

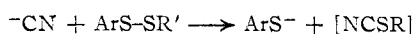
[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY, THE UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL, N. C.]

Chemistry of Aliphatic Disulfides. II.<sup>1</sup> Cyanide Cleavage of Unsymmetrical Disulfides<sup>2</sup>BY RICHARD G. HISKEY AND F. I. CARROLL<sup>3,4</sup>

RECEIVED MAY 17, 1961

The cyanide ion cleavage of five unsymmetrical aliphatic disulfides have been investigated. A quantitative method for estimation of cleavage products (alkyl thiocyanate and alkyl mercaptide ion) is also described. In each case the disulfides were cleaved in the direction which afforded the more stable alkyl mercaptide ion and corresponding alkyl thiocyanate as the predominant products.

Nucleophilic cleavage of a sulfur-sulfur bond has been considered<sup>5,6</sup> to occur by the bimolecular displacement of mercaptide ion. The suggestion<sup>5</sup> that the bond-breaking step is of greater relative importance than the bond-forming step has been supported<sup>7</sup> for diaryl and arylalkyl disulfides by studies of the cleavage of disulfides I-IV. In each case the mercaptide of greater anionic stability was isolated.

I, Ar = 2,4-(NO<sub>2</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>, R = C<sub>2</sub>H<sub>5</sub>II, Ar = 2,4-(NO<sub>2</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>, R = C<sub>6</sub>H<sub>5</sub>III, Ar = 2,4-(NO<sub>2</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>, R = CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>IV, Ar = *o*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>, R = C<sub>2</sub>H<sub>5</sub>

The reversible nature of the nucleophilic fission of the disulfide bond was suggested<sup>7</sup> by a comparison of the reactivity of substrates I-IV toward several nucleophiles and by the fact that symmetrical disulfides such as dimethyl and diphenyl disulfide, are cleaved only in the presence of a mercaptide scavenger. The direction of the cyanide cleavage of I-IV was, however, not affected by the presence or absence of 2,4-dinitrochlorobenzene.

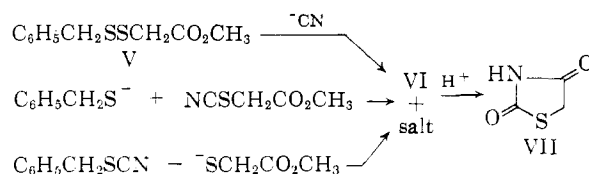
Although the proposed cleavage mechanism correctly predicts the experimental observations in the case of diaryl and arylalkyl disulfides, it could be argued that the correlation was due to the large values of the " $\Delta pK_a$ 's"<sup>8</sup> of disulfides I-IV. Hence purely aliphatic unsymmetrical disulfides might cleave in a different manner. Few cleavages of molecules of this type have been reported and with the availability<sup>1</sup> of a number of such substrates the cyanide ion cleavage has been investigated. In previous work<sup>7</sup> isolation and characterization of both primary cleavage products was not achieved. Further, no data were obtained on the amount of cleavage that occurred to give the more basic mercaptide. A complete product analysis was clearly desirable.

The present work includes: (a) a quantitative investigation of the cleavage of unsymmetrical disulfides with cyanide ion and (b) data relating

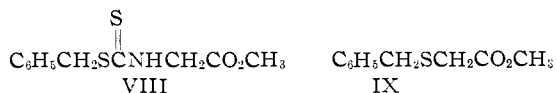
the direction of cleavage of unsymmetrically substituted aliphatic disulfides with the  $pK_a$ 's of the constituent mercaptans. In the accompanying paper<sup>9</sup> the effect of substituents on the nature of products obtained from the cleavage reaction and positive evidence for the equilibrium nature of the cyanide ion cleavage of disulfides is presented.

When methyl 5-phenyl-3,4-dithiapentanoate (V) in methanol solution was cleaved with cyanide ion in the absence of a mercaptide scavenger a quantitative yield of dibenzyl disulfide (VI) resulted. Acidification of the remaining black salt afforded 9.7% of 2,4-diketothiazolidine (VII) and an unidentified red oil.

