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Synthesis of Nereistoxin and Related Compounds. II[1,2]

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An improved synthesis of nereistoxin (VII or XIII; $R_3=CH_3$) was achieved *via* the intermediates VIII ($R_3=CH_3$), X ($R_3=CH_3$) and XII ($R_3=CH_3$) as summarized in Chart 2. Applying the reactions formulated in Chart 1 and Chart 2, a number of amines were prepared, whereby the occurrence of intermediates, cyclic sulfonium (III) in the amination reaction in Chart 1 and cyclic immonium (IX) in the thiolation reaction in Chart 2 respectively, was suggested.

Synthesis of nereistoxin, 4–N,N–dimethylamino–1,2–dithiolane (VII), was first accomplished in these laboratories as summarized in Chart 1 wherein R_1 was $C_6H_5CH_2$– and R_2 was CH_3–.[4] A serious drawback of the method, however, was that the yield of the desired symmetrical amine (IV) was rather low in the amination of the chloride mixture (I and II) with dimethylamine. The reason appeared to be due to that the amination proceeded *via* a cyclic sulfonium intermediate (III), which was subsequently attacked by the incoming dimethylamine preferentially at the less hindered outer carbon to afford the asymmetrical amine (V) rather than the symmetrical one (IV).

The present paper deals with an improved synthesis of nereistoxin (VII) and a number of its derivatives.

As in many of these reactions, the characteristic reactivities[5] of 2–haloalkyl sulfides and 2–haloalkyl amines, such as high solvolyses rates and neighboring group effects in the

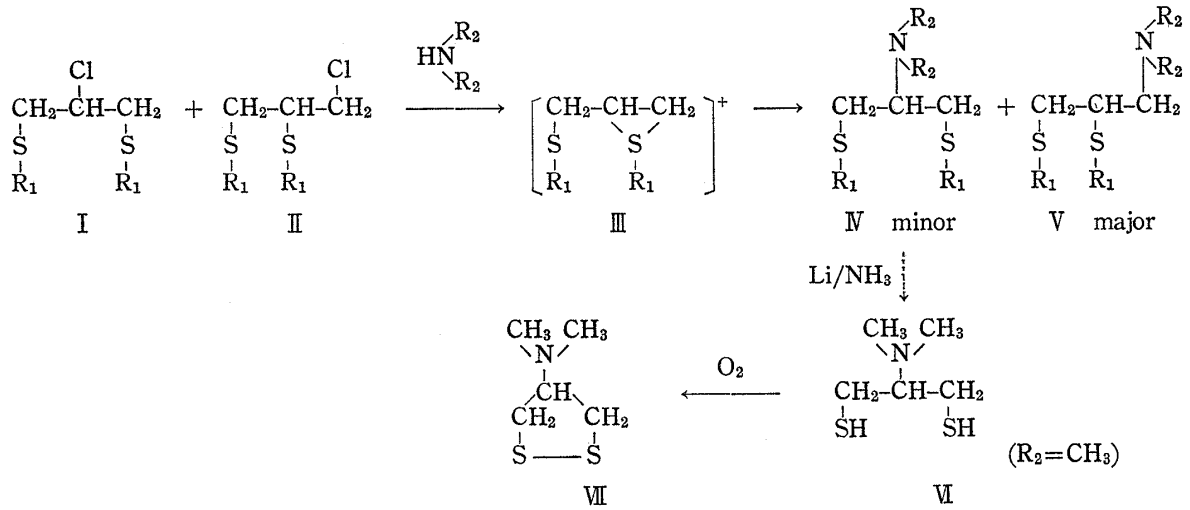


Chart 1

1) Part I: *Chem. Pharm. Bull.* (Tokyo), **13**, 253 (1965).
2) This paper was presented at the 16th Annual Meeting of the Pharmaceutical Society of Japan, at Shizuoka, on November 2 (1962).
3) Location: *Juso–Nishino–cho, Higashiyodogawa–ku, Osaka.*
4) Part I.
5) We can seed iscussions and summaries elsewhere, for example, see E.S. Gould, "Mechanism and Structure in Organic Chemistry", Henry Holt and Company, Inc., 1960, pp. 570.

