facilitating the expression of biological activity by these materials.

Cross Linking and Carcinogenicity.—The monofunctional epoxides are largely devoid of carcinogenic activity[1,2] but are potent mutagenic agents.[19] Bifunctional epoxides, on the other hand, are carcinogenic[1,2] and exhibit mutagenicity on the same order as that of monoepoxides.[19] These characteristics raise the question of the role of the often-mentioned, cross-linking ability of bifunctional alkylating agents in accounting for their biological activity.

It has been suggested, for example, that bifunctional alkylating agents cross link the strands of the double helix of DNA at two guanine moieties. This cross linking may then result in incomplete duplication of genetic material and these processes may be involved in carcinogenesis.[20]

Nevertheless, it must be remembered that the classical carcinogenic alkylating agent, β-propiolactone, has only one active alkylating center. This compound is one of the few alkylating agents which has noticeable carcinogenic as well as mutagenic activity.

In order to evaluate the role of cross linking of DNA by these alkylating agents more accurately, the interatomic distances between the reactive centers in several epoxides were measured by use of scale drawings and Dreiding atomic models. Because of free rotation in the open-chain epoxides, the distances of closest approach and of greatest separation between terminal reactive centers were measured and are listed in Table III. Several observations become apparent from these measurements. Thus, in glycidaldehyde, which has only one epoxide function, the distance between the terminal oxygen-bearing carbon atoms is only 2.6 Å. which would make it impossible to reach from a guanine moiety on one strand to the nearest base on the adjacent strand of the DNA helix. Similarly, for β-propiolactone, cross linking of this type between bases cannot occur. The relatively short distances between epoxide functions in the diepoxybutanes and diepoxypentane also render cross linking between bases unlikely. Even without exact measurements of interatomic distances between the N-7 positions on two adjacent base pairs it is immediately apparent that cross linking can occur only when there is a much longer distance between epoxide functions. However, resorcinol diglycidyl ether, in which there are eleven atoms between the terminal epoxy-bearing carbon atoms, is inactive as a carcinogen.[1] These considerations suggest a re-evaluation of the possible sites of action of alkylating agents concerned with carcinogenesis.

TABLE III
INTERATOMIC DISTANCES IN EPOXIDES

Compd.	Distance between reactive carbon atoms (Å.) Closest approach	Greatest separation
dl-Diepoxybutane	2.5	4.0
meso-Diepoxybutane	2.5	4.0
1,2,4,5-Diepoxypentane	1.5	5.2
1,2,5,6-Diepoxyhexane	0.0	6.6
1,2,6,7-Diepoxyheptane	Overlap	7.7
1-Ethyleneoxy-3,4-epoxycyclohexane	4.6	5.4
Glycidaldehyde	2.6 (fixed)	

Acknowledgments.—This work was supported by Grant L-46 from the American Cancer Society, Inc., and by Grants CA-05946, CA-06989, and ES-00014 from the National Institutes of Health, U. S. Public Health Service. The assistance of C. E. Bardi, E. Karafiath, and C. M. Mercado is gratefully acknowledged.

(19) Summarized in ref. 2.
(20) P. Brookes and P. D. Lawley, *Brit. Med. Bull.*, **20**, 91 (1964).

Synthesis and Study of β-Chloroethylamines, Sulfides, and Sulfones Structurally Related to Dibenzyline

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Several N-arylthioisopropyl-N-benzyl-2-chloroethylamines and their corresponding sulfones were obtained. The former do not have a sulfonium structure despite their rapid rate of hydrolysis, especially the disulfurated derivative. In general they lack adrenolytic activity as do the sulfones of low hydrolytic rate. From this it can be inferred that no relationship can be established between the rate of hydrolysis and the pharmacological activity of this group of substances. The hydrolysis mechanism takes place probably *via* the sulfonium ion.

The advent of dibenzyline, N-phenoxyisopropyl-N-benzyl-2-chloroethylamine,[1] and its promising activity as an adrenolytic agent induced us to attempt the synthesis of analogous sulfides, with the object of studying their properties and the possibility of obtaining new drugs in this series. In 1950[2] a series of adrenolytic 2-haloethylamines were obtained with the following formula. The cited patent included only one

$$\mathrm{ArO(CH_2)_nCHR}$$
$$\mathrm{ArCH_2NCH_2CH_2X}$$

R = alkyl, aryl, or aryloxy
X = Cl or Br

sulfide, N-phenylthioisopropyl-N-benzyl-2-chloroethylamine hydrochloride; its properties were not described.

