Water and then hydrochloric acid were added to the reaction vessel; the mixture was extracted with ether. The ether solution was extracted with 2 *N* sodium hydroxide solution. Work-up of the alkaline aqueous solution yielded 129 mg. of crude phenol, identified by its characteristic odor and infrared spectrum. Work-up of the ether solution yielded 7.121 g. of a yellow oil, the infrared spectrum of which was almost reproduced by a mixture of 80% benzophenone and 20% triphenylcarbinol. (The ratio of intensities of absorption at 6.72 and 6.94 μ can be used for quantitative analysis of such mixtures.)

A portion of the crude product, 0.951 g., was chromatographed on 40 g. of acid-washed alumina (Merck). Oily fractions 4–28, eluted with hexane through 50:50 hexane–benzene, were combined (589 mg.), dissolved in ether–pentane, and cooled to −20°, yielding 557 mg. of benzophenone in three crops, m.p. 46–48°. The yield of benzophenone based on 2-phenyl-1,3-dioxolane is therefore no less than 70%. Crystalline fractions 30–35, eluted with benzene, all showed the characteristic infrared spectrum of triphenylcarbinol. They were combined, yielding 184 mg. with m.p. >150°, corresponding to a yield of triphenylcarbinol based on 2-phenyl-1,3-dioxolane of 15%. Crystallization of the combined triphenylcarbinol fractions from ether–pentane at room temperature yielded 131 mg., m.p. 159–161°, almost indistinguishable from twice crystallized authentic triphenylcarbinol, m.p. 160–162°.

Bisdithiocarbonate and Related Analogs of 2-Aminoethanethiol[1]

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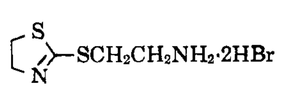
Certain modifications of the mercapto group of 2-aminoethanethiol have resulted in compounds whose radioprotective properties are not dependent *a priori* on simple release of the parent agent.[2] Continued evaluation of such changes may lead to an effective, yet relatively nontoxic antiradiation agent. In this work the excellent method provided by Crawhall and Elliott[3] for the conversion of 2-(alkylthio)-2-thiazolines to the corresponding *S*-alkyl *S'*-2-aminoethyl dithiocarbonate hydrochlorides has been extended to the preparation of several other dithiocarbonate derivatives of 2-aminoethanethiol.

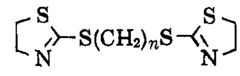
2-(2-Aminoethylthio)-2-thiazoline dihydrobromide (I) was hydrolyzed in refluxing 6 *N* hydrobromic acid to give *S,S'*-bis(2-aminoethyl) dithiocarbonate dihydrobromide (II). The dihydrochloride corresponding to II had previously been isolated as one of the products of prolonged hydrolysis of 2-thiazolidinethione in refluxing concentrated hydrochloric acid.[4] Hydrolysis of the 2,2'-(alkylenedithio)bis-2-thiazolines (IIIa–e) in 6 *N* hydrochloric (or hydrobromic) acid gave the corresponding *S,S'''*-bis(2-aminoethyl) *S',S''*-alkylene bisdithiocarbonate dihydrohalides (IVa–e). The intermediate bisthiazolines were obtained in good yields from 2-thiazolidinethione and the appropriate dibromoalkane in *N,N*-dimethylformamide with potassium carbonate as acid acceptor, the crude products so obtained being used without further purification. The two lower members of the series, 2,2'-(methylenedithio)bis-2-thiazoline (IIIa) and 2,2'-(ethylenedithio)bis-2-thiazoline (IIIb), were isolated as characterizable solids. Hydrolysis of IIIb was carried out in 6 *N* hydrobromic acid instead of the usual 6 *N* hydrochloric acid, and therefore *S,S'''*-bis(2-aminoethyl) *S',S''*-ethylene bisdithiocarbonate was isolated as the dihydrobromide IVb.



