

2. Fluorene has similarly been converted to fluorene-9-carboxylic acid.

3. The potassium salt of *t*-butyl diphenylacetate, prepared by means of potassium amide, has been benzoylated and acetylated and the resulting  $\beta$ -keto esters cleaved to  $\alpha,\alpha$ -diphenylaceto-

phenone and  $\alpha,\alpha$ -diphenylacetone, respectively.

4. Ethyl  $\alpha,\alpha$ -diphenylbenzoylacetate, prepared by benzoylating the potassium salt of ethyl diphenylacetate, is stable toward ketonic cleavage.

DURHAM, N. C.

RECEIVED JANUARY 29, 1947

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

## Reactions of Mercaptans with Acrylic and Methacrylic Derivatives

BY CHARLES D. HURD AND LEON L. GERSHBEIN

That hydrogen sulfide adds to methyl acrylate, acrylonitrile or crotonaldehyde when a basic catalyst is present, but not to methyl methacrylate, was established recently.<sup>1</sup> The present paper reports an extension of this type of reaction to mercaptans and thiophenols. Both acrylic and methacrylic esters give high yields of  $\beta$ -substituted propionates and isobutyrate:  $\text{RSH} + \text{CH}_2=\text{CHCOOCH}_3 \rightarrow \text{RSCH}_2\text{CH}_2\text{COOCH}_3$ ; but unless a basic condensing agent is present, the reaction is very slow and the yield small.

A few instances are on record involving the addition of methanethiol, ethanethiol, or thiophenol to acrylic acid, cinnamic acid, methyl methacrylate, or acrolein, but the specified reaction conditions often involve relatively long periods of reaction,<sup>2</sup> the presence of mercuric salts,<sup>3</sup> or irradiation.<sup>4</sup> It should be pointed out that  $\beta$ -mercaptopropionic or  $\beta$ -mercaptoisobutyric acids or esters frequently have been made by the metathetic approach. New interest in methyl  $\beta$ -methylmercaptpropionate stems from the fact that it has been isolated<sup>5</sup> from pineapple fruit pulp.

The presence of two functional groups (SH and OH) in 2-mercaptoethanol makes this substance one of particular interest, since alcohols are known to undergo addition<sup>6</sup> to acrylic ester in the presence of a basic catalyst. We found that only the mercapto group of 2-mercaptoethanol participates in the reaction with methyl acrylate. Methyl  $\beta$ -(2-hydroxyethylmercapto)-propionate,  $\text{HOCH}_2\text{CH}_2\text{SCH}_2\text{CH}_2\text{COOCH}_3$ , (I), was isolated in a yield of 97% when benzyltrimethylammonium hydroxide was the catalyst, but only 52% when sodium methoxide was employed.

Seven  $\beta$ -mercapto esters were prepared from methyl acrylate and five from methyl methacrylate in the present work:  $\text{R} \text{ in } \text{RSCH}_2\text{CH}_2\text{-}$

(1) Gershbein and Hurd, *THIS JOURNAL*, **69**, 241 (1947).

(2) Holmberg and Schjånberg, *Arkiv Kemi, Mineral Geol.*, **A15**, No. 20, 14 (1942); *C. A.*, **38**, 2943 (1944); *Chem. Zentr.*, **114**, I, 388 (1943); Posner, *Ber.*, **40**, 4791 (1907).

(3) Kaneko and Mii, *J. Chem. Soc. Japan*, **59**, 1383 (1938).

(4) Jacobson, U. S. Patent 2,199,799 (1940).

(5) Haagen-Smit, Kirchner, Deasy and Prater, *THIS JOURNAL*, **67**, 1651 (1945).

(6) (a) Koelsch, *ibid.*, **65**, 437 (1943); (b) Rehberg, Dixon and Fisher, *ibid.*, **68**, 544 (1946); (c) Purdie and Marshall, *J. Chem. Soc.*, **59**, 468 (1891).