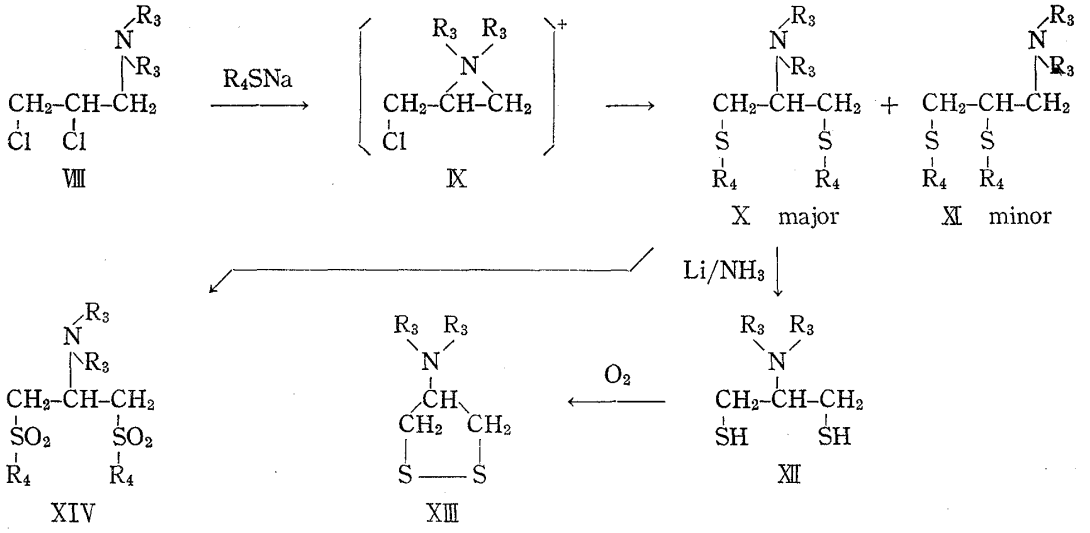
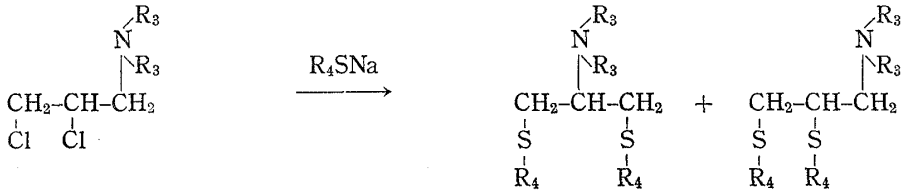
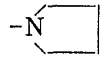
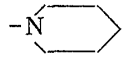
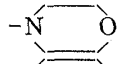
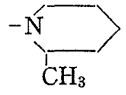


Chart 2

substitution, have been ascribed to the intervention of ethylene–sulfonium (such as III) and –immonium ions (such as IX) respectively in the transition states. Since it might be said that a similar steric factor is operating in these small ring systems, our presumption was that a certain propylene–1,2–immonium ion (such as IX) would preferentially attacked at the terminal carbon to give the corresponding symmetrical amine (X). In fact, the treatment of known N,N–dimethyl–2,3–dichloropropylamine (VIII; $R_3=CH_3$)[8] with sodium benzylmercaptide afforded the symmetrical amine, 2–dimethylamino–1,3–bis(benzylthio)propane (X; $R_3=CH_3$, $R_4=C_6H_5CH_2$), in a good yield and this approach has proved to be satisfactory for the synthesis of nereistoxin (VII).

Table I. The Thiolation of VIII with R_4SNa



$-N(R_3)(R_3)$	R_4-	X %	XI %
$-N(CH_3)(CH_3)$	CH_3-	63[a]	30[a]
$-N(CH_3)(CH_3)$	$C_6H_5CH_2-$	77[b]	23[b]
	$C_6H_5CH_2-$	62[d]	—
	$C_6H_5CH_2-$	77[c]	—
	$C_6H_5CH_2-$	59[c]	—
	$C_6H_5CH_2-$	71[d]	—
$-N(C_3H_7)(C_3H_7)$	$C_6H_5CH_2-$	68[d]	—

a) Calculated on gas chromatogram.
b) Calculated on the integral of NMR spectrum.
c) Calculated on the crystalline product isolated.
d) Calculated on the derived sulfone (XIV).

Apparently, it should be noted that schema in Chart 1 and in Chart 2 provide the complementary synthesis of asymmetrical amines and symmetrical amines, respectively. Thus starting with several monochlorides (I and II) and dichlorides (VIII) a number of symmetrical and asymmetrical amines were prepared. Whereby it was seen, when a substituent was bulky, that the amination in Chart 1 gave predominantly asymmetrical amines (V) and the alkylthiolation in Chart 2 the symmetrical amines (X) respectively. On Birch reduction followed by the oxidation with air the symmetrical amines (X) gave the corresponding 4–N,N–dialkylamino–1,2–dithiolanes (XIII).