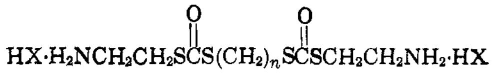
I

$$HBr\cdot H_2NCH_2CH_2SCSCH_2CH_2NH_2\cdot HBr \quad (C{=}O)$$

II



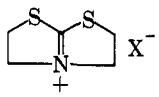
IIIa, $n = 1$
b, $n = 2$
c, $n = 3$
d, $n = 4$
e, $n = 5$



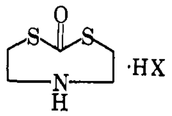
$$HX\cdot H_2NCH_2CH_2S\overset{O}{\overset{\|}{C}}S(CH_2)_nS\overset{O}{\overset{\|}{C}}SCH_2CH_2NH_2\cdot HX$$

IVa, $n = 1$; X = Cl
b, $n = 2$; X = Br
c, $n = 3$; X = Cl
d, $n = 4$; X = Cl
e, $n = 5$; X = Cl

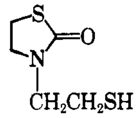
The preparation of 2,3,5,6-tetrahydrothiazolo[2,3-*b*]thiazolium chloride (Va) from 2,2'-dichlorodiethylamine and carbon disulfide has been recently described,[5,6] and the structural similarity of Va to the thiazolines described above suggests that it might be converted in hydrochloric acid to the cyclic dithiocarbonate hydrochloride VI. Refluxing a solution of Va in 6 *N* hydrochloric acid in the usual way resulted in a rather high recovery of unchanged starting material, but prolonged refluxing of a solution of Va in concentrated hydrochloric acid gave in medium yield a distillable nitroprusside-positive oil, whose infrared absorption spectrum is incompatible with the spectra of the dithiocarbonates described above. The identity of the oil as 3-(2-mercaptoethyl)-2-thiazolidinone (VII) was strongly indicated by a spectral comparison with 2-thiazolidinone itself and confirmed by elemental analyses and iodometric assay. Seto and Ikegami[6] iso-



Va, X = Cl
b, X = Br



VI



VII

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[1] This investigation was supported by the U. S. Army Medical Research and Development Command under Contract No. DA-49-193-MD-2028.

[2] For example: (a) R. Shapira, D. G. Doherty, and W. T. Burnett, Jr., *Radiation Res.*, **7**, 22 (1957); (b) B. Holmberg and B. Sörbo, *Nature*, **183**, 832 (1959); (c) B. Hansen and B. Sörbo, *Acta Radiol.* **56**, 141 (1961); (d) W. O. Foye, J. R. Marshall, and J. Mickles, *J. Pharm. Sci.*, **52**, 406 (1963); (e) L. Field, A. Ferretti, R. R. Crenshaw, and T. C. Owen, *J. Med. Chem.*, **7**, 39 (1964).

[3] J. C. Crawhall and D. F. Elliott, *J. Chem. Soc.*, 3094 (1952).

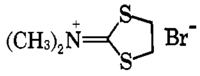
[4] R. J. Gaul and W. J. Fremuth, *J. Org. Chem.*, **25**, 869 (1960).

[5] W. Schulze, G. Letsch, and H. Willitzer, *J. prakt. Chem.*, [4]**19**, 101 (1963).

[6] S. Seto and Y. Ikegami, *Bull. Chem. Soc. Japan*, **36**, 730 (1963).

lated VII from the reaction of Va with water alone and characterized their product as a lead salt. Apparently the hydrolysis of Va proceeds more readily in water alone than in hydrochloric acid, in which the yield of VII may be limited by equilibrium. The thiazolidinone VII has also been proposed as an intermediate in the reaction of Va in sodium hydroxide solution.[5,6]

In the preparation of IIIb the formation of the bromide Vb as a by-product was considered a possibility, since ring closure is known to occur by the interaction of similar thioanions and 1,2-dihaloethanes: for example, ring closure (on N-1) occurred in an attempted 2-chloroethylation of purine-6(1*H*)-thione.[7] It was also been observed in this laboratory that the reaction of sodium dimethyldithiocarbamate with either 1-bromo-2-chloroethane or 1,2-dibromoethane gives 1,3-dithiolan-2-ylidenedimethylammonium bromide (VIII), ring closure occurring on sulfur instead of nitrogen.[8] The formation of Vb was not observed, even when a favorable ratio of reactants was used.