(1) J. F. Kerwin, G. C. Hall, F. J. Milnes, I. H. Witt, R. A. McLean, E. Macko, E. J. Fellows, and G. E. Ullyot, *J. Am. Chem. Soc.*, **73**, 4162 (1951).
(2) Smith Kline and French International Co., British Patent 673,509 (June 4, 1952).

TABLE I

N,N-DISUBSTITUTED AMINOETHANOLS

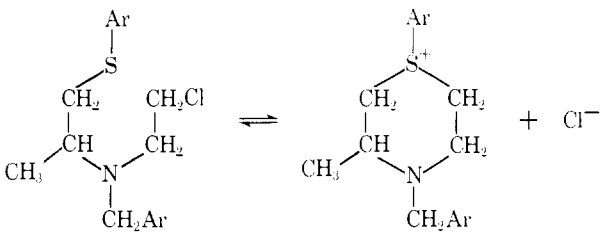
$RCH_3CHNCH_2CH_2OH$
CH_3
R'

No.	R	R'	Form Base/hydrochloride	B.p., °C. (1 mm.)	Yield, %	Formula	N, % Calcd.	N, % Found
IX	C_6H_5S	$C_6H_5CH_2$	Oil/paste	192–201	81[a] 87[b]	$C_{15}H_{31}ClNOS_2$[c]	4.65	4.60
X	$CH_3C_6H_4S$	$C_6H_5CH_2$	Oil/paste	195–205	73[a] 73[b]	$C_{19}H_{25}NOS$	4.44	4.39
XI	$C_6H_5CH_2S$	$C_6H_5CH_2$	Oil/paste	[d]	91[a]	$C_{19}H_{28}ClNOS$[c]	3.98	3.87
XII	$C_6H_5SO_2$	$C_6H_5CH_2$	Oil/hygroscopic soft flakes	[d]	73[b]	$C_{15}H_{23}NO_3S$	4.20	4.23
XIII	$CH_3C_6H_4SO_2$	$C_6H_5CH_2$	Dense oil/hygroscopic amorphous solid	[d]	72[b]	$C_{16}H_{25}NO_3S$	4.03	4.17
XIV	$C_6H_5CH_2SO_2$	$C_6H_5CH_2$	Oil/paste	[d]	86[b]	$C_{19}H_{25}NO_3S$	4.03 3.87	3.95 3.69
XV	C_6H_5S	$C_6H_5SCH_2CHCH_3$	Oil/dense oil	195–200	75[b]	$C_{20}H_{27}NOS_2$	S: 17.2	S: 17.7

[a] Method A. [b] Method B. [c] Hydrochloride. [d] Not distillable.

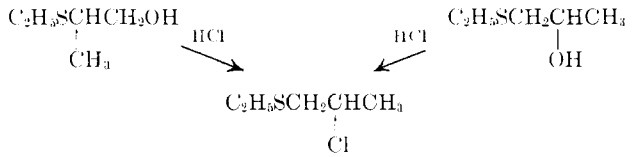
Subsequently, Kerwin and Ullyot[3] patented a series of sulfides, including this sulfide, indicating that it was "a hygroscopic oil." The hydrochloride of the oxygenated compound (dibenzyline) is a solid, while all of the sulfides (bases and hydrochlorides) were hygroscopic oils.

An interesting possibility was that the compounds of type I could possess a structure different from dibenzyline, one having a cyclic thiazine ring (sulfonium ion type, II). This was suggested by the observa-

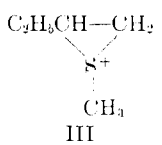


I II

tion of Fuson, *et al.*,[4] that on treating ethyl 2-hydroxyisopropyl sulfide and ethyl 2-hydroxy-*n*-propyl sulfide with hydrochloric acid or thionyl chloride, they yielded the same product, 2-chloro-*n*-propyl ethyl sulfide, probably by rearrangement of the isopropyl to the *n*-

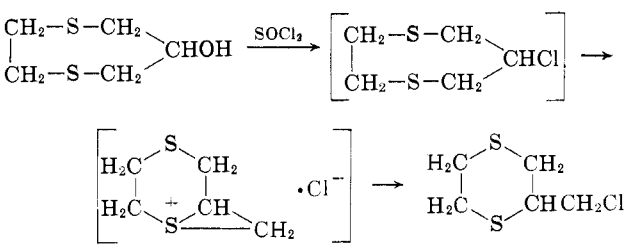


propyl structure through a cyclic sulfonium ion (III).



