Anal. Calcd. for $C_8H_{11}ClN_2O \cdot H_2O$: C, 47.1; H, 6.4; Cl, 17.4; neut. equiv., 204. Found: C, 47.1; H, 6.4; Cl, 17.4; neut. equiv., 200; pK_a 4.0.

O-Methyl-6-methylpicolinaldehyde Oxime Hydroiodide (III).—The same procedure of anion conversion described for II was followed to give yellow needles, m.p. 150°. Ultraviolet spectrum: pH 1, λ_{max} 306 mμ, log ε 4.18; pH 7.0, λ_{max} 285, log ε 4.05; pH 14, λ_{max} 285, log ε 4.05.

Anal. Calcd. for $C_8H_{11}IN_2O \cdot 1/2H_2O$: C, 33.4; H, 4.2; I, 44.3; neut. equiv., 287. Found: C, 33.2; H, 4.6; I, 44.3; neut. equiv., 282.

1,6-Dimethyl-2-formylpyridinium Iodide Dimethyl Acetal (IV).—Freshly distilled (b.p. 76° at 10 mm.) 6-methylpicolinaldehyde (43 g., 0.36 mole) was dissolved in 100 ml. of methyl alcohol. Hydrogen chloride gas was passed for 20 min. through the refluxing solution. The cooled (ice water) pale yellow solution was added slowly to a saturated solution of potassium carbonate. Distillation of the red oil which separated gave 40.0 g. (67.5%) of the colorless acetal, b.p. 94–96° at 10 mm. This material was heated in a capped bottle for 15 hr. at 60° with 41 g. (0.28 mole) of methyl iodide. The reaction mixture was cooled and the supernatant liquid was decanted. The remaining yellow solid and red gum were dissolved in methyl alcohol. Ether was added to the point of cloudiness; cooling in a Dry Ice chest gave 19 g. (49%) of a yellow crystalline solid, m.p. 146–149°.

Anal. Calcd. for $C_{10}H_{16}INO_2$: C, 38.8; H, 5.2; N, 4.6. Found: C, 38.8; H, 5.1; N, 4.7.

1,6-Dimethyl-2-formylpyridinium Iodide Oxime (V).[8]—To 15 g. (0.049 mole) of V was added 90 ml. of 10% hydrochloric acid. The solution was refluxed for 90 min. and allowed to stand overnight. The pH was adjusted to 7.0 with sodium carbonate and a solution of hydroxylamine hydrochloride (7.0 g., 0.10 mole) and sodium hydroxide (4.0 g., 0.10 mole) in 25 ml. of water was added and the resulting mixture heated on a steam bath for 30 min. Upon cooling in a freezer, 4.5 g. of a pale yellow crystalline solid (m.p. 191–192° dec.) was obtained. Cooling overnight gave an additional 2.2 g. (total yield 49.5%). The compound was recrystallized from ethanol–ether to give yellow needles m.p. 212°. Ultraviolet spectrum: pH 1, λ_{max} 297 mμ, log ε 4.10; pH 7.0, λ_{max} 2.97, log ε 4.10; pH 14, λ_{max} 336, log ε 4.24.

Anal. Calcd. for $C_8H_{11}IN_2O$: C, 34.6; H, 4.0; I, 45.7; neut. equiv., 278. Found: C, 34.5; H, 4.1; I, 45.7; neut. equiv., 272; pK_a 8.1.

Acknowledgment.—We wish to express our gratitude to the Analytical Research Branch of the U.S. Army Chemical Research and Development Laboratories for the analyses here reported.

(8) The same procedure described for the preparation of VI was used to prepare O-methyl-1,6-dimethyl-2-formylpyridinium iodide oxime with the exception that O-methylhydroxylamine was used in place of the hydroxylamine. Yellow solid, 38%, m.p. 155°, calcd. for $C_9H_{13}IN_2O$: C, 37.0; H, 4.5; I, 43.3. Found: C, 36.8; H, 4.5; I, 43.7.