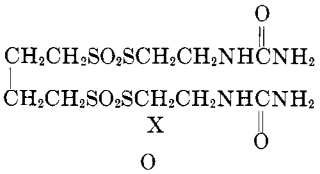


VIII

The 2-aminoethylation of disodium 1,4-butanebisthiosulfonate was accomplished in a manner similar to that already described[9] for the reaction of 2-bromoethylamine hydrobromide and potassium methanethiosulfonate. The product, *S,S'*-bis(2-aminoethyl) 1,4-butanebisthiosulfonate dihydrobromide (IX), is the first bis analog of this type to be reported. The conversion of IX to *S,S'*-bis(2-ureidoethyl) 1,4-butanebisthiosulfonate (X) was brought about by the action of potassium cyanate in water, as was the conversion of *S*-2-aminoethyl 2-aminoethanethiosulfonate dihydrochloride to the corresponding bisureido derivative XI. Similar attempts to prepare the bisureido derivatives of the dithiocarbonates described above gave erratic results. The isolation of pure bisurea from II could not be repeated on a larger scale. Attempted conversions of IVa resulted in cleavage of the dithiocarbonate linkage; products of low nitrogen content were isolated from IVb and IVd. Analyses and infrared absorption spectra of the recrystallized product from IVd suggested formation (at 45 and 90°) of a bisureido biuret from two molecules of the desired bisurea.

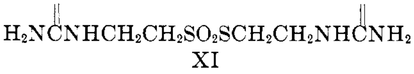
$$\begin{array}{l}CH_2CH_2SO_2SCH_2CH_2NH_2\cdot HBr\\ |\\ CH_2CH_2SO_2SCH_2CH_2NH_2\cdot HBr\end{array}$$

IX



$$\begin{array}{l}CH_2CH_2SO_2SCH_2CH_2NH\overset{O}{\overset{\|}{C}}NH_2\\ |\\ CH_2CH_2SO_2SCH_2CH_2NH\underset{O}{\underset{\|}{C}}NH_2\end{array}$$

X



$$H_2N\overset{O}{\overset{\|}{C}}NHCH_2CH_2SO_2SCH_2CH_2NH\overset{O}{\overset{\|}{C}}NH_2$$

XI

Experimental[10]

***S,S'*-Bis(2-aminoethyl) Dithiocarbonate Dihydrobromide (II).**—A solution of crude 2-(2-aminoethylthio)-2-thiazoline dihydrobromide[11] (3.24 g., *ca.* 10 mmoles) in 6 *N* hydrobromic acid (17 ml.) was refluxed for 4 hr., filtered, and chilled. The white solid that precipitated was dried *in vacuo* over sodium hydroxide and phosphorus pentoxide; the yield of crude II, which decomposed at 229-231° without melting, was 2.09 g. (*ca.* 61%). For analysis a small sample was recrystallized from methanol, ground fine, and dried *in vacuo* over phosphorus pentoxide at 100°; the analytical sample decomposed at 238-239° without melting, ν_{max}^{KBr} 1645 (C=O) and 870 cm.$^{-1}$ (S-C-S).

Anal. Calcd. for $C_5H_{12}N_2OS_2\cdot HBr$: C, 17.55; H, 4.12; S, 18.74. Found: C, 17.84; H, 4.14; S, 18.9.

This procedure carried out on a 0.1-mole scale gave a 58% yield of recrystalllized II in two crops.

General Procedure for the Preparation of 2,2'-(Alkylenedithio)-bis-2-thiazolines (IIIa-e).—To a well-stirred mixture of anhydrous potassium carbonate (29 g., 0.21 mole), 2-thiazolidinethione (25 g., 0.21 mole), and *N,N*-dimethylformamide (75 ml.) was added dropwise over a 1-hr. period a solution of the appropriate dibromoalkane (0.10 mole) in the same solvent (25 ml.) at such a rate that the reaction temperature did not exceed 50°. The resulting mixture was heated at 60-70° for 2 hr., cooled, and poured into water (1 l.). The first two members of the series precipitated as solids, the others as oils.

Crude 2,2'-(methylenedithio)bis-2-thiazoline (IIIa) was obtained as a yellow solid in 94% yield by evaporation of a filtered benzene solution of the precipitate to dryness under reduced pressure. Triturating a 0.5-g. sample in two 2.5-ml. portions of ethanol and drying *in vacuo* gave a 49% recovery of IIIa, m.p. 53-54°, ν_{max}^{KBr} 1565 cm.$^{-1}$ (C=N).

Anal. Calcd. for $C_7H_{10}N_2S_4$: C, 33.57; H, 4.02; S, 51.21. Found: C, 33.83; H, 4.04; S, 51.7.