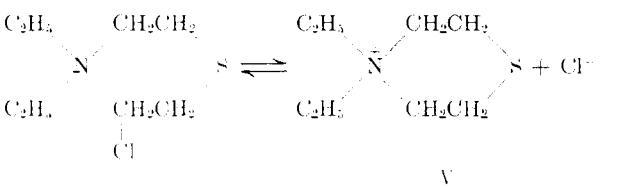
III

Fuson and Speziale[5] treated 6-hydroxy-1,4-dithiacycloheptane with thionyl chloride in chloroform and obtained 2-chloromethyl-1,4-dithiane (IVb) which probably formed by rearrangement of the 6-chloro-1,4-dithiacycloheptane through a cyclic sulfonium ion intermediate (IVa).



IVa IVb

Another type of cyclization (ammonium cyclization) was observed by Clinton[6] on treating 2-hydroxyethyl N,N-diethylaminoethyl sulfide with thionyl chloride. The obtained compound was the open chloro derivative in equilibrium with the 1,4-thiazonium structure V.



V

We prepared, then, a series of sulfides and sulfones analogous to dibenzyline and measured their relative rates of hydrolysis and their adrenolytic activity to correlate the two properties and to determine if the hydrolytic mechanism proceeds *via* the sulfonium or imonium ion intermediate.

Chemistry.—Derivatives of thiophenol, *p*-thiocresol, and benzyl mercaptan and the corresponding sulfones were obtained (Tables I and II). All of the amine bases were uncrystallizable dense oils, while the hydrochlorides were viscous oils, and in some cases very hygroscopic amorphous solids.

The synthesis of these derivatives was effected by two methods. The first (A) was according to the mentioned patents[1,2] and the second (B) involved the condensation of the benzylaminoethanol with the 2-

(3) J. F. Kerwin and C. E. Ullyot, U. S. Patent 2,774,770 (Dec. 18, 1956).

(4) R. C. Fuson, C. C. Price, and D. M. Burness, *J. Org. Chem.*, **11**, 475 (1946).

(5) R. C. Fuson and A. J. Speziale, *J. Am. Chem. Soc.*, **71**, 1582 (1949).

(6) R. O. Clinton, *ibid.*, **67**, 594 (1945).

Table II

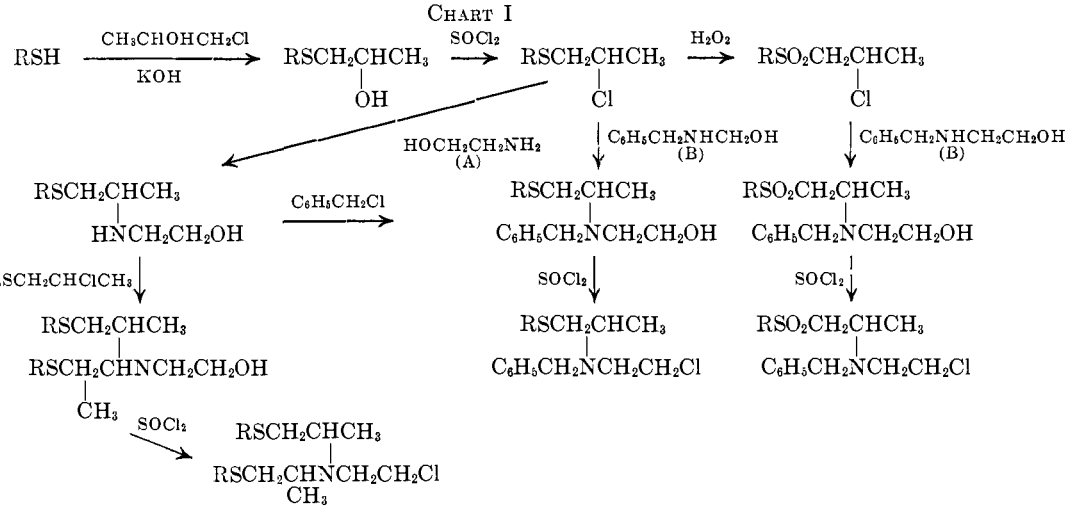
N,N-Disubstituted β-Chloroethylamines

$RCH_2CHNCH_2CH_2Cl$
CH_3
R'