Thiolethylation of Amines with Ethylene Sulfide[1]

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The use of ethylene sulfide as a direct thiolethylation reagent has been extended to a variety of aliphatic amino compounds. Amines of varying polarity, diamines, and alkanolamines, have been thiolethylated without extensive polymer formation. The aminothiols were converted to the hydrochloride salts for characterization.

In the search for agents that offer chemical protection against radiation effects in animal tissue much interest has centered around 2-aminoethanethiol, its derivatives, and other aminothiols.[2,3] This paper reports the synthesis of a number of 2-mercaptoethylated amines and amino alcohols *via* thiolethylation with ethylene sulfide.

Several routes are available for the synthesis of 2-aminoethanethiols starting with S-blocked compounds using established procedures. Examples are the alkylation of amines with benzyl 2-chloroethyl sulfide,[4] followed by debenzylation[5]; and the amination of epoxides[6] and ethylenimines[7] with 2-(benzylthio)ethylamine, followed by debenzylation.[5]

$$RNH_2 \xrightarrow{ClCH_2CH_2SCH_2C_6H_5} RNHCH_2CH_2SCH_2C_6H_5 \xrightarrow[2.\ HCl]{1.\ Na/NH_3} RNHCH_2CH_2SH\cdot HCl$$

$$\underset{\diagdown O \diagup}{CH_2—CH_2} \xrightarrow{H_2NCH_2CH_2SCH_2C_6H_5} HOCH_2CH_2NHCH_2CH_2SCH_2C_6H_5 \xrightarrow[2.\ HCl]{1.\ Na/NH_3} HOCH_2CH_2NHCH_2CH_2SH\cdot HCl$$

$$\underset{\diagdown N \diagup \\ H}{CH_2—CH_2} \xrightarrow{H_2NCH_2CH_2SCH_2C_6H_5} H_2NCH_2CH_2NHCH_2CH_2SCH_2C_6H_5 \xrightarrow[2.\ HCl]{1.\ Na/NH_3} H_2NCH_2CH_2NHCH_2CH_2SH\cdot 2HCl$$

Direct thiolethylation of amines and amino

(1) This investigation was supported by the U. S. Army Medical Research and Development Command under Contract No. DA-49-193-MD-2109.

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(3) A. Pihl and L. Eldjarn, *Pharmacol. Rev.*, **10**, 437 (1958), and references therein cited.

(4) G. Cavallini and F. Ravenna, *Farmaco (Pavia) Ed. sci.*, **12**, 151 (1957).

(5) J. Baddiley and E. M. Thain, *J. Chem. Soc.*, 800 (1952).

(6) S. Winstein and R. B. Henderson, "Heterocyclic Compounds," Vol. 1, R. C. Elderfield, ed., J. Wiley and Sons, Inc., New York, N. Y., 1950, p. 1, and references therein cited.

(7) L. B. Clapp, *J. Am. Chem. Soc.*, **70**, 184 (1948).

alcohols offers a shorter route adaptable to solutions of the amino compounds in solvents of low polarity.

Previous investigators have generally used one of two procedures for amine–ethylene sulfide reactions. One of these was the use of a solvent of low polarity (benzene) with the reaction mixture kept at room temperature. Rachinskii and associates[8] have distinguished between strongly basic amines such as dimethylamine and weakly basic amines. For the former they used a nonprotonic solvent (anhydrous benzene) and reaction at 25° and for the latter, alcohol solutions in a sealed tube at 100°. Of the amine–ethylene sulfide reactions relatively few have been run on primary aliphatic amines. Rachinskii reported twenty products of which only four were from primary aliphatic amines with no yields given.

Reppe and Nicolai[9] have reported neither details nor yields on the preparation of two examples of mercaptoethylated primary aliphatic amines they cited. Their process is equivalent to the sealed tube process using benzene or an aliphatic hydrocarbon solvent.

