[CONTRIBUTION FROM THE REGA INSTITUTE, UNIVERSITY OF LOUVAIN]

Phenoxazines. II.[1] 10-Dialkylaminoalkylphenoxazines

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The preparation of a number of 10-dialkylaminoalkyl derivatives of phenoxazine and of 2-ethylphenoxazine is described. Various methods of synthesis are examined.

After the discovery of the potent antihistaminic activity of 10-(2′-dimethylaminopropyl)phenothiazine (promethazine)[2] and the tranquilizing properties[3] of 10-(3′-dimethylaminopropyl)-2-chlorophenothiazine (chlorpromazine),[4] a large number of other derivatives of phenothiazine have been introduced in the clinic.[5,6]

Very few phenoxazine derivatives have been studied, probably because 10-(2′-dimethylaminoethyl)phenoxazine has no antihistaminic activity.[7] Certain 10-(piperazinoalkyl)phenoxazines, however, have been reported to have anti-epileptic properties.[8] Very recently a few other 10-(dialkylaminoalkyl)phenoxazines have been described.[9,10]

Most products given in Tables I and II were prepared by the reaction of phenoxazine or 2-ethylphenoxazine[1] with dialkylaminoalkyl chlorides[11] in refluxing toluene, using sodamide as the condensing agent (Method A). No reaction was observed when diethylaminoethyl chloride was heated with phenoxazine in benzene at 150°.[12]

In analogy with the observations in the methadone[13] and phenothiazine series.[14] a rearrangement was expected during the reaction of phenoxazine with 1-dialkylamino-2-chloropropane.[15] From the reaction of 1-diethylamino-2-chloropropane with phenoxazine, two products, *viz.* 10-(2′-diethylaminoisopropyl)phenoxazine (II, R = H, R′ = CH_3, $m = 0$, $n = 1$, $N^A_{A'} = N(C_2H_5)_2$) and 10-(2′-diethylaminopropyl)phenoxazine (II, R = H, R′ = CH_3, $m = 1$, $n = 0$, $N^A_{A'} = N(C_2H_5)_2$), were obtained. The structure of the second product was proved by the unambiguous synthesis, used by Dahlbom in the phenothiazine series.[19] Phenoxazine was condensed with propylene oxide in the presence of sodamide to give 10-(2′-hydroxypropyl)-phenoxazine (VI). The *p*-toluene sulfonate of this intermediate (VII) gave by reaction with diethylamine, 10-(2′-diethylaminopropyl)phenoxazine, identical with the product prepared by the other method. The yields obtained in the reaction of various amines with the *p*-toluenesulfonates of 10-(2′- and 3′-hydroxypropyl)phenoxazine and -2-ethylphenoxazine (VII and X) in 1-propanol solution were rather low (Method C in Tables I and II).

Several compounds were also prepared in good yield by the reaction of various amines with 10-(3′-halogenoalkyl)phenoxazine or -2-ethylphenoxazine (V) in benzene solution (Methods B and D). These intermediates (V) were obtained either by the reaction of 1-chloro-3-bromopropane with phenoxazine (or ethylphenoxazine) or by the action of phosphorus tribromide on 2-ethyl-10-(3′-hydroxypropyl)phenoxazine (IV). The 10-(3′-hydroxypropyl)-phenoxazines have been prepared by hydrolysis of the tetrahydropyranyloxypropyl derivative (III) or by reduction of ethyl β-(10-phenoxazinyl)propionate (VIII) with lithium aluminum hydride.

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(2) B. Halpern and R. Ducrot, *Compt. rend. soc. biol.*, **140**, 361 (1946).

(3) J. Delay, P. Deniker, and J. Hyri, *Ann. med. psych.*, **2**, No. 1–2 (1952).

(4) P. Charpentier, P. Gaillot, R. Jacob, J. Gaudechon, and P. Buisson, *Compt. rend.*, **235**, 59 (1952).

(5) P. Viaud, *J. Pharm. Pharmacol.*, **6**, 361 (1954).

(6) M. Gordon in A. Burger, *Medicinal Chemistry*, Interscience, New York, 1960.

