toluene (Table I, compounds V through IX). The reaction mixture was refluxed until upon cooling a semi-solid waxy mass was formed. The time required varied from 4–82 hr. Compound I was formed by reaction at room temperature. Compound X required heating in an oil bath for five hours at 200° to complete the reaction.

At the end of the reaction period the solidified waxy mass was washed several times with ether, and recrystallized twice from ethyl acetate. The products are insoluble in ether and cold ethyl acetate, soluble in alcohol, and from slightly soluble to very soluble in water.

*N-Alkyl pyrrolidines* (Table II) were prepared by refluxing for 24 hr. 0.3 mole pyrrolidine, 0.2 mole of the alkyl bromide and 0.11 mole anhydrous potassium carbonate in a 100 ml. of methanol. The reaction mixture was filtered while hot on a sintered glass filter, and the insoluble salts were washed with two portions of boiling methanol.

The alcoholic filtrate was treated with 1 g. of decolorizing carbon and filtered while hot. The methanol and excess pyrrolidine were removed at reduced pressure and the residue was taken up in ethyl acetate and again filtered to remove a small amount of inorganic salts. The ethyl acetate was removed at reduced pressure and the N-alkyl pyrrolidine was isolated by fractional distillation *in vacuo*.

N-Alkyl pyrrolidines were also prepared by long refluxing of the appropriate primary amine with a 10% excess of 1,4-dichlorobutane in the presence of a large excess of potassium carbonate in ethyl alcohol solution. The yields obtained by this procedure were lower than those obtained by alkylation of pyrrolidine.

*Symmetrical N,N-dialkyl pyrrolidinium alkyl sulfates* (Table III) were prepared by reacting equimolar quantities (approximately 0.01 mole) of the N-alkyl pyrrolidine and redistilled dimethyl or diethyl sulfate in 5 g. of acetone.[3] The alkyl sulfate was added gradually with stirring to the boiling acetone solution of the N-alkyl pyrrolidine. The reaction mixture was allowed to cool slowly to room temperature and was then allowed to stand overnight. The *n*-decyl and *n*-dodecyl pyrrolidinium alkyl sulfates which formed as yellow oils were triturated several times with small volumes of petroleum ether and crystallized upon drying *in vacuo* over phosphorous pentoxide. The *n*-tetradecyl, *n*-hexadecyl and *n*-octadecyl pyrrolidinium alkyl sulfates formed as waxy solids. These were triturated three times with small volumes of petroleum ether, recrystallized three times from acetone or ethyl acetate, and finally dried *in vacuo* over phosphorous pentoxide. These compounds are all white, water soluble solids. The lower members of the series are hygroscopic.

CHEMICAL LABORATORIES
LAFAYETTE COLLEGE
EASTON, PA., and

ST. JOHN'S UNIVERSITY
BROOKLYN, N. Y.

## Hydrazinolysis of 1-(Alkyldithioate)-piperidine

EUGENE LIEBER AND RONALD C. ORLOWSKI

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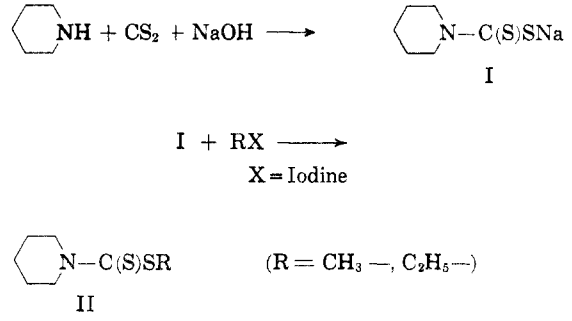
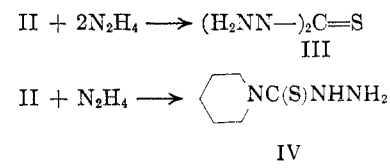
A study of the hydrazinolysis of 1-(alkyldithioate)-piperidine,[1] II, was undertaken for the purpose of preparing a thiosemicarbazide in which the fourth position embraced a reduced ring system including the nitrogen. These have not been previously described in the literature. The required II, also not previously described in the literature, were prepared by the following sequence of reactions:



I + RX ⟶
X = Iodine



It was found that the I need not be isolated and that the alkylation step could be carried out in the suspension of I obtained in the initial reaction. Surprisingly, the hydrazinolysis of II (R = $C_2H_5$-) proceeded chiefly with the elimination of both the thioalkyl- and piperdyl-radicals, thiocarbohydrazide, III, being the major product, while the desired product, 1-(aminothiocarbamyl)-piperidine,[2] IV, was obtained in only minor quantity.



