[COMMUNICATION NO. 1970 FROM THE KODAK RESEARCH LABORATORIES]

Dithiocarbamates. II. The Formation of 1,3-Dithiane, 1,3-Dithiolane, and 1,3-Dithiepane Quaternary Salts

KENNETH C. KENNARD AND JAMES A. VANALLAN

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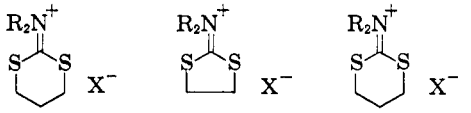
The hitherto unknown 1,3-dithiolan-, 1,3-dithian-, and 1,3-dithiepan-2-dialkylimmonium salts have been prepared by the reaction of 2-hydroxyethyl, 3-hydroxypropyl, and 4-hydroxybutyl dialkyldithiocarbamate, respectively, with *p*-toluenesulfonyl chloride. 1,3-Dithian-2-diethylimmonium perchlorate is decomposed by alkali to 1,3-propanedithiol, 3-mercaptopropyl diethylthiolcarbamate, and bis(3-diethylthiolcarbamatopropyl)disulfide. The 4-, 5-, and 6-membered ring compounds show a characteristic absorption peak between 262 and 276 mμ.

It has been discovered that certain hydroxyalkyl dialkyldithiocarbamates cyclize in the presence of *p*-toluenesulfonyl chloride. The product of this reaction is a 1,3-dithiane (I), a 1,3-dithiolane (II), or a 1,3-dithiepane (III), depending on whether the starting dithiocarbamate ester is the 3-hydroxypropyl, the 2-hydroxyethyl, or the 4-hydroxybutyl, respectively. Presumably, the *p*-toluenesulfonate ester is an intermediate in this reaction.

$$R_2NCS_2CH_2CH_2CH_2OH + C_7H_7SO_2Cl \longrightarrow R_2NCS_2CH_2CH_2CH_2O_3SC_7H_7$$

$$R_2NCS_2CH_2CH_2CH_2O_3SC_7H_7 \xrightarrow{\Delta} I$$



I II III

The ring closure was effected by two methods. Method A consisted in the addition of *p*-toluenesulfonyl chloride to the dithiocarbamate in dimethylformamide with a flow of nitrogen to entrain the by-product, hydrogen chloride. The product was isolated as the perchlorate or the tetraphenylboron salt.

One drawback to this method is the strong solubilizing effect of the dimethylformamide in the solution from which the product was recovered. The use of a more concentrated reaction solution produced resinous by-products which contaminated the salts.

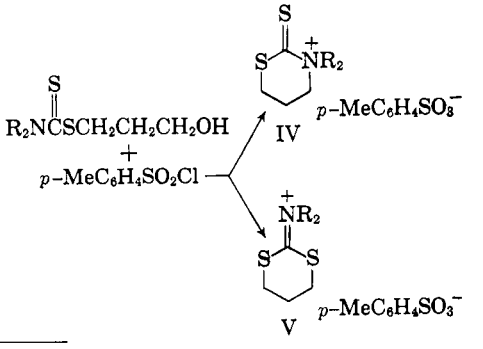
In Method B, the initial reaction was carried out in benzene in the presence of triethylamine. After removal of the triethylamine hydrochloride by filtration, ring closure was effected by heating under reflux. The product was isolated as described previously. This method suffered from the lack of a highly polar solvent which would facilitate the transformation of nonpolar reactants to ionic products. Ultimate yields would probably require the use of a solvent with a high dipole which could be removed after the reaction was completed.

Method B was used to prepare the five-membered ring compound, 1,3-dithiolan-2-diethylimmonium tetraphenylboron, and the seven-membered ring compound, 1,3-dithiepan-2-diethylimmonium perchlorate.

The intermediate hydroxyalkyl dialkyldithiocarbamates are high-boiling or undistillable oils of fair thermal stability. The pure compounds are slightly yellow in color and possess unusually high refractive indices. As may be seen in Table I, their ultraviolet absorption characteristics closely resemble those of other dithiocarbamates.[1]

The dithianes are white, crystalline solids. The *p*-toluenesulfonate salts are hygroscopic and water-soluble, while the perchlorate and tetraphenylboron salts are nonhygroscopic and less water-soluble. The tetraphenylboron salt is especially convenient for homologs bearing small groups on the nitrogen atom. Unlike the dithiocarbamates which show two ultraviolet absorption peaks, the dithianes show only one peak. The dithianes are readily hydrolyzed by dilute alkali. Only one dithiolane and dithiepane were prepared, but they appeared to resemble the dithianes in all respects.

