The following fractions could not be identified by their physical properties nor by their derivatives: The fraction boiling at 210.5° had d^{25}_4 0.9525, n^{25}_D 1.4878, a picrate and a phenyl urea melting at 202 and 221°, respectively.

Anal. Calcd. for ethyl-di-(2-aminoethyl)-amine: N, 32.1; 1° amine N, 21.4; N of phenyl urea 18.9. Found: N, 32.1; 1° amine N, 21.4; N of phenyl urea, 18.3. Specific dispersion did not indicate unsaturation. *MR* calcd., 41.1; found, 39.8.

The fraction boiling at 233.5° had d^{25}_4 0.997, n^{25}_D 1.5098 and a picrate decomposing at 208°.

Anal. Calcd. for 1-[N-(2-aminoethyl)-2-aminoethyl]-pyrroline: N, 27.0; 1° amino N, 9.00. Found: N, 26.9; 1° amino N, 9.00. The double bond was indicated by its specific dispersion of 155 instead of the usual 120. *MR* calcd. 47.9; found: 46.5.

The products isolated are the type that would be expected from the splitting of the C–N linkage in the primary reaction. Piperazine derivatives might be expected as products in this kind of pyrolysis due to their stability and volatility. They are relatively more volatile than the corresponding linear polyethylene amines.

Summary

Pyrolyses of "amine residue" in the apparatus described has been found to yield as high as 24% ethylenediamine. Higher boiling fractions consisting mainly of cyclized amines can be formed in yields of 5 to 15% at the expense of ethylene diamine yield.

Analyses and physical properties indicate that some of the other fractions are diethylene triamine, 1,2-di-(N-piperazyl)-ethane, and 1,4-di-(2-aminoethyl)-piperazine.

Pyrolysis of tetraethylenepentamine yielded somewhat similar results but two of the above products did not appear while two new fractions were formed. Analyses and physical properties indicate that these were ethyl-di-(2-aminoethyl)-amine and 1-[N-(2-aminoethyl)-2-aminoethyl]-pyrroline.

MORGANTOWN, WEST VIRGINIA
RECEIVED SEPTEMBER 10, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF KENTUCKY]

The Condensation of Diethylamine and Formaldehyde with Phenol, *o*-, *m*- and *p*-Cresols[1]

BY GERALD F. GRILLOT AND WILLIAM T. GORMLEY, JR.[2]

Studies of the Mannich reaction in which a variety of phenols were condensed with formaldehyde and secondary amines such as dimethylamine[3] or piperidine[4] have been reported, but we have been unable to find in the literature[5] any reference to the interaction of a phenol with formaldehyde and diethylamine. The latter amine appears to be less reactive than certain other secondary amines.[5]

The authors have been successful in the condensation of phenol and *o*-, *m*- and *p*-cresol with formaldehyde and diethylamine. When about equimolar quantities of the reacting materials were employed, 2-diethylaminomethylphenol, 6-diethylaminomethyl-2-methylphenol, 2- or 6-diethylaminomethyl-3-methylphenol and 2-diethylaminomethyl-4-methylphenol, respectively, were formed. When an excess of diethylamine and formaldehyde was condensed with phenol, 2,6-di-(diethylaminomethyl)-phenol was isolated. Although the position of the entering diethylaminomethyl group was not determined, it has been assumed, in view of the experiments of Décombe[3b] with dimethylamine, that the substituent entered the benzene ring in a position ortho to that of the phenolic hydroxyl group.

Experimental

2-Diethylaminomethylphenol.—General Procedure. Diethylamine (13.4 g., 0.18 mole) was added dropwise with stirring to 15.7 g. (0.17 mole) of pure phenol. The temperature was kept below 20° during this addition and was maintained in the same range while 15.8 g. of formalin (35–40% formaldehyde solution, 0.18 mole of formaldehyde) was added drop by drop. When about half of the formalin had been added, the reaction mixture separated into an oily and an aqueous layer. The mixture was allowed to stand for one hour at about 20° and was then warmed for two hours on a water-bath at about 80°.

