THE REACTION BETWEEN DIETHYLAMINE AND ETHYLENE OXIDE

BY W. H. HORNE AND R. L. SHRINER

β-Diethylaminoethanol is an important intermediate in the preparation of alkylamino esters. The reaction between diethylamine and ethylene oxide should furnish a method of preparation which would be superior to the reduction of diethylaminoacetic ester[1] or the action of diethylamine on ethylene chlorohydrin[2] because of the greater ease in the isolation of the product. The starting materials are now available commercially and inexpensive. The purposes of the present investigation were (1) to determine the optimum conditions for the preparation of β-diethylaminoethanol and (2) to separate and identify some of the higher boiling compounds which are always formed in reactions involving ethylene oxide.

In 1863, just four years after he had first prepared ethylene oxide,[3] Wurtz noted its reaction with ammonia.[4] Since that time the action of ethylene oxide on ammonia,[5] primary, secondary and tertiary amines,[6] hydrazines,[7] amides and imides[8] has been investigated. Substituted ethylene oxides[3,9] have also been shown to react with ammonia and amines to yield various amino alcohols. These investigations were carried out before ethylene oxide was readily available, so no complete study of the combination of diethylamine and ethylene oxide has been published. Quite different experimental conditions were used by the previous investigators and no general procedures were described.

It was found that pure dry diethylamine did not react with ethylene oxide but in the presence of water or alcohol the reaction would take place. A study was made of the effect of various solvents and the data obtained are summarized in Table I of the Experimental Part. It is evident that methyl and ethyl alcohols afford a smooth, rapid absorption of ethylene

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[1] Gault, *Compt. rend.*, **145**, 126 (1907); Bouveault and Blanc, *Bull. soc. chim.*, **31**, 1210 (1904).

[2] Ladenburg, *Ber.*, **14**, 1878 (1881).

[3] Wurtz, *Ann. chim. phys.*, **55**, 427 (1859).

[4] Wurtz, *ibid.*, **69**, 381 (1863).

[5] (a) Knoor, *Bull. soc. chim.*, **22**, 499 (1899); (b) Henry, *ibid.*, **25**, 978 (1901); (c) Krassuskii, *Compt. rend.*, **146**, 236 (1908).

[6] (a) Demole, *Ann.*, **173**, 127 (1874); (b) Knoor and Matthes, *Bull. soc. chim.*, **28**, 592 (1902); (c) Knoor and Brownsdon, *ibid.*, **30**, 921 (1903); (d) Gabel, *ibid.*, **38**, 600 (1925); (e) Roithner, *Monatsh.*, **15**, 655 (1894).

[7] Barnett, *Proc. Chem. Soc.*, **28**, 259 (1912); Ref. 6e.

[8] Gabriel, *Ber.*, **50**, 819 (1917).

[9] Krassuskii, *Compt. rend.*, **146**, 236 (1908); *Bull. soc. chim.*, **42**, 1151 (1927); *J. chim. Ukraine*, 1, 65, 68, 398 (1925); *Chem. Abs.*, **20**, 2820 (1926).

oxide resulting in a good yield of β-diethylaminoethanol. Methyl alcohol was easier to separate by fractional distillation and hence is the best solvent. There was no evidence that the ethylene oxide reacted with the solvent under the conditions used.

A series of experiments was carried out to determine the best temperature for the reaction. If diethylamine containing a little water and liquid ethylene oxide are mixed at room temperature in a closed vessel the combination takes place slowly at first, but as the mixture warms up it finally proceeds with explosive violence.[10] It seems probable that an addition compound is first formed similar to that between Grignard reagents and ethylene oxide[11] which must be subsequently rearranged. It was found that a temperature range of 45–60° permitted a smooth, rapid absorption of gaseous ethylene oxide. Below 45° the absorption was slow and above 60° the reaction also slowed down due to the diminished solubility of the ethylene oxide in the amine. By carrying out the reaction at 45–60° the addition compound is rearranged as fast as it is formed, thus avoiding a violent reaction. It is interesting to note that this temperature range is the same as that used to rearrange the Grignard addition compounds.

The results of variations in the mole ratio of reactants are also given in Table I. It is evident that the best yield was obtained with a ratio of about 1.3 moles of ethylene oxide to one mole of diethylamine (Run 9). The very slightly higher yield in Run 10 does not justify the use of the additional half mole of ethylene oxide. From Table II it will be noted that as the amount of ethylene oxide was increased the amount of unreacted diethylamine decreased but the percentage of material boiling above β-diethylaminoethanol was increased. These high boiling fractions from several runs were combined and carefully fractionated and two of the fractions definitely identified as the mono-β-diethylaminoethyl ether of ethylene glycol (II) and mono-β-diethylaminoethyl ether of diethylene glycol (III). Analyses and molecular refractivities of the two highest boiling fractions indicated that they are the mono-β-diethylaminoethyl ethers of triethylene glycol (IV) and tetraethylene glycol (V), respectively. These compounds represent the progressive addition of ethylene oxide and are of considerable theoretical interest, since they constitute further examples of bifunctional reactions discussed by Carothers in connection with chain polymerization.[12] They are evidently formed according to the reactions shown.