No.	R	R′	Form Base/ hydrochloride	Yield, %	Chloroplatinate m.p., °C.	Formula	—C, %— Calcd.	Found	—H, %— Calcd.	Found	—N, %— Calcd.	Found
XVI	C_6H_5S	$C_6H_5CH_2$	Oil/paste	75	155	$C_{18}H_{22}ClNS$	67.6	66.9	6.88	6.70	4.39	4.36
XVII	$CH_3C_6H_4S$	$C_6H_5CH_2$	Oil/hygroscopic amorphous solid	72	189	$C_{19}H_{25}Cl_2NS$[a]	61.6	60.8	6.70	6.41	3.79	4.09
XVIII	$C_6H_5CH_2S$	$C_6H_5CH_2$	Oil/paste	92	...	$C_{19}H_{24}ClNS$	67.6	66.8	6.88	6.70	4.39	4.40
XIX	$C_6H_5SO_2$	$C_6H_5CH_2$	Oil/paste	90	213	$C_{18}H_{22}ClNO_2S$	61.5	62.0	6.25	6.02	3.95	3.72
XX	$CH_3C_6H_4SO_2$	$C_6H_5CH_2$	Oil/amorphous solid (m.p. 41–43°)	82	216	$C_{19}H_{25}Cl_2NO_2S$[a]	56.7	56.9	6.21	6.66	3.48	3.43
XXI	$C_6H_5CH_2SO_2$	$C_6H_5CH_2$	Dense oil/hygroscopic amorphous solid	92	217	$C_{19}H_{24}ClNO_2S$	62.4	62.5	6.61	6.60	4.06	4.04
XXII	C_6H_5S	$C_6H_5SCH_2CHCH_3$	Dense oil/paste	84	...	$C_{20}H_{26}ClNS_2$	63.2	63.8	6.85	7.20	3.72	3.89

[a] Hydrochloride.

Chart I



chloropropyl aryl sulfides or sulfones (Chart I). Attempts to obtain the bis sulfones by treating 1-(4-methylphenyl sulfone)-2-chloropropane with monoethanolamine failed, giving only the corresponding alcohol. It was shown to be identical with a sample

$$CH_3C_6H_4SO_2CH_2CHClCH_3 \xrightarrow[K_2CO_3]{H_2NCH_2CH_2OH} CH_3C_6H_4SO_2CH_2CHOHCH_3$$

obtained by aqueous alkaline hydrolysis of the chloro sulfone.

N.m.r. Spectra.—The n.m.r. spectra (Table III) of dibenzyline and sulfide XVI (as bases) indicated that they exist in the open form and not in the cyclic thiazonium structure.

Table III

N.m.r. Spectra[a]

Hydrogen	$C_6H_5OCH_2\overset{a}{C}H\overset{e}{C}H_3$ / $C_6H_5CH_2\overset{a}{N}CH_2\overset{b}{C}H_2\overset{d}{N}\overset{c}{C}l$	$C_6H_5\overset{a}{S}CH_2\overset{e}{C}HCH_3$ / $C_6H_5CH_2\overset{a}{N}CH_2\overset{b}{C}H_2\overset{d}{N}\overset{c}{C}l$	$H_2\overset{f}{N}CH_2\overset{d}{C}H_2\overset{c}{N}Cl$
	δ	δ	δ
H_a	7.0	7.1	...
H_b	3.7	3.6	...
H_c	3.2	3.2	3.3
H_d	2.7	2.7	3.0
H_e	1.1	1.2	...
H_f			1.2

[a] Given in δ values; δ = 0 for TMS internal standard; taken in CCl_4 on a Varian A-60 spectrometer.