(7) P. Viaud, *Prods. pharm.*, **2**, 53 (1947).

(8) Rhône-Poulenc (R. Horclois), Belgian Pat. **537,690** (1955).

(9) H. Linde, *Arch. Pharm.*, **293**, 537 (1960).

(10) G. Frangatos, G. Kohan, and F. L. Chubb, *Canad. J. Chem.*, **38**, 1021 (1960).

(11) The preparation of many dialkylaminoalkyl chlorides has been summarized recently by J. P. Bourquin *et al.*, *Helv. Chim. Acta*, **41**, 1972 (1958).

(12) This method has been described for phenothiazine by Cassella Farbwerke, German Pat., **922,467** (1955); *Chem. Abstr.*, **52**, 5485 (1958).

(13) E. M. Schultz, C. M. Robb, and J. M. Sprague, *J. Am. Chem. Soc.*, **69**, 188 (1947); M. Bockmühl and G. Ehrhart, *Ann.*, **561**, 52 (1948).

(14) P. Charpentier, *Compt. rend.*, **225**, 306 (1947); P. Charpentier and R. Ducrot, *Compt. rend.*, **232**, 415 (1951); W. B. Reid, J. B. Wright, H. G. Kolloff, and J. H. Hunter, *J. Am. Chem. Soc.*, **70**, 3100 (1948).

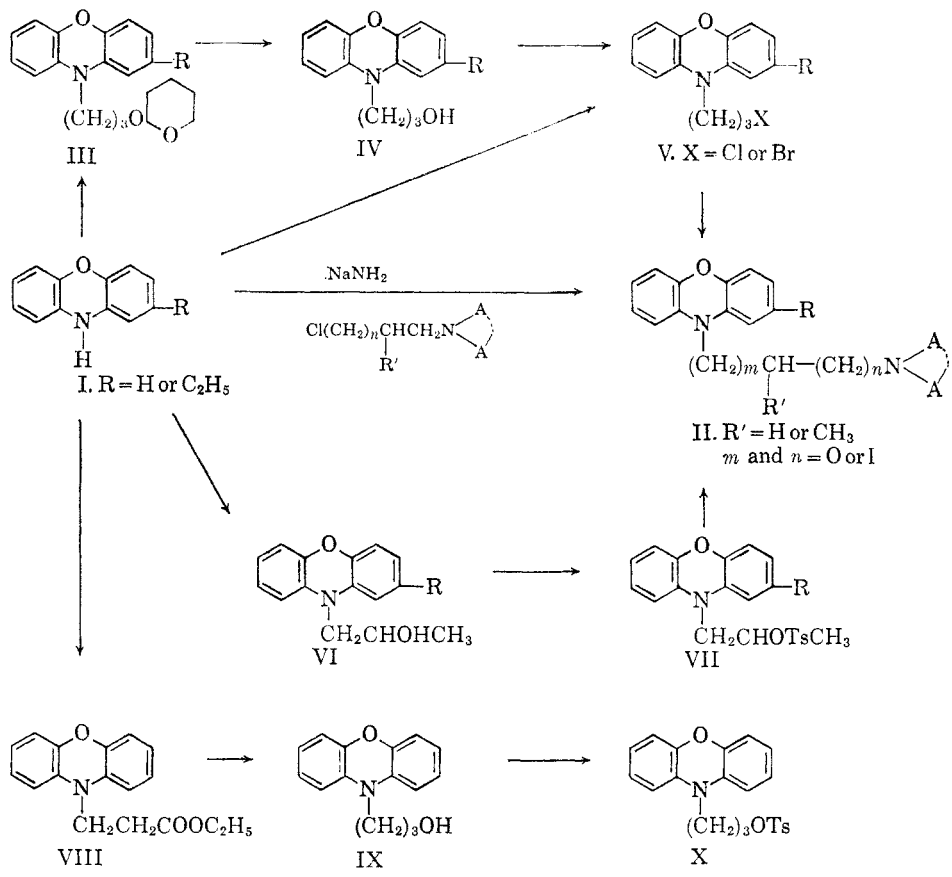
(15) The rearrangement of the 2-dialkylaminopropyl chlorides has been examined by W. R. Brode and M. W. Hill, *J. Am. Chem. Soc.*, **69**, 724 (1947); J. F. Kerwin, G. E. Ullyot, R. C. Fuson, and C. L. Zirkle, *J. Am. Chem. Soc.*, **69**, 2961 (1947); R. C. Fuson and C. L. Zirkle, *J. Am. Chem. Soc.*, **70**, 2760 (1948). This rearrangement has also been observed with $ClCH_2(CH_2NR_2)_2$[16] $ClCH(CH_3)CH_2CH_2NR_2$[17] and 1-methyl-4-chloromethylpiperidine.[18] For a review see W. Lwowski, *Angew. Chem.*, **70**, 483 (1958).