Snyder, Stewart, and Ziegler[10] have reported only one example of a primary aliphatic amine as reactant in their mercaptoethylation procedure. No yield is given. A sealed tube reaction at 90–100° was used without solvent.

Yur'ev and co-workers[11,12] have reported a number of examples of primary and secondary aryl amines in reactions with ethylene sulfide but no examples of aliphatic amines. The procedure used was a sealed tube reaction at 100° with benzene solvent.

Braz[13] gave three examples of the mercaptoethylation of primary aliphatic amines together with yields and reaction conditions. His procedure, a sealed tube reaction at 100° using benzene solvent, resulted in yields of 46–68%. Braz obtained N,N - diethyl - N′ - 2 - mercaptoethylethylenediamine in 46% yield. This is the sole example found of the mercaptoethylation of a primary aliphatic amine containing another polar group directly with ethylene sulfide.

Recently Reynolds and co-workers[14–17] have reported the thiolethylation of various amines with several ethylene sulfide precursors. Of these, ethyl 2-mercaptoethylcarbonate offers wide utility except for highly polar amines as 2-aminoethanol.

Initially, in this work direct thiolethylation of amines with ethylene monothiolcarbonate[18] was attempted and was successful for a secondary amine such as piperidine; 2-(1-piperidyl)ethanethiol was obtained in 55% yield by refluxing for five hours a toluene solution of equimolar quantities of the monothiolcarbonate and amine.

In the major portion of this work ethylene sulfide was generated prior to use and used in benzene solution. The episulfide was prepared by two routes, the sodium carbonate-catalyzed decomposition of ethylene monothiolcarbonate[18] and the reaction of ethylene carbonate with potassium thiocyanate,[19] and could be stored with minimum polymerization at −25°, preferably in benzene solution.

Initially, the thiolethylation involved the addition of a solution of ethylene sulfide to a stirred solution of the amine in benzene at 50° under anhydrous conditions and nitrogen. Such a procedure was satisfactory in some cases but led to substantial polymer formation in the case of more polar amines. The gradual addition of the episulfide solution to a refluxing solution of the primary or secondary amine in benzene has worked reasonably well for polar amines. Small amounts of polymer were formed, usually less than 1% of the ethylene sulfide charged. Removal of the solvent generally yielded a viscous liquid thiolic residue from which the product was isolated by reduced pressure distillation. The aminothiols were converted to the hydrochloride salts for characterization.

In Table I are listed the various aminothiols prepared by the ethylene sulfide thiolethylation of aliphatic amines, diamines, and amino alcohols. The yields listed are isolated yields.

Generally, for the compounds containing primary amine groups a high molar ratio of amine to episulfide favored the desired monothiolethylation except where branching occurred at the carbon alpha to the amine group. For example, the isolated yields of the products derived from *t*-butylamine and 4-amino-1-diethylaminopentane were low (12 and 21%, respectively) despite amine:ethylene sulfide molar ratios of 6 and 2.2, respectively.

For secondary amines the observed yields of monothiolethylated products were not as sensitive to amine:ethylene sulfide molar ratios. In the case of 2,6-dimethylpiperidine steric hindrance probably decreased the extent of reaction.

For the more polar compounds, *i.e.*, amino alcohols and diamines with two primary amine groups, a high molar ratio of amine to episulfide favored monothiolethylation. For example, the reactions with ethanolamine and 3-amino-2-butanol yielded

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(17) D. D. Reynolds, D. L. Fields, and D. L. Johnson, *ibid.*, **26**, 5125 (1961).

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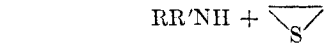
(19) S. Searles, Jr., and E. F. Lutz, *ibid.*, **80**, 3168 (1958).