The cyclization of 3-hydroxypropyl dialkyldithiocarbamates conceivably might result in a compound possessing either of two structures. Ring closure on the nitrogen atom would produce the thiazine structure, IV, while alkylation of the un-



IV V

(1) See Part I for a discussion of the properties of the dithiocarbamates.

(2) C. H. Grogan, L. M. Rice, and E. E. Reid, *J. Org. Chem.*, **20**, 50 (1955).

(3) F. Arndt and F. Bielich, *Ber.*, **56**, 2276 (1923).

(4) H. L. Wheeler and B. Barnes, *Am. Chem. J.*, **24**, 60 (1900). H. L. Wheeler and T. B. Johnson, *Am. Chem. J.*, **24**, 189 (1900). H. L. Wheeler and G. K. Dustin, *Am. Chem. J.*, **24**, 424 (1900).

TABLE I

DITHIOCARBAMATES

$R_2NCS_2(CH_2)_\eta OH$

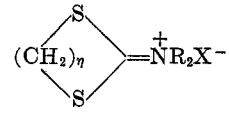
No.	R	η	% Yield	B.P., °C./mm. Hg	n_D^{25}	λ_{max}[a] (mμ)	$10^{-3}\epsilon$	Analysis Calcd./Found % C	% H	% N	% S
XII	CH_3	3	87	139–141/0.5	1.6005[b]	248	9.3	40.2	7.3	7.8	
						276	10.5	40.3	7.4	7.5	
XIII	C_2H_5	3	75	121–122/0.1	1.5726	252	9.4	46.4	8.3	6.8	
						279	10.0	46.1	8.3	6.9	
XIV	n-C_3H_7	3	75	129.5/0.1	1.5559	253	9.3	51.1	9.0	5.9	27.3
						279	10.5	51.0	9.2	5.6	27.4
XV	C_5H_{10}	3	50	162–163/0.2	1.5923			49.4	7.8	6.4	29.2
								48.9	7.7	6.0	28.7
XVI	$C_6H_5CH_2$	3	62	[c]	1.6273	254	11.0	65.3	6.4	4.3	19.2
						282	10.5	65.2	6.4	4.0	19.1
XVII	C_2H_5	2	80	122/0.2	1.5861	251	9.2	43.5	7.8	7.2	
						270	10.9	43.6	7.9	7.1	
XVIII	C_2H_5	4	82	[c]	1.5650					6.3	
										6.2	

XII. 3-Hydroxypropyl dimethyldithiocarbamate.
XIII. 3-Hydroxypropyl diethyldithiocarbamate.
XIV. 3-Hydroxypropyl di-*n*-propyldithiocarbamate.
XV. 3-Hydroxypropyl piperidine-*N*-carbodithioate.
XVI. 3-Hydroxypropyl dibenzyldithiocarbamate.
XVII. 2-Hydroxyethyl diethyldithiocarbamate.
XVIII. 4-Hydroxybutyl diethyldithiocarbamate.

[a] In methanol solution. [b] Temperature of 24°. [c] Purified chromatographically.

TABLE II

QUATERNARY SALTS



No.	R	η	X^-	% Yield	M.P., °C.	λ_{max}[a] (mμ)	$10^{-3}\epsilon$	Analysis Calcd./Found % C	% H	% N	% S
XIX	CH_3	3	$C_7H_7SO_3$	35	136–138	262	12.7	46.7	5.7	4.2	
								46.9	5.7	4.2	
XX	C_2H_5	3	ClO_4[b]	64–69	125.5–127	266	18.4	33.2	5.6	4.8	21.1
								33.3	5.4	5.0	21.1
XXI	n-C_3H_7	3	ClO_4	53	153–155	268	14.8	37.9	6.3	4.4	20.2
								38.0	6.3	4.2	20.2
XXII	C_5H_{10}	3	ClO_4	26	142.5–144.5	268	12.0	35.9	5.4	4.6	21.2
								35.4	5.1	4.5	21.1
XXIII	$C_6H_5CH_2$	3	ClO_4	36	134	271	13.7	52.2	4.9		
								52.1	4.8		
XXIV	C_2H_5	2	$(C_6H_5)_4$[b]	42	208	256[c]	17.2	75.2	6.9		
								75.4	7.0		
XXV	C_2H_5	4	ClO_4	29	99–100	276[d]	11.2	35.6	5.9	4.6	
								35.6	5.8	4.5	