The fact that VI and the salt represented products resulting from thermodynamic control of the reaction was indicated by separate experiments involving the primary cleavage products. When sodium benzylmercaptide and methyl  $\alpha$ -thiocyano-



acetate were allowed to react under the cleavage conditions, the same characteristic color changes were observed. The reaction mixture afforded a 97.4% yield of VI and a salt which gave a red oil and 18.4% of VII when acidified. Likewise, the treatment of benzyl thiocyanate with sodium carbomethoxymethylmercaptide afforded 99% of VI and 15.4% of VII. Although the nature of the salt and the mechanism of formation of the observed products is unknown at present, VI and VII were shown not to result from the action of methoxide ion on methyl dithiocarbonyloxyglycinate (VIII) or from thiocyanate ion on methyl 4-phenyl-3-thiabutanoate (IX).



In order to clarify the initial course of cleavage the reaction was studied in the presence of various mercaptide scavengers. When an equivalent of 2,4-dinitrochlorobenzene was employed rather low yields (42.9%) of carbomethoxymethyl 2,4-dinitrophenyl sulfide were obtained and no pure alkyl thiocyanate or symmetrical disulfide could be iso-

(1) Part I, R. G. Hiskey, F. I. Carroll, R. M. Babb, J. O. Bledsoe, R. T. Puckett and B. W. Roberts, *J. Org. Chem.*, **26**, 1152 (1961).

(2) Supported in part by a Fredrick Gardner Cottrell Grant, from the Research Corporation.

(3) Abstracted in part from the Ph.D. Dissertation of Mr. F. I. Carroll, June, 1961.

(4) Tennessee Eastman Corp. Fellow, 1959-1960; National Science Foundation Coöperative Fellow, 1960-1961.

(5) O. Foss, *Acta Chem. Scand.*, **4**, 401 (1950).

(6) A. J. Parker and N. Kharasch, *Chem. Revs.*, **59**, 583 (1959).

(7) A. J. Parker and N. Kharasch, *J. Am. Chem. Soc.*, **82**, 3071 (1960).

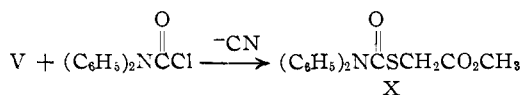
(8) The " $\Delta pK_a$ " of a disulfide is defined as the difference in  $pK_a$  values of the two mercaptans comprising the disulfide.

(9) R. G. Hiskey and F. I. Carroll, *J. Am. Chem. Soc.*, **83**, 4647 (1961).

TABLE I  
% YIELD OF CYANIDE CLEAVAGE PRODUCTS OF UNSYMMETRICAL DISULFIDES IN PRESENCE OF N,N-DIPHENYL-CARBAMYL CHLORIDE IN ACETONITRILE SOLUTION AT 50°

R	R-S-S-R'	R'	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> NCO SR'	RSCN	R'SCN	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> NCO SR	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> NCO CN
(V) C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>		CH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>	53.8	43.7	4.15		
(XI) C <sub>6</sub> H <sub>5</sub> CH(CH <sub>2</sub> )		CH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>	60.5	48.3	3.22		
(XII) CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub>		CH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>	83.2	68.0	0.0		
(XIII) C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>		CHCO <sub>2</sub> CH <sub>3</sub>	73.9	70.3	0.0		
		CH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>					
(XIV) C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>		CH <sub>2</sub> CH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>	10.7	12.2	13.4	8.3	55.6
(XV) (CH <sub>3</sub> ) <sub>3</sub> C		CH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>					87.7

lated. The use of 2,4-dinitrofluorobenzene provided no characterizable products and *p*-chloromercuritoluene and *N*-phenylmaleimide gave low yields of oily derivatives. *N,N*-Diphenylcarbonyl chloride<sup>10</sup> proved to be a satisfactory mercaptide scavenger. Cyanide ion cleavage of V in the presence of this agent afforded 41.8% of the *N,N*-diphenylthiocarbamate derivative of methyl mercaptoacetate (X). Although the yield of trapped mercaptide was the same with either scavenger,



use of the latter reagent greatly enhanced the ease of product isolation. A similar cleavage of methyl 5-phenyl-3,4-dithiahexanoate (XI) with cyanide ion afforded a 45.2% yield of X but no other characterizable products.

