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Some N-Basically Substituted Derivatives of *o*-Nitroaniline

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Some syntheses designed by us to lead to 9-(dialkylaminoalkyl)-isoalloxazine derivatives as potential metabolite antagonists to natural flavines were interrupted by the war four years ago, and the appearance of several recent articles based on similar thoughts[1,2,3,4] made resumption of this work inadvisable. We wish to report the syntheses and properties of some of the intermediates prepared in these studies.

TABLE I

Deriv. of chlorobenzene	Amine	Product	Yield, %	M. p., °C.	B. p., °C. (mm.)	Formula	% Composition		
								Calcd.	Found
2-Nitro-5-methoxy[a]	N-β-Aminoethylmorpholine	3-(2-Morpholinoethyl)amino-4-nitroanisole	63[b]	85–86[c]	235–245 (9–10)[d]	$C_{13}H_{19}N_3O_4$	N,	14.94	15.03
Same	1-Diethylamino-4-aminopentane	3-(1-Methyl-4-diethylaminobutyl)-amino-4-nitroanisole	51[e]		193[f] (4–5)	$C_{28}H_{33}N_9O_{17}$[g]	N,	16.43	16.83
Same	Cyclohexylamine	3-Cyclohexylamino-4-nitroanisole	36	76–77[h]	195–205 (2–3)	$C_{13}H_{18}N_2O_3$	N, OCH₃,	11.19 12.40	10.75 12.02
Same	Piperazine	1,4-Bis-(2-nitro-5-methoxyphenyl)-piperazine	29	240–242[i]		$C_{18}H_{20}N_4O_6$	N, OCH₃,	14.43 15.98	14.55 15.98
2-Nitro-	N-β-Aminoethylmorpholine	2-(2-Morpholinoethyl) aminonitrobenzene[j]	47	44–45[k]	190–195 (2)	$C_{12}H_{17}N_3O_3$	N,	16.72	16.69
2-Nitro-	2-Amino-2-methylpropanol	2-(1,1-Dimethyl-2-hydroxyethyl)-aminonitrobenzene	8		150–160[l] (1–2)	$C_{12}H_{16}N_2O_4$[m]	N,	11.11	11.33

[a] Prepared by the method of Hodgson and Handley, *J. Chem. Soc.*, **128**, 543 (1926). [b] 20% of unchanged chloronitroanisole was recovered by steam distillation. [c] Yellow crystals from ethanol or benzene–ligroin. [d] Distilled at 150° (2 mm.), and collected crystalline on a cold surface. [e] 16% of unchanged chloronitroanisole recovered. [f] Yellow oil. [g] Dipicrate m. p. 112–113°. [h] Red crystals from ligroin. [i] The insoluble orange solid was washed with ether and sublimed at 1 mm. [j] Dipicrate m. p. 210–212° (dec.); $C_{24}H_{23}N_9O_{17}$: % N calcd., 17.76; found, 17.56. [k] Red crystals from dilute ethanol. [l] Red oil. [m] O-Acetyl derivative prepared with acetic anhydride in pyridine at 100°, *cf.* Karrer and Naef, *Helv. Chim. Acta*, **19**, 1029 (1936), yellow crystals m. p. 64–65° from ethanol.

Experimental

Alkylaminonitrobenzenes.—Approximately equivalent amounts of 2-nitrochlorobenzene or its 5-methoxy derivative and the amine were refluxed for several hours in two equivalents of dry pyridine, 0.5 mole of the 2-nitrochlorobenzene and 0.01 to 0.05 mole of the 5-methoxy derivative being taken. Four to five hours of reaction time was used for runs of one-twentieth mole or less; eight hours for those of one-half mole. In some cases, unreacted chloronitroanisole was then removed by steam distillation. The residue was extracted with several portions of ether, and the reaction product obtained by evaporation of the solvent. Data as to the percentage composition and the physical properties of the substances prepared from the derivatives of chlorobenzene are given in Table I.

2-(2-Morpholinoethyl)-aminoaniline.—When a solution of 7.5 g. of 2-(2-morpholinoethyl)-aminonitrobenzene in 150 cc. of hot 50% ethanol was treated with a freshly prepared solution of 20.7 g. of sodium hydrosulfite dihydrate in 100 cc. of hot water, the red color soon changed to green. After brief boiling, the mixture was acidified with 80 cc. of 10% hydrochloric acid, the solution was cleared with norite, and evaporated to dryness under reduced pressure. The residue was washed with ether, and then decomposed with a cold 20% sodium hydroxide solution under ether. The aniline derivative was extracted into ether and worked up, yielding 5.3 g. (80%) of a red oil. Its *tripicrate* crystallized from ethanol, m. p. 201–203° (dec.).

Anal. Calcd. for $C_{30}H_{28}N_{12}O_{22}$: N, 18.50. Found: 18.33, 18.75.

1,4-bis-(2-Nitro-ethylaminophenyl)-piperazine.—A mixture of 3.0 g. of *o*-(β-chloroethyl)-aminonitrobenzene, 2.8 g. of piperazine and 0.05 g. of sodium iodide reacted exothermically, and was then refluxed for six hours. It was poured into water, the small amount of precipitated solid was filtered from much red oil, and washed with water. The oil from the filtrate was treated with alcohol and deposited another crop of the same orange crystals. Recrystallization from ethanol raised the melting point to 140–141°. The yield was 0.9 g.

Anal. Calcd. for $C_{20}H_{26}N_6O_4$: N, 20.28. Found: N, 20.27.

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(1) Hall and Turner, *J. Chem. Soc.*, 699 (1945).

(2) Neeman, *ibid.*, 812 (1946).

(3) Adams, Weisel and Mosher, THIS JOURNAL, **68**, 883 (1946).

(4) Kipnis, Weiner and Spoerri, *ibid.*, **69**, 799 (1947).

Preparation of 2- and 4-Benzylpyridine

BY KENNETH E. CROOK

Several investigators have reported the preparation of 2- and 4-benzylpyridines by heating a