(16) M. Jacob, R. Horclois, R. Vaupré, and M. Messer, *Compt. rend.*, **243**, 1637 (1956).

(17) Rhône-Poulenc (P. Gaillot and J. Gaudechon), Brit. Pat., **797,172** (1958); *Chem. Abstr.*, **53**, 416 (1959).

(18) H. Henecka, U. Hörlein, and K. H. Risse, *Angew. Chem.*, **72**, 960 (1960).

(19) R. Dahlbom, *Acta Chem. Scand.*, **3**, 247 (1949).



Several phenoxazines were injected into mice (10 mg./kg. i.p.) and the prolongation of the narcosis induced by hexobarbital (50 mg./kg. i.p.) was determined (*cf.* ref. 5). The products 13, 18, and 20 (Tables I and II) showed the same activity as promazine, while *n*° 27 was slightly more active. The conditioned escape response of rats which received an intraperitoneal injection of these products was also examined. Their activity was only one-tenth that of chlorpromazine.[20]

EXPERIMENTAL[21]

10-(3'-N-Pyrrolidinopropyl)phenoxazine hydrochloride (compound 13). Method A. A mixture of 51.6 g. (0.282 mole) of phenoxazine, 12.4 g. (0.31 mole) of sodamide and 150 ml. of dry toluene was stirred and refluxed for 1 hr. A solution of 42.1 g. (0.285 mole) of 3-*N*-pyrrolidinopropyl chloride in 50 ml. of toluene was added dropwise, with stirring, and refluxing was continued for 2 hr. Subsequently, the mixture was cooled and water was added. The toluene layer was extracted with dilute hydrochloric acid. The acid extracts were made alkaline and extracted with benzene. The toluene gave upon evaporation 3 g. of unchanged phenoxazine. The benzene was evaporated and the residue was distilled to give 62 g. (76% yield) of an oil, b.p. 220–222° (3 mm.). The base was dissolved in an alcoholic solution of hydrochloric acid, and the hydrochloride was precipitated by adding dry ether. There was obtained 56 g. of a white crystalline product, m.p. 162–163°, unchanged upon recrystallization in the same solvent mixture.

Method B. To a suspension of sodamide, prepared by dissolving 1.01 g. (0.044 g.-atom) of sodium in 40 ml. of liquid ammonia containing a crystal of ferric nitrate, 7.32 g. (0.04 mole) of phenoxazine was added. After stirring for an 0.25 hr., 6.3 g. (0.04 mole) of 1-chloro-3-bromopropane was added slowly and with stirring. After an 0.5 hr., the ammonia was allowed to evaporate, and water was added. The mixture was extracted three times with ether. The ether solution was washed with water, dried over sodium sulfate, and evaporated. The residue was taken up in 25 ml. of toluene, 5.68 g. (0.08 mole) of pyrrolidine and a small amount of copper powder were added, and the solution was heated at 100–110° for 48 hr. in a closed reaction level. The reaction mixture was worked up, as described above, to give 7.61 g. (63% yield) of an oil, b.p. 190° (0.5 mm.). The base was transformed into 6.8 g. of crystalline hydrochloride, m.p. 160–162°.

The residue, obtained after evaporation of the ether, may also be distilled (195°/0.7 mm). In this way, 10-(3'-chloropropyl)phenoxazine (V. R = H; X = Cl) was obtained (77% yield) and was crystallized from ethanol, m.p. 54–55°.