Absence of appreciable amounts of alkyl thiocyanate (the other expected product) was attributed to decomposition by potassium methoxide, generated by hydrolysis of potassium cyanide in methanol. To avoid this, and also possible base-catalyzed decomposition of the unsymmetrical disulfide, another solvent was desirable. The choice of acetonitrile was governed by its ability to dissolve sodium cyanide and the decreased likelihood of base formation. The preferred conditions employ substrate cleavage with sodium cyanide at 50°, in acetonitrile, using *N,N*-diphenylcarbonyl chloride as the trapping agent. The thiocarbamate derivatives were conveniently isolated by crystallization and elution chromatography. The percentages of the alkyl thiocyanate present (Table I) were obtained from vapor fractograms of the mother liquors after separation of the derivatives. In several experiments the predominant alkyl thiocyanate formed was isolated by distillation and compared with an authentic sample.

In agreement with previous proposals,<sup>5,7</sup> the least basic mercaptide (Table II) was displaced preferentially. No quantitative relationship between the *pK<sub>a</sub>*'s of the two mercaptans and the ratio of attack on the individual sulfur atoms could be derived from the present data. Cleavage of XII ("Δ*pK<sub>a</sub>*" 2.86) afforded a single thiocyanate as did cleavage of XIII ("Δ*pK<sub>a</sub>*" 1.80). However, decomposition of V ("Δ*pK<sub>a</sub>*" 1.63) gave two thiocyanates and presumably two thiocarbamate derivatives, although only the major one could be iso-

(10) R. G. Hiskey, F. I. Carroll, R. L. Smith and R. T. Corbett, *J. Org. Chem.*, **26**, in press (1961).

TABLE II  
ACID DISSOCIATION CONSTANTS OF MERCAPTANS, RSH

R	<i>pK<sub>a</sub></i>	Ref.
C <sub>6</sub> H <sub>5</sub>	6.52	11
C <sub>6</sub> H <sub>5</sub>	7.78	12
CH <sub>3</sub> O <sub>2</sub> CCH <sup>a</sup>		
	7.63	
CH <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub>		
CH <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub>	7.8	11
	7.68	12
CH <sub>3</sub> COCH <sub>2</sub>	7.86	11
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	9.43	11
CH <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> CH <sub>2</sub> <sup>a</sup>	10.48	
<i>n</i> -C <sub>4</sub> H <sub>9</sub> <sup>b</sup>	10.66	11
<i>t</i> -C <sub>4</sub> H <sub>9</sub>	11.05	11

<sup>a</sup> Value determined by Mr. T. L. Eisenhour and Mr. W. P. Harrington. <sup>b</sup> Value used for *n*-hexyl mercaptan.

lated. The importance of the anionic stability of the two potential mercaptans involved is shown in the attempted cleavage of XV. Attack of cyanide on the sulfur atom of the *t*-butyl group is prevented by steric hindrance and, although the second sulfur atom is not hindered, no cleavage occurred. The present results indicate that in the absence of "secondary effects"<sup>6</sup> (cyclization, sulfide formation or other side reactions of the primary cleavage products) cleavage of a disulfide with a "Δ*pK<sub>a</sub>*" of 1.80 or greater occurs in a single direction; "Δ*pK<sub>a</sub>*" values of 1.63–1.05 result in attack on both sulfur atoms by cyanide ion. With a Δ*pK<sub>a</sub>* of 1.05 or less the disulfide is relatively inert to cyanide ion while a disulfide with a Δ*pK<sub>a</sub>* of 0, *i.e.*, a symmetrical disulfide, is not cleaved by cyanide ion.

### Experimental<sup>13</sup>

**Cyanide Cleavage of Methyl 5-Phenyl-3,4-dithiapentanoate(V) in Methanol.**—To a solution of 1.71 g. (0.026 mole) of potassium cyanide in 300 ml. of dry methanol was added 6 g. (0.026 mole) of V in 200 ml. of dry methanol. The addition was carried out dropwise with rapid stirring over a period of 1 hour. The colorless solution turned yellow, then red, and, on standing 5 hours, black. Removal of solvent afforded a black mass which yielded 3.20 g. (98.8%) of VI, m.p. 68–70° when diluted with water. A mixture melting with an authentic sample was not depressed. The aqueous solution was acidified with sulfuric acid and continuously extracted with ether. Removal of ether afforded an oily solid from which 0.44 g. of a red oil was obtained by washing with cold chloroform. The infrared spectrum of the oil exhibited an absorption peak at 2150 cm.<sup>-1</sup>. The remaining solid afforded 0.30 g. (9.7%) of

(11) M. M. Kreevoy, E. T. Harper, R. E. Duvall, H. S. Wilgus and L. T. Ditsch, *J. Am. Chem. Soc.*, **82**, 4899 (1960).