$\text{COOCH}_3$ , representing methyl, isopropyl, carboxymethyl, benzyl, phenyl, *t*-butyl and 2-hydroxyethyl; and  $\text{R}'$  in  $\text{R}'\text{SCH}_2\text{CH}(\text{CH}_3)\text{COOCH}_3$  being the same as the first five R groups listed above. All were distillable liquids with a density of 1.0–1.1. Some of them were oxidized by hydrogen peroxide to the corresponding sulfone esters.

Extension of the addition reaction to sodium acrylate revealed that the alkalinity of a hot aqueous solution of the latter was sufficient to produce an excellent yield of 3-benzylmercaptpropionic acid from phenylmethanethiol without using any added base.

Acrolein and crotonaldehyde were converted into 3-methylmercaptopropanal and 3-benzylmercaptobutanal, respectively, by reaction with methanethiol and phenylmethanethiol. Synthesis of the former has been reported by reaction of methanethiol with acrolein in the presence of a mercury salt.<sup>3</sup>

The reaction between acrylonitrile<sup>7</sup> and alkanethiols or thiophenols also proceeds practically quantitatively if a small amount of alkaline condensing agent is present:  $\text{RSH} + \text{CH}_2=\text{CHCN} \rightarrow \text{RSCH}_2\text{CH}_2\text{CN}$ , R representing methyl, ethyl, butyl, isobutyl, *t*-butyl, isopropyl, carboxymethyl, benzyl, 2-hydroxyethyl, phenyl, *o*-, *m*-, and *p*-tolyl, 2-benzoxazolyl, 2-benzothiazolyl. Although in most of the runs where alkaline agents were employed, the product was allowed to stand overnight, the reaction yielding  $\text{RSCH}_2\text{CH}_2\text{CN}$ <sup>8</sup> was virtually complete within the first hour.

Of the simple mercaptans tested some (2-propanethiol, 2-methyl-1-propanethiol, ethyl mercaptoacetate) were almost non-reactive<sup>9</sup> at 25°

(7) Since completion of this work, Gribbins, Miller and O'Leary, U. S. Patent 2,397,960 (1946), list examples of ethyl-, benzyl-,  $\beta$ -hydroxyethyl- and  $\beta$ -mercaptoethyl-mercaptpropionic acids. These were produced by hydrolyzing the corresponding nitriles which, in turn, were made by adding mercaptans to acrylonitrile in the presence of piperidine; but the nitriles were not characterized by analysis.

(8)  $\beta$ -Methylmercaptpropionitrile is the only simple compound of this type to have been previously prepared and analyzed. It was made by metathesis of sodium cyanide and 2-methylmercaptoethyl bromide: Akabori, Kaneko and Matizuki, *J. Chem. Soc. Japan*, **59**, 1186 (1938).

(9) We found 2-propanol also to be completely indifferent toward acrylonitrile at 25° (eleven days) when no basic agent was present.

(sixteen hours) when alkaline reagents were absent, whereas others (phenylmethanethiol, 2-mercaptoethanol, thiophenol<sup>10</sup>) gave excellent yields under the same conditions; but even these compounds reacted more vigorously if catalyzed by base. Mercuric acetate, benzoyl peroxide or light were all ineffective in bettering the yields of product from alkanethiols and acrylonitrile.

The effect of these factors was studied on the cyanoethylation of thiophenol, in view of the high yields involved with no catalyst. The same high yields were obtained by irradiating the mixture, and only a slight lessening of yield was noted if traces of hydroquinone or pyrogallol were present. Benzoyl peroxide, however, with or without irradiation, caused diminution of the yield from 93% (three hours) to 62–65%. A trace of hydrochloric acid was still more inhibitory (20–28%), and mercuric acetate almost stopped any tendency for reaction. The last observation is particularly significant in view of the stated<sup>3</sup> catalytic activity of mercuric salts toward acrolein or acrylic acid. In view of the non-reaction of mercaptoacetic acid and acrylonitrile during sixteen hours, evidently a carboxyl group also represses the reaction.