TABLE I
AMINOTHIOLS FROM ETHYLENE SULFIDE



Aminothiols					
R	R′	Amine:ethylene sulfide Molar ratio	Yield, %	B.p., °C./mm.	$n^{20}D$
$CH_3(CH_2)_4CH_2$—	H	6	66	85–86/3.5	1.4709[a]
$CH_3(CH_2)_5CH_2$—	H	3	39	87/2	1.4713
$CH_3(CH_2)_7CH_2$—	H	3	41	92/0.3	1.4710
$CH_3(CH_2)_9CH_2$—	H	3	26	104–106/0.13	1.4760
$CH_3(CH_2)_3CH(C_2H_5)CH_2$—	H	3	56	66/0.06	1.4827
$(CH_3)_3C$—	H	6	12	58–64/20	Solid[b]
$CH_3(CH_2)_6CH_2$—	$CH_3(CH_2)_6CH_2$—	3	31	131/0.13	1.4679
$H_2NCH_2CH_2CH_2$—	H	8.3	66[c]	62/0.1	Solid
$(C_2H_5)_2NCH_2CH_2$—	H	1	32	82/1	1.4796[e]
$H_2N(CH_2)_5CH_2$—	H	8.3	57	88/0.13	Solid[f]
$(CH_3)_2NCH_2CH_2CH_2$—	H	2.8	69	60/0.1	1.4849
$(C_2H_5)_2NCH_2CH_2CH_2$—	H	3.3	72	80/0.02	1.4820
$(C_2H_5)_2NCH_2CH_2CH_2CH(CH_3)$—	H	2.2	21	94/0.4	1.4800
$HOCH_2CH_2$—	H	10[g]	40[h]	66–69/0.03	1.5379
$HOCH_2CH_2CH_2$—	H	5	39[i]	81–88/0.12	Solid
$HOCH_2CH_2CH_2CH_2$—	H	2	12	80–86/0.02	1.5150
$HOCH_2CH(C_2H_5)$—	H	3.2	48	83–88/0.25	1.5036
$HOCH(CH_3)CH(CH_3)$—	H	2.2	24[j]	64–67/0.1	1.4985
$HOC(CH_3)(C_3H_7)CH_2$—	H	1.4	28	67–87/0.08	1.4884
$(C_2H_5)_2NCH_2CH(OH)CH_2$—	H	2	37	98–99/0.1	1.4942
$HOCH_2CH_2$—	CH_3CH_2—	2.2	72	71/0.5	1.4966
$CH_3OCH_2CH_2$—	H	4	57	84/17	1.4767
$CH_3OCH_2CH_2CH_2$—	H	1	36	80/4	1.4800
$(CH_3)_2CHOCH_2CH_2CH_2$—	H	2	48	73/0.8	1.4679
p-$CH_3OC_6H_4CH_2$—	H	1.8	28	106–108/0.15	1.5622
—$CH_2CH_2CH_2CH_2CH_2$—[k]		1	66[l,m]	60/7	1.5014[n]
—$CH_2CH_2CH_2CH_2CH_2CH_2$—[q]		2.3	84	86/5	1.5076
—$CH(CH_3)CH_2CH_2CH_2CH(CH_3)$—		1	11	57/0.5	1.5014
—$CH_2CH(OH)CH_2CH_2CH_2$—		1.9	77	97–99/0.7	1.5282
—$CH_2CH(CH_3)OCH(CH_3)CH_2$—		1[r]	56	68/1	1.4852
$CH_2CH_2CH_2CH_2OCHCH_2$—	H	1.9	58	79–80/0.3	1.5040
$CH_2CH_2OCH_2CH_2NCH_2CH_2$—	H	4	48	93–104/0.2–0.8	1.5103
$CH_2CH_2OCH_2CH_2NCH_2CH_2CH_2$—	H	4.8	46	119/0.4	1.5086