The precipitate of 2,2'-(ethylenedithio)bis-2-thiazoline (IIIb) was washed with water and dried *in vacuo* (yield 91%), and for analysis a small sample was recrystallized from ethanol as white plates, m.p. 124-126°, ν_{max}^{KBr} 1575 cm.$^{-1}$ (C=N).

Anal. Calcd. for $C_8H_{12}N_2S_4$: C, 36.33; H, 4.57; S, 48.49. Found: C, 36.45; H, 4.63; S, 48.5.

The bisthiazolines that separated as oils were extracted with four 250-ml. portions of benzene; and the benzene extracts, which were washed with three 50-ml. portions of water and dried over magnesium sulfate, were evaporated under reduced pressure, the evaporations being repeated several times after successive additions of ethanol. Finally the oils were dried for 1 hr. at 60° at about 1 mm. 2,2'-(Trimethylenedithio)bis-2-thiazoline (IIIc), 2,2'-(tetramethylenedithio)bis-2-thiazoline (IIId), and 2,2'-(pentamethylenedithio)bis-2-thiazoline (Vc) were thus obtained as crude oils in 90-95% yields, and were used without further purification.

General Procedure for the Preparation of *S,S'''*-Bis(2-aminoethyl) *S',S''*-Alkylene Bisdithiocarbonate Dihydrohalides (IVa-e).—A suspension of crude 2,2'-(alkylenedithio)bis-2-thiazoline in 6 *N* hydrochloric (or hydrobromic) acid (16.7 ml. per mmole of bisthiazoline) was heated under reflux for 4 hr. The reaction mixture was filtered hot to remove a small amount of insoluble gum and cooled. The solid that precipitated was dried *in vacuo* over phosphorus pentoxide and sodium hydroxide. For analysis small samples were recrystallized from ethanol with Norit treatment; the remaining larger samples, from methanol. These recrystallizations gave fair recoveries (30-70%) of purified products. Typical preparations by this procedure are summarized in Table I.

3-(2-Mercaptoethyl)-2-thiazolidinone (VII).—A solution of unrecrystallized hydrated 2,3,5,6-tetrahydrothiazolo[2,3-*b*]thiazolium chloride[7] (Va, 18 g.) in concentrated hydrochloric acid (21 ml.) was refluxed for 72 hr. The cooled solution was diluted with water (79 ml.) and extracted with three 50-ml. portions of chloroform. The chloroform extract was washed with three 25-ml. portions of water, dried over magnesium sulfate, and evaporated to dryness under reduced pressure; the residue was an oil (7.8 g., n^{25}D 1.5833). Vacuum distillation through a Claisen head gave IX as a colorless oil, b.p. 113-116° (0.3 mm.). The yield was 6 8 g. (50% based on Va as a dihydrate), iodometric assay 98%. Redistillation gave the analytical sample, b.p. 106-108° (0.2 mm.), n^{25}D 1.5828, ν_{max}^{film} 2550 (SH, weak) and 1670 cm.$^{-1}$ (C=O, strong).

Anal. Calcd. for $C_5H_9NOS_2$: C, 36.78; H, 5.55; N, 8.58. Found: C, 36.64; H, 5.69; N, 8.67.

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[7] R. W. Balsiger, A. L. Fikes, T. P. Johnston, and J. A. Montgomery, *J. Org. Chem.*, **26**, 3446 (1961).

[8] *Cf.* K. C. Kennard and J. A. VanAllan, *ibid.*, **24**, 470 (1959).

[9] T. P. Johnston and A. Gallagher, *ibid.*, **26**, 3780 (1961).

[10] Melting points were determined with a Mel-Temp apparatus (unless indicated otherwise) and are uncorrected; infrared absorption spectra, with a Perkin-Elmer Model 221 spectrophotometer.

[11] R. C. Clapp, L. Long, Jr., and T. Hasselstrom, *J. Org. Chem.*, **26**, 1666 (1961).