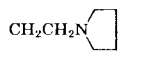
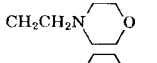
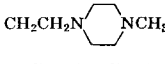
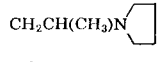
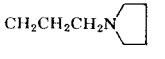
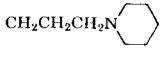
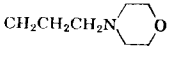
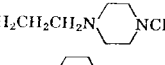
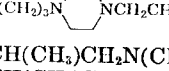
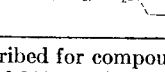
10-(2'-Hydroxypropyl)phenoxazine (VI. R = H). A mixture of 29.2 g. (0.016 mole) of phenoxazine and 6.4 g. (0.016 mole) of sodamide in 80 ml. of dry toluene was refluxed with stirring for 1 hr. After cooling, a solution of 10 g. (0.172 mole) of propylene oxide in 30 ml. of toluene was added and stirring was continued for 3 hr. After standing overnight, the mixture was filtered through a layer of sand, and the solution was treated with 50 ml. of water. The aqueous phase was removed and extracted twice with 50 ml. of benzene. The organic solutions were collected, washed with water, and dried. The solvent was evaporated and the residue was distilled under reduced pressure to give 30.4 g. (76% yield) b.p. 195/0.5 mm. The solid was crystallized

(20) We are indebted to Dr. W. Lammers (Utrecht) and Dr. P. Kolosy (Genval) for these biological data.

(21) All melting points are uncorrected. The microanalyses were performed by Dr. A. Bernhardt, Mülheim, Germany.

TABLE I

10-(DIALKYLAMINOALKYL)PHENOXAZINES. (FORMULA II, R = H)

Compound Number	Side Chain	Method[a]	B.P. of Base	Yield, %	M.P. of Salt	Formula	Nitrogen Calcd.	Nitrogen Found
1	$CH_2CH_2N(CH_3)_2$	A	145–150/1 mm.	51	237–238[b]	$C_{16}H_{18}N_2O\cdot HCl$	9.64	9.45
2	$CH_2CH_2N(C_2H_5)$	A	160–170/1 mm.	57	167–169[c]	$C_{18}H_{22}N_2O\cdot HCl$	8.79	8.58
3		A	170/0.3 mm.	44	203–205	$C_{18}H_{20}N_2O\cdot HCl$	8.84	8.76
4		A	170/1 mm.	30	226–227	$C_{18}H_{20}N_2O_2\cdot HCl$	8.42	8.49
5		A	185/1 mm.	50	258–260	$C_{19}H_{23}N_3O\cdot 2HCl$[d]	11.00	10.85
6	$CH_2CH(CH_3)N(CH_3)_2$	A	160–170/1 mm.	70	175–177	$C_{17}H_{20}N_2O\cdot HCl$[e]	9.20	8.99
7	$CH_2CH(CH_3)N(C_2H_5)_2$	C		30	208–210	$C_{19}H_{24}N_2O\cdot HCl$	8.42	8.20
		A	180/1 mm.	67[f]				
8	$CH(CH_3)CH_2N(C_2H_5)_2$	A			162–164	$C_{19}H_{24}N_2O\cdot HCl$	8.42	8.26
9		C	200/0.7 mm.	24	198–200	$C_{19}H_{22}N_2O\cdot HCl$	8.47	8.68
10	$CH_2CH_2CH_2N(CH_3)_2$	A	190/0.5 mm.	58	132–134	$C_{17}H_{20}N_2O\cdot HCl$[g]	9.20	9.30
11	$CH_2CH_2CH_2N(C_2H_5)_2$	A		70	112–114	$C_{19}H_{24}N_2O\cdot C_4H_6O_4$[h]	6.76	6.85
12	$CH_2CH_2CH_2N(nC_3H_7)_2$	B	210/1 mm.	64	152–153	$C_{21}H_{28}N_2O\cdot HCl$	7.76	7.86
13		A	220/3 mm.	76	162–163	$C_{19}H_{22}N_2O\cdot HCl$	8.47	8.19
		B	190/0.5 mm.	63				
14		B		76	197–199	$C_{20}H_{24}N_2O\cdot HCl$	8.12	8.11
		C		30				
15		B	230/1 mm.	65	195–196	$C_{19}H_{22}N_2O_2\cdot HCl$	8.07	8.12
16		A	190/1 mm.	66	245–246	$C_{20}H_{25}N_3O\cdot 2HCl$[i]	10.61	10.53
17		B	250/1 mm.	53	236–237	$C_{21}H_{27}N_3O_2\cdot 2HCl$	9.85	9.74
18	$CH_2CH(CH_3)CH_2N(CH_3)_2$	A	170/1 mm.	64	161–163	$C_{18}H_{22}N_2O\cdot HCl$	8.78	8.82
19	$CH_2CH(CH_3)CH_2N(C_2H_5)_2$	A	190/0.5 mm.	60	156–158	$C_{20}H_{26}N_2O\cdot HCl$	8.07	8.13
20		A	200/0.8 mm.	56	170–171	$C_{20}H_{24}N_2O\cdot HCl$	8.12	8.30