Both III and IV were identified by analysis and conversion to benzylidene derivatives which were also analyzed. III was first described by Stolle and Bowles.[3] Its preparation by hydrazinolysis of various thiocarbonic acid derivatives has recently been reported.[4]

### EXPERIMENTAL[5,6]

*1-(Sodium carbodithioate)-piperidine.* In a three-necked 1-l. round bottomed flask, surrounded by an ice-salt bath and fitted with mechanical stirrer, reflux condenser, thermometer, and dropping funnel were placed 82.2 g. (63 cc., 1.08 moles) carbon disulfide and a cold solution of 43.2 g. (1.08 moles) of sodium hydroxide in 96 cc. water. The mixture was cooled to 0 to 5°. While stirring, 91.8 g. (1.08 mleos) of piperidine as a cold 35% aqueous solution was added over a period of 30 minutes. Stirring was continued for two hours in order to insure complete precipitation. The product recovered by filtration weighed 178 g. (90%) and was used without further purification.

*1-(Ethyl carbodithioate)-piperidine.* A mixture comprising 183 g. (1 mole) of 1-(sodium carbodithioate)-piperidine, 161 g. (1 mole) ethyl iodide and 200 cc. ethanol (95%) was refluxed for two hours. At the end of this period, 200 cc. of

(1) The name for this structure is derived from the *C. A.*, 39, 5968 (1945) nomenclature for the radical-C(S)SH, carbodithioic and the 1-position of the piperidine ring.

(2) Several different names for this structure can be derived from official sources of nomenclature. The name selected was for the purpose of emphasizing that the substance is a derivative of piperidine.

(3) R. Stolle and P. E. Bowles, *Ber.*, 41, 1099 (1908).

(4) L. F. Audrieth, E. S. Scott and P. S. Kippur, *J. Org. Chem.*, 19, 733 (1954).

(5) Melting points are uncorrected.

(6) Microanalyses by Dr. C. Weiler and Dr. F. B. Strauss, Oxford, England.

water was added and the two layers separated. The bottom oil phase was washed with two 100-cc. portions of water. The combined aqueous extract was washed with two 100-cc. portions of benzene. The benzene extract, combined with the oil, was dried with sodium sulfate. After removal of the benzene the residue was vacuum fractionated at 3 mm. pressure, the product being recovered at 155–159°, $n_D^{22}$ 1.6012, yield 123 g. (65%).

*Anal.* Calc'd for $C_8H_{15}NS_2$: S, 33.86. Found: S, 33.48.

*1-(Methyl carbodithioate)-piperidine.* Without recovering the product, an aqueous suspension of 1-(sodium carbodithioate)-piperidine was prepared from a mixture comprising 40 g. (1 mole) NaOH in 100 cc. $H_2O$, carbon disulfide (60 cc., 1 mole) and 85 g. (99 cc., 1 mole) piperidine in 100 cc. water. The piperidine was added in 1 hr. and the mixture allowed to stir for 30 min. The ice-salt bath was removed and 142 g. (1 mole) of methyl iodide added at once and the mixture refluxed for 1 hr. and allowed to cool to room temperature. The oil layer was recovered as described previously and after drying, vacuum fractionated at 6 mm., the product being collected over the range 171–176°.

*Anal.* Calc'd for $C_7H_{13}NS_2$: N, 8.00; S, 36.58. Found: N, 7.85; S, 36.30.

*Thiocarbohydrazide.* A mixture comprising 40 g. (0.21 mole) of 1-(ethyl carbodithioate)-piperidine, 10 cc. of 85% hydrazine hydrate (0.26 mole) and 150 cc. ethanol was refluxed for 6 hours. No precipitation of product took place after cooling at 5° for 48 hr. However, precipitation occurred after concentrating the reaction mixture by distillation of the solvent and cooling. Cooling of the mother liquor resulted in the precipitation of a crystalline solid having properties different from thiocarbohydrazide. This is described below. From the new mother liquid additional yield of thiocarbohydrazide was obtained by the addition of water. Yield, 9.4 g. (42.3%), m.p. 164–174° (Parr Block) dec.

*Anal.* Calc'd for $CH_6N_4S$: N, 52.79. Found: N, 53.0.

*1-(Aminothiocarbamyl)-piperidine.* The first mother liquor obtained in the above preparation yielded 1.5 g. (3.9%) of a white crystalline material which, after recrystallization from a minimum quantity of aqueous methanol, melted at 92–95°.