The structures of the products and the yields of the thiolation of N,N–dialkyl–2,3–dichloropropylamines (VIII) with sodium alkylmercaptides are listed in Table I.

Treatment of N,N–dimethyl–2,3–dichloropropylamine (VIII; $R_3=CH_3$) with sodium benzylmercaptide gave an oily mixture of the isomers, 2–dimethylamino–1,3–bis(benzylthio)-propane (X; $R_3=CH_3$, $R_4=C_6H_5CH_2$) and N,N–dimethyl–2,3–bis(benzylthio)propylamine (XI; $R_3=CH_3$, $R_4=C_6H_5CH_2$). The oil was crystallized as the hydrogen oxalate salt, which showed the correct analysis for $C_{21}H_{27}O_4NS_2$, but any attempts to isolate a pure isomer from the other by recrystallization were unsuccessful. The mixture, therefore, was directly put into the Birch reduction followed by the oxidation with air to afford nereistoxin in a 32% over–all yield.

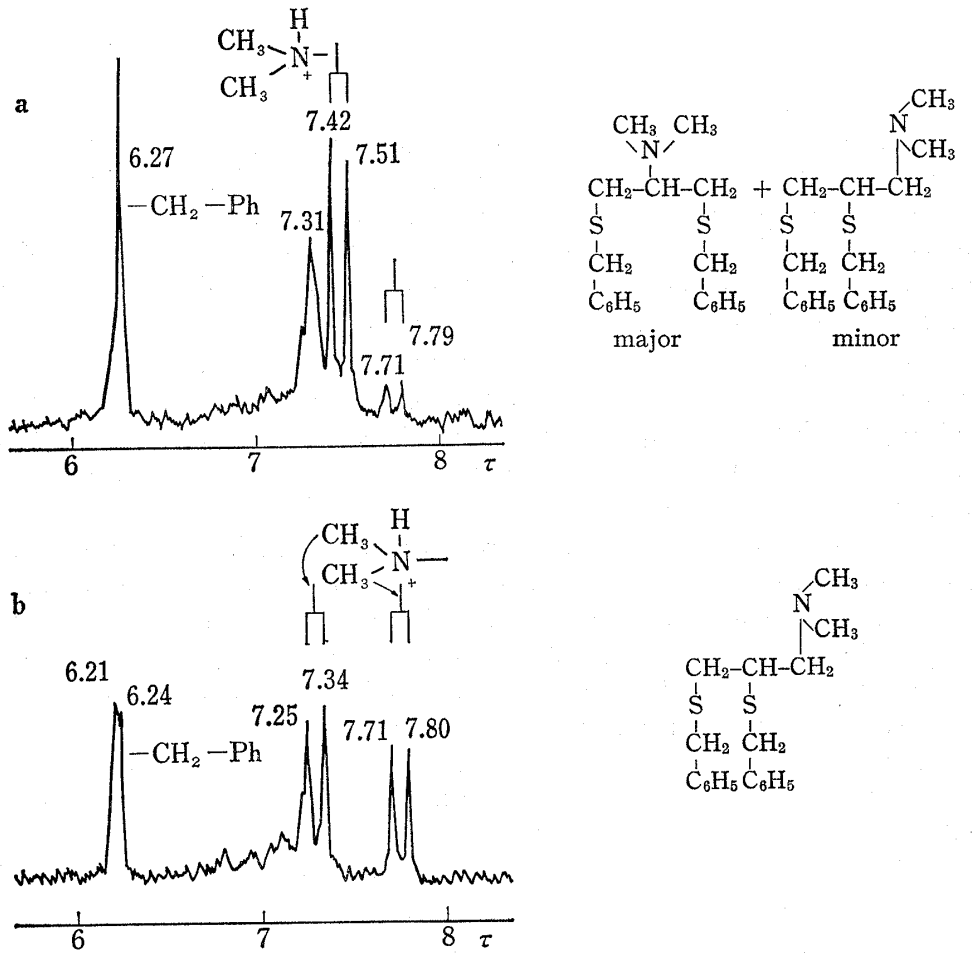
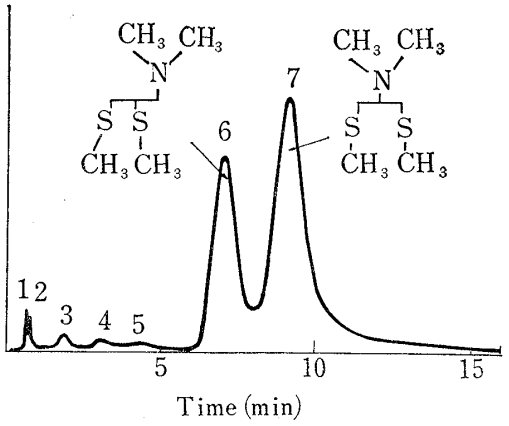