Compounds II, III, IV and V represent very low molecular weight chain molecules with different functional groups on the ends of the chain. Cyclic

[10] Staudinger [*Ber.*, **62**, 2395 (1929)] has also recorded the explosive polymerization of ethylene oxide.

[11] "Organic Syntheses," J. Wiley and Sons, Inc., New York, Vol. VI, 1926, p. 56.

[12] Carothers, *Chem. Rev.*, **8**, 353 (1931).

$$(C_2H_5)_2NH + \underset{\underset{O}{\diagdown\diagup}}{CH_2\!-\!CH_2} \longrightarrow (C_2H_5)_2NCH_2CH_2OH$$

$$I$$

$$\underset{\underset{O}{\diagdown\diagup}}{CH_2\!-\!CH_2}\Big\downarrow$$

$$(C_2H_5)_2NCH_2CH_2OCH_2CH_2OCH_2CH_2OH \xleftarrow{\quad\underset{\underset{O}{\diagdown\diagup}}{CH_2\!-\!CH_2}\quad} (C_2H_5)_2NCH_2CH_2OCH_2CH_2OH$$

$$III \qquad\qquad\qquad\qquad\qquad\qquad II$$

$$(C_2H_5)_2NCH_2CH_2(OCH_2CH_2)_3OH \longrightarrow (C_2H_5)_2NCH_2CH_2(OCH_2CH_2)_4OH$$

$$IV \qquad\qquad\qquad\qquad V$$

polymerization was blocked by the tertiary amino group. The presence of the alcohol group was demonstrated by reaction with p-nitrophenyl isocyanate[13] or with p-nitrobenzoyl chloride. The amino group was indicated by the formation of a salt with hydrochloric acid. In the transformation of I $\longrightarrow$ II $\longrightarrow$ III the addition of the ethylene oxide can take place at only one end of the chain instead of both ends as in the linear polymers of ethylene oxide alone. That compound II was actually formed from I was shown by treating pure β-diethylaminoethanol in methyl alcohol solution with ethylene oxide and isolating the compounds II and III. Similarly III can be obtained from II, IV from III and V from IV.

TABLE I

EFFECT OF SOLVENTS

Run	Solvent, g.	Diethyl-amine, g. A	Ethylene oxide, g. B	Mole ratio B/A	Yield Grams	%	Time, hours
1	None	60.0	0.5	0.0138	..	0.00	6
2	H₂O 2.5	54.5	21	.639	39	45.0	10
3	H₂O 2.5	49.0	30	1.02	38	48.4	15
4	C₆H₆ 50, H₂O 5	40.0	18	0.747	30	46.8	4
5	C₆H₆ 100, H₂O 5	58.5	94	2.67	40	42.7	15
6	C₂H₅OH (95%) 40	40	26	1.08	43	67.1	1.5
7	C₂H₅OH (95%) 40	40	44	1.83	48	74.9	4
8	CH₃OH 40	40	28	1.16	40.5	63.2	1.33
9	CH₃OH (absolute), 40	40	32	1.33	48	74.9	2
10	CH₃OH 40	40	43	1.78	49	76.5	2.5

TABLE II

EFFECT OF INCREASING AMOUNTS OF ETHYLENE OXIDE ON COMPOSITION OF THE REACTION MIXTURE

Run	Ethylene oxide added, g.	Diethylamine recovered, g.	β-Diethylamino-ethanol, g.	Higher fraction 80–135°, 7–10 mm., g.	Residue, above 135°, g.
1	18	7.64	34	5	1.0
2	26	7.15	43	7.5	2.5
3	28	6.7	40.5	7.0	1.5
4	32	6.17	48	10.0	2.0
5	43	3.87	49	17.5	4.0

[13] Horne and Shriner, THIS JOURNAL, **53**, 3186 (1931); Shriner and Cox, *ibid.*, **53**, 1601 (1931).

Experimental Part

The results of the experiments carried out to determine the optimum conditions for the preparation of β-diethylaminoethanol are summarized in the two tables.

The best procedure for the production of β-diethylaminoethanol (Run 9) was the following.