TABLE I

S,S'''-BIS(2-AMINOETHYL) *S',S''*-ALKYLENE BISDITHIOCARBONATE DIHYDROHALIDES

Compound	Crude yield, %	M.p.,[a] °C.	ν_{max}^{KBr}, cm.$^{-1}$ C=O[b]	ν_{max}^{KBr}, cm.$^{-1}$ S-C-S[b]	Formula	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	S, % Calcd.	S, % Found
IVa	57	184–185 dec.	1645	875	$C_7H_{14}N_2O_2S_4 \cdot 2HCl$	23.39	23.51	4.49	4.64	35.69	35.5
IVb	63	240–241 dec.	1640	880	$C_8H_{16}N_2O_2S_4 \cdot 2HBr$	20.78	20.94	3.92	3.59	27.74	27.8
IVc	59	215–216 dec.	1650	875	$C_9H_{18}N_2O_2S_4 \cdot 2HCl$	27.90	28.06	5.20	5.46	33.10	33.1
IVd	51	210–211 dec.	1650	875	$C_{10}H_{20}N_2O_2S_4 \cdot 2HCl$	29.91	29.86	5.52	5.49	31.94	32.1
IVe	55	197–199 dec.	1650	875	$C_{11}H_{22}N_2O_2S_4 \cdot 2HCl$	31.79	31.94	5.82	5.70	30.87	30.6

[a] Varied widely with rate of heating, typical values being reported. [b] Strong absorption; *cf.* ref. 4.

1,3-Dithiolan-2-ylidenedimethylammonium Bromide (VIII).—A solution of sodium dimethyldithiocarbamate hemihydrate[12] (4.00 g., 26.3 mmoles) in methanol (75 ml.) was added dropwise to a solution of 1,2-dibromoethane (4.5 ml., 53 mmoles) in the same solvent (10 ml.) over a period of 15–20 min. The reaction mixture was then stirred for 3 hr., maximum temperature being 31°. The methanol was removed under reduced pressure and the residual yellow solid was triturated in chloroform (100 ml.). The insolubles were removed by filtration, and the filtrate was evaporated to dryness under reduced pressure. The white residue after trituration in benzene was dried *in vacuo* at 63° over phosphorus pentoxide, yielding 3.86 g. (64%) of VIII, m.p. 174° (Kofler Heizbank). The same product was obtained from 1-bromo-2-chloroethane, sodium chloride having precipitated from the reaction mixture. The analytical sample was obtained as white prisms, m.p. 174°, by recrystallization from acetonitrile; λ_{max} in mμ ($\epsilon \times 10^{-3}$): 249 (12.2) at pH 1, 249 (12.7) at pH 7, 250 (13.3) in methanol; ν_{max}^{KBr} 1595 cm.$^{-1}$ (C=N, strong). The product isolated was the same when the ratio of dihalide to dithiocarbamate was varied from 1:1 to 4:1, and also when the reaction temperature was increased to 66° by external heating.

Anal. Calcd. for $C_5H_{10}BrNS_2$: C, 26.32; H, 4.42; N, 6.14. Found: C, 26.48; H, 4.59; N, 6.24.

***S,S'*-Bis(2-aminoethyl) 1,4-Butanebisthiosulfonate Dihydrobromide (IX)**.—Crude 1,4-butanedisulfonyl chloride[13] (m.p. 76–77°, 17.8 g., about 70 mmoles) was added in portions over a 30-min. period to a cold and well-stirred aqueous solution (100 ml.) of sodium hydroxide (11.2 g.) that had been saturated with hydrogen sulfide at 15°. The resulting mixture was stirred at 5° for 2 hr., the pH changing from 11 to 5, and at room temperature for 4 hr., the pH being maintained at 8 by the addition of 0.2 *N* sodium hydroxide solution (total about 30 ml.). A small amount of solid was removed by filtration, and the filtrate was evaporated to dryness under reduced pressure. The residual solid was extracted with *N,N*-dimethylformamide, first with four 50-ml. portions at room temperature and then with three 50-ml. portions hot. Evaporation *in vacuo* of the combined extracts left a yellow solid, which was rendered white by trituration in 2-propanol. The yield of crude disodium 1,4-butanedbisthiosulfonate (20.0 g.) was nearly quantitative.