[a] *Anal.* Calcd. for $C_8H_{19}NS$: S, 19.9. Found: S (thiol), 19.4. d^{20}_4 0.892. [b] M.p. 46–48°. [c] Yield of crude solid. [d] N calcd.: 13.5. Found: 13.6. [e] Reported[13] 1.4795. [f] M.p. 38–40°. [g] Reaction run in 9:1 mixture of benzene and ethanol. [h] Also isolated was a 21% yield of $HOCH_2CH_2NHCH_2CH_2SCH_2CH_2SH$ b.p. 123–124°/0.1 mm., $n^{20}D$ 1.5563. *Anal.* Calcd. for $C_6H_{16}ClNOS_2$: C, 33.1; H, 7.4; Cl, 16.3; S, 29.5; S (thiol), 14.7. Found: C, 33.1; H, 7.5; Cl, 16.4; S, 29.2; S (thiol), 14.6. [i] Also isolated in 10% yield was $HOCH_2CH_2CH_2NHCH_2CH_2SCH_2CH_2SH$, b.p. 139–140°/0.12 mm., $n^{20}D$ 1.5500. *Anal.* Calcd. for $C_7H_{17}NOS_2$: C, 43.0; H, 8.8; S, 32.8; S (thiol), 16.4. Found: C, 44.2; H, 8.7; S, 32.4; S (thiol), 16.0. [j] Also isolated was a 29% yield of $HOCH(CH_3)CH(CH_3)NHCH_2CH_2SCH_2CH_2SH$, b.p. 120–125°/18.

substantial quantities of the telomeric mercaptoethylthioethyl derivatives. The formation

$HOCH_2CH_2NHCH_2CH_2SCH_2CH_2SH$ (21%) (A)

$HOCH(CH_3)CH(CH_3)NHCH_2CH_2SCH_2CH_2SH$ (29%) (B)

of such compounds has been observed by Reppe and Nicolai[9] and Reynolds and co-workers[14,17,20] in thiolethylation reactions.

The structure assignments for A and B (as the hydrochloride salts) were based on the observed ratios of total sulfur to thiol sulfur content and the presence of —OH and —NH absorption in the infrared spectra,[21] as outlined in Table II. For A this sulfur ratio was 2.02; for B the ratio was 2.1.

Since the solubility in benzene of highly polar amines, such as ethanolamine, is limited, a 10% (by vol.) solution of absolute ethanol in benzene was found satisfactory as a reaction medium to which the benzene solution of ethylene sulfide was added. Extensive polymer formation was not observed in this more polar solvent mixture.

In an attempt to study the process variables in the thiolethylation of amines with ethylene sulfide a number of experiments was carried out using a relatively nonpolar amine, *n*-hexylamine. The solvent was anhydrous benzene.

Table III outlines the results of this study.

The above data indicate the important favorable variables to be high amine:ethylene sulfide molar

(20) D. D. Reynolds, D. L. Fields, and D. L. Johnson, *J. Org. Chem.* **26**, 5111 (1961).

(21) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed., J. Wiley and Sons, Inc., New York, N. Y., 1958, pp. 96, 259.

TABLE I (*Continued*)

