into the ether layer (16 hr.). The ether extract was dried over anhydrous magnesium sulfate and fractionated. After removal of the ether, the product, 25.2 g. (70%) was collected in the range 41–42° at 10 mm. as a light yellow oil (f.p. −7°).

Anal. Calcd. for $C_3H_9N_3O$: C, 34.94, H, 8.80, N, 40.75. Found: C, 35.50, 35.41; H, 8.87, 8.83; N, 41.50, 41.45.

Nitrosotrimethylhydrazine gave a positive Lieberman test for the nitroso group when the reactions were carried out at about 0°. At higher temperatures oxidation of the test samples by concentrated sulfuric acid occurred.

Catalytic hydrogenation of nitrosotrimethylhydrazine. A solution of 7.35 g. (0.0713 mole) of nitrosotrimethylhydrazine in 133 ml. of water was reduced with hydrogen in the presence of 3.502 g. of a catalyst consisting of 10% palladium-on-charcoal at 25° and one atmosphere. The reduction was attended by a steadily decreasing rate of hydrogenation until a total of 1.2 moles of hydrogen per mole of nitroso compound had been adsorbed. The catalyst was removed by filtration, the filtrate was saturated at 30° with sodium hydroxide pellets, and the yellow oil which separated was dried over fresh sodium hydroxide and fractionated to give 1.5 g. of a colorless liquid, b_{749} 59–60°, and 0.5 g. of a yellow oil, b_{10} 42°. The latter fraction was considered to be nitrosotrimethylhydrazine on the basis of the boiling point and a positive Lieberman test. The former was shown to be trimethylhydrazine through the preparation of trimethylhydrazine picrate in ethereal picric acid. The recrystallized product (from absolute ethanol) melted at 113–114.5°. Mixed melting point determinations with an authentic sample of trimethylhydrazine picrate (m.p. 114–115°) at 2 compositions showed no depression. An analysis of the trimethylhydrazine fraction with standard potassium iodate indicated that trimethylhydrazine was present to the extent of 95.3% (four-electron change).

Reduction of nitrosotrimethylhydrazine with lithium aluminum hydride. Seven grams (0.068 mole) of nitrosotrimethylhydrazine in 100 ml. of ether was added over a period of 1 hr. at 25° to 5.0 g. (0.132 mole) of lithium aluminum hydride in 150 ml. of absolute ether. The reaction mixture was stirred for an additional hour, followed by the dropwise addition of water until the reaction mixture appeared white, and subsequently the addition of 75 ml. of 30% aqueous sodium hydroxide. The ether layer was removed, and the gelatinous solid was extracted with three 50-ml. portions of ether. The ether extracts were combined with the original ether layer, and the solution was dried over anhydrous magnesium sulfate. An appreciable liquid residue remained when the ether was distilled off. The distillate (200 ml.) was treated with ethereal picric acid (20 g. = 0.075 mole of acid), and the resulting precipitate was recrystallized three times from absolute ethanol to give 5.2 g. (28%) of dimethylamine picrate, m.p. 158–159°. Mixed melting point determinations at two compositions with authentic dimethylamine picrate (m.p. 158–159°) showed no depression.

Reduction of nitrosotrimethylhydrazine with sodium amalgam. Thirty grams of 3% sodium amalgam (0.9 g., 0.039 mole of sodium) was added in one portion to 2.0 g. (0.019 mole) of nitrosotrimethylhydrazine in 40 ml. of absolute ethanol at 0°, and the mixture was shaken for 6 hr. at 0°. The solution was filtered, and the filtrate was acidified with acetic acid. A twofold volume of water was added, followed by 2.1 g. (0.020 mole) of benzaldehyde. When the mixture was shaken, a yellow precipitate formed. The solution was filtered and the solid recrystallized from 95% ethanol to give 0.59 g. (15%) of benzalazine, m.p. 91–92°. Mixed melting point determinations at two compositions with authentic benzalazine (m.p. 92–93°) showed no depression. The alcohol and water were removed from the filtrate on the steam bath, and the residue was extracted with ether to remove benzaldehyde. The crude acetate residue was dissolved in 10 ml. of water, and half of the solution was saturated at 25° with solid sodium hydroxide and extracted 4 times with 5-ml. portions of ether. The ether extracts were dried over anhydrous magnesium sulfate, and the clear solution was treated with ethereal picric acid (2.3 g. = 0.010 mole of the acid). The precipitate which formed was recrystallized from absolute ethanol to give 0.39 g. (15%) of dimethylamine picrate, m.p. 157–158.5°. Mixed melting point determinations at two compositions with authentic dimethylamine picrate (m.p. 158–159°) showed no depression. The Hinsburg test, when applied to the other portion of the aqueous solution, confirmed the presence of dimethylamine, and indicated the absence of methylamine.