[a] Methods A and B are described for compound 13 in the Experimental part. Method C is described for compound 7. [b] J. W. Cusic, U.S. Pat **2,687,414**; *Chem. Abstr.*, **50**, 1092 (1956) gives 241°, and a m.p. of 232–233 is given in ref. 9. [c] Ref. 9 gives 168.5–170°. The m.p. of 241–242° cited in ref. 10 must be an error. [d] Ref. 8 gives 240° for the dimaleate. [e] The orange-red picrate melts at 154–155°. [f] See Experimental. [g] The m.p. of the maleate is 130–132°. (ref. 9). [h] Succinate. The m.p. of the red picrate is 138–142° dec. [i] Ref. 10 gives 89–91° as melting point for the base. [j] The melting point of the acid oxalate is 194–196°.

TABLE II

2-ETHYL-10-(DIALKYLAMINOALKYL)PHENOXAZINES (FORMULA II, R = C_2H_5)

Compound Number	Side Chain	Method[a]	B.P. of Base	Yield, %	M.P. of Salt	Formula	Nitrogen Calcd.	Nitrogen Found
21	$CH_2CH_2N(C_2H_5)_2$	A	210/1 mm.	69	158–160	$C_{20}H_{26}N_2O\cdot HCl$	8.08	7.85
22		A	210/0.5 mm.	65	267–269	$C_{21}H_{27}N_3O\cdot 2HCl$	10.24	9.98
23	$CH_2CH(CH_3)N(C_2H_5)_2$	C	180/0.3 mm.	17	178–180	$C_{21}H_{28}N_2O\cdot HCl$	7.76	7.81
24		C	200/0.5 mm.	20	201–203	$C_{22}H_{28}N_2O\cdot HCl$	7.51	7.56
25	$CH_3CH_2CH_2N(CH_3)_2$	A	200/1 mm.	64	208–209	$C_{19}H_{24}N_2O\cdot HCl$	8.42	8.21
26	$CH_3CH_2CH_2N(C_2H_5)_2$	A	210/0.9 mm.	50	119–121	$C_{21}H_{28}N_2O\cdot C_4H_4O_4$[b]	6.33	6.36
		B	200/0.6 mm.	33				
27		A	230/1 mm.	92	174–175	$C_{21}H_{26}N_2O\cdot HCl$	7.80	8.00
		B	210/0.7 mm.	40				
		D		33				
28		A	230/1 mm.	68	256–257	$C_{22}H_{29}N_3O\cdot 2HCl$	9.90	9.84
29		D	250/0.2 mm.	26	238–240	$C_{23}H_{31}N_3O_2\cdot 2HCl$	9.25	8.95
30	$CH_3CH(CH_3)CH_2N(CH_3)_2$	A	185/0.7 mm.	68	144–146	$C_{20}H_{26}N_2O\cdot C_4H_4O_4$[c]	6.56	6.56
31	$CH_3CH(CH_3)CH_2N(C_2H_5)_2$	A	190/0.3 mm.	74	126–129	$C_{22}H_{30}N_2O\cdot C_4H_4O_4$[c]	6.12	6.16
32		A	190/0.3 mm.	73	171–173	$C_{22}H_{28}N_2O\cdot HCl$	7.59	7.42
33		A	210/0.3 mm.	78	215–217	$C_{23}H_{31}N_3O\cdot 2HCl$	9.58	9.35