(12) J. P. Danehy and C. P. Noel, *ibid.*, **82**, 2511 (1960).

(13) Melting points and boiling points are uncorrected. Elemental analysis by Micro Tech Laboratories, Skokie, Ill.

2,4-diketothiazolidene, m.p. 122–124°. A mixture melting point with an authentic sample<sup>14</sup> was not depressed.

In other experiments, extraction of the black mass with benzene to remove the dibenzyl disulfide afforded a black solid whose infrared spectrum was similar to, but not identical with, that of sodium thiocyanacetate. Experiments involving shorter reaction times produced essentially the same products.

When 3.65 g. (0.025 mole) of sodium benzyl mercaptide was allowed to react with 3.28 g. (0.025 mole) of methyl thiocyanacetate in 80 ml. of dry methanol the color sequence described above was observed. Isolation of products in the same manner afforded 3.0 g. (97.4%) of dibenzyl disulfide, 0.4 g. of red oil and 0.54 g. (18.4%) of 2,4-diketothiazolidene.

Likewise, treatment of sodium carbomethoxymethyl mercaptide (0.051 mole) with 7.45 g. (0.05 mole) of benzyl thiocyanate in 300 ml. of dry methanol afforded 6.1 g. (99%) of dibenzyl disulfide, 0.85 g. of red oil and 0.9 g. (15.4%) of 2,4-diketothiazolidene.

**Reaction of Methyl Dithiocarbonyloxyglycinate (VIII) with Sodium Methoxide.**—Treatment of dithiocarbonyloxyglycinate<sup>15</sup> with dry hydrogen chloride in methanol afforded a 91.52% yield of methyl ester, m.p. 51–52°.

*Anal.* Calcd. for  $C_{11}H_{18}NO_2S_2$ : C, 51.75; H, 5.13; N, 5.49; S, 25.10. Found: C, 51.75; H, 5.16; N, 5.32; S, 25.14.

When VIII was treated with one equivalent of sodium methoxide in methanol no color change occurred and no dibenzyl disulfide was produced.

Treatment of 0.025 mole of sodium carbomethoxymethyl mercaptide with 3.16 g. (0.025 mole) of benzyl chloride in methanol followed by addition of 2.30 g. (0.025 mole) of potassium thiocyanate produced no color change.

**Cyanide Cleavage of Methyl 5-Phenyl-3,4-dithiapentanoate(V) in the Presence of 2,4-Dinitrochlorobenzene.**—One gram (4.38 mmoles) of V in 100 ml. of dry methanol was cleaved by 0.255 g. (4.38 mmoles) of potassium cyanide in the presence of 0.885 g. (4.38 mmoles) of 2,4-dinitrochlorobenzene. Removal of methanol afforded a red oil which gave 0.51 g. (42.9%) of carbomethoxymethyl-2,4-dinitrophenyl thioether, m.p. 93–95°. A mixture melting point with an authentic sample<sup>16</sup> was not depressed. Removal of ether afforded a red oil whose odor and infrared spectrum (2160, 1730  $cm^{-1}$ ) suggested the presence of benzyl thiocyanate. All attempts to purify the mixture were unsuccessful.

When potassium cyanide and 2,4-dinitrochlorobenzene were added simultaneously to the disulfide at 0° a 43.3% yield of thioether resulted.

**Cyanide Cleavage of Methyl 5-Phenyl-3,4-dithiapentanoate(V) in the Presence of N,N-Diphenylcarbonyl Chloride.**—Cleavage of 1.0 g. (4.38 mmoles) of V in the presence of 1.01 g. (4.38 mmoles) of N,N-diphenylcarbonyl chloride was conducted in the usual manner. Removal of methanol afforded a yellow solid which yielded 0.55 g. (41.8%) of X, m.p. 111–115°. A mixture melting point with an authentic sample<sup>10</sup> was not depressed. Evaporation of the filtrate and recrystallization from methanol afforded 0.23 g. (42.6%) of dibenzyl disulfide. No other pure products could be obtained.

**Cyanide Cleavage of Methyl 5-Phenyl-3,4-dithiohexanoate(XI) in the Presence of N,N-Diphenylcarbonyl Chloride.**—Cleavage of 1.0 g. (4.13 mmoles) of XI using the previous conditions afforded 0.56 g. (45.2%) of X and 1.33 g. of a yellow oil which could not be characterized. The infrared spectrum of the oil exhibited a weak absorption peak at 2150  $cm^{-1}$  indicating very little alkyl thiocyanate was present.