XIX. 1,3-Dithian-2-dimethylimmonium *p*-toluenesulfonate, recrystallized from acetone. This compound is very hygroscopic.
XX. 1,3-Dithian-2-diethylimmonium perchlorate.
XXI. 1,3-Dithian-2-di-*n*-propylimmonium perchlorate, recrystallized from acetone.
XXII. 1,3-Dithian-2-cyclopentamethylenimmonium perchlorate, recrystallized from acetone.
XXIII. 1,3-Dithian-2-dibenzylimmonium perchlorate, recrystallized from alcohol.
XXIV. 1,3-Dithiolan-2-diethylimmonium tetraphenylboron.
XXV. 1,3-Dithiepan-2-diethylimmonium perchlorate, recrystallized from water.

[a] In methanol solution. [b] Tetraphenylboron salt had m.p. 184°. [c] In dimethyl sulfoxide solution. [d] In water solution.

saturated sulfur atom would produce the dithiane structure, V. By analogy with the alkylation of thiourea,[2] monoalkyldithiocarbamates,[3] or thionocarbamates,[4] the dithiane seems to be the obvious answer. Furthermore, alkylation of the amide nitrogen atom, which is required for the thione formation, seems unlikely.

In order to establish the structure of the 1,3-

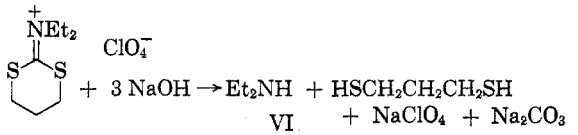
TABLE III

HYDROLYSIS FRAGMENTS

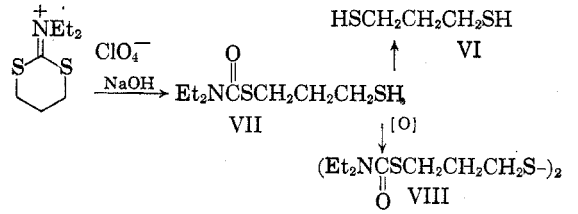
No.	Compound	B.P., °C./mm Hg	n_D^{25}	Analysis Calcd./Found %C	%H	%N	%S
VI	$HSCH_2CH_2CH_2SH$[a]	64/13	1.5406				
VII	$Et_2NC(=O)SCH_2CH_2CH_2SH$[b]	153–154/9	1.5258	46.4 46.4	8.2 8.2	6.8 6.8	30.9 31.2
VIII	$(Et_2NC(=O)SCH_2CH_2CH_2S)_2$[c]	228–230/0.1	1.5522	47.0 47.0	7.7 8.2	7.1 7.0	30.9 31.0

[a] S. D. Simpson, *Can. J. Res.*, **25B**, 20 (1947), b.p. 57°; J. R. Meadow and E. E. Reid, *J. Am. Chem. Soc.*, **56**, 2177 (1934), n_D^{20} 1.5403. [b] Distillation performed by Dr. Dorothy J. Beavers, of these Laboratories. This substance is a strong skin irritant. [c] The distillate, a slightly brown oil, was further purified chromatographically. Mol. wt. in benzene, 411; calculated, 412.

dithianes, the alkaline hydrolysis of a representative compound was studied. The complete alkaline hydrolysis of 1,3-dithian-2-diethylimmonium perchlorate was expected to proceed as shown in the formula. In practice, several organic fragments were

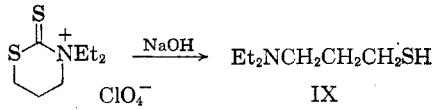


isolated, including 1,3-propanedithiol (VI), 3-mercaptopropyl diethylthiolcarbamate (VII), and bis(3-diethylthiolcarbamatopropyl) disulfide (VIII). Consequently, the hydrolysis scheme can be amended as follows:



That the carbamates were the thiol isomers and not the thione isomers was shown by their transparency to ultraviolet radiation. The properties of the hydrolysis fragments are summarized in Table III.

Under similar hydrolytic conditions, the thione would be expected to provide diethyl-3-mercaptopropylamine (IX). No trace of this amine was detected.