The oily layer was extracted with ether and the ether was evaporated. Low-boiling impurities were removed by warming the residue to 80° at a pressure of about 17 mm. The pale amber oil boiled at 63–67° (1–2 mm.); yield 21 g. (68.6%); d^{25}_4 0.9780; n^{25}_D 1.5108; *MR* calcd. 55.01; found 54.81.

Anal. Calcd. for $C_{11}H_{17}NO$: N, 7.82. Found: N, 7.85; 7.82.

2,6-Di-(diethylaminomethyl)-phenol.—Using the procedure described above, 51.1 g. (0.7 mole) of diethylamine and 60 g. (0.7 mole) of formalin were condensed with 18.8 g. (0.2 mole) of phenol. A fraction, b. p. 63–80° (1–2 mm.), yielded on redistillation 13 g. of 2-diethylaminomethylphenol, b. p. 63–67° (1–2 mm.).

In addition, there was obtained 12 g. (22.4%) of the disubstituted phenol boiling at 120–125° (1–2 mm.); d^{25}_4 0.9561; n^{25}_D 1.5120; *MR* calcd. 86.85; found, 84.05.

Anal. Calcd. for $C_{16}H_{32}N_2O$: N, 14.44. Found: N, 14.44.

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[1] Abstracted from the M. S. thesis of William T. Gormley, Jr., submitted in 1945.

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[3] (a) German Patent 92,309; (b) Décombe, *Compt. rend.*, **196**, 866 (1933); (c) Décombe, *ibid.*, **197**, 258 (1933); (d) Bruson and MacMullen, THIS JOURNAL, **63**, 270 (1941); (e) Caldwell and Thompson, *ibid.*, **61**, 765 (1939).

[4] (a) Hildebrandt, *Arch. für exp. Path. Pharmakol.*, **44**, 278 (1900); *Ber.*, **37**, 4456 (1904); (b) Auwers and Dombrowski, *Ann.*, **344**, 280 (1906).

[5] F. F. Blicke, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, chapter 10.

With a molar ratio of diethylamine and formaldehyde to phenol of 3.5 to 1, it appeared that appreciable amounts of mono- and di-substituted phenols were formed.[6]

***o*-, *m*- and *p*-Cresol.**—Preparation of the three cresols was based on the conversion of *m*-nitroaniline to *m*-nitrophenol which is described in "Organic Syntheses."[7]

A cold solution of 120 cc. of water and 80 cc. of concd. sulfuric acid was stirred by hand while 43 g. (0.4 mole) of *p*-toluidine and then 200 g. of finely crushed ice were added. A solution of 27 g. of sodium nitrite dissolved in 125 cc. of water was added rapidly (15–20 min.) from a separatory funnel whose stem was immersed below the surface of the liquid. The temperature during the diazotization was maintained between 0 and 5°. Urea (2 g.) was added and stirring was continued for ten minutes.

While diazotization was in progress, 270 cc. of concd. sulfuric acid was added to 200 cc. of water in a 2-liter, round-bottomed flask. The acid was heated to boiling and the diazonium solution was then added at such a rate that the acid mixture was kept boiling vigorously. The *p*-cresol was steam-distilled and extracted with ether from the distillate. The ether extract was dried over magnesium sulfate, the ether evaporated, and the *p*-cresol distilled at atmospheric pressure. It boiled at 195–200°; yield 20 g. (46%).

By a similar synthesis, *o*-cresol, b. p. 69–71° (6 mm.), was made in 40.1% yield, and *m*-cresol, b. p. 80–82° (6 mm.), in 41.2% yield.

2-(Diethylaminomethyl)-4-methylphenol.—Fifty-four grams (75%) of this compound was obtained when 40 g. (0.46 mole) of *p*-cresol was condensed with 37.2 g. (0.51 mole) of diethylamine, and 43.7 g. (0.51 mole) of formalin. It was a pale amber oil, b. p. 90–93° (1–2 mm.); d^{25}_4 0.9675; n^{25}_D 1.5140; *MR* calcd. 59.65; found, 60.21.

Anal. Calcd. for $C_{12}H_{19}NO$: N, 7.25. Found: N, 7.09, 7.12.