β-Diethylaminoethanol.—Forty grams of diethylamine was dissolved in 40 g. of methyl alcohol as solvent. The mixture was warmed to 45–60° and a fairly rapid stream of ethylene oxide passed through the reaction mixture. The flow of ethylene oxide was adjusted to keep the heat of the reaction from raising the temperature of the mixture above 60°. The maximum rate of addition was achieved in this manner. After two hours, 32 g. (8 g. excess) of ethylene oxide had been added. By fractional distillation *in vacuo* 48 g. of β-diethylaminoethanol (74.9% of the theoretical) was obtained. The residues in the flask (about 15 g.) from several runs were combined and fractionated as described below.

The product of the reaction was identified as β-diethylaminoethanol by means of its chemical and physical properties. It was found to contain hydrogen replaceable by metallic sodium, and to produce a distinctly alkaline aqueous solution. It was soluble in water, ether, benzene, petroleum ether and acetone. Its hydrochloride salt was precipitated from ether solution. This salt is very hygroscopic. Physical Properties: colorless, hygroscopic liquid, which turns yellow on standing; b. p. 163° at 760 mm. and 42–44° at 8 mm.; n_D^{25} 1.4400; d_{25}^{25} 0.8601; M_D calcd., 35.02; found, 35.81.

Anal. Calcd. for $C_6H_{15}ON$: N, 11.95. Found: N, 11.40.

To establish further the identity of the compound the *p*-nitrophenyl urethan was prepared by mixing β-diethylaminoethanol with *p*-nitrophenyl isocyanate in benzene solution. Evaporation of the benzene left the urethan, which was recrystallized from carbon tetrachloride as yellow crystals, m. p. 59–60° (corr.).

Anal. Calcd. for $C_{13}H_{19}O_4N_3$: N, 14.95. Found: N, 14.66.

The hydrochloride salt of this urethan was obtained by dissolving the urethan in dry acetone and precipitating as yellow crystals with dry hydrogen chloride. This derivative was recrystallized from 95% alcohol as fine yellow crystals, decomp. 200–210°.

Anal. Calcd. for $C_{13}H_{20}O_4N_3Cl$: Cl, 11.17. Found: Cl, 11.12.

Fractionation of the High Boiling Residues.—The residues from the distillation of ten runs from the preparation of β-diethylaminoethanol were combined and fractionally distilled *in vacuo* with the following results.

Fraction	Temp. at 7 mm., °C.	Vol. (approx.), cc.
1	80– 90	4
2	90– 95	15
3	95–100	25
4	100–120	15
5	120–130	30
6 (Residue)	Above 130	10
	Total	99

Fractions 2 and 3 were combined and redistilled, yielding about 27 cc. of material boiling between 92 and 95° (Fraction A). Fraction 5 was redistilled and about 22 cc. of material was obtained between 123 and 128° (Fraction B). In this way these two

fractions represented the two chief components of the mixture. The residue was a dark brown viscous material from which no definite product could be isolated.

Identification of Fraction A as the Mono-(β-diethylaminoethyl) Ether of Ethylene Glycol.—Fraction A was a colorless hygroscopic liquid with an odor similar to that of β-diethylaminoethanol. It reacted with sodium and was soluble in water, benzene, alcohol, ether and acetone. The aqueous solution was alkaline. Its hydrochloride was precipitated from ether by dry hydrogen chloride and found to be very hygroscopic. Physical properties: b. p. 92–95° at 7 mm.; n_D^{25} 1.4457; d_{25}^{25} 0.9399; M_D, calcd., 44.52; found, 45.65.

Anal. Calcd. for $C_8H_{19}O_2N$: N, 8.70. Found: N, 8.77.

To further establish the identity of this compound the *p*-nitrophenyl urethan hydrochloride was obtained by treating fraction A with *p*-nitrophenyl isocyanate in benzene solution. Addition of dry hydrogen chloride gave an orange oil which was crystallized from 95% alcohol and washed with acetone; light yellow crystals, m. p. 152–153° (corr.).

Anal. Calcd. for $C_{15}H_{24}O_5N_3Cl$. Cl, 9.81. Found: Cl, 9.77.

Identification of Fraction B as the Mono-(β-diethylaminoethyl) Ether of Diethylene Glycol.—Fraction B was also a light yellow, hygroscopic, viscous liquid. It reacted with metallic sodium, and produced a distinctly alkaline aqueous solution. It was soluble in water, ether, acetone and benzene. Its hydrochloride salt was precipitated from ether and found to be hygroscopic. Physical properties: b. p. 123–128° at 7 mm.; n_D^{25} 1.4534; d_{25}^{25} 0.9763; M_D, calcd., 55.00; found, 56.80.

Anal. Calcd. for $C_{10}H_{23}O_3N$: N, 6.83. Found: N, 6.71.

The *p*-nitrobenzoate was obtained by treatment with *p*-nitrobenzoyl chloride. The product was obtained as light yellow crystals from 95% alcohol; m. p. 121.5–122° (corr.).