Rate of Hydrolysis.—The rate of hydrolysis (SN1 solvolytic reaction) was carried out to establish the relative maximum per cent of hydrolysis (Figure 1 and Table IV). The experimental data allowed us to classify the compounds in three groups: (a) sulfides, showing the greatest hydrolytic rates especially the bis sulfide; (b) phenoxy derivative (dibenzyline), hav-

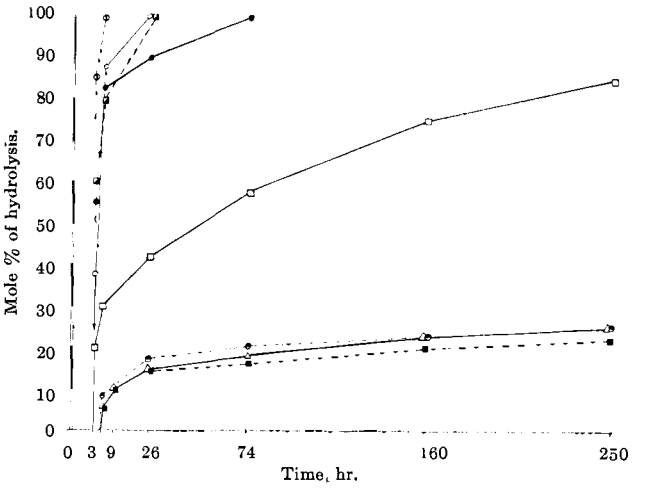


Figure 1.—Hydrolysis curves of N,N-disubstituted β-chloroethylamines (mole %/hour): O—O, C_6H_5S; □—□, C_6H_5O; ◪—◪, p-$CH_3C_6H_4S$; ■-—■, $C_6H_5SO_2$; ⦶—⦶, $(C_6H_5S-)_2$; △—△, p-$CH_3C_6H_4SO_2$; ●—●, $C_6H_5CH_2S$; ◓-·—·-◓, $C_6H_5CH_2SO_2$.

TABLE IV

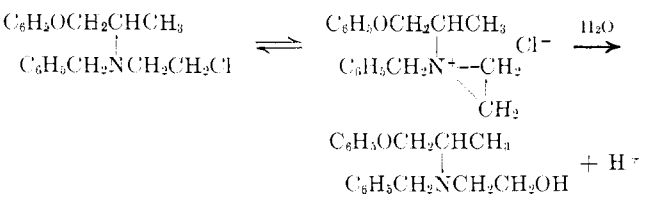
RATE OF HYDROLYSIS (MOLE %/HOUR) OF N,N-DISUBSTITUTED β-CHLOROETHYLAMINES[a]

Compd.	3 hr.	9 hr.	26 hr.	74 hr.	160 hr.	250 hr.
Dibenzyline	20	30	42	57	75	86
XVI	37	87	100	---	---	---
XVII	60	80	100	---	---	---
XVIII	55	82	90	100	---	---
XIX	5	10	15	17	20	22
XX	5	10	15	18	22	25
XXI	7	12	17	20	22	25
XXII	86	100	---	---	---	---

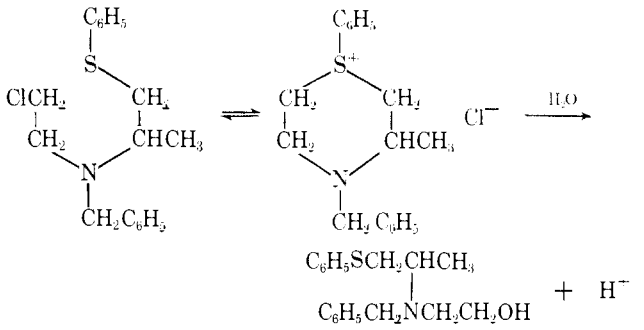
[a] 2 m*M* % in acetone with 30% water.

ing medium rate and used as a reference; (c) sulfones, which were the least reactive, considerably less than dibenzyline. In general, it was observed that the presence of a methyl group in the *para* position of the thioethers increased the hydrolytic reactivity; in the case of the benzyl mercaptan the greater distance of the sulfur atom from the benzene ring had the same effect.

It has been demonstrated[7] that the 2-haloethylamines undergo hydrolysis *via* a cyclic imonium ion, a mechanism also valid for the alkylating action of nitrogen mustards and probably for dibenzyline.[8] In the thio-



ethers, the presence of sulfur would allow the possibility of the formation of a thiazine sulfonium ion during hydrolysis which would explain their greater reactivity especially of the bis sulfide derivative. In the



sulfones where there is no possibility of a sulfonium structure, the hydrolysis takes place at a lower rate probably through an ethylene–imonium ion mechanism.

Between the two alternatives of the SN1 mechanism, formation of the ethylene–imonium ion or of the thiazoline–sulfonium ion, the latter is then the favored one. It was not possible to detect the presence of an ethylene–imonium ion by the method of Golumbic, Fruton, and Bergmann[7] in the tested sulfide derivative.