[a] Methods A and B are described in the Experimental for compound 13. Method C is described for compound 7. Method D is identical to Method B, except that the crude 2-ethyl-10(γ-bromopropyl)phenoxazine, obtained by the reaction of phosphorus tribromide with 2-ethyl-10-(3-hydroxypropyl)phenoxazine, described in the Experimental, was used. [b] Succinate. [c] Fumarate.

from ethanol, to give 29.5 g. of a white product, m.p. 95–98°. When propylene chlorohydrin was used instead of propylene oxide, only unchanged phenoxazine was isolated.

2-Ethyl-10-(2'-hydroxypropyl)phenoxazine (VI. R = C_2H_5). This product was prepared by the reaction of 8.4 g. (0.04 mole) of 2-ethylphenoxazine with 3.5 g. (0.06 mole) of propylene oxide in the presence of sodamide as described above. There was obtained 5.35 g. (50% yield) of a white solid, b.p. 190°/0.4 mm., m.p. 78–80°.

10-(2'-p-Toluenesulfonyloxypropyl)phenoxazine (VII. R = H). A suspension of 25 g. (0.131 mole) of *p*-toluenesulfonyl chloride in 30 ml. of pyridine was added slowly, with cooling, to a stirred solution of 29.5 g. (0.123 mole) of 10-(2'-hydroxypropyl)phenoxazine in 40 ml. of pyridine. After stirring for another 2 hr. and standing overnight, the mixture was treated with ice water. The precipitate was filtered off, washed, and recrystallized in an ethanol-acetone mixture. There was obtained 40 g. (81% yield), m.p. 136–138°. A m.p. of 142° is given in ref. 8.

2-Ethyl-10-(2'-p-toluenesulfonyloxypropyl)phenoxazine (VII R = C_2H_5) was prepared by the same method. The oil solidified after several days, and was recrystallized from ethanol, m.p. 85–86°.

10-(2'-Diethylaminopropyl)phenoxazine (compound 7) (Method C). A 3-g. sample of VII (R = H) was added to a solution of 3 g. of diethylamine in 30 ml. of 1-propanol and the mixture was heated in a closed reaction vessel at 120° for 48 hr. The solution was evaporated, the residue was taken up with a 10% sodium hydroxide solution and with ether. The organic base was extracted with dilute hydrochloric acid and re-extracted in ether after having been made alkaline. The residue, obtained by evaporation of the ether, was dissolved in an alcoholic solution of hydrochloric acid, and the hydrochloride was precipitated by adding dry ether. There was obtained 0.75 g. (30% yield), m.p. 197–204°. After recrystallization in absolute ethanol, 0.3 g. with a m.p. of 208–210° was obtained.

10-(2'-Diethylaminopropyl)- and 10-(2'-diethylaminoisopropyl)phenoxazine. (compounds 7 and 8). A 7.32-g. sample (0.04 mole) of phenoxazine was treated with 1-diethylamino-2-chloropropane in the presence of sodamide as described for compound 13. The base was distilled at 180°/1 mm., 7.1 g. (67% yield, taking into account 1.1 g. of recovered phenoxazine). The base was neutralized with a solution of hydrochloric acid in absolute ethanol, and a first crop of the hydrochloride (4.53 g., m.p. 190–195°) was precipitated by adding ether. A second crop (2.14 g., m.p. 149–156°) was obtained by adding a larger volume of ether. The first product was dissolved in water, and extracted with ether, after having been made alkaline with sodium hydroxide. The ether solution was evaporated, and the residue was dissolved in methanol and neutralized with a methanolic solution of picric acid. In this way, 4.78 g. of a yellow picrate, m.p. 152–153° dec. was obtained. The picrate was transformed into the hydrochloride by extraction with ether, after having been made alkaline with lithium hydroxide, evaporation of the organic solvent, and neutralization with a solution of hydrochloric acid in absolute ethanol. The melting point of pure 10-(2'-diethylaminopropyl)phenoxazine was 208–210°, undepressed upon admixture of the same product prepared by Method C, described above.

