid was made in the same way, and melted at 168–169.5° (reported[12,22] 169–171°). The two samples showed no depression in melting point on mixing.

The quinine salt crystallizes with water and after drying at room temperature over phosphorus pentoxide (16 hours) melted at 184–186° and analyzed for the monohydrate.

Anal. Calcd. for $C_{20}H_{24}N_2O_2 \cdot C_5H_8O_4 \cdot H_2O$: C, 67.65; H, 7.32. Found: C, 67.63; H, 7.30.

After drying at 138° (P_2O_5, 27 hours) the salt melted at 188–190° and was anhydrous.

Anal. Calcd. for $C_{20}H_{24}N_2O_2 \cdot C_5H_8O_4$: C, 69.20; H, 7.23. Found: C, 68.97; H, 7.27.

The salt from the synthetic acid, treated in the same way, formed the monohydrate (m.p. 182–184°; found: C, 67.64; H, 7.48) and the anhydrous form (m.p. 188–189°; found: C, 69.11; H, 7.36).

Carbon-linked methyl groups were determined by the use of the procedure of Barthel and LaForge.[23] In Table III are collected the C-methyl values for the compounds analyzed.

TABLE III

Compound	C-Methyl groups
Xanthinin	2.45
Xanthatin	1.44
Dihydroxanthinin	2.96
Dihydroxanthatin	1.95
Xanthinin-pyrazoline	2.55
Xanthatin-pyrazoline	1.47
Xanthatin-dipyrazoline	1.42
Xanthatic acid	0.53
Dihydroxanthatic acid	1.39
Methyl xanthatate pyrazoline	0.64

Ultraviolet absorption spectra were determined with a Beckman model DU spectrophotometer.

Infrared absorption spectra were determined with a Perkin–Elmer model 21 recording spectrophotometer equipped with a sodium chloride prism. Samples were in chloroform solution, as a film, or in a potassium bromide disk as noted in Table II.

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(21) D. Vorländer, P. Weissheimer and F. Sponnagel, *Ann.*, **345**, 232 (1906).

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(23) W. F. Barthel and F. B. LaForge, *Ind. Eng. Chem., Anal. Ed.*, **16**, 434 (1944).

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[CONTRIBUTION OF THE DEPARTMENT OF RESEARCH AND DEVELOPMENT, U. S. NAVAL POWDER FACTORY]

The Reaction of Thiopseudoureas with 1,3-Diamino-2,2-bis-(hydroxymethyl)-propane[1]

BY L. S. HAFNER AND ROBERT EVANS

RECEIVED DECEMBER 14, 1956

The reaction of 1,3-diamino-2,2-bis-(hydroxymethyl)-propane with the salts of 2-methyl-2-thiopseudourea or with 1-nitro-2-alkyl-2-thiopseudourea formed the following products: the salt of 1,3-bis-(guanidino)-2,2-bis-(hydroxymethyl)-propane, the salt of 1-guanidino-3-amino-2,2-bis-(hydroxymethyl)-propane, 1,3-bis-(nitroguanidino)-2,2-bis-(hydroxymethyl)-propane, 2-nitrimino-5,5-bis-(hydroxymethyl)-1,3-diazacyclohexane and 2-imino-5,5-bis-(hydroxymethyl)-1,3-diazacyclohexane, which may have formed from the nitrimino compound by a secondary reaction involving the addition of ammonia and the elimination of nitramide. These compounds when nitrated yielded 1,3-bis-(nitroguanidino)-2,2-bis-(nitroxymethyl)-propane and 2-nitrimino-5,5-bis-(nitroxymethyl)-1,3-diazacyclohexane. The 1,3-diamino-2,2-bis-(hydroxymethyl)-propane was prepared from the diacetate of 1,3-dibromo-2,2-bis-(hydroxymethyl)-propane by the Gabriel synthesis.