Fig. 1. Nuclear Magnetic Resonance Spectra measured at 60 Mc in CF_3COOH, Me_4Si as an Internal Reference

a; Product by the thiolation of N,N–dimethyl–2,3–dichloropropylamine (VIII; $R_3=CH_3$) with sodium benzylmercaptide.
b; N,N–dimethyl–2,3–bis(benzylthio)propylamine (V; $R_1=C_6H_5CH_2$, $R_2=CH_3$).

A nuclear magnetic resonance study of these isomers revealed that the nitrogen atom of these compounds in trifluoroacetic acid is protonated and that the two methyl groups of the symmetrical isomer (X; $R_3=CH_3$, $R_4=C_6H_5CH_2$) are coupled to the protonated proton to show two peaks at 7.42τ and 7.51τ (Fig. 1a). On the other hand, the two methyl groups in the asymmetrical isomer (XI; $R_3=CH_3$, $R_4=C_6H_5CH_2$) were nonequivalent presumably



Peak No.	Peak area (%)
1	
2	
3	7.9
4	
5	
6	29.8
7	62.4

Fig. 2. Gas Chromatogram of the Product obtained by the Thiolation of N,N-Di-methyl-2,3-dichloropropylamine (VIII; $R_3=CH_3$) with Sodium Methylmercaptide

Column: 25% Apiezon L/C-22 (30—60 mesh); 1 m×6 mm *i.d.*
Column temperature: 185° Carrier gas: He, 60 ml/min

because of the steric hindrance of the free rotation and of further coupling to the protonated proton eventually to show four peaks at 7.25τ, 7.34τ, 7.71τ and 7.80τ (Fig. 1b). The latter two peaks which correspond to one of the methyl groups of the asymmetrical isomer are apart from the other and are not influenced by any other peaks. It is, therefore, possible to calculate the content of the asymmetrical amine (XI; $R_3=CH_3$, $R_4=C_6H_5CH_2$) in the reaction mixture on relative intensities of these two peaks.

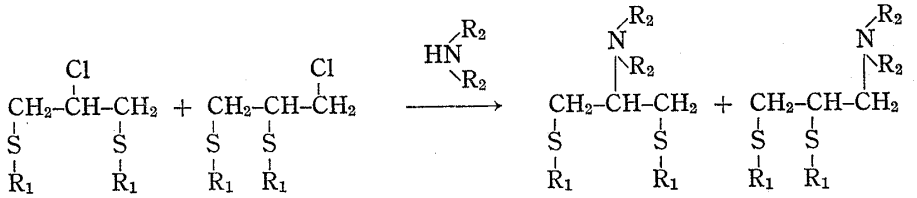
Treatment of N,N-dimethyl-2,3-dichloropropylamine (VIII; $R_3=CH_3$) with sodium methylmercaptide gave similarly an oily mixture of the isomers, 2-dimethylamino-1,3-bis(methylthio)propane (X; $R_3=CH_3$, $R_4=CH_3$) and N,N-dimethyl-2,3-bis(methylthio)propylamine (XI; $R_3=CH_3$, $R_4=CH_3$), and the proportion of two isomers was measured by gas chromatography as shown in Fig. 2.

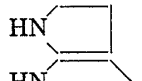
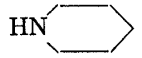
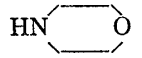
Treatment of N,N-dialkyl-2,3-dichloropropylamines (VIII) which have an amino group bulkier than the dimethylamino group, with sodium benzylmercaptide, gave predominantly symmetrical amines (X) while the asymmetrical isomers (XI) were detected only in minor quantities by thin-layer chromatography. In cases where $(R_3)_2N-$ is morpholino and piperidino, the symmetrical amines (X) were obtained as crystals without any difficulties. Other symmetical isomers, which failed to crystallize, were converted into the corresponding crystalline sulfones (XIV). The yields listed in Table I are mostly calculated on the basis of quantity of the isolated products or derived sulfones (XIV), therefore, the actual formation ratio should be more than the values in the Table.

The data listed in Table I apparently indicate that our presumption was valid, *i.e.*, the thiolation in Chart 2 proceeded *via* a cyclic immonium intermediate (IX) and that the alkylthio anions attacked on the terminal carbon.