Aminothiol hydrochlorides										
		Carbon, %		Hydrogen, %		Chlorine, %		Total sulfur, %		Thiol sulfur, %
M.p., °C.	Formula	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Found
203–204	$C_9H_{22}ClNS$	51.0	50.7	10.5	10.5			15.1	15.3	15.6
204–207	$C_{11}H_{26}ClNS$	55.1	55.1	10.9	10.9			13.4	13.3	13.4
206–209	$C_{13}H_{30}ClNS$	58.3	58.6	11.3	11.4			12.0	11.6	12.1
115–116	$C_{10}H_{24}ClNS$	53.2	53.1	10.7	10.6			14.2		14.6
193–196	$C_6H_{16}ClNS$	42.5	42.8	9.5	9.5			18.9		18.9
97–99	$C_{18}H_{40}ClNS$	64.0	64.2	11.9	12.0			9.2		9.1
165 dec.	$C_5H_{16}Cl_2N_2S$[d]	29.0	29.4	7.8	7.7	34.2	33.8	15.5	15.6	14.1
147–150	$C_8H_{22}Cl_2N_2S$	38.5	38.4	8.9	8.8			12.9	13.0	
193–196	$C_8H_{22}Cl_2N_2S$	38.5	38.7	8.9	8.9			12.9	12.8	13.2
200 dec.	$C_7H_{20}Cl_2N_2S$	35.7	35.9	8.6	8.5	30.1	30.1	13.6		13.5
197–202	$C_9H_{24}Cl_2N_2S$	41.0	41.0	9.2	9.2	26.9	26.8	12.2	12.3	12.2
193–196	$C_{11}H_{28}Cl_2N_2S$	45.4	45.5	9.7	9.9	24.3	24.3	11.0	11.2	10.9
Oil	$C_4H_{12}ClNOS$	30.5	30.4	7.7	7.6	22.5	22.3	20.3	20.2	20.2
Oil	$C_5H_{14}ClNOS$	35.0	34.7	8.2	8.0	20.7	21.0	18.7	19.0	17.3
Oil	$C_6H_{16}ClNOS$	38.8	40.2	8.7	8.6	19.1	18.7	17.3	16.7	16.8
Oil	$C_6H_{16}ClNOS$	38.8	38.8	8.7	8.7	19.1	19.0	17.3	17.1	17.1
60–62	$C_6H_{16}ClNOS$	38.8	39.0	8.7	8.6	19.1	18.9	17.3	17.3	16.8
76–82	$C_8H_{20}ClNOS$	44.9	44.6	9.4	9.7	16.6	16.4	15.0	15.0	14.6
191–193	$C_9H_{24}Cl_2N_2OS$	38.7	38.8	8.7	8.7	25.4	25.4	11.5	11.6	12.0
Oil	$C_6H_{16}ClNOS$	38.8	39.1	8.7	8.5	19.1	16.5	17.3	16.2	16.6
93–107	$C_5H_{14}ClNOS$	35.0	35.0	8.2	8.2	27.0	29.0	18.7	18.0	18.7
58–66	$C_6H_{16}ClNOS$	38.8	39.0	8.7	8.9	19.1	19.3	17.3	19.3	16.8
96–108	$C_8H_{20}ClNOS$	44.9	45.0	9.4	9.5	16.6	16.5	15.0	15.2	14.3
184–188[p]	$C_{10}H_{16}ClNOS$	51.4	51.7	6.9	7.0	15.2	14.9	13.7	13.8	14.0
189–193 dec.	$C_8H_{18}ClNS$	49.1	49.0	9.3	9.3	18.1	18.2	16.4		16.6
192–196 dec.	$C_9H_{20}ClNS$	51.5	51.5	9.6	9.6			15.3	15.4	
125 dec.	$C_7H_{16}ClNOS$	42.5	42.5	8.2	8.2	17.9	18.0	16.2	16.3	15.8
231–233	$C_8H_{18}ClNOS$	45.4	45.5	8.6	8.6			15.1	14.8	15.0
155–170 dec.	$C_8H_{18}ClNOS$	45.4	45.7	8.6	8.5	16.7	16.5	15.1	15.1	15.5
185–188	$C_8H_{20}Cl_2N_2OS$	36.5	36.2	7.6	7.3			12.2		12.1
225–230 dec.	$C_9H_{22}Cl_2N_2OS$	39.0	39.0	8.0	8.0	25.6	25.5	11.6		11.3