Both straight chain and cyclic guanidine and nitroguanidine derivatives of 2,2-bis-(hydroxymethyl)-1,3-propanediol have been prepared by the reaction between 1,3-diamino-2,2-bis-(hydroxymethyl)-propane and 1-nitro-2-alkyl-2-thiopseudoureas[2] or the salts of 2-methyl-2-thiopseudoreas.[3–5] The 1,3-diamino-2,2-bis-(hydroxymethyl)-propane used in the synthesis of these compounds was prepared from the diacetate of 1,3-dibromo-2,2-bis-(hydroxymethyl)-propane by the Gabriel synthesis. 1,3-Bis-(phthalimido)-2,2-bis-(hydroxymethyl)-propane could not be prepared from 1,3-dibromo-2,2-bis-(hydroxymethyl)-propane. The recovery of over 50% of the potassium phthalimide used in this reaction as phthalimide indicated that hydrogen bromide had split from the 1,3-dibromo-2,2-bis-(hydroxymethyl)-propane with the probable formation of an oxacyclobutane ring. Phthalimide would then be formed by the reaction between hydrogen bromide and potassium phthal-

(1) Published with permission of the Bureau of Ordnance, Navy Department. The opinions and conclusions are those of the authors.

(2) L. Fishbein and J. A. Gallaghan, THIS JOURNAL, **76**, 1877 (1954).

(3) B. Rathke, *Ber.*, **17**, 297 (1884).

(4) H. L. Wheeler and G. S. Jamieson, *J. Biol. Chem.*, **4**, 111 (1907).

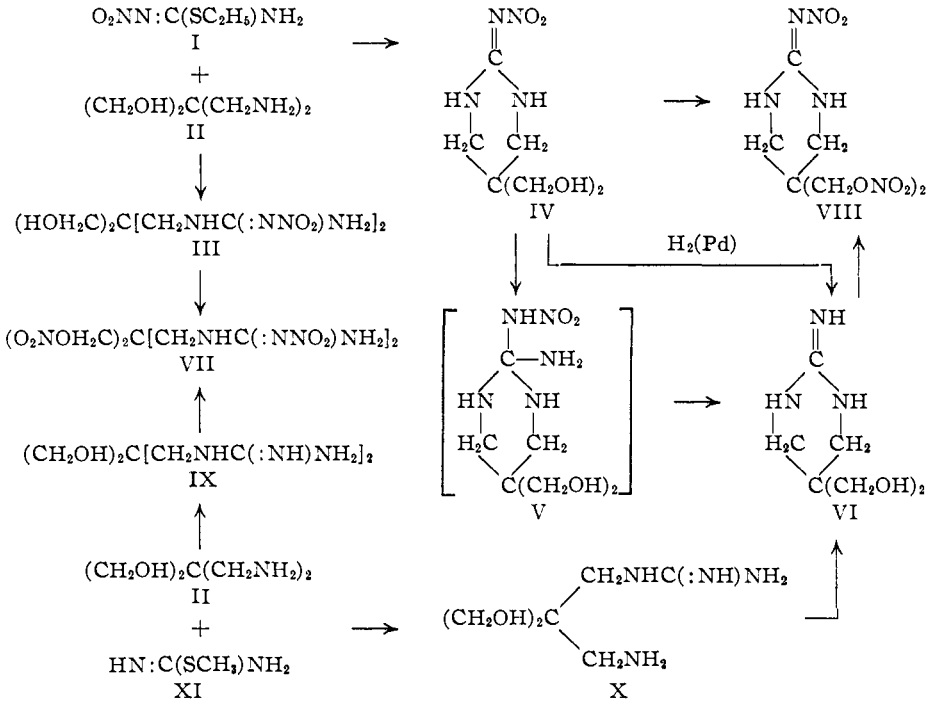
(5) W. Schoeller and H. Schotte, U. S. Patent 1,805,889 (1931).

imide. Phthalimide formation was greatly reduced by the acetylation of the hydroxyl groups of the 1,3-dibromo-2,2-bis-(hydroxymethyl)-propane, and by this method a 60% yield of the phthalimido compound was obtained. The hydrolysis of the phthalimido compound with hydrogen bromide was unsatisfactory due to a partial bromination of the hydroxyl groups. However, with aqueous hydrazine,[6] 1,3-diamino-2,2-(hydroxymethyl)-propane was obtained in 45% yield. Slight variations in the hydrazinolysis procedure led to the formation of alcohol-soluble sirups that were difficult to process. Under the conditions used, however, the hydrochloride and nitrate salts of the amine were obtained readily in the crystalline state and were not hygroscopic. Govaert and Beyert,[7] who prepared the amine by the ammonolysis of 1,3-dibromo-2,2-bis-(hydroxymethyl)-propane, stated that these salts were deliquescent and difficult to obtain in a pure state, and elemental analyses were not reported.

uct VI also was prepared by the hydrogenolysis of the cyclic nitrimino compound in the presence of a palladium catalyst.