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Formation of Isothiouronium Salts and Pseudothiohydantoins

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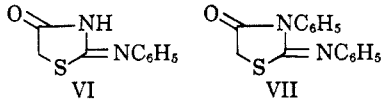
Taniyama and Yusa[1] have recently shown that 2'-chloroacetanilide and 2'-chloro-4-nitroacetanilide with 1-phenyl and 1,3-diphenyl thiourea gave *N*-substituted pseudothiohydantoins (VI and VII) in alcohol at reflux. However, Knott and Morgan[2] have reported that thiourea and the chloroacetamides derived from ammonia, 2-aminothiazole, and 2-aminopyridine gave the corresponding isothiouranium salts



VI VII

(III, R = amino, 2-thiazolylamino, and 2-pyridylamino) in refluxing ethanol.

Other investigators have reported that thiourea with chloroacetic acid,[3] methyl or ethyl chloroacetates[4] formed the corresponding isothiouranium salts (III, R = OH, OCH_3, OC_2H_5) in acetone at room temperature and that chloroacetic acid[5] in water at 80° formed pseudothiohydantoin (IV). A preparative method for IV and its hydrochloride from ethyl chloroacetate and thiourea in refluxing ethanol has been developed by Allan and Van Allan.[6]

In view of these results we wish to report an extension of our previous work.[7] Thiourea and 2-chloro-*N*,*N*-dipropylacetamide in dimethylformamide (DMF) at 30°, gave a 75% yield of the

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(2) E. B. Knott and J. Morgan, U. S. Patent **2,461,987.**
(3) P. C. Ray and F. V. Fernandes, *J. Chem. Soc.*, **105**, 2159 (1914).
(4) J. Taylor, *J. Chem. Soc.*, **117**, 4 (1920).
(5) R. Andreasch, *Monatsh.*, **8**, 407 (1887).
(6) C. F. H. Allan and J. A. Van Allan, *Org. Syntheses*, **27**, 71 (1947).
(7) A. J. Speziale and P. C. Hamm, *J. Am. Chem. Soc.*, **78**, 5580 (1956).

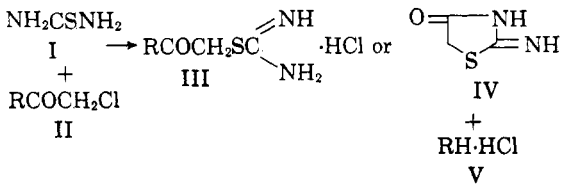
isothiouronium salt [III, R = $(C_3H_7)_2N$] and a 21% yield of pseudothiohydantoin (IV). In 95% ethanol at 25°, the dipropylamide and thiourea afforded a 57% yield of the isothiouronium salt and 17% yield of IV. In refluxing ethanol, none of III [R = $(C_3H_7)_2N$] was isolated but rather an 86% yield of IV and a 74% yield of dipropylamine hydrochloride. III [R = $(C_3H_7)_2N$] was converted to IV in refluxing ethanol.[4] 2-Chloro-*N*,*N*-diethylacetamide and thiourea in benzene at 80° for 2 hrs gave a 51.8% yield of IV.

Ethyl chloroacetate and thiourea gave a 57% yield of III(R = C_2H_5O) and 26% yield of IV (as the hydrochloride) at 25° in ethanol, and a 62% yield of III(R = C_2H_5O) and a 14% yield of IV·HCl in DMF at 25°. A slightly higher yield of the isothiouronium salt was obtained when the reaction was carried out for only 4 hr. rather than 24 hr. at 25° in ethanol.