To a well-stirred suspension of crude disodium 1,4-butanebisthiosulfonate (6.5 g., about 20 mmoles) in *N,N*-dimethylformamide (30 ml.) was added a solution of 2-bromoethylamine hydrobromide (8.61 g., 42.0 mmoles) in the same solvent (20 ml.). The resulting solution was heated at 80-90° for 5 hr. and evaporated to dryness under reduced pressure, the evaporation being repeated several times after successive additions of ethanol. The solid residue was extracted with three 50-ml. portions of methanol to remove sodium bromide, and the methanol-insoluble solid was dried *in vacuo* (8.03 g.). A solution of the crude product in water (100 ml.) was treated with Norit and evaporated to dryness *in vacuo*. Trituration of the white crystalline residue with two 25-ml. portions of methanol left 6.18 g. of IX, m.p. 177–178° dec. An additional 1.30 g., m.p. 176–177° dec., was obtained from the methanol washings, the total yield being about 75%. For analysis a small sample was recrystallized from methanol-ether (m.p. 171-172° dec.).

Anal. Calcd. for $C_8H_{20}N_2O_4S_4 \cdot 2HBr$: C, 19.28; H, 4.45; S, 25.74. Found: C, 19.55; H, 4.52; S, 25.7.

***S,S'*-Bis(2-ureidoethyl) 1,4-Butanebisthiosulfonate (X)**.—To a stirred solution of *S,S'*-bis(2-aminoethyl) 1,4-butanebisthiosulfonate dihydrobromide (IX, 2.7 g., 5.5 mmoles) in water (50 ml.) was added dropwise a solution of potassium cyanate (0.89 g., 11 mmoles) in the same solvent (25 ml.). After about 15 min. the solution became cloudy, and solid began to precipitate. The mixture was stirred overnight at room temperature; the solid was collected, washed with water, and dried *in vacuo* over phosphorus pentoxide, yielding 1.8 g. (79%) of crude X, m.p. 177–179° dec. with predarkening. The crude product was recrystallized from water in 84–92% recovery and dried as described above, m.p. 183–184°.

Anal. Calcd. for $C_{10}H_{22}N_4O_6S_4$: C, 28.42; H, 5.25; N, 13.25. Found: C, 28.44; H, 5.21; N, 13.27.

***S*-2-Ureidoethyl 2-Ureidoethanethiosulfonate (XI)**.—A solution of potassium cyanate (0.811 g., 10.0 mmoles) in water (5 ml.) was added dropwise to a stirred solution of *S*-2-aminoethyl 2-aminoethanethiosulfonate dihydrochloride[14,15] (1.28 g., 5.00 mmoles) in water (10 ml.). The resulting solution was stirred at room temperature for 5 hr. and then evaporated to dryness under reduced pressure (oil pump) at room temperature, the evaporation being repeated several times after successive additions of methanol. The solid residue was extracted with three 5-ml. portions of *N,N*-dimethylformamide and the combined extracts were evaporated to dryness *in vacuo* at less than 50°. Evaporations were again repeated after successive additions of methanol until the oily residue solidified. Recrystallization from ethanol (100 ml.) gave crude XI as a cream-colored solid, which was dried *in vacuo* (0.62 g., m.p. 115–117° dec. with presoftening). Analytically pure XI, m.p. 151–153° dec., was obtained by diluting a Norit-treated solution of the crude product (250 mg.) in warm methanol (10 ml.) with an equal volume of ether. The recovery (108 mg.) corresponded to an over-all yield of 20%.

Anal. Calcd. for $C_6H_{14}N_4O_4S_2$: C, 26.65; H, 5.22; S, 23.72. Found: C, 26.81; H, 5.25; S, 23.9.

The yield was little improved when the above described procedure was repeated on a 25-mmole scale with omission of the initial ethanol recrystallization. The product, twice recrystallized from 1:1 methanol–ether, melted at 145–146° dec.

Acknowledgment.—The authors are indebted to Mrs. T. N. Carruthers, Jr., and Mr. G. S. McCaleb for preparation of VIII, and to Dr. W. J. Barrett and associates of the Analytical Section of this institute for microanalyses and spectra.

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[12] M. Delépine, *Bull. soc. chim. France*, [4]**3**, 650 (1908).

[13] B. Helferich and H. Grünert, *Ber.*, **74B**, 1531 (1941).

[14] L. Field, T. C. Owen, R. R. Crenshaw, and A. W. Bryan, *J. Am. Chem. Soc.*, **83**, 4414 (1961).

[15] Distillation Products Industries, Rochester 3, N. Y.

The Preparation of Hexaphenylcyclotrisilthiane and of Tetraphenylcyclodisilthiane[1]

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In the course of investigations on the displacement of halogen or amino groups on silicon with sulfhydryl or $-S-SiR_3$ groups, two cyclosilthianes, I and II, have

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