A number of asymmetrical amines (V), isolable as crystalline hydrogen oxalate salts, were synthesized in high yields by the amination reaction of the chloride mixture (I and II; $R_1=C_6H_5CH_2$) with various secondary amines other than dimethylamine. Table II represents the yields of the isolated hydrogen oxalate salts.

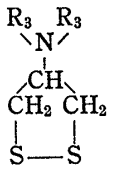
Table II. The Amination of a Mixture of I and II with Secondary Amines

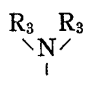
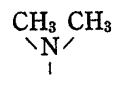
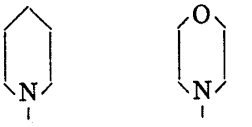
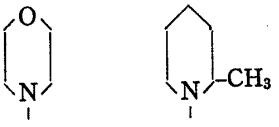


R_1	$HN(R_2)_2$	IV %	V %
$C_6H_5CH_2-$	$HN(CH_3)_2$	minor[a]	major[a]
$C_6H_5CH_2-$		—	59[b]
$C_6H_5CH_2-$		—	91[b]
$C_6H_5CH_2-$		—	78[b]
$C_6H_5CH_2-$	$HN(CH_2CH_2OH)_2$	—	65[b]

a) Result in the preceding paper.[1]
b) Calculated on the isolated hydrogen oxalate salts.

Table III. 4-N,N-Dialkylamino-1,2-dithiolanes (XIII)



					
mp (°C)	172—174 (oxal.)	192—193 (oxal.)	180—184 (oxal.)	186—189 (oxal.)	87—89 (pic.)
max (mμ) in H_2O	320	324	321	320	—
ε	125	116	134	113	—

The structures of the amines thus obtained in both reactions were determined mainly on the basis of the nuclear magnetic resonance spectra. In the nuclear magnetic resonance spectra of some bis(benzylthio) derivatives the benzylmethylene protons of the symmetrical isomer, being equivalent, showed a single peak near 6.2τ while those of the asymmetrical isomer showed a doublet or more complex peaks at this region.[6] One example of this still unveiled feature is provided by the spectra of two isomers of N,N-dimethyl propylamine as in Fig. 1. On thin-layer chromatography the symmetrical isomer flow faster than the asymmetrical one as was described in the preceding paper.[1]

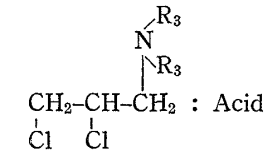
On reduction followed by the oxidation with air the symmetrical amines (IV) were converted into the corresponding 4-N,N-dialkylamino-1,2-dithiolanes (XIII), which showed the UV maximum near 320 mμ characteristic of a dithiolane ring.

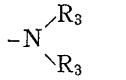
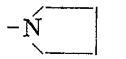
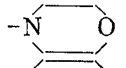
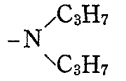
6) More detailed discussions will be presented in future.

Experimental[7]

N,N-Dialkyl-2,3-dichloropropylamines (VIII)——These were prepared according to the procedure of Cromwell and Hassner[8] with some modification. N,N-Dialkylallylamines were obtained by the treatment of allylbromide with two equivalents of the corresponding secondary amines. The modification was derived from the observation that, in the reaction of allylbromide with two equivalents of a secondary amine in ether the precipitate formed was the secondary amine hydrobromide and the desired allylamine had remained in the solution. Thus the treatment of the precipitate followed by distillation described in the literature was omitted.[8]

To a stirred solution of allylbromide (60 g, 0.5 mole) in ether (200 ml), a solution of secondary amine (1 mole) in ether (100 ml) was added dropwise under ice cooling. The mixture was allowed to stand overnight in a refrigerater keeping away from moisture. The precipitate was filtered and the filtrate was treated with dry HCl until no more precipitation occurred. The precipitated allylamine hydrochloride was collected by filtration. The solid material was dissolved in $CHCl_3$ (300 ml), to which Cl_2 was introduced until the calculated amount was absorbed. The mixture was evaporated to dryness to afford oily N,N-dialkyl-2,3-dichloropropylamine (VIII)hydrochloride which generally crystallized after being left standing. All the products thus prepared were found to be homogeneous by thin-layer chromatography, on which a single spot was visualized with Dragendorff reagent. In some cases, where new compounds were obtained, crystalline hydrogen oxalates or picrates were prepared for the identification.