Pharmacological Tests.—The adrenolytic activity was determined in dogs anesthetized with nembutal with intraperitoneal doses of 50 mg./kg., prepared for direct carotid arterial pressure recording. Actual reversal of the pressor response to epinephrine was selected as the criterion of activity. The epinephrine was administered intravenously in doses of 2.0 mg./kg. Those agents which failed to produce a reversal were tested by injecting repeatedly higher doses at intervals of 0.5–1 hr. over a period of 4 hr. until the limit of tolerance of the animal was reached or reversal of the epinephrine response was obtained. The dose used was 1–6 mg./kg. i.v. injected slowly. The solution of the drugs was prepared with propylene glycol, acidified with HCl, and diluted with equal parts of 0.9% NaCl solution, giving a final dilution of 5 mg./ml. immediately before injection. The activity of the tested compounds was determined using dibenzyline at the dose of 1 mg./kg. as a reference drug. Those compounds that showed activity like dibenzyline were classified as active. The only active compounds were XVIII and XX, but at a dose of 6 mg./kg.; their adrenolytic activity was considered 1/6 that of dibenzyline (Table V). No correlation seems to exist then between the adrenolytic activity and the rate of hydrolysis.

TABLE V

PHARMACOLOGICAL TESTS OF N,N-DISUBSTITUTED β-CHLOROETHYLAMINES. ADRENOLYTIC ACTIVITY

Compd.	Dosage, mg./kg.	Adrenolytic activity
Dibenzyline	1	Active (standard)
XVI	1–6	Inactive
XVII	1–6	Inactive
XVIII	6	Active
XIX	1–6	Inactive
XX	6	Active
XXI	1–6	Inactive
XXII	1–6	Inactive

Experimental Section

Arylthiopropanols. General Method.—A solution of KOH (57 g.) in 30 ml. of water and 120 ml. of ethanol was added slowly with stirring to 0.91 mole of redistilled thiol. The mixture was boiled for 1 hr. after which time 0.95 mole of propylene chlorohydrin was added. After refluxing for 3 hr., the solution was cooled, the KCl was removed, and the alcohol was distilled. The remaining oil was poured into water, extracted with CCl_4, washed with 10% NaOH and again with water, and dried. After distilling the solvent, the product was distilled under vacuum. With this procedure the following compounds were prepared: 1-phenylthio-2-propanol, yellow oil, b.p. 115–116° (2–3 mm.), yield 72%; 1-(4-methylphenylthio)-2-propanol, yellow oil, b.p. 125–126° (2–3 mm.), yield 75%; 1-benzylthio-2-propanol, yellow oil, b.p. 126–128° (2–3 mm.), yield 65%.

Arylthioisopropyl Chlorides.—1-Phenylthio-2-chloropropane was obtained by three methods. (1) To 0.36 mole of 1-phenylthio-2-propanol in a three-necked flask equipped with a dry-air injector, a condenser, and a separatory funnel, was added slowly at 0° 0.27 mole of thionyl chloride. The gases were eliminated by air injection for 3 hr. Another 0.27 mole of thionyl chloride was added, when injection of air was stopped, and 0.5 ml. of pyridine was added; the mixture was heated at 80–90° for 3 hr. and poured into water. The oil was separated, washed with 10% NaOH, extracted with CCl_4, washed with water, dried, and distilled; b.p. 106–108° (5 mm.), yield 97%.[3]

(2) To 50 ml. of dry $CHCl_3$ and 22 ml. of dry pyridine was added 0.18 mole of 1-phenylthio-2-propanol and the mixture was cooled in an ice bath, while 40 g. of thionyl chloride was slowly added. After 2 hr. of stirring under reflux the mixture was cooled and treated as in method 1, yield 85%.

(3) The conversion of 2-hydroxyisopropyl phenyl sulfide as indicated by Fuson and Koehneke[9] was used.

1-(4-Methylphenylthio)-2-chloropropane was obtained by

(7) C. Golumbic, J. S. Fruton, and M. Bergmann, *J. Org. Chem.*, **11**, 518 (1946).

(8) M. Nickerson and W. S. Gump, *J. Pharmacol. Exptl. Therap.*, **97**, 25 (1949).