The reaction between 55% of the molar quantity of 1-nitro-2-methyl-2-thiopseudourea and II produced 26% of the cyclic imino compound VI, 20% of the cyclic nitrimino compound IV and none of the bis-(nitroguanidino) compound III. 2-Nitrimino-5,5-bis-(nitroxymethyl)-1,3-diazacyclohexane (VIII) was prepared from either the cyclic nitrimino compound IV or the nitrate salt of the cyclic imino compound VI by the selection of the proper nitrating conditions.

The free base II reacted with 60% of the molar quantity of the nitrate salt of 2-methyl-2-thiopseudourea (XI) to form the dinitrate salts of both 1,3-bis-(guanidino)-2,2-bis-(hydroxymethyl)-propane (IX, 13%) and 1-amino-3-guanidino-2,2-bis-(hydroxymethyl)-propane (X, 21.5%). The reaction between II and a 20% molar excess of XI gave a 52% yield of the bis-(guanidino) compound



Three compounds were isolated from the reaction between 1-nitro-2-ethyl-2-thiopseudourea (I) (20% molar excess) and 1,3-diamino-2,2-bis-(hydroxymethyl)-propane (II). The principal product was 1,3-bis-(nitroguanidino)-2,2-bis-(hydroxymethyl)-propane (III, 26% yield). The other two products were 2-nitrimino-5,5-bis-(hydroxymethyl)-1,3-diazacyclohexane (IV) (6.3%) and 2-imino-5,5-bis-(hydroxymethyl)-1,3-diazacyclohexane (VI, 20%). The cyclic imino compound VI probably was not an initial reaction product. Possibly it resulted from the elimination of nitramide from an addition compound V formed when the ammonia liberated as IV was produced added to IV.[8] Product IX. By selecting the proper conditions, either the bis-(nitroguanidino) compound III or the nitrate salt of the bis-(guanidino) compound IX could be nitrated to form 1,3-bis-(nitroguanidino)-2,2-bis-(nitroxymethyl)-propane (VII). The free base 1-amino-3-guanidino-2,2-bis-(hydroxymethyl)-propane (X) was converted to the cyclic imino compound VI (20% yield) in refluxing methanol.

Experimental[9]

1,3-Bis-(phthalimido)-2,2-bis-(hydroxymethyl)-propane Diacetate.—The conditions employed for this preparation were a modification of those used by Sheehan and Bolhofer[10] to prepare dimethyl α,δ-diphthalimidoadipate. A solution

(6) A. F. Child, *et al.*, *J. Chem. Soc.*, 2174 (1948).

(7) F. Govaert and M. Beyert, *Proc. Koninkl. Akad. Wetenschap. Amsterdam*, **42**, 641 (1939).

(8) A. F. McKay, *Chem. Revs.*, **51**, 301 (1952).

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

(10) J. C. Sheehan and W. A. Bolhofer, THIS JOURNAL, **72**, 2786 (1950).

of 1,3-dibromo-2,2-bis-(hydroxymethyl)-propane diacetate (194 g., 0.561 mole) in 675 ml. of dimethylformamide was placed in a 2-liter flask equipped with a stirrer, condenser and thermometer. The temperature was maintained at 152° with stirring, while seven portions (24.4 g. each) of potassium phthalimide were added at 10-minute intervals. The temperature was then lowered to 144°, and two more portions of potassium phthalimide were added at 20-minute intervals. The mixture was heated for an additional 4.3 hr. at 144°. The reaction was then cooled to approximately 100° and the sodium bromide removed by filtration. The filtrate was allowed to stand at room temperature overnight, and the precipitate that formed was removed and washed in turn with dimethylformamide, ethanol, water and hot ether. The crude product, 164 g. (62%), was used for the preparation of 1,3-diamino-2,2-bis-(hydroxymethyl)-propane. A pure sample prepared by recrystallizing three times from benzene melted at 199.5–200.5°.