*Anal.* Calc'd for $C_6H_{13}N_3S$: N, 26.39; S, 20.48. Found: N, 26.4; S, 20.13.

*1-(Benzylideneaminothiocarbamyl)-piperidine* was prepared from 1 cc. benzaldehyde, 0.5 g. 1-(aminothiocarbamyl)-piperidine, 0.4 g. sodium acetate and 10 cc. ethanol by refluxing and cooling. Recrystallized from ethanol, m.p. 125–128°.

*Anal.* Calc'd for $C_{13}H_{17}N_3S$: N, 17.00; S, 12.98. Found: N, 17.01; S, 12.96.

*Benzaldehyde 3-thiocarbohydrazone* was prepared from 0.5 g. thiocarbohydrazide prepared above. M.p. 190–200° with dec.

*Anal.* Calc'd for $C_{15}H_{14}N_4S$: N, 19.85; S, 11.35. Found: N, 19.6; S, 11.25.

DEPARTMENT OF CHEMISTRY
DE PAUL UNIVERSITY
CHICAGO 14, ILL.

## Synthesis of 6-Nitro-2,3-dimethoxybenzaldehyde

ARTHUR F. ROSENTHAL[1]

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In connection with the synthesis of compounds related to mescaline, it was found necessary to prepare both 5-nitro-2,3-dimethoxy benzaldehyde and 6-nitro-2,3-dimethoxybenzaldehyde. Murakami's method[2] for the synthesis of the 5-nitro compound was found to be the most satisfactory. The synthesis of 6-nitro-2,3-dimethoxybenzaldehyde recently reported by Ried and Schiller[3] however, has the disadvantage that the last step, the methylation of 6-nitro-*o*-vanillin, gave a low yield and a product that required considerable purification.

An attempt to apply Murakami's acetal procedure[2] to this methylation failed; apparently the dimethyl acetal of 6-nitro-*o*-vanillin is formed much less readily than the corresponding 5-nitro acetal. However, it was found that with methyl iodide and silver oxide, which was used by Davies[4] in the preparation of 5-nitro-2,3-dimethoxybenzaldehyde, the methylation proceeded smoothly to give 6-nitro-2,3-dimethoxybenzaldehyde of satisfactory purity in moderately good yield.

An interesting peculiarity of the 6-nitro intermediates as well as of 6-nitro-2,3-dimethoxybenzaldehyde is a considerable sensitivity to light.[3] Thus, the entire preparation from the benzenesulfonate ester of *o*-vanillin is best performed all at once and the final product stored in the dark.

### EXPERIMENTAL[5]

*6-Nitro-2,3-dimethoxybenzaldehyde.* 6-Nitro-*o*-vanillin, freshly prepared from 63 g. (0.21 mole) of 6-nitro-*o*-vanillin benzenesulfonate ester, was used immediately after recrystallization without drying. It was refluxed in a mixture of 90 ml. of chloroform and 15 ml. of methyl iodide with 21 g. of powdered silver oxide. After filtration, the chloroform solution was washed twice with 50 ml. portions of 10 per cent sodium hydroxide, then with water, and finally evaporated to dryness. The residue after recrystallization from methanol weighed 10.5 g., m.p. 107–109°. A second recrystallization gave 8.5 g. of fine, faintly yellow needles (22 per cent overall from the nitrated ester), m.p. 109–110.5° (reported[3] 108–110°).

The 6-nitro-*o*-vanillin benzenesulfonate ester had a m.p. of 154–155°, instead of the reported[3,4] 145°.

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FELS RESEARCH INSTITUTE AND
CHEMISTRY DEPARTMENT
ANTIOCH COLLEGE
YELLOW SPRINGS, OHIO

(2) M. Murakami, *Ann.*, **496**, 122 (1932).
(3) W. Ried and H. Schiller, *Ber.*, **85**, 216 (1952).
(4) W. Davies, *J. Chem. Soc.*, **123**, 1575 (1923).
(5) All melting points are uncorrected.

## Cleavage of Phthalylglycine by Substituted Hydrazines

ARTHUR F. ROSENTHAL[1]

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The cleavage of N-substituted phthalimides by hydrazine, which was studied extensively by Ing

(1) Present address: c/o Dr. Robert P. Geyer, Department of Nutrition, Harvard School of Public Health, Boston 15, Massachusetts.

(1) Present address, c/o Dr. Robert P. Geyer, Department of Nutrition, Harvard School of Public Health, Boston 15, Massachusetts.