**Cyanide Cleavage of Unsymmetrical Disulfides in Acetonitrile Using N,N-Diphenylcarbonyl Chloride. A. Chromatography Conditions.**—All experiments involving chromatography on alumina were conducted in the following manner. Merck reagent grade alumina was neutralized with ethyl acetate, washed with methanol and petroleum ether and dried at 200°. The column was made up in petroleum ether (30–60°)–benzene (4:1). The sample in

the same solvent, was eluted from the column with 100-ml. portions of solvent starting with petroleum ether–benzene (4:1) and progressing in 10% solvent changes through petroleum ether–benzene, benzene–chloroform to chloroform–methanol(4:1).

Vapor phase chromatograms were obtained on a Perkin-Elmer model 154-C vapor fractometer using a 40 in., 4 mm. glass column packed with 30/60 mesh Celite containing 4% Carbowax. Yields of the volatile cleavage products were obtained from standard calibration curves of each pure component. Ethyl phenylacetate was used as the internal standard.

**B. Cyanide Cleavage Conditions. Methyl 5-Phenyl-3,4-dithiapentanoate(V).**—A stirred solution of 1.01 g. (4.38 mmoles) of N,N-diphenylcarbonyl chloride in 100 ml. of acetonitrile was treated simultaneously with solutions of 1.0 g. (4.38 mmoles) of V and 0.222 g. of 97% sodium cyanide (previously powdered and weighed in a dry-box) in acetonitrile. The rapidly stirred reaction mixture was kept at 45–50° for 11 hours. Filtration of suspended solids, followed by removal of solvent *in vacuo*, afforded a yellow oil which partially crystallized when triturated with cold ether. Recrystallization from ethanol afforded 0.61 g. (46.2%) of X.

The ethanolic filtrate was concentrated *in vacuo* and dried to a constant weight (1.19 g.). A vapor fractogram of the residual oil indicated the presence of 4.15% methyl thiocyanacetate and 43.7% benzyl thiocyanate (ethyl phenylacetate; 140°; helium flow, 235 cc./min.; elution time, 45 and 110 sec.). Chromatography of the remaining oil on alumina afforded an additional 0.10 g. (7.6%) of X.

In a separate experiment the residual oil was steam distilled. A 22.8% yield of benzyl thiocyanate, m.p. 40–41°, was obtained. A mixture melting point with an authentic sample<sup>17</sup> was not depressed. The temperature of the cleavage reaction proved to be critical. In reactions run below 25° no cleavage occurred and only recovered disulfide and trapping agent could be isolated. When reaction mixture was refluxed for 7 hours the yield of thiocarbamate derivative was reduced to 45.2% and no pure benzyl thiocyanate was obtained.

**Methyl 5-Phenyl-3,4-dithiahexanoate(XI).**—Cleavage of 1.0 g. (4.13 mmoles) of XI in the manner described afforded 0.65 g. (52.4%) of X. Evaporation of ether gave 1.22 g. of an oil consisting of 3.22% methyl thiocyanacetate and 48.3%  $\alpha$ -phenethyl thiocyanate as shown by the vapor fractogram (ethyl phenylacetate; 110°; 264 cc./min.; 123 and 297 sec.). Alumina chromatography of the remaining oil afforded an additional 0.10 g. (8.1%) of X.

The "authentic"  $\alpha$ -phenethyl thiocyanate<sup>18</sup> contained approximately 10%  $\alpha$ -phenethyl isothiocyanate as determined by the vapor fractogram. The cleavage product also contained a small amount of  $\alpha$ -phenethyl isothiocyanate.

**Methyl 3,4-Dithiadecanoate(XII).**—When 1.0 g. (4.5 mmoles) of XII was subjected to cleavage, 1.0 g. (75.8%) of X was obtained. Analysis of the residual oil indicated the presence of only *n*-hexyl thiocyanate<sup>19</sup> in 68% yield (ethyl phenylacetate; 110°; 264 cc./min.; 52 sec.). An additional 7.4% of X was obtained by alumina chromatography of the residual oil.

In a separate experiment the liquid fraction obtained from the mother liquor was distilled and afforded 0.40 g. (62%) of *n*-hexyl thiocyanate, b.p. 43–45° at 0.1 mm. The infrared spectrum of this material was identical with that of an authentic sample.