TABLE V.  : Acid

	Acid	mp (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
	oxalic	130—131	$C_9H_{15}O_4NCl_2$	39.72	5.55	—	39.85	5.59	—
	oxalic	143—145	$C_9H_{15}O_5NCl_2$	37.52	5.25	4.86	37.66	5.36	4.80
	picric	121—123	$C_{15}H_{20}O_7N_4Cl_2$	41.01	4.59	12.75	41.25	4.92	12.73
	oxalic	108—110	$C_{11}H_{21}O_4NCl_2$	43.71	7.01	—	45.06	7.44	—

2-Dimethylamino-1,3-bis(benzylthio)propane (X; $R_3=CH_3$, $R_4=C_6H_5CH_2$) and N,N-Dimethyl-2,3-bis(benzylthio)propylamine (XI; $R_3=CH_3$, $R_4=C_6H_5CH_2$)——A mixture of N,N-dimethyl-2,3-dichloropropylamine (VIII; $R_3=CH_3$) hydrochloride (19.2 g) MeOH (50 ml) and EtOH (150 ml) was added to a solution of KOH (5.6 g) in EtOH (200 ml) under stirring, and the precipitated KCl was filtered off. To the filtrate was added a solution of sodium benzylmercaptide in EtOH, which was prepared from Na (5.8 g), benzylmercaptan (31 g) and EtOH (50 ml), and the mixture was heated to reflux for 2 hr. The precipitated NaCl was filtered off and the filtrate was evaporated to dryness. The residual oil dissolved in ether was washed with H_2O, dried, and evaporated to afford a brown oil (26.4 g). This was shown to be a mixture of 2-dimethylamino-1,3-bis(benzylthio)propane (X; $R_3=CH_3$, $R_4=C_6H_5CH_2$) (major constituent) and N,N-dimethyl-2,3-bis(benzylthio)propylamine (XI; $R_3=CH_3$, $R_4=C_6H_5CH_2$) (minor constituent) by thin-layer chromatography. The nuclear magnetic resonance spectrum of the mixture was shown in Fig. 1a. The oil was crystallized as hydrogen oxalate salt, which was recrystallized from MeOH to give white powder, mp 90—93°. *Anal.* Calcd. for $C_{21}H_{27}O_4NS_2$: C, 59.82; H, 6.46; N, 3.32; S, 15.12. Found: C, 59.60; H 6.47; N, 3.35; S, 15.56.

Nereistoxin (VII) Hydrogen Oxalate——An oily mixture (8 g) of 2-dimethylamino-1,3-bis(benzylthio)-propane (X; $R_3=CH_3$, $R_4=C_6H_5CH_2$) and N,N-dimethyl-2,3-bis(benzylthio)propylamine (XI; $R_3=CH_3$,

7) All melting points are uncorrected. All the compounds included in the table are new in the literature.
8) N.H. Cromwell and A. Hassner, *J. Am. Chem. Soc.*, **77**, 1568 (1955).

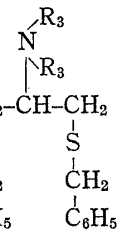
$R_4=C_6H_5CH_2$) prepared as described above was dissolved in a solution of liquid NH_3 (240 ml) in ether (160 ml) and the reaction vessel was cooled over solid CO_2–acetone. To the stirred mixture Li (2.4 g) was added, whereupon the color of the mixture turned dark blue. After 20 min, EtOH (24 ml) was added under vigorous stirring, the cooler was taken off, and NH_3 was evaporated off in a hood. To the residue H_2O (150 ml) was added and the mixture was extracted repeatedly with ether. The ether extracts were combined, washed with saturated aqueous NaCl solution, dried, and finally treated with oxalic acid until no more solid is deposited. The yellow solid (2.3 g) collected by filtration and recrystallized from 95% EtOH afforded yellow leaflets, mp 172—174°, which was identical with a specimen prepared in the preceding paper[1] (Yield 32%).

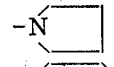
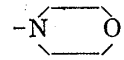
2-Dimethylamino-1,3-bis(methylthio)propane (X; $R_3=CH_3$, $R_4=CH_3$) Hydrogen Oxalate——Nereistoxin (VII) hydrogen oxalate (1 g) was suspended in 50% MeOH (20 ml), to the stirred mixture a solution of $NaBH_4$ (0.5 g) in MeOH (5 ml) was added under ice cooling. After 5 min, the excess $NaBH_4$ was decomposed by addition of drops of CH_3COOH. Keeping the solution alkaline with simultaneous addition of 10% NaOH, Me_2SO_4 (11.6 g) was added dropwise under vigorous stirring over a period of one hour. The mixture was extracted with ether and the ether solution, after drying over Na_2SO_4, was treated with oxalic acid. The solid deposited (200 mg) was collected by filtration, mp 132° (decomp.). The compound thus obtained gave a single spot visualized with Dragendorff reagent at *Rf* 0.35 on thin-layer chromatography, which was run with MeOH on a mixture of 9 parts Merck 100 mesh silicagel and one part of Mallinkrodt 100 mesh silicagel as an adsorbent without binder. *Anal.* Calcd. for $C_9H_{19}O_4NS_2$: C, 40.13; H, 7.11. Found: C, 39.64; H, 7.21.