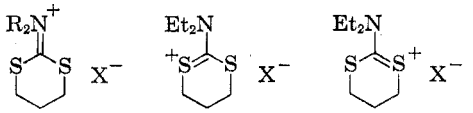


A polarographic study[5] of the alkaline hydrolysis of 1,3-dithian-2-diethylimmonium perchlorate also furnished evidence for the dithian structure. The polarogram recorded immediately after solution of the sample showed an anodic wave at −0.6 volt *vs.* S.C.E. (saturated calomel electrode) and a cathodic wave at −1.2 volts *vs.* S.C.E. These reduction waves were attributed to the sulfhydryl and carbon-nitrogen groups, respectively. After exhaustive hydrolysis, the reduction wave due to the carbon-nitrogen bond was absent, whereas the reduction wave due to the mercaptan appeared to increase.

In an independent experiment, the mercaptan formed in this alkaline hydrolysis was precipitated as the silver salt. Analysis of this precipitate showed the empirical formula of the mercaptide to agree well with 1,3-propanedithiol, the expected hydrolysis product of 1,3-dithian-2-diethylimmonium perchlorate.

Evidence for the presence of the unstable diethylcarbamic acid as a product of the complete alkaline hydrolysis was noted when the alkaline hydrolyzate was made slightly acid (to phenolphthalein) and refluxed. The solution gradually turned alkaline, as evidenced by the reappearance of the phenolphthalein color. The cycle could be repeated by adding more acid and refluxing. This was attributed to the decomposition of diethylcarbamic acid to carbon dioxide and its removal by refluxing.

It has been pointed out (Part I) that dithiocarbamates exhibit several resonance forms, and these have been assigned, both for theoretical and experimental reasons, to specific excited states of the molecule.[1,6] In the dithianes under discussion, there is also opportunity for resonance. Since



two of the states are equivalent, only one ultraviolet absorption peak is expected and only one was observed (Table II).

(5) The authors are grateful to Dr. E. P. Przybylowicz, of these Laboratories, for conducting the work with the polarograph and for analyzing the data.

(6) H. P. Koch, *J. Chem. Soc.*, 401, (1949).

EXPERIMENTAL

The boiling and melting points of all substances described here are uncorrected.

The hydroxyalkyl dialkyldithiocarbamates mentioned here were prepared from 2-bromoethanol, 3-bromopropanol, or 4-chlorobutanol, and the sodium salt of the requisite dithiocarbamic acid, using the general procedure described in Part I.

The syntheses of two of the cyclic quaternary salts, one by Method A and one by Method B, illustrate the general technique employed. The individual compounds are named, associated by Roman numerals, with the data in the tables and accompanied by any pertinent miscellaneous information below them.

Method A. 1,3-Dithian-2-diethylimmonium perchlorate (XX). A solution of 20.7 g. of 3-hydroxypropyl diethyldithiocarbamate (XIV) and 19.1 g. of *p*-toluenesulfonyl chloride in 50 ml. of dimethylformamide, with a stream of nitrogen to dispel the by-product, hydrogen chloride, was maintained for 1 hr. at 60° by intermittent cooling. The reaction solution, without the nitrogen stream, was heated further at 60° for 24 hr. The cooled solution was then poured into 200 ml. of water containing 15 g. of sodium perchlorate. The resulting white crystalline solid was recrystallized from water–acetone solution.

A solution of 0.005 mole of XX in 30 ml. of water was mixed with 0.0055 mole of sodium tetraphenylboron in 30 ml. of water. The resulting white solid was removed by filtration and recrystallized from dimethyl sulfoxide. The pure 1,3-dithian-2-diethylimmonium tetraphenylboron melted at 184°.

Method B. 1,3-Dithiolan-2-diethylimmonium tetraphenylboron (XXIV). A solution of 19.5 g. of 2-hydroxyethyl diethyldithiocarbamate (XVII) in 100 ml. of benzene containing 18 ml. of triethylamine was treated with 22 g. of *p*-toluenesulfonyl chloride. After the solution had been stirred for 3 hr., it was filtered; 16 g. of triethylamine hydrochloride remained on the filter. The filtrate was heated under reflux for 1.5 hr., after which 32 ml. of benzene-insoluble oil was separated. Volatiles were removed *in vacuo* from the warmed oil; the final weight of viscous oil was 20 g. A solution of 1.73 g. of this oil in 25 ml. of water was treated with 1.71 g. of sodium tetraphenylboron in 80 ml. of water. The white crystalline solid was removed from the cooled solution by filtration and recrystallized from dimethylsulfoxide.