(9) R. C. Fuson and J. H. Koehneke, *J. Org. Chem.*, **14**, 706 (1949).

method 1; yellow oil, b.p. 114–116° (5 mm.), yield 93%.

1-Benzylthio-2-chloropropane was obtained by method 1. Care should be taken not to heat above 60° during chlorination; yield 97%, yellow oil, b.p. 122–128° (5 mm.).

1-(Phenyl sulfone)-2-chloropropane.[9]—To 0.07 mole of 1-phenylthio-2-chloropropane and 70 ml. of glacial acetic acid was added (stirring) during 20 min., 23 ml. of 30% hydrogen peroxide. Stirring and warming were maintained for 6 hr. at 70–80°. After distilling the solvents at reduced pressure, the remaining oil was distilled *in vacuo;* colorless oil, b.p. 166–168° (5 mm.), yield 93%.

1-(4-Methylphenyl sulfone)-2-chloropropane, using the previous method, was obtained as a colorless oil, b.p. 154–158° (2 mm.), yield 94%.

1-(Benzyl sulfone)-2-chloropropane.—Using the previous method and after distilling the acetic acid, the residue crystallized on cooling. Crystallization from petroleum ether (b.p. 60–80°) afforded white needles, m.p. 80°. The yield was 85%. Distillation at 2 mm. occurred with great decomposition at 176–182°.

N-(Phenylthioisopropyl)-β-hydroxyethylamine (VI).—To 0.65 mole of boiling monoethanolamine was added 0.13 mole of 1-phenylthio-2-chloropropane in 1 hr. The mixture was refluxed for 4 hr., cooled, poured into water, and diluted with ether. The separated organic layer was washed twice with 2 *N* HCl, then with water, dried, and evaporated to give an oily product which was distilled *in vacuo* at 152–158° (2–3 mm.); yield 89%. The dense oil was freely soluble in ethanol and insoluble in water.

Anal. Calcd. for $C_{11}H_{16}NOS$: N, 6.63. Found: N, 6.49.

N-(4-Methylphenylthioisopropyl)-β-hydroxyethylamine (VII).—Condensation was carried out in the same way, but the greater part of the monoethanolamine was distilled *in vacuo* and the residual oil was poured into water. The mixture was made alkaline with 10% aqueous NaOH and extracted with benzene; oil, b.p. 162–164° (3 mm.), yield 96%.

Anal. Calcd. for $C_{12}H_{18}NOS$: N, 6.22. Found: N, 6.22.

N-Benzylthioisopropyl-β-hydroxyethylamine (VIII) was obtained as VI; dense syrup, b.p. 170–175° (5 mm.), yield 76%.

Anal. Calcd. for $C_{12}H_{18}NOS$: N, 6.22. Found: N, 6.19.

N-N-Disubstituted aminoethanols (Table I) were obtained by two methods. (1) To 0.09 mole of VI, VII, or VIII were added 0.09 mole of benzyl chloride, 7 g. of anhydrous K_2CO_3, and 50 ml. of absolute ethanol. The mixture was heated under reflux for 8 hr. After distilling 40 ml. of the solvent, the mixture was heated at 120° for 3 hr., then cooled, poured into water, made basic with 10% NaOH, and extracted with benzene. The benzene solution was washed with water, dried, and distilled under vacuum.

(2) Arylthio-2-chloropropane (0.08 mole) (including 1-benzylthio-2-chloropropane) was mixed with 0.08 mole of N-benzylaminoethanol, 7 g. of anhydrous K_2CO_3 and 35 ml. of absolute ethanol. The mixture was heated at reflux for 8 hr., 25 ml. of the solvent was distilled, and the mixture was heated again in an oil bath at 120° for 3 hr. The procedure was continued as in 1. Compound XV, N,N-bis(phenylthioisopropyl)-β-hydroxyethylamine, was obtained in the same way by replacing the N-benzylaminoethanol with compound VI.

N-(Aryl isopropyl sulfone)-N-benzyl-β-hydroxyethylamine (XII–XIV).—A mixture of 0.07 mole of N-benzylaminoethanol and 0.07 mole of the (aryl sulfone)-2-chloropropane [including 1-(benzyl sulfone)-2-chloropropane] was cooled in an ice bath. Absolute ethanol (40 ml.) and 4 g. of anhydrous K_2CO_3 were added and the mixture was heated under reflux for 2 hr. The alcohol was evaporated, and the heating was continued for 3 hr. Cold water was added to the residue, and the mixture was extracted with ether. The organic phase was washed with 1 *N* HCl, then with water. The ether was evaporated and the product again was dissolved in anhydrous ether. Anhydrous acetone saturated with HCl was slowly added with stirring. The hydrochloride of the products crystallized as soft flakes; they are very hygroscopic. The free bases were obtained by dissolving the salts in dilute NaOH and extracting with ether. They are undistillable syrups, soluble in organic solvents and concentrated HCl.