2-Dimethylamino-1,3-bis(methylthio)propane (X; $R_3=CH_3$, $R_4=CH_3$) Hydrogen Oxalate and N,N-Dimethyl-2,3-bis(methylthio)propylamine (XI; $R_3=CH_3$, $R_4=CH_3$) Hydrogen Oxalate——N,N-Dimethyl-2,3-dichloropropylamine (VIII; $R_3=CH_3$) hydrochloride (7 g) was added to a solution of KOH (2.1 g) in EtOH (100 ml), and the precipitated KCl was filtered off. To the filtrate was added a solution of sodium methylmercaptide in EtOH, which was prepared from Na (3.3 g), methylmercaptan (6.9 g) and EtOH, and the mixture was heated to reflux for 2 hr, and then allowed to stand overnight at room temperature. The precipitated NaCl was filtered off, the filtrate was acidified with ethanolic HCl, and the solvent was evaporated to dryness. The oily resdiue was dissolved in H_2O (150 ml), the solution was made alkaline with K_2CO_3 and extracted with ether. To the organic layer an ether solution saturated with oxalic acid was added until no more precipitate deposit. The solid material (6.7 g) was collected by filtration and recrystallized from MeOH to give white powder mp 122—123°. *Anal.* Calcd. for $C_9H_{19}O_4NS_2$: C, 40.13; H, 7.11; N, 5.20. Found: C, 40.23; H, 7.39; N, 5.02. The compound thus obtained was shown to be a mixture of isomers by thin-layer chromatography developed with similar condition described above, on which two spots—deeply colored one at *Rf* 0.35 due to X ($R_3=CH_3$, $R_4=CH_3$) and slightly colored the other one at *Rf* 0.18 ascribable to XI ($R_3=CH_3$, $R_4=CH_3$)—were brought out with Dragendorff reagent. The gas chromatogram of the free base was shown in Fig. 2. The peaks were assigned as above, because it was known from the thin-layer chromatogram that the symmetrical isomer was the major and the asymmetrical one the minor concomitant of the mixture.

2-N,N-Dialkylamino-1,3-bis(benzylthio)propane (X; $R_4=C_6H_5CH_2$)——A mixture of N,N-dialkyl-2,3-dichloropropylamine (VIII) hydrochloride (1 mole), MeOH (50 ml) and EtOH (150 ml) was added to a solution of KOH (5.6 g) in EtOH (200 ml) under stirring and the precipitated KCl was filtered off. To the filtrate was added a solution of sodium benzylmercaptide in EtOH, which was made from Na (5.8 g), benzylmercaptan (31 g) and EtOH (50 ml), and the mixture was heated to reflux for 2 hr. The NaCl formed was filtered off and the filtrate was evaporated to dryness. The residual oil was dissolved in ether, and

Table V.

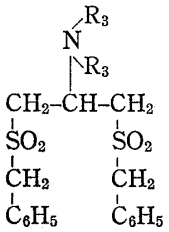


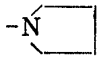
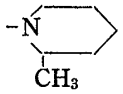
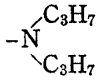
$-N^{R_3}_{R_3}$	mp (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
	52—54	$C_{22}H_{29}NS_2$	71.11	7.87	3.77	70.95	7.64	3.43
	81—84	$C_{21}H_{27}ONS_2$	67.52	7.29	3.75	67.48	7.17	3.58

the solution was washed and dried. The solvent was evaporated to afford brown oil of X ($R_4=C_6H_5CH_2$) which gradually crystallized after being left standing. In cases of oily amines, they were converted into the corresponding sulfones (XIV) as described in the next column for the identification and the calculation of the yields. The yields are listed in Table I.

2-N,N-Dialkylamino-1,3-bis(benzylsulfonyl)propane(XIV)——To the suspension of above obtained amine (0.03 mole) in HCOOH (100 ml), 30% H_2O_2 (14 g) was added under violent stirring. After a while exothermic reaction set in, the temperature rised to about 80° and the mixture became homogeneous. After the reaction had subsided, stirring was continued for 3 hr, and the solvent was removed under reduced pressure. The residue was poured into ice–H_2O and the mixture was made alkaline with the addition of 10% K_2CO_3. The precipitated solid was collected and recrystallized from EtOH to give cyrstalline XIV.

