and the lactones, D-glucurone and D-mannurone (see Table I). All the acids and lactones tested appeared as compact spots on the chromatograms.

The R_f values of the amino acids tested on the *O*-(carboxymethyl)cellulose paper were of the same order of magnitude as previously observed[7] and lower than those observed with phenol as the solvent.[8] In the case of histidine and proline the R_f values 0.04 and 0.17, respectively, were so much lower than those found on chromatograms developed with phenol:water[8] that the difference might be used to characterize these two amino acids.

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Synthesis and Reduction of Nitrosotrimethylhydrazine[1]

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As a logical extension to an investigation in this laboratory of the lower alkylhydrazines, an attempt was made to prepare an alkyl derivative of the unknown triazane, H_2NNHNH_2. A survey of the literature did not disclose any attempts to prepare compounds of this type, although a few aromatic triazanes have been prepared and characterized.[2] One route to the synthesis of such a compound appeared to lie in the reduction of nitrosotrimethylhydrazine: This compound was selected as a pos-

$$(CH_3)_2NNCH_3NO + 4\ [H] \longrightarrow (CH_3)_2NN(CH_3)NH_2 + 2H_2O$$

sible precursor to *N,N,N'*-trimethyltriazane because (*1*) nitrosamines can be reduced to hydrazines with little or no reductive cleavage of the N—N bond,[3] (*2*) *N*-nitroso-*N*-phenyl-*N'*-formylhydrazine has been successfully reduced to *N*-formyl-*N'*-phenyltriazane, which was characterized through its benzaldehyde derivative,[4] and (*3*) trimethyltriazane may be considerably more stable than a triazane containing fewer alkyl groups. This is suggested by the high order of stability of tetramethylmethylenediamine, $[(CH_3)_2N]_2CH_2$,[5] compared to that of the nonisolable parent compound, methylenediamine.

The unknown nitrosotrimethylhydrazine was synthesized from trimethylhydrazine and nitrous acid. It gives a positive Lieberman test for the nitroso group, and is miscible with water to give a neutral solution. The compound is stable for long periods of time at Dry Ice temperatures, but at room temperature it slowly decomposes. A sample stored at 23° became orange-yellow in about three days, and orange-brown in a week. An elemental analysis gave somewhat high values for nitrogen, but the results are considered satisfactory in view of the instability of the compound. The reduction of nitrosotrimethylhydrazine was characterized by cleavage of at least one of the N—N bonds in attempts to prepare the triazane by three different methods. In the direct hydrogenation of the nitroso compound under mild conditions with a catalyst of 10% palladium-on-charcoal, trimethylhydrazine was isolated in addition to unreacted nitroso compound. With lithium aluminum hydride in ether dimethylamine was obtained, while with sodium amalgam in ethanol, hydrazine and dimethylamine were obtained. The course of the reduction to produce hydrazine is not clear, although other nitroso compounds have also been found to yield hydrazine when reduced with sodium amalgam under similar conditions.[6]

EXPERIMENTAL[7]

Starting materials. Trimethylhydrazine was prepared by the method of Class.[8] A value of 100.5% was obtained for the purity of the product, b.p. 59–60° 749 mm., by titration with standard potassium iodate (four-electron change).[9] Lithium aluminum hydride was obtained from Metal Hydrides, Inc., Beverly, Mass. Sodium amalgam was prepared by the method given by Fieser.[10]

Preparation of nitrosotrimethylhydrazine. A solution of 25.9 g. (0.35 mole) of trimethylhydrazine in 100 ml. of water was neutralized to a *p*H of 7.00 with 1:1 hydrochloric acid, diluted to 280 ml. with water, and cooled to 0°. A solution of 72.5 g. (1.05 moles) of sodium nitrite in 200 ml. of water was then added dropwise to the well stirred trimethylhydrazine hydrochloride solution at such a rate that the temperature did not rise above 5°. After the addition, the *p*H was adjusted to 5.18 by the dropwise addition of 1:1 acetic acid. When the resulting solution, which degassed continuously, was stored overnight at 0°, the *p*H increased to 5.83 and the solution deepened in color (yellow). The *p*H was adjusted to 8.00 by the addition of solid potassium carbonate, and the solution was extracted continuously with 150 ml. of ether until nearly all of the yellow color had passed

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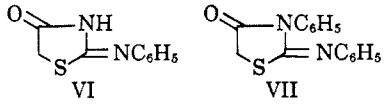
Taniyama and Yusa[1] have recently shown that 2'-chloroacetanilide and 2'-chloro-4-nitroacetanilide with 1-phenyl and 1,3-diphenyl thiourea gave *N*-substituted pseudothiohydantoins (VI and VII) in alcohol at reflux. However, Knott and Morgan[2] have reported that thiourea and the chloroacetamides derived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