One interesting effect of the presence of a trace of hydrochloric acid on the reaction between thiophenol and acrylonitrile was the appearance of a small amount of higher condensation product, analogous to the one reported by Jacobson<sup>4</sup> with thiophenol and methyl methacrylate. No such product was noticed unless acid was present. Evidently the rate of addition of thiophenol to acrylonitrile is so much retarded by acid that a competing condensation reaction, involving two moles of nitrile, becomes important. The same type of retarded reaction, leading to the formation of condensed products, was observed in our reactions of thiophenol with acrylic or methacrylic esters in the absence of basic catalysts, or in the presence of a small amount of hydrochloric acid.

Tertiary butyl alcohol has been reported to be inert toward both acrylonitrile<sup>11</sup> and methyl acrylate.<sup>6b</sup> The sulfur analog of *t*-butyl alcohol, 2-methyl-2-propanethiol, in the presence of a base reacts to form high yields of  $\beta$ -*t*-butylmercapto-propionitrile and methyl  $\beta$ -*t*-butylmercapto-propionate from acrylonitrile and methyl acrylate, respectively.

The behavior of 2-mercaptoethanol is interesting. It needed no basic agent to form a 95% yield of  $\beta$ -(2-hydroxyethylmercapto)-propionitrile,  $\text{HOCH}_2\text{CH}_2\text{SCH}_2\text{CH}_2\text{CN}$ , (II). The yield dropped to 82% when sodium methoxide was employed, small amounts of a polymer containing sulfur and nitrogen being recognized. This formation of (II) by monocyanoethylation is

(10) The facility with which thiophenol reacts with acrylonitrile is in decided contrast to the drastic conditions required for phenol: Ufer, U. S. Patent 2,163,176 (1939).

(11) Bruson and Riener, *THIS JOURNAL*, **65**, 23 (1943), employed *t*-butyl alcohol as an inert reaction medium.

analogous to the results obtained when 2-mercaptoethanol and methyl acrylate interacted. Quite unexpected, therefore, was the finding that other strong basic catalysts (alcoholic sodium hydroxide, or trimethylbenzylammonium hydroxide) promoted bis-cyanoethylation with the formation of 4-oxa-7-thiadenecanodinitrile,  $\text{NCCH}_2\text{CH}_2\text{SCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{CN}$  (III),<sup>12</sup> in practically quantitative yields. The latter catalysts also were effective in the conversion of II into III by further reaction with acrylonitrile, whereas this did not occur if sodium methoxide was the basic condensing agent. It is interesting to note that ester (I),  $\text{HOCH}_2\text{CH}_2\text{SCH}_2\text{CH}_2\text{COOCH}_3$ , corresponding to (II), is practically indifferent toward methyl acrylate at 25° (Triton B), and the reaction proceeded only to 29% at refluxing temperature.

2-Hydroxyethyl sulfide,  $(\text{HOCH}_2\text{CH}_2)_2\text{S}$ , behaved similarly. In the presence of Triton B<sup>12</sup> it reacted at refluxing temperature with acrylonitrile to yield both mono- and dicyanoethylated products, but there was practically no reaction at 25°. The 2-hydroxyethyl sulfide was indifferent toward methyl acrylate at refluxing temperature. No reaction occurred at 100° between acrylonitrile and thiourea, using dioxane or water in the presence of a strong base. Acrylonitrile polymer was the only product isolated, this polymerization being favored by higher temperatures.

Two new reactions of the nitriles were developed in the present study. One was a reduction to 3-methylmercapto-propanal (5% yield) by Stephen's method, and the other was an oxidation of the  $\beta$ -arylmercapto-propionitriles to the sulfones with hydrogen peroxide. The sulfones were formed in high yields, but some hydrolysis to the amide and acid also was observed.  $\beta$ -Arylmercapto-propionic esters underwent similar reaction with hydrogen peroxide to yield the  $\beta$ -substituted sulfonylpropionic esters.