Anal. Calcd. for $C_{25}H_{22}O_8N_2$: C, 62.75; H, 4.64; N, 5.86. Found: C, 62.78; H, 4.64; N, 5.82.

1,3-Diamino-2,2-bis-(hydroxymethyl)-propane Dihydrochloride.—The phthalimido compound was converted to the diamine by the method of Child and co-workers.[6] 1,3-Bis-(phthalimido)-2,2-bis-(hydroxymethyl)-propane diacetate, 153.8 g. (0.324 mole), and 358 ml. of ethanol were placed in a flask equipped with a condenser, stirrer and dropping funnel. The mixture was heated to the reflux temperature, with stirring, and 38.9 g. of aqueous hydrazine (61%, 0.741 mole) was added over a period of 10 minutes. After stirring at the reflux temperature for 15 minutes, the heat was removed, and the mixture was stirred for an additional 50 minutes. At the end of this interval, 55 ml. of concentrated hydrochloric acid was added and the solution stirred for an additional 35 minutes. Concentrated hydrochloric acid (18 ml.) was added to the reaction mixture which was then heated and the ethanol–ethyl acetate azeotrope removed by distillation. Four hundred ml. of additional alcohol was put in as required. The alcoholysis was complete in about 2 hr. The phthalyl hydrazide and undissolved reaction products were then filtered, washed with ethanol and with water and the combined filtrates and wash solutions concentrated under vacuum to a sirup. This sirup was washed twice with absolute ethanol and once with ether, dissolved in water (60 ml.) and filtered. The filtrate was agitated for 1 hr. with salicylaldehyde to remove excess hydrazine. The insoluble material was removed, and the filtrate, after extracting with ether to remove excess salicylaldehyde, was concentrated under vacuum to a sirup. The sirup was washed twice in a Waring blender with absolute ethanol. Recrystallization from ethanol gave 30.8 g. (45.8%) of product with a melting point of 246–247°.

Anal. Calcd. for $C_5H_{16}O_2N_2Cl_2$: C, 28.99; H, 7.79; N, 13.53; Cl, 34.24. Found: C, 29.25; H, 8.02; N, 13.55; Cl, 34.58.

1,3-Diamino-2,2-bis-(hydroxymethyl)-propane Dinitrate Salt.—This compound was prepared from the dipicrate salt of the diamine and after recrystallization from ethanol melted at 117–118°.

Anal. Calcd. for $C_5H_{16}O_8N_4$: C, 23.08; H, 6.20; N, 21.53. Found: C, 23.19; H, 5.99; N, 21.46.

1,3-Bis-(phthalimido)-2,2-bis-(hydroxymethyl)-propane Monoacetate.—A solid sometimes separated from the alcoholic solution remaining after the insoluble phthalyl hydrazide was removed. After purification by crystallizing from methanol, dissolving in chloroform and precipitating with *n*-heptane and crystallizing again from methanol, the compound melted at 142–143°.

Anal. Calcd. for $C_{23}H_{20}O_7N_2$: C, 63.29; H, 4.62; N, 6.42. Found: C, 63.30; H, 4.77; N, 6.58.

1,3-Bis-(phthalimido)-2,2-bis-(hydroxymethyl)-propane.—The attempt to hydrolyze the diacetyldiphthalimido compound to the diamino compound with dilute hydrochloric acid was unsuccessful. The product after crystallization from benzene melted at 220.5–222.0°.

Anal. Calcd. for $C_{21}H_{18}O_6N_2$: C, 63.95; H, 4.60; N, 7.11. Found: C, 64.09; H, 4.44; N, 7.37.