2-(Diethylaminomethyl)-6-methylphenol.—From 21.4 g. (0.20 mole) of *o*-cresol, 15.8 g. (0.22 mole) of diethylamine and 19 g. (0.22 mole) of formalin, there resulted 22 g. (57.7%) of the phenol boiling at 93–97° (1–2 mm.); d^{25}_4 0.9708; n^{25}_D 1.5141; *MR* calcd. 59.65; found, 59.95.

Anal. Calcd. for $C_{12}H_{19}NO$: N, 7.25. Found: N, 7.23, 7.21.

2- or 6-(Diethylaminomethyl)-3-methylphenol.—Eighteen grams (0.17 mole) of *m*-cresol was condensed with 13.4 g. (0.18 mole) of diethylamine and 15.8 g. (0.18 mole) of formalin to yield 13 g. (40.4%) of a fraction which boiled at 107–110° (1–2 mm.); d^{25}_4 0.9677; n^{25}_D 1.5130; *MR* calcd. 59.65; found 60.03.

Anal. Calcd. for $C_{12}H_{19}NO$: N, 7.25. Found: N, 7.40, 7.42.

There is not yet sufficient evidence to indicate whether the entering group occupies the 2- or the 6-position.

Summary

1. Diethylamine and formaldehyde have been condensed with phenol and with *o*-, *m*- and *p*-cresol; 2-diethylaminomethylphenol, 6-diethylaminomethyl-2-methylphenol, 2- or 6-diethylaminomethyl-3-methylphenol and 2-diethylaminomethyl-4-methylphenol, respectively, were formed.

2. 2,6-Di-(diethylaminomethyl)-phenol was isolated when an excess of diethylamine and formaldehyde was condensed with phenol.

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(6) Bruson and MacMullen (ref. 3d) have reported the formation of 2,4,6-tri-(dimethylaminomethyl)-phenol in 86% yield under conditions similar to those which we used. Dimethylamine, formaldehyde and phenol were employed in a molar ratio of 4, 3.5 and 1 in their experiment.

(7) Gilman, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 396.

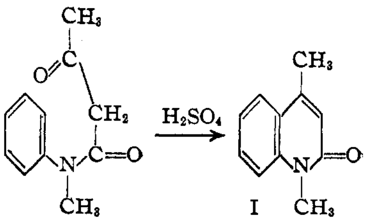
[Contribution from the Chemistry Laboratory of Indiana University]

N-Substituted 4-Methylcarbostyrils[1]

By C. E. Kaslow and D. J. Cook[2,3]

A study has been made of the preparation of N-alkyl-4-methylcarbostyrils by the reaction between a secondary aromatic amine and ketene dimer. The reaction is illustrated by the following equation showing the formation of 1,4-dimethylcarbostyril.

$$C_6H_5NHCH_3 \xrightarrow{CH_3COCHCO}$$



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1,4-Dimethylcarbostyril has been prepared by Knorr[4] through rearrangement of 2-methoxylepidine and also by treating the crude condensation product of methylaniline and acetoacetic ester with sulfuric acid.

The above synthesis has made available several 1-alkyl-4-methylcarbostyrils which may be obtained in yields of 44–83% (see Table II of Experimental).

A study has also been made of some reactions of 1,4-dimethylcarbostyril which was chosen as a typical representative of this class of compounds. For example, the nitration of 1,4-dimethylcarbostyril with excess fuming nitric acid gave a mixture from which a mononitro- and a trinitro-compound was isolated. On the basis of previous work on the nitration of 1-methylcarbostyril[5,6] these compounds may be tentatively assigned the structures of 6-nitro- and 3,6,8-trinitro-1,4-dimethylcarbostyril.

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(1) Presented in part before the Division of Organic Chemistry, American Chemical Society, New York, N. Y., September 13, 1944.

(2) Abstracted from a thesis submitted to the Faculty of the Graduate School in partial fulfillment of the requirements for the degree, Doctor of Philosophy, in the Department of Chemistry, Indiana University.

(3) Present address: DePauw University, Greencastle, Indiana.

(4) Knorr, *Ann.*, **236**, 69 (1886).

(5) Decker, *J. prakt. Chem.*, **64**, 85 (1901).

(6) Kaufman and dePetherd, *Ber.*, **50**, 336 (1916).