When the cleavage was performed at 25°, 0.86 g. (86%) of N,N-diphenylcarbonyl chloride was recovered; at 80° the yield of X was reduced to 61.5%.

**Methyl 6-Phenyl-3-carbomethoxy-3,4-dithiahexanoate(X-III).**—Removal of acetonitrile from the cleavage mixture of 1.0 g. (3.3 mmoles) of XIII afforded no solid product when triturated with ether. Analysis of the oil (1.70 g.) in a vapor fractometer indicated benzyl thiocyanate (70.3%) as the only volatile product (ethyl phenylacetate; 140°; 235 cc./min.; 102 sec.).

The N,N-diphenylthiocarbonyl derivative of dimethyl  $\alpha$ -mercaptosuccinate, 0.72 g. (58.5%), m.p. 98–100°,<sup>10</sup>

(14) D. Libermann, J. Himbert and L. Henyl, *Bull. soc. chim.*, [5], **15**, 1120 (1948).

(15) A. H. Cook, G. Harris, I. Heilbron and G. Shaw, *J. Chem. Soc.*, 1056 (1948).

(16) P. Friedlaender and A. Chwala, *Monatsh. Chem.*, **28**, 247 (1907).

(17) L. Henry, *Ber.*, **2**, 636 (1869).

(18) P. A. S. Smith and D. W. Emerson, *J. Am. Chem. Soc.*, **82**, 3076 (1960).

(19) R. Riemschneider and G. Orlick, *Monatsh. Chem.*, **84**, 313 (1953).

crystallized when the oil was dissolved in ethanol. Removal of alcohol and chromatography of the residue afforded two solid fractions. The first, after recrystallization from alcohol, afforded 0.25 g. (50.8%) of benzyl thiocyanate, m.p. 39–41°. The second fraction, upon recrystallization from alcohol, gave an additional 0.19 g. (15.4%) of the thiocarbamate ester derivative.

**Methyl 6-Phenyl-4,5-dithiahexanoate (XIV).**—When 1.0 g. (4.13 mmoles) of XIV was cleaved under the usual conditions 0.31 g. (33.8%) of N,N-diphenylcarbamylnitrile, m.p. 124–125°, was obtained. The nitrile was obtained in 91.5% yield when N,N-diphenylcarbanyl chloride and sodium cyanide were allowed to react under the cleavage conditions. Removal of ether afforded 1.57 g. of an oil consisting of 13.4% methyl  $\beta$ -thiocyanopropionate and 12.2% benzyl thiocyanate (ethyl phenylacetate; 140°; 235 cc./min.; 49 and 96 sec.).

The remaining oil was chromatographed on alumina and afforded four solid fractions. The first, recrystallized from petroleum ether (30–60°), yielded 0.35 g. (69.4%) of dibenzyl disulfide. The second, recrystallized from ethanol, gave 0.2 g. (21.8%) of N,N-diphenylcarbamylnitrile. Recrystallization of the third and fourth fractions from eth-

anol afforded 0.11 g. (8.3%) of the thiocarbamate derivative of benzyl mercaptan, m.p. 120–123°, and 0.14 g. (10.7%) of the derivative of methyl  $\beta$ -mercaptoacetate, m.p. 95–96°. Mixture melting points with authentic samples<sup>10</sup> were not depressed.

**Preparation of Methyl  $\beta$ -Thiocyanopropionate.**—The ester used for the calibration curve in the preceding experiment was prepared in 82.1% yield from methyl  $\alpha$ -bromopropionate and potassium thiocyanate; b.p. 98° at 3 mm.,  $n_D^{25}$  1.4770,  $d_4^{25}$  1.1913.

*Anal.* Calcd. for C<sub>6</sub>H<sub>7</sub>NO<sub>2</sub>S: C, 41.36; H, 4.86; N, 9.65; S, 22.09. Found: C, 41.55; H, 4.97; N, 9.67; S, 22.16.

**Methyl 5,5-Dimethyl-3,4-dithiahexanoate (XV).**—Trituration of the oil, resulting from the cleavage of 1.0 g. (5.15 mmoles) of XV with ether, afforded 0.80 g. (70.2%) of N,N-diphenylcarbamylnitrile. Analysis of the residue in the vapor fractometer indicated only unchanged disulfide was present (140°; 235 cc./min.; 43 sec.). Distillation of the residue yielded 0.79 g. (79%) of XV,  $n_D^{25}$  1.4987; reported<sup>1</sup>  $n_D^{25}$  1.4985. The residue from the distillation was recrystallized from ethanol and afforded an additional 0.20 g. (17.5%) of the carbamylnitrile.