mm., $n^{20}D$ 1.5328. *Anal.* Calcd. for $C_8H_{20}ClNOS_2$: C, 39.1; H, 8.2; Cl, 14.4; S, 26.1; S (thiol), 13.0. Found: C, 39.1; H, 8.4; Cl, 14.3; S, 26.2; S (thiol), 12.5. [k] S-Acetyl derivative, b.p. 57/0.05 mm., $n^{20}D$ 1.5036. *Anal.* Calcd. for $C_9H_{17}NOS$: C, 57.7; H, 9.1; S, 17.1. Found: C, 57.4; H, 9.3; S, 17.3. [l] Amine added to ethylene sulfide in benzene; allowed to react at 25°. [m] Direct reaction of piperidine with ethylene sulfide generated *in situ* by decomposition of ethylene monothiocarbonate[14] gave a 55% yield. [n] Reported[10] 1.5015. [p] Hydrochloride salt not prepared. [q] S-Acetyl derivative, b.p. 60–65°/0.025 mm., $n^{20}D$ 1.5081. *Anal.* Calcd. for $C_{10}H_{19}NOS$: C, 59.7; H, 9.5; S, 15.9. Found: C, 60.8; H, 9.9; S, 16.8. [r] Reaction run at 50°; ethylene sulfide added in benzene.

ratio and long reflux periods. In the case of the nonpolar amine, slow addition of the episulfide was not important.

The number and variety of aminothiols prepared in this work illustrate the applicability of ethylene sulfide as a general thiolethylation reagent for primary and secondary amines. For polar amines which have a low solubility in the solvent of choice, benzene, a more polar solvent mixture of benzene–ethanol (9:1 by vol.) is satisfactory and does not cause extensive polymerization of ethylene sulfide.

Experimental[22,23]

Ethylene Sulfide.—The episulfide was prepared by both the procedures of Reynolds[18] and Searles and Lutz.[19] In the former, the sodium carbonate-catalyzed decomposition of ethylene monothiolcarbonate (D.P.I), a steam-jacketed reflux condenser was necessary to minimize carry-over of the starting cyclic ester.[24] The latter procedure was found to be convenient in that no impurities in the product were detected *via* infrared and vapor phase chromatography.

The ethylene sulfide was conveniently stored in benzene solution at −25°.

Thiolethylation Procedures.—The following are typical examples of the procedures used for the thiolethylation of various amino compounds.

a. 2-(2-Methoxyethyl)aminoethanethiol.—A solution of 146 g. (1.92 moles) of 2-methoxyethylamine (D.P.I., previously dried over potassium hydroxide and redistilled) in 200 ml. of anhydrous benzene in a 1-l. four-necked flask,

(22) Melting points and boiling points are uncorrected.

(23) Elemental analyses were performed by Dr. Carol K. Fitz, 115 Lexington Avenue, Needham Heights 94, Massachusetts. Thiol analyses by titration with iodine and infrared spectra were determined by the Analytical Section of this laboratory.

(24) Less than 1% by carbonyl absorption in the infrared.

TABLE II

CHARACTERIZATION OF N-(2-MERCAPTOETHYLTHIOETHYL) DERIVATIVES OF ALKANOLAMINES

Compound	Total S/thiol S	Infrared absorption, μ —NH2+	Infrared absorption, μ —OH
$HOCH_2CH_2NHCH_2CH_2SCH_2CH_2SH \cdot HCl$	2.02	3.65(s) 6.30(s)	3.03(s) 9.25–9.45(s)
$HOCH(CH_3)CH(CH_3)NHCH_2CH_2SCH_2CH_2SH \cdot HCl$	2.1	3.66(s) 6.30(s)	3.03(s) 8.93–9.40(s)

TABLE III

EXPERIMENTAL VARIABLES IN THE THIOLETHYLATION OF *n*-HEXYLAMINE IN BENZENE

Amine: S molar ratio	S addition time, min.	Additional reflux time, min.	n-$C_6H_{13}NHCH_2CH_2SH$, % yield
2[a]	60	15	28
2	60	120	55
2	240	15	45
2	240	120	56
4	150	67.5	60
4	150	67.5	55
6	15	165	66
6	15	165	62
6	60	15	33
6	60	120	68
6	240	15	39
6	240	15	48
6	240	120	59

[a] Toluene used as reaction solvent.

fitted with stirrer, thermometer, ethylene sulfide capillary tube inlet, nitrogen inlet, Dean–Stark trap, and reflux condenser protected with drying tube, was heated to reflux with stirring under nitrogen. A solution of 29 g. (0.48 mole) of ethylene sulfide in 100 ml. of anhydrous benzene was added over a 4-hr. period at reflux.[25] The mixture was then refluxed for 2 hr.