Reaction of 1-Nitro-2-methyl-2-thiopseudourea with an Excess of 1,3-Diamino-2,2-bis-(hydroxymethyl)-propane.—The free base of the diamine was prepared by the reaction between the dihydrochloride and sodium ethoxide. To 3.743 g. (0.0279 mole) of the free base in a 50-ml. flask was added 3.957 g. (0.0293 mole) of the thiopseudourea in small portions over a period of about 15 minutes. The well stirred reaction mixture became warm, and ammonia and methyl mercaptan were evolved. At the end of the addition period, the flask was evacuated with a water aspirator (about 30 mm.) for 15 minutes. Fourteen ml. of absolute ethanol was added, and the flask was evacuated for an additional 15 minutes. The reaction product was filtered and washed with absolute ethanol. The precipitate, which weighed 1.4 g. and melted at 185–193° dec., was set aside. The filtrate was treated with a picric acid–methanol solution. The precipitate that formed (7.3 g.) was dissolved in 500 ml. of ethanol, and, by taking off successive fractions, two products were obtained. The first, consisting of 2.8 g. (17%), was determined to be the dipicrate of the original diamine. The second picrate, 3.9 g. (36.2%), after two crystallizations from ethanol melted at 179–180° and by proof outlined in the discussion was determined to be the picrate of 2-imino-5,5-bis-(hydroxymethyl)-1,3-diazacyclohexane VI.

Anal. Calcd. for $C_{12}H_{16}O_9N_6$: C, 37.12; H, 4.15; N, 21.64. Found: C, 37.10; H, 4.46; N, 21.64.

This picrate was converted to the nitrate salt which, after two crystallizations from absolute ethanol, melted at 114–115°.

Anal. Calcd. for $C_6H_{14}O_8N_4$: C, 32.46; H, 6.36; N, 25.24. Found: C, 32.64; H, 6.22; N, 25.40.

The crude alcohol-insoluble reaction product was dissolved in water and fractionated by slow evaporation. The fractions which melted at 203–207° dec. and weighed 1.01 g. (18.8%) were combined. Crystallization from alcohol and then from water raised the melting point to 207.5–208.5° dec. This product was 2-nitrimino-5,5-bis-(hydroxymethyl)-1,3-diazacyclohexane (IV).

Anal. Calcd. for $C_6H_{12}O_4N_4$: C, 35.29; H, 5.93; N, 27.46. Found: C, 35.43; H, 6.05; N, 27.02.

The nitrimino compound IV was converted to the imino compound VI by hydrogenolysis in the presence of palladium black by the following procedure. The nitrimino compound IV (0.469 g., 0.00296 mole) was added to 50 ml. of 15% acetic acid solution containing 0.06 g. of palladium black in a modified Skita[11] hydrogenation apparatus and agitated, slightly above atmospheric pressure, for 20 hr. The catalyst was removed, the filtrate treated with picric acid and the picrate (57% yield) after crystallization from methanol melted at 179–180°. A mixed melting point with the picrate of compound VI was not depressed.

Reaction of an Excess of 1-Nitro-2-ethyl-2-thiopseudourea with 1,3-Diamino-2,2-bis-(hydroxymethyl)-propane.—A solution of 3.214 g. (0.02175 mole) of the thiopseudourea in 11 ml. of tetrahydrofuran was added to 1.2075 g. (0.009 mole) of the diamine. The mixture was stirred for 25 minutes, the tetrahydrofuran removed under a vacuum, 10 ml. of absolute ethanol added and the stirring continued for 2.5 hr. The solid material was removed and washed with absolute ethanol and then with ether. The filtrate was treated with picric acid. The only product isolated was the picrate of 2-imino-5,5-bis-(hydroxymethyl)-1,3-diazacyclohexane (VI, 20.1%). The insoluble reaction product weighed 1.14 g. and melted at 158–160° dec. Washing with water, alcohol and finally ether reduced the weight to 0.83 g. and increased the melting point to 164–168° dec. This material was dissolved in concentrated hydrochloric acid, filtered and precipitated by dilution with water. The product, compound III (26%), melted at 200–201° dec.

Anal. Calcd. for $C_7H_{16}O_6N_8$: C, 27.23; H, 5.23; N, 36.35. Found: C, 27.43; H, 5.28; N, 36.24.