The data, summarized in Table I, clearly indicate that solvents have no appreciable effect on the course of reaction of I and II, and that the amounts of III and IV formed are dependent on reaction temperature. Temperatures of about 25–30° favor the formation of the isothiouronium salts (III) while temperatures of about 80° favor the formation of IV.

TABLE I

REACTION OF THIOUREA WITH 2-HALOACETAMIDES AND 2-HALOACETATES



R	Solvent	Temp., °C.	Time, Hr.	% Yield III	% Yield IV
$(C_2H_5)_2N$	C_6H_6	80	2.0	—	51.8[a]
$(C_3H_7)_2N$	EtOH	80	1.5	—	86.0[b]
	DMF	30	18.0	75.0	20.7
	EtOH	25	23.0	57.0	17.3
	DMF	30	20.0	59.0	—[c]
C_2H_5O[d]	EtOH	25	24.0	56.8	25.6[f]
	DMF	25	24.0	61.8	14.1[f]
	DMF	25	4.0	70.4	—[c]
[e]	EtOH	80	3.0	—	79–82[f]

[a] 45.5% yield of diethylamine hydrochloride isolated. [b] 74% yield of dipropylamine hydrochloride isolated. [c] Attempt to isolate IV was unsuccessful. [d] With esters, IV is isolated as the hydrochloride (IV HCl) which on treatment with NaOAc gives IV. [e] Data from reference 6. [f] Yield of IV HCl.

EXPERIMENTAL

Thiourea and ethyl chloroacetate. The procedure used in the reactions of thiourea with 2-chloroacetates and 2-chloroacetamides[7] is illustrated by this typical example. A solution of 15.2 g. (0.2 mole) of thiourea and 24.5 g. (0.2 mole) of ethyl chloroacetate in 100 ml. of DMF was stirred at 25° for 24 hr. One liter of acetone was added to the clear solution and the precipitated solid was filtered; wt. 32.8 g. This was dissolved in 200 ml. of absolute ethanol and 4.3 g (14.1% yield) of pseudothiohydantoin hydrochloride was recovered by filtration of the alcohol insoluble material. The alcohol filtrate, diluted with 1.5 liters of ethyl acetate, afforded 24.5 g. (61.8% yield) of the isothiouronium hydrochloride [III, R = C_2H_5O], m.p. 110° (dec.).

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Prodigiosin Hydrochloride[1]

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Efimenko and co-workers[3] have claimed the isolation of prodigiosin hydrochloride from *Serratia marcescens* through a process involving chromatography of the bacterial pigment. Identification of the compound, which is described as red needles melting at 149°, rests solely upon analysis for carbon and hydrogen and apparently its absorption spectrum, λ_{max} 538–539 mμ[4] (presumably in ethanol). In a previous paper[5] we described the isolation of a magenta colored solid, m.p. 150.0–150.5° (dec.), from a powdered sugar chromatogram of the mixture resulting from the reaction of prodigiosin perchlorate with sodium hydroxide. At that time the similarity in the properties of the two products was noted. We have now established that the compound isolated by us is definitely prodigiosin hydrochloride. The substance gives a positive Beilstein test and elemental analyses are in good agreement with the calculated values for the hydrochloride, $C_{20}H_{26}ON_3Cl$. The ultraviolet-visible absorption spectrum is like that for prodigiosin perchlorate[5] with a main absorption maximum in isopropyl alcohol at 540 mμ ($\epsilon = 7.07 \times 10^4$) and a second very much weaker maximum at 294 mμ ($\epsilon = 1.08 \times 10^4$). The addition of aqueous sodium hydroxide to a solution of the magenta colored solid in isopropyl alcohol gave a mixture exhibiting absorption like that for prodigiosin with λ_{max} 468 mμ (ϵ 4.2×10^4). The observed[5] maximum

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(3) O. M. Efimenko, G. A. Kutnesova, and P. A. Yakimov, *Biokhimiya*, **21**, 416 (1956).

(4) Estimated by us from reported curve.

(5) A. J. Castro, A. H. Corwin, F. J. Waxham, and A. L. Beilby, submitted for publication in *J. Org. Chem.*