Anal. Calcd. for $C_{17}H_{26}O_6N_2$: N, 7.91. Found: N, 8.09.

Attempts to prepare derivatives of fractions A and B with the following reagents failed: with α-naphthyl isocyanate and methyl-*p*-toluenesulfonate, viscous, non-crystallizing products were obtained; with chloroplatinic acid and picric acid no insoluble products were produced.

Conversion of β-Diethylaminoethanol into Mono-(β-diethylaminoethyl) Ether of Ethylene Glycol.—Twelve grams of β-diethylaminoethanol was dissolved in 10 g. of methyl alcohol and ethylene oxide passed into the solution which was kept at 50°. In thirty minutes 14 g. of ethylene oxide was absorbed. The solvent was distilled and the residual oil fractionated. About 7 g. of unreacted β-diethylaminoethanol was recovered and 4 g. of material boiling 92–95° at 7 mm. was obtained. This last fraction agreed in its properties with the mono-(β-diethylaminoethyl) ether of ethylene glycol.

Separation of Fraction 6.—After a considerable number of the residues constituting fraction 6 above had been obtained, they were combined and carefully fractionated *in vacuo* using a column packed with carborundum. After repeated distillation two fractions were obtained; C, boiling between 164–172° at 7 mm.; and D, boiling 190–200° at 7 mm.

Identification of Fraction C as the Mono-(β-diethylaminoethyl) Ether of Triethylene Glycol.—Fraction C was a yellow, very viscous hygroscopic liquid. It was soluble in water, ether, alcohol and acetone but was less soluble in benzene than fraction B. Physical properties: b. p. 164–172 at 7 mm., n_D^{25} 1.4570, d_{25}^{25} 1.0237, M_D calcd. 65.48, found 66.31.

Anal. Calcd. for $C_{12}H_{27}O_4N$: N, 5.61. Found: N, 5.65.

Identification of Fraction D as the Mono-(β-diethylaminoethyl) Ether of Tetraethylene Glycol.—Fraction D was a dark yellow viscous hygroscopic liquid.

It was soluble in water, ether, alcohol, acetone but slightly soluble in benzene and insoluble in petroleum ether. Physical properties: b. p. 190–200° at 7 mm., n_D^{25} 1.4622, d_{25}^{25} 1.0510, M_D calcd. 75.96, found, 74.92.

Anal. Calcd. for $C_{14}H_{31}O_5N$: N, 4.77. Found: N, 4.72.

No solid derivatives of Fractions C and D could be obtained.

Summary

1. β-Diethylaminoethanol may be prepared conveniently by the combination of diethylamine with ethylene oxide in methyl alcohol solution at a temperature range of 45–60°.

2. The above reaction also produces chain molecules corresponding to the addition of two, three, four and five molecules of ethylene oxide to one of diethylamine. The mono-(β-diethylaminoethyl) ethers of ethylene glycol, diethylene glycol, triethylene glycol and tetraethylene glycol have been isolated and characterized.

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THE TOXICITY TO GOLDFISH OF CERTAIN ORGANIC THIOCYANATES AND ISOTHIOCYANATES[1]

BY NATHAN L. DRAKE AND RUTH L. BUSBEY

There appear in the literature several scattered references to investigations concerned with the possible value of thiocyanates and isothiocyanates as insecticides.

Moore[2] reported that, molecule for molecule, allyl isothiocyanate is more toxic against house flies (*Musca domestica* L.) than chloropicrin. Later, allyl isothiocyanate was found by Tattersfield and Roberts[3] to be the most toxic to wireworms (*Agriotes*) of all compounds tested by them. Probably two or more species were used in the tests. More recently, Neifert and co-workers[4] in tests with fumigants against the rice weevil (*Calendra oryzae* L.) and the flour beetle (*Tribolium confusum* Duv.) and the granary weevil (*Calendra granaria* L.) found that methyl and ethyl thiocyanates, and allyl isothiocyanates were more effective than carbon bisulfide.

In another investigation of possible fumigants, Roark and Cotton[5] found

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[1] From a thesis submitted by Ruth Lawless to the Graduate School of the University of Maryland in partial fulfilment of the requirements for the degree of Master of Science.

[2] Moore, *J. Agr. Research*, 10, 365–71 (1917).

[3] Tattersfield and Roberts, *J. Agr. Sci.*, 10, 119–232 (1920).

[4] Ira E. Neifert and co-workers, "Fumigation against Grain Weevils with Various Volatile Organic Compounds," U. S. D. A. Dept. Bull. 1313 (1925).

[5] Roark and Cotton, "Tests of Various Aliphatic Compounds as Fumigants," Tech. Bull. 162 of the U. S. Dept. of Agriculture, March, 1930.