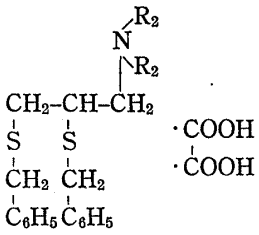
Table VI.

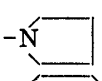
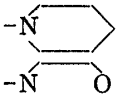
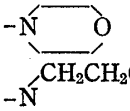
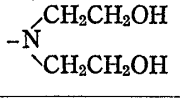


$-N^{R_3}_{R_3}$	mp (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Found C	Found H
	151—153	$C_{21}H_{27}O_4NS_2$	59.83	6.46	59.94	6.31
	188—189	$C_{23}H_{31}O_4NS_2$	61.44	6.95	61.40	6.94
	146—148	$C_{23}H_{33}O_4NS_2$	61.16	7.36	61.41	7.25

N,N-Dialkyl-2,3-bis(benzylthio)propylamine (V; $R_1=C_6H_5CH_2$) Hydrogen Oxalate——A mixture (15 g) of 2-chloro-1,3-bis(benzylthio)propane (I; $R_1=C_6H_5CH_2$) and 1-chloro-2,3-bis(benzylthio)propane (II; $R_1=C_6H_5CH_2$) prepared by the method described in the preceding paper,[1] was heated with secondary amine (20 g)

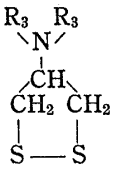
Table VII.

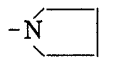
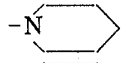
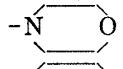
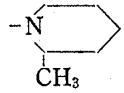


$-N^{R_2}_{R_2}$	mp (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
	135—137	$C_{23}H_{29}O_4NS_2$	61.72	6.53	3.13	61.76	6.43	2.93
	129—132	$C_{24}H_{31}O_4NS_2$	62.44	6.77	3.04	62.47	6.95	3.04
	105—109	$C_{23}H_{29}O_5NS_2$	59.60	6.31	3.02	59.67	6.36	2.80
	125—128	$C_{23}H_{31}O_6NS_2$	57.36	6.49	2.91	57.09	6.71	2.85

and C_6H_6 (40 ml) at 160° for 16 hr in an autoclave. The excess amine and C_6H_6 were evaporated off under reduced pressure, and the residual oil was dissolved in C_6H_6 and the solution was washed and dried. The solution was evaporated to dryness to afford a brown oil containing V ($R_1=C_6H_5CH_2$). The amines thus prepared were converted into crystalline hydrogen oxalate salts for the identification and the calculation of the yields. The results attained are listed in Table II.

4-N,N-Dialkylamino-1,2-dithiolane(XIII)——2-N,N-Dialkylamino-1,3-bis(benzylthio)propane(X; $R_4=C_6H_5CH_2$, 8 g) was dissolved in a solution of liquid NH_3 (240 ml) and ether (160 ml) and the reaction vessel was cooled over a solid CO_2–acetone mixture. To the stirred solution Li (2.4 g) was added, whereupon the color of the mixture turned dark blue. After 20 min, EtOH (24 ml) was added under stirring, the cooler was taken off, and NH_3 was evaporated off in a hood. To the residual solid, H_2O (150 ml) was added, and the mixture was extracted with ether. After two layers were separated, air was bubbled into the aqueous layer under ice cooling for 40 min and the solution was again extracted with ether. The ether extracts were combined, washed with a saturated NaCl solution and dried. To the etherial solution a saturated ether solution of oxalic acid was added until no more solid is formed. The yellow solid deposited was collected and recrystallized from 95% EtOH to afford yellow leaflets of XIII–hydrogen oxalates. Physical constants of the compounds are listed in Table III.

Table VIII.  : Acid

	Acid	Formula	Analysis (%) Calcd. C	Calcd. H	Found C	Found H
	oxalic	$C_9H_{15}O_4NS_2$	40.74	5.70	41.21	5.79
	oxalic	$C_{10}H_{17}O_4NS_2$	42.99	6.13	43.23	6.24
	oxalic	$C_9H_{15}O_5NS_2$	38.42	5.37	38.20	5.55
	picric	$C_{15}H_{20}O_7N_4S_2$	41.66	4.64	41.82	5.28

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