The second product was also purified through the picrate (red crystals, m.p. 152–153° dec.); the melting point of the hydrochloride was 162–164°.

Ethyl β-(10-phenoxazinyl)propionate (VIII). A mixture of 11 g. (0.06 mole) of phenoxazine and 2.8 g. (0.06 mole) of sodamide in 30 ml. of dry toluene was refluxed with stirring for 1 hr. After cooling, 10.9 g. (0.06 mole) of ethyl β-bromopropionate was added slowly and with stirring. After reacting for 4 hr. at room temperature and for 0.5 hr. under reflux, the mixture was treated with water. The aqueous layer was separated and extracted with 20 ml. of benzene. The organic solutions were collected, washed, and dried, and then evaporated. The residue was taken up in petroleum ether (b.p. 40–60°), and the insoluble portion (2 g. of unchanged phenoxazine) was filtered off. The solution was evaporated and the residue was distilled under reduced pressure. There was obtained 7.3 g. (51% yield, taking into account the recovered phenoxazine), b.p. 210°/2 mm.

10-(3'-Hydroxypropyl)phenoxazine (IX). A solution of 7.3 g. (0.026 mole) of VIII in 40 ml. of dry ether was added, slowly and with stirring, to a suspension of 1.40 g. (0.035 mole) of lithium aluminum hydride in 60 ml. of ether. The mixture was refluxed for 2 hr. After cooling, the excess hydride was destroyed with ethyl acetate. The mixture was further treated with wet ether and concentrated hydrochloric acid. The aqueous layer was removed and extracted with ether. The combined extracts were washed, dried and and evaporated. The residue was distilled *in vacuo*, to give 4.54 g. (71% yield) of a solid product. A melting point of 68° is given in refs. 8 and 10.

10-(3'-p-Toluenesulfonyloxypropyl)phenoxazine (X). Compound IX was treated with *p*-toluenesulfonyl chloride in pyridine as described for VII. The product was crystallized in ethanol, m.p. 158°, after melting at 52–54° and resolidification.

2-Ethyl-10-(3'-hydroxypropyl)phenoxazine (IV. R = C_2H_5). A mixture of 12.6 g. (0.06 mole) of 2-ethylphenoxazine and 2.5 g. (0.062 mole) of sodamide in 60 ml. of dry xylene was refluxed for 1 hr. A solution of 10.8 g. (0.06 mole) of 2-(3'-chloropropoxy)tetrahydropyran in 20 ml. of xylene was added and refluxing was continued for 48 hr. After cooling, the reaction mixture was treated with water. The water layer was extracted with ether, and the organic solutions were washed and dried. After evaporation of the solvent, under reduced pressure (20 mm.), the residue was distilled *in vacuo* (0.5 mm.). At 160° 2.5 g. of unchanged 2-ethylphenoxazine and at 230° 12 g. of III were obtained.

This product (III) was taken up in 80 ml. of 75% ethanol and 1.5 ml. of concd. hydrochloric acid and the solution was refluxed for 1 hr. The alcohol was then distilled and the residue was extracted with ether. The ether was washed with a sodium bicarbonate solution and with water. The dried ether extracts were concentrated and distilled to give 7.2 g. (55%), of IV, b.p. 210°/0.5 mm., m.p. 37–40°. When ethylphenoxazine was treated with trimethylene chlorohydrin in the presence of sodamide, only unchanged ethylphenoxazine was isolated.

2-Ethyl-10-(3'-bromopropyl)phenoxazine (V. R = C_2H_5; X = Br). Phosphorus tribromide (20 g.) was added to a solution of 12 g. of IV in 20 ml. of dry chloroform, and the mixture was refluxed for 1 hr. on the steam bath. After cooling, the reaction mixture was washed with a solution of sodium bisulfite and water. The chloroform solution, after drying over calcium chloride, was evaporated to give 1.3 g. of crude V.

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