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.

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Synthesis of 6-Nitro-2,3-dimethoxybenzaldehyde

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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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Cleavage of Phthalylglycine by Substituted Hydrazines

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

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and Manske,[2] has recently been modified by Schumann and Boissonnas,[3,4] who replaced the hydrazine of the original procedure with phenylhydrazine.

The work of the latter authors has shown that the reaction products with phthalylglycine and phenylhydrazine, using tri-*n*-butylamine as a catalyst, are glycine and N-phenylphthalhydrazide. The alternative reaction, which would result in the formation of phthalhydrazide and N-phenylglycine, does not appear to occur to any significant degree.

The use of four additional substituted hydrazines has now been studied. Of three which are derivatives of phenylhydrazine, neither 2,4-dinitrophenylhydrazine nor hydrazobenzene underwent the reaction under the usual conditions. Only 2,5-dichlorophenylhydrazine attacked phthalylglycine and gave the expected N-(2,5-dichlorophenyl)-phthalhydrazide in moderate yield.

The other compound studied, methylhydrazine, was found to enter the reaction readily to give an excellent yield of N-methylphthalhydrazide. Thus, the course of the reaction brought about by this alkylhydrazine was the same as that effected by the arylhydrazines so far reported. Unlike hydrazine itself, however, none of its derivatives appear to react at an appreciable rate in the absence of the catalyst. Whether this is due to steric or other factors has not yet been investigated.

N - (2,5 - dichlorophenyl)phthalhydrazide was found to be inactive against *M. tuberculosis* in concentrations up to 100 γ per ml. *in vitro*.

EXPERIMENTAL[5,6]

N-(2,5-Dichlorophenyl)phthalhydrazide. A solution of 1.8 g. (0.010 mole) of 2,5-dichlorophenylhydrazine, 1.03 g. (0.00500 mole) of phthalylglycine,[7] and 0.93 g. (0.005 mole) of tri-*n*-butylamine in 5 ml. of 95% ethanol was refluxed on a steam bath for 12 hr. Fifteen ml. of acetone was then added and the mixture refluxed for 15 min. more. The precipitated glycine was filtered off and the filtrate evaporated *in vacuo*, leaving a clear golden oil as residue. This was dissolved in 15 ml. of ether and treated with dry hydrogen chloride for one min. The ether was evaporated and the orange solid which remained was ground with water, filtered, and thoroughly washed with water. The dry solid weighed 1.2 g. (40%). After two recrystallizations from 95% ethanol it was faintly yellow, m.p. 204–205°.

Anal. Calc'd for $C_{14}H_8Cl_2N_2O_2$: N, 9.02; Cl, 23.09. Found: N, 8.88; Cl, 22.74, 23.03.

N-Methylphthalhydrazide. 1.03 g. (0.00500 mole) of phthalylglycine and 1.85 g. of tri-*n*-butylamine (0.0100 mole) were dissolved in 30 ml. of 95% ethanol. To this was added a solution of methylhydrazine prepared by distilling 1.44 g. (0.0100 mole) of methylhydrazine sulfate with excess alcoholic potassium hydroxide. The mixture was heated under reflux for 20 hours, after which it was evaporated to one-third its volume and 40 ml. of 2-butanone added. The mixture was refluxed for 15 min., cooled, and the glycine filtered off and washed with ether. It weighed 346 mg. (92%) and gave a benzoyl derivative, m.p. 188–190°, unchanged on mixing with authentic hippuric acid.

The filtrate and washings were evaporated to give a clear yellow oil. Forty ml. of ether and 100 ml. of pentane were added and the mixture allowed to stand overnight. The faintly yellow precipitate of N-methylphthalhydrazide was separated by filtration. It weighed 770 mg. (88%) and was insoluble in cold water, ether, and dilute hydrochloric acid, but soluble in dilute aqueous potassium hydroxide. Recrystallization from 95% ethanol gave white granular crystals, m.p. 238.5–239.5° after some sublimation above 180°. (Reported[8] m.p. 239°.) Refluxing 30 min. with acetic anhydride, followed by addition of water and sodium carbonate, gave a white crystalline precipitate, m.p. 139.5–140.5° (reported[8] for N-acetyl-N′-methylphthalhydrazide, 140°).

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The Preparation of Aliphatic Propynylcarbinols[1]

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In connection with a research program in these laboratories, it was necessary to prepare 1-propynylcyclohexanol(I) and 1-propynylcyclopentanol(II). Propynylcarbinols of the general type RR′C(OH)C≡C—CH_3 have been prepared by Iotsitch and coworkers[2] by the reaction of propynylmagnesium bromide with various ketones. Zakharova[3] has recently reported the preparation of several of these compounds by the reaction between methylacetylene and aliphatic ketones, using KOH as a condens-

(1) Paper I from the Acetylene Research Program, St. Edward's University; based in part on the B.S. thesis of James E. Kmiecik.

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