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY, THE UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL, N. C.]

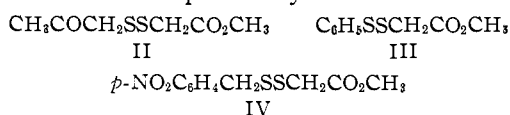
## The Chemistry of Aliphatic Disulfides. III.<sup>1</sup> Formation of Sulfides During Cleavage by Cyanide Ion<sup>2</sup>

BY RICHARD G. HISKEY AND F. I. CARROLL<sup>3,4</sup>

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Cyanide ion cleavage of three unsymmetrical disulfides yield unsymmetrical sulfides as the major product and, in addition, small amounts of thiocyanates and trapped mercaptides. The more stable mercaptide is preferentially produced. Formation of sulfide occurs as the result of a secondary reaction between mercaptide and thiocyanate formed in the initial cleavage. Evidence is presented for the equilibrium nature of the reaction. Possible mechanisms are discussed.

The direction of cyanide ion cleavage of several unsymmetrical aliphatic disulfides has been found<sup>1</sup> to be related to the stability of the mercaptide ion produced: the mercaptide of greater anionic stability and the corresponding alkyl thiocyanate predominate. In order to provide a more thorough test of this proposal,<sup>5,6</sup> substrates containing a potential mercaptide of stability equal to or greater than the previously used sodium carboxymethyl mercaptide (I) were desirable. Thus methyl 6-keto-3,4-dithiaheptanoate (II), " $\Delta pK_a$ " 0.06,<sup>7</sup> methyl 4-phenyl-3,4-dithiabutanoate (III), " $\Delta pK_a$ " 1.28, and methyl 5-(4-nitrophenyl)-3,4-dithiapentanoate (IV) were cleaved using the general conditions previously described.<sup>1</sup> The re-



sults, reported in Table I, were obtained from ex-

(1) Part II, R. G. Hiskey and F. I. Carroll, *J. Am. Chem. Soc.*, **83**, 4644 (1961).

(2) Supported in part by a Fredrick Gardner Cottrell Grant from the Research Corporation.

(3) Abstracted from the Ph.D. dissertation of Mr. F. I. Carroll, June, 1961.

(4) Tennessee Eastman Corp. Fellow, 1959–1960; National Science Foundation Cooperative Fellow, 1960–1961.

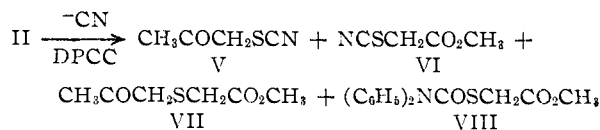
(5) O. Foss, *Acta Chem. Scand.*, **4**, 401 (1950).

(6) (a) A. J. Parker and N. Kharasch, *J. Am. Chem. Soc.*, **82**, 3071 (1960); (b) A. J. Parker and N. Kharasch, *Chem. Revs.*, **59**, 583 (1959).

(7) The  $pK_a$ 's of the various mercaptans are recorded in ref. 1, Table II.

periments involving small amounts of the disulfides or mercaptides and thiocyanates. The yields reported undoubtedly represent minimum values and must be considered qualitative. Additional products may well be formed.

Treatment of II with cyanide ion (Table I, a) afforded approximately equal amounts of thiocyanacetone (V) and methyl thiocyanacetate (VI) as would be expected from a consideration of the  $\Delta pK_a$  value. The major product of reaction was, however, methyl 5-keto-3-thiahexanoate (VII) obtained in 39.7% yield together with a similar amount of sodium thiocyanate and unreacted N,N-diphenylcarbanyl chloride (DPCC). A 16.1% yield of the N,N-diphenylthiocarbamate derivative of methyl mercaptoacetate (VIII) was isolated although no derivative of mercaptoacetone was obtained, presumably due to oxidation or dimerization.



The cleavage of IV (Table I, e) provided 40.5% of sodium thiocyanate and 35.3% of recovered trapping agent. Although no pure sulfide was obtained, a liquid fraction with an infrared spectrum virtually identical to authentic sulfide was isolated by elution chromatography. The absence of VI was indicated by the vapor fractogram of the reaction mixture. The di-*p*-nitrobenzyl disulfide pro-