N,N-Disubstituted β-Chloroethylamines (Table II).—The corresponding hydroxyethylamine (0.05 mole) in 40 ml. of dry $CHCl_3$ was cooled in an ice bath and saturated with HCl. Redistilled thionyl chloride (0.06 mole) in 15 ml. of dry chloroform was added dropwise. The resulting solution was heated at 70° for 3 hr., the solvent was removed, and the semisolid residue was dissolved by warming with 40 ml. of ethanol which contained 10 ml. of concentrated HCl. The filtered solution, treated with charcoal, was cooled and adjusted to pH 8 with dilute NaOH. The oil which settled to the bottom was extracted with $CHCl_3$ and the $CHCl_3$ extract was washed with water, dried over sodium sulfate, and distilled under reduced pressure. The yields are listed in Table II. An attempt was made to distil the oily, free base at 0.025 mm. but decomposition took place. The hydrochlorides were obtained by passing a stream of dry HCl over a cooled solution of the free base in dry ether.

Chloroplatinates.—To a 10% alcoholic solution of the free base was added dropwise a 10% aqueous solution of chloroplatinic acid and the mixture was left 24 hr. at room temperature. The precipitate was collected, washed with water then acetone, and dried *in vacuo*. All of the chloroplatinates were yellow-orange crystals.

Attempted Synthesis of N,N-Bis(4-methylphenyl isopropyl sulfone)-β-hydroxyethylamine.—1-(4-Methylphenyl sulfone)-2-chloropropane (0.1 mole), 0.05 mole of dry monoethanolamine, 6 g. of anhydrous K_2CO_3, and 20 ml. of absolute ethanol were refluxed for 3 hr. After distilling the alcohol, the mixture was heated in an oil bath at 120° for 2 hr., then cooled, poured into water, made alkaline, and extracted with $CHCl_3$. Removal of the $CHCl_3$ at reduced pressure gave an oil, b.p. 142–158° (3 mm.). The distilled product was cooled giving 15 g. of a crystalline solid. Crystallization from acetone–petroleum ether gave white needles, m.p. 94°. The product was identified (mixture melting point) as 1-(4-methylphenyl sulfone)-2-propanol which was also obtained by alkaline hydrolysis of the starting material.

Anal. Calcd. for $C_{10}H_{14}O_3S$: C, 56.07; H, 6.54; mol. wt., 214. Found: C, 55.94; H, 6.28; mol. wt., 210 (Rast).

Hydrolysis Curves.[7]—The chloroethylamine (free base, listed in Table IV) (2 mmoles) was dissolved in 70 ml. of acetone and diluted to 100 ml. with distilled water in a flask with a ground-glass stopper. The solution was maintained at 37°. Aliquots of 20 ml. were extracted and ionic chloride was determined with 0.1 *N* $AgNO_3$ using dichlorofluorescein (in 0.1% aqueous alcohol) as an indicator.

Ethylene-Imonium Cation Test.[7]—To 20 ml. of 2 m*M* % aqueous acetone solution of the chloroethylamine, 10 ml. of 0.1 *N* $Na_2S_2O_3$ was added, and the solution was allowed to stand for 10 min. at 37°. Excess thiosulfate was determined with 0.1 *N* iodine. In every case the test was negative.

Infrared spectra were made for one sulfide, one sulfone, and the bis sulfide, showing the following maxima: XVI, 2990, 2980, 1700, 1650, 1490, 1450, 1385, 1110, 1090, 1080, 1030, 740, and 700 cm.$^{-1}$; XIX, 3500, 2990, 2980, 1700, 1650, 1490, 1450, 1385, 1300, 1150, 1110, 1090, 1080, 740, and 690 cm.$^{-1}$; XXII, 3000, 2990, 1750, 1650, 1480, 1450, 1385, 1300, 1250, 1120, 1090, 1050, 1030, 740, and 690 cm.$^{-1}$.

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