It was air-dried and redistilled at 20 mm.: (a) 120–150°, 19.4 g.; (b) 150–195°, 11.9 g.; (c) 195–215°, 51.3 g. Fraction (a) contained 10.7 g. of diphenyl, a 7.0% recovery. Fractions (b) and (c) were recrystallized several times from 95% alcohol and yielded 45.9 g. of *p*-phenylacetophenone, m. p. 121°. This represented a 23.4% yield.

Summary

Factors influencing the yield of acetophenone from benzene and ketene have been studied. Conditions have been determined for the preparation of methyl α-naphthyl ketone to the practical exclusion of the β-isomer. The preparations of methyl β-tetrahydronaphthyl ketone and *p*-phenylacetophenone, using ketene, are reported.

COLLEGE PARK, MARYLAND RECEIVED OCTOBER 5, 1939

[CONTRIBUTION FROM THE ORGANIC CHEMISTRY LABORATORIES OF THE UNIVERSITY OF FLORIDA]

alpha,omega-Amino Alcohols. I. N-Phenyl-N'-(ω-hydroxyalkyl)-piperazines from α,ω-Chlorohydrins. Derivatives of Piperazine. XVII

BY GEORGE W. ANDERSON[1] AND C. B. POLLARD

Pyman and Levene[2] have synthesized α,ω-amino alcohols by the reaction of secondary amines with α,ω-chlorohydrins. We have now employed this reaction for the synthesis of a series of N-phenyl-N'-(ω-hydroxyalkyl)-piperazines.

The general procedure followed was to heat 0.2 mole of the chlorohydrin with 0.4 mole of N-phenylpiperazine for five hours on a water-bath. The white solid product was heated with 40 cc. of 5 *M* potassium carbonate, the resulting orange colored oily layer was separated and after it had cooled and solidified, was washed with water and recrystallized from 250 cc. of 60% ethyl alcohol. The white crystals were dried to constant weight in a vacuum over fused potassium hydroxide. Two recrystallizations from ligroin (70–100°) gave a material of constant melting point. The urethans were prepared in hot ligroin solution and were recrystallized from this solvent.

With one exception, the amino alcohols were obtained in a quantitative crude yield. That of N-phenyl-N'-(4-hydroxybutyl)-piperazine was reduced because of the formation of tetramethylene oxide. Neutral equivalents of the amino alcohols and their phenylurethans and analytical data are recorded in Table I.

TABLE I

N-PHENYL-N'-(ω-HYDROXYALKYL)-PIPERAZINES OF THE GENERAL FORMULA $C_6H_5NC_4H_8N(CH_2)_nOH$ AND THEIR PHENYLURETHANS

	Neutral equivalent (methyl orange)					Phenylurethans		
				Anal., % N			Anal., % N	
n	Calcd.	Found	M. p., °C. (corr.)	Calcd.	Found	M. p., °C. (corr.)	Calcd.	Found
4	234.3	236.0	59.0–60.0	11.96	11.81	91.0–92.0	11.98	11.64
5	248.4	248.3	74.0–75.0	11.28	11.13	100.0–101.5	11.44	11.24
6	262.4	262.7	65.5–67.0	10.68	10.52	91.5–93.0	11.01	10.91
7	276.4	274.9	75.5–76.5	10.14	10.06	96.5–97.5	10.63	10.46
8	290.4	292.1	57.0–58.5	9.65	9.43	99.5–100.5	10.26	10.09
9	304.5	303.1	80.0–80.5	9.20	9.14	94.0–95.0	9.92	9.78
10	318.5	317.1	67.0–68.0	8.80	8.74	95.0–96.0	9.60	9.45

N-Phenyl-N'-(8-hydroxyoctyl)-piperazine readily absorbs water from air to form a monohydrate. The other amino alcohols absorb water less rapidly.

The α,ω-chlorohydrins of four and five carbon atoms were obtained in 35% yield by the method of Kirner and Richter.[3] The higher members were prepared in approximately 65% yield by continuous extraction of the reaction mixtures of the corresponding glycols and hydrochloric acid.[4]

Final purification was effected by fractionation at 10 mm. The boiling points of the α,ω-chlorohydrins showed a regular increase with increasing number of carbon atoms.

Phenyl- or α-naphthylurethans were prepared from the chlorohydrins. New urethans prepared were the α-naphthylurethans of hexamethylene-

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(1) This paper is abstracted from a portion of a dissertation submitted by George W. Anderson to the Graduate Council of the University of Florida in partial fulfilment of the requirements for the degree of Doctor of Philosophy, May, 1939.

(2) Pyman and Levene, British Patent 402,159, Nov. 30, 1933, to Boot's Pure Drug Co.