Purification of 3-hydroxypropyl dibenzyldithiocarbamate (XVI). This compound appeared to decompose above 200° at a pressure of 0.03–0.04 mm. Consequently, it was purified chromatographically, by means of a 22-in. column of alumina with an outside diameter of 1.25 in., and benzene as the solvent. Fractions of about 50 ml. were collected; only those fractions which gave the proper analysis were employed. The pure compound is a very viscous oil.

Hydrolysis of 1,3-dithian-2-diethylimmonium perchlorate (XX). The relative yields of hydrolysis fragments varied with the mode of hydrolysis. A solution of 87 g. of XX and 48 g. of sodium hydroxide in 300 ml. of water was heated on the steam bath for 4 hr. The reaction solution was cooled, acidified, and extracted with ether. The ether was evaporated and the residual oil was distilled, giving 7 g. of VI, 3 g. of VII, and 21 g. of VIII. VII was further purified chromatographically, using a 24-in. column (outside diameter = 2 in.) filled with alumina and benzene as the solvent.

A solution of 20 g. of XX and 7.5 g. of sodium carbonate in 100 ml. of water was steam-distilled. The distillate was extracted with ether, the ether was evaporated, and the residue was distilled, giving 1 g. of VI and 6 g. of VII.

The polarographic study was made with a Sargent Model XXI polarograph. Polarograms were recorded on millimolar solutions of the dithiane in 0.5*M* ammonium sulfate–ammonium hydroxide buffer containing 50% methanol by volume. The maxima suppressor employed was 0.001% Triton-X-100. Polarograms were recorded on solutions 0, 15, and 30 min. after mixing. The hydrolysis reaction was essentially complete after 30 min.

The silver mercaptide was isolated by precipitating it from an ammoniacal solution of the hydrolyzed dithiane. This salt was dried *in vacuo* and identified by its silver, carbon, hydrogen, and sulfur analyses.

ROCHESTER 4, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MICHIGAN STATE UNIVERSITY]

Cyanoethylation of the 5-Aminotetrazoles[1]

DONALD W. RENN[2,3] AND ROBERT M. HERBST

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Cyanoethylation of 5-aminotetrazole gave a mixture of 1- and 2-β-cyanoethyl-5-aminotetrazole. The same mixture of products was obtained by alkylation of 5-aminotetrazole with β-bromopropionitrile. Interaction of 1-benzyl-5-aminotetrazole and acrylonitrile gave both 1-benzyl-5-β-cyanoethylaminotetrazole and 1-benzyl-5-di-β-cyanoethylaminotetrazole. 1-β-Cyanoethyl-5-aminotetrazole was also obtained from β-aminopropionitrile by interaction successively with cyanogen bromide and hydrazoic acid. Under similar conditions β,β′-iminodipropionitrile gave 5-di-β-cyanoethylaminotetrazole. 1-Benzyl-4-β-cyanoethyl-5-iminotetrazoline hydrochloride was formed on alkylation of 1-benzyl-5-aminotetrazole with β-chloropropionitrile or on benzylation of 1-β-cyanoethyl-5-aminotetrazole.

Many compounds containing active hydrogen atoms will undergo the cyanoethylation reaction.[4] The purpose of this investigation was to determine the conditions for the cyanoethylation of 5-aminotetrazole and to establish the structures of the resulting products. Tautomerism of the 5-aminotetrazole structure[5] makes conceivable the formation of three monocyanoethylated products: 1-β-cyanoethyl-5-aminotetrazole (I), 2-β-cyanoethyl-5-aminotetrazole (II), and 5-β-cyanoethylaminotetrazole (VII). An even greater number of

(1) Based on a doctoral thesis submitted to Michigan State University in 1957 by Donald W. Renn.

(2) American Viscose Corporation Fellow, 1955–1956. Monsanto Chemical Company Fellow, 1956–1957.

(3) Present address: John L. Smith Memorial for Cancer Research, Chas. Pfizer and Company, Inc., Maywood, N. J.

(4) H. A. Bruson, *Org. Reactions*, V, 79–135 (1949).

(5) R. M. Herbst, C. W. Roberts, and E. K. Harvill, *J. Org. Chem.*, 16, 139 (1951).