The mixture was filtered through Celite, the solvent removed from the filtrate, and the liquid thiolic residue distilled under reduced pressure under nitrogen to give 37.1 g. (57%) of 2-(2-methoxyethyl)aminoethanethiol, b.p. 82–86° (17 mm.), $n^{20}D$ 1.4767.

b. **2-*n*-Hexylaminoethanethiol.**—A solution of 101 g. (1.0 mole) of *n*-hexylamine in 200 ml. of anhydrous benzene in a five-necked 1-l. flask fitted with stirrer, addition funnel, thermometer, nitrogen inlet tube, and Dean–Stark trap with condenser connected to a gas bubbler was dried azeotropically by refluxing for 1 hr. To the dried refluxing solution was added in 15 min. a solution of 10 g. (0.166 mole) of ethylene sulfide in 100 ml. of anhydrous benzene followed by refluxing for 165 min. After solvent removal and recovery of unchanged amine by distillation at 20 mm., the pressure was reduced further to distil the product; yield 17.5 g. (66%), b.p. 85–86° (3.5 mm.), $n^{20}D$ 1.4709, d^{20}_4 0.892.

c. **2-(2-Mercaptoethyl)aminoethanol.**—A solution of 55 g. (0.92 mole) of ethylene sulfide in 100 ml. of benzene was added dropwise in 200 min. to a refluxing solution of 560 g. (9.2 moles) of ethanolamine in a mixture of 2880 ml. of benzene and 320 ml. of absolute ethanol contained in a three-necked, 5-l. flask fitted with stirrer, reflux condenser, and pressure-equalizing dropping funnel through which a flow of nitrogen was admitted. Refluxing was continued an additional hour. The oily residue which remained after solvent removal was distilled under reduced pressure to yield 44.4 g. (40% yield) of the monothiol, b.p. 66–69° (0.03 mm.), $n^{20}D$ 1.5379, d^{20}_4 1.139.

A higher boiling fraction, identified as 2-(2-mercaptoethylthioethyl)aminoethanol, was also obtained, yield 17.8 g. (21%), b.p. 123–124° (0.1 mm.), $n^{20}D$ 1.5563.

d. **2-(6-Aminohexyl)aminoethanethiol.**—A solution of 200 g. (1.72 moles) of 1,6-hexanediamine in 300 ml. of benzene in a five-necked, 1-l. flask fitted with stirrer, addition funnel, thermometer, nitrogen inlet tube, and Dean–Stark trap with condenser connected to a gas bubbler was dried azeotropically by refluxing for 1 hr. To the dried refluxing mixture was added dropwise in 2 hr. a solution of 12.9 g. (0.215 mole) of ethylene sulfide in 100 ml. of benzene followed by refluxing for 2 hr. After solvent removal the product was distilled under reduced pressure to give the desired 2-(6-aminohexyl)aminoethanethiol, 21.7 g. (57%), b.p. 88° (0.13 mm.), m.p. 38–40°.

Aminothiol Hydrochlorides.—The hydrochloride salts were prepared from the free aminothiols by use of either anhydrous hydrogen chloride in ethanol solution or aqueous hydrochloric acid solution. The resulting solid derivatives were purified by recrystallization from appropriate alcoholic solvents; the oils were purified by extraction.

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(25) For this addition the episulfide solution was pumped from a reservoir by a small metering pump (Distillers Co., Ltd., distributed by Marton Equip., Inc., Beverly, Massachusetts) through 2-mm. Kel-F tubing to a capillary inlet placed 3–6 cm. above the liquid level. The rate of addition was 0.4–0.5 ml./min.