The material recovered by the evaporation of the diluted hydrochloric acid solvent and by the evaporation of the water wash of the crude material was crystallized from ethanol. The product was the nitrimino compound IV (6.3%). A mixed melting point with an authentic sample of IV was not depressed.

Reaction of 1,3-Diamino-2,2-bis-(hydroxymethyl)-propane with an Excess of the Nitrate Salt of 2-Methyl-2-thiopseudourea.—To a stirred solution of 2.459 g. (0.0183 mole) of the diamine in 2 ml. of water was added a 10% excess of the nitrate salt of 2-methyl-2-thiopseudourea, 6.184 g.

(11) A. Skita and W. A. Meyer, *Ber.*, **45**, 3589 (1912).

(0.0403 mole), dissolved in 8 ml. of water. The reaction was stirred for 5.5 hr. at room temperature, allowed to stand overnight and then stirred for an additional 5 hr. with a current of air blowing over the surface of the liquid to remove methyl mercaptan and ammonia. The reaction mixture was filtered, the precipitate washed with absolute ethanol and all the filtrates combined and treated with picric acid. The reaction precipitate was dissolved in warm water (60°) and successive fractions of crystals collected by slow evaporation of the water. A total of 3.27 g. (51.8%) of material was recovered. After recrystallizing twice from water, the product, the dinitrate salt of compound IX, melted at 196–198° dec.

Anal. Calcd. for $C_7H_{20}O_8N_8$: C, 24.41; H, 5.86; N, 32.55. Found: C, 24.59; H, 5.98; N, 32.33.

The dipicrate was prepared from the nitrate salt and after crystallization from methanol melted at 257–259° dec.

Anal. Calcd. for $C_{19}H_{24}O_{16}N_{12}$: C, 33.74; H, 3.58; N, 24.85. Found: C, 33.81; H, 3.68; N, 24.85.

The picrates from the filtrate could not be separated. Conversion to the nitrate salts and extraction with acetone gave a small amount of the nitrate salt of the starting material, 2-methyl-2-thiopseudourea (XI).

Reaction of the Nitrate Salt of 2-Methyl-2-thiopseudourea with an Excess of 1,3-Diamino-2,2-bis-(hydroxymethyl)-propane.—To the diamine (2.951 g., 0.022 mole) dissolved in 2 ml. of water was added 3.719 g. (0.0275 mole) of the thiopseudourea salt in 2 ml. of water. The mixture was stirred for 5.5 hr., absolute ethanol added and the insoluble material removed and washed with absolute ethanol. This product was crystallized from water, and its properties indicated that it was the dinitrate salt of compound IX (13% yield).

The filtrate was heated with picric acid, and the picrates were collected and converted to the nitrate salts. Fractional crystallization from ethanol gave 1.43 g. (21.4%) of product X which melted at 128–129°.

Anal. Calcd. for $C_6H_{18}O_8N_6$: C, 23.84; H, 6.00; N, 27.80. Found: C, 24.50; H, 5.63; N, 27.49.

The dipicrate was prepared from the purified nitrate and after crystallization from methanol melted at 209.5–211.5° dec.

Anal. Calcd. for $C_{18}H_{12}O_{16}N_{10}$: C, 34.20; H, 3.51; N, 22.10. Found: C, 34.18; H, 3.42; N, 21.93.

It was found that 1-amino-2-guanidino-2,2-bis-(hydroxymethyl)-propane (X) could be cyclized to VI by the following procedure. The salt (0.365 g.) was converted to the free base with sodium ethoxide, dissolved in methanol and refluxed for 1.2 hr. The product was neutralized with dilute nitric acid and concentrated in a current of air. Absolute ethanol was then added and 0.163 g. of sodium nitrate removed. The filtrate was treated with picric acid and the picrate removed. After crystallization from water the product weighed 0.093 g. (20%) and melted at 179–180°. A mixed melting point with an authentic sample of the picrate of VI was not depressed.