(3) Kirner and Richter, THIS JOURNAL, **51**, 2503 (1929).

(4) Bennett and Moses, *J. Chem. Soc.*, 1697 (1931).

α,ω-chlorohydrin, m. p. 49–50°, and of decamethylene-α,ω-chlorohydrin, m. p. 63–64°. The melting point of the phenylurethan of nonamethylene-α,ω-chlorohydrin was 70–70.5°, 3° higher than previously reported.[4]

N-Phenyl-N′-(8-hydroxyoctyl)-piperazine Hydrate.—N-phenyl-N′-(8-hydroxyoctyl)-piperazine of m. p. 57–58.5° and neut. equiv. 292.1 (mol. wt. is 290.4) gave a compound of m. p. 80–82° and neut. equiv. 306.5 (theoretical 308.4 for a monohydrate) upon exposure to air.

Summary

A series of seven new amino alcohols, the N-phenyl-N′-(ω-hydroxyalkyl)-piperazines, with the alkyl group having four through ten carbon atoms, has been synthesized from α,ω-chlorohydrins and N-phenylpiperazine. Their phenylurethans are reported. The formation of the monohydrate of N-phenyl-N′-(8-hydroxyoctyl)-piperazine upon exposure to air has been ascertained.

alpha,omega-Chlorohydrins of four through ten carbon atoms have been made by methods reported in the literature. The phenylurethan of nonamethylene chlorohydrin was found to melt 3° higher than previously reported. The α-naphthylurethans of hexamethylene and decamethylene chlorohydrins are reported for the first time.

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[CONTRIBUTION FROM THE ORGANIC CHEMISTRY LABORATORIES OF THE UNIVERSITY OF FLORIDA]

alpha,omega-Amino Alcohols. II. Morpholino Alcohols. Derivatives of Morpholine. II

BY GEORGE W. ANDERSON[1] AND C. B. POLLARD

Paden and Adkins[2] in their study of the reaction of amines with glycols at 200–250° in the presence of copper–chromium oxide reported one experiment in which equivalent quantities of phenethylamine and tetramethylene glycol in dioxane solution were heated for half an hour with hydrogen at 200–400 atm. with the production of 35% of 4-(N-phenethylamino)-butanol-1, 19% of 1-phenethylpyrrolidine, and 43% of unchanged amine and glycol.

On the basis of this experiment we have investigated the reaction of morpholine with α,ω-glycols of four through ten carbon atoms and, as was to be expected, have obtained only two products, namely, the morpholino alcohol and the dimorpholinoalkane. Data are shown in Tables I, II and III.

Approximately 0.5 mole of each reactant in 300 cc. of dioxane was heated at 235–270° for six hours at a pressure of 100 atm. After cooling, the dioxane was distilled off at atmospheric pressure and the remainder fractionated in an efficient electrically heated air-jacketed column 2 cm. in bore, 70 cm. long, packed with 6 × 6 mm. Raschig rings, and having a total condensation, variable take-off head. In several cases, a similar column, 1.8 cm. in bore and 30 cm. long, packed with 5 × 5 mm. Raschig rings, and having a total condensation, variable take-off head was used.

The morpholino alcohols, with the exception of 7-morpholinoheptanol-1, were also prepared from morpholine and the corresponding chlorohydrins. Almost quantitative yields were obtained by this method. Physical and analytical data for the seven new morpholino alcohols are recorded in Table II.

The aryl urethans of the morpholino alcohols were prepared by mixing hot solutions of the aryl isocyanate and the alcohol and heating the mix-

TABLE I

MORPHOLINO ALCOHOLS BY ALKYLATION[a]

Glycol	Moles used	Moles of morpholine	Yields[b] of pure compd., % Amino alcohol	Dia-mine	Cu–Cr–O cat. used
Tetramethylene	0.75	0.94	36	22	22
Pentamethylene	.80	1.0	31	28	24
Hexamethylene	.60	0.60	21	18	20
Heptamethylene	.33	.42	19	28	10
Octamethylene	.50	.75	26	41	15
Nonamethylene	.34	.43	38	28	11
Decamethylene	.40	.40	21	13	9

[a] Between 125 and 300 cc. of dioxane was used in each case as solvent. The reaction was carried out under about 100 atm. of hydrogen at 235–270° for six hours. [b] Yields are based on the glycol used. Some of the glycol did not react in each case, but was not recovered pure, so yields were not adjusted for it.

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[1] This paper is abstracted from a portion of a dissertation submitted by George W. Anderson to the Graduate Council of the University of Florida in partial fulfilment of the requirements for the degree of Doctor of Philosophy, May, 1939.

[2] Paden and Adkins, THIS JOURNAL, 58, 2487 (1936).