2-Nitrimino-5,5-bis-(nitroxymethyl)-1,3-diazacyclohexane (VIII).—The nitrate salt of the imino compound VI (0.7 g., 0.0032 mole) was added to a nitration mixture consisting of 1.29 g. of 99% nitric acid and 2 ml. of 98% sulfuric acid at −15°. The mixture was kept below 10° for 12 minutes and then allowed to warm and stand at room temperature (21°) for 1.7 hr. It was then poured over 30 g. of crushed ice and the precipitate collected on a medium sintered-glass funnel. The product VIII (0.61 g., 65.9%) after crystallization from ethanol melted at 214–215° dec.

The nitrimino compound IV (0.465 g., 0.0023 mole) was added to 5 g. of 99% nitric acid at −10°. The solution was held at 10–15° for 30 minutes, poured over 30 g. of crushed ice, filtered and the precipitate washed with cold water. The product VIII (0.601 g., 89%) after crystallization from water melted at 214–215° dec.

Anal. Calcd. for $C_6H_{10}O_8N_6$: C, 24.49; H, 3.43; N, 28.57. Found: C, 24.56; H, 3.28; N, 28.63.

1,3-Bis-(nitroguanidino)-2,2-bis-(nitroxymethyl)-propane (VII).—The dinitrate salt of IX (1.008 g., 0.0029 mole) was nitrated by the procedure used to produce the nitrate salt of VI except that the holding time at room temperature was increased to 2.7 hr. The product VII (0.613 g., 53%) after crystallization from water melted at 158.5–160° dec.

The nitroguanidino compound III (0.39 g., 0.00129 mole) was nitrated in 4 ml. of 99% nitric acid using the same procedure as for the cyclic nitrimino compound IV. The product VII weighed 0.4393 g. (85.5%) and melted at 158–160° dec.

Anal. Calcd. for $C_7H_{14}O_{10}N_{10}$: C, 21.11; H, 3.54; N, 35.17. Found: C, 21.37; H, 3.66; N, 34.82.

Acknowledgment.—We wish to thank Mrs. P. P. Wheeler for the microanalyses and Dr. J. A. Gallaghan for his helpful suggestions.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF DELAWARE]

2,2-Disubstituted-1,3-propanediamines and Related Diurethans, Diureides and Hexahydropyrimidin-2-ones

BY GLENN S. SKINNER, RICHARD H. HALL AND PETER V. SUSI

RECEIVED FEBRUARY 20, 1957

2,2-Disubstituted-1,3-propanediamines have been prepared and converted to diurethans, diureides and hexahydropyrimidin-2-ones. A practical synthesis of 5-alkyl-5-phenylhexahydropyrimidin-2-ones has been the major achievement. As a cyclization reagent diphenyl carbonate was superior to diethyl carbonate.

Since the replacement of carbonyl by methylene at position 2 in 5-ethyl-5-phenylbarbituric acid gave a compound[1] which still possessed anticonvulsant properties, it seemed of interest to prepare analogs with methylene groups at positions 4 and 6 in the ring. Our experimental work was practically complete when there appeared a paper[2] describing the preparation of one of these compounds (Table III) by reduction of the corresponding barbituric acid derivative.

Our syntheses depend upon the preparation of the 2,2-disubstituted-1,3-propanediamines. The method involving the condensation of ketones[3] with nitromethane generally gave poor yields when both radicals were larger than ethyl. In the case of propiophenone none of the intermediate dinitro compound was obtained.

The 2-alkyl-2-phenyl-1,3-propanediamines were therefore prepared from phenylcyanoacetamide[4] which was alkylated[5] and then reduced to the di-

(1) W. R. Boone, H. C. Carrington and C. H. Vasey, *C. A.*, **46**, 6162*a* (1952).

(2) F. J. Marshall, THIS JOURNAL, **78**, 3696 (1956).

(3) (a) H. B. Hass and J. F. Bourland, U. S. Patent 2,343,256 (1944); (b) M. S. Larrison and H. B. Hass, U. S. Patent, 2,383,603 (1945).

(4) J. C. Hessler, *Am. Chem. J.*, **32**, 120 (1904).

(5) T. J. Thompson, H. L. Bedell and G. M. Buffet, THIS JOURNAL, **47**, 875 (1925).