Hydrolysis of  $\beta$ -benzenesulfonylpropionitrile and its homologs to the corresponding amides,  $\text{ArSO}_2\text{CH}_2\text{CH}_2\text{CONH}_2$ , was accomplished in practically quantitative yield by allowing a mixture of the nitrile and concentrated sulfuric acid to stand overnight at 25°. Hydrolysis to the respective acids was accomplished by refluxing the nitrile with 70% sulfuric acid. Treatment of the acid with thionyl chloride, followed by reaction with ammonia, also yielded the amide.

$\beta$ -Benzenesulfonylpropionic acid and its amide have been classified<sup>13</sup> in the triclinic (or monoclinic) and rhombic systems, respectively, and both stated to melt at 123–124°. In reinvestigating this subject, it was found that both derivatives possessed practically the same melting point and showed a high birefringence. The amide was triclinic; the acid, which was uniaxial and definitely not triclinic or monoclinic, belonged to the hexagonal or tetragonal systems.

(12) Bruson and Riener<sup>11</sup> used aqueous potassium hydroxide or powdered sodium methoxide and reported dicyanoethylation only.

(13) Otto, *Ber.*, **21**, 96, 98 (1888).

TABLE I  
 β-SUBSTITUTED PROPIONITRILES, RSCH<sub>2</sub>CH<sub>2</sub>CN

RSH R	g.	Catalyst Base <sup>a</sup>	g.	Yield, %	B. p. °C.	RSCH <sub>2</sub> CH <sub>2</sub> CN			Analyses, % N		
						Mm.	<i>d</i> <sub>20</sub> <sup>20</sup>	<i>n</i> <sub>D</sub> <sup>20</sup>	Formula	Calcd.	Found
CH <sub>3</sub>	34 <sup>b</sup>	A	0.30	91	97	15	1.032	1.4840	.....	...	...
C <sub>2</sub> H <sub>5</sub>	16	A	0.8	83	108-109	21	0.996	1.4790	C <sub>6</sub> H <sub>9</sub> NS	12.16	12.27
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	41	A	1.2	96 <sup>n</sup>	126-127	14	.958	1.4735	C <sub>7</sub> H <sub>13</sub> NS	9.78	10.20
<i>i</i> -C <sub>4</sub> H <sub>9</sub>	14 <sup>c</sup>	A	0.15	85	132.5-133	30	.950	1.4730	C <sub>7</sub> H <sub>13</sub> NS	9.78	9.53
<i>i</i> -C <sub>4</sub> H <sub>9</sub>	7	..	..	1	106						
<i>i</i> -C <sub>8</sub> H <sub>7</sub>	32	A	.80	95	102.5-103	12	.970	1.4751	C <sub>6</sub> H <sub>11</sub> NS	10.83	11.00
<i>i</i> -C <sub>8</sub> H <sub>7</sub>	21	..	..	1							
<i>i</i> -C <sub>8</sub> H <sub>7</sub>	7 <sup>f</sup>	..	..	24							
<i>t</i> -C <sub>4</sub> H <sub>9</sub>	19	A	.20	95	113.5-114	17	.946	1.4733	C <sub>7</sub> H <sub>13</sub> NS	9.78	9.52
C <sub>2</sub> H <sub>5</sub> OOCCH <sub>2</sub>	13 <sup>d</sup>	A	.15	89	169	16	1.128	1.4810	C <sub>7</sub> H <sub>11</sub> NO <sub>2</sub> S	8.09	8.33
C <sub>2</sub> H <sub>5</sub> COCCH <sub>2</sub>	10 <sup>d</sup>	A	.30	85							
C <sub>2</sub> H <sub>5</sub> OOCCH <sub>2</sub>	20	..	..	1.8							
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	7	..	..	92	192	19	1.090	1.5625	C <sub>10</sub> H <sub>11</sub> NS	7.90	7.95
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	25 <sup>k</sup>	A	.25	92	152-153	2					
C <sub>6</sub> H <sub>5</sub>	18	B	.70	97	154	8	1.116	1.5735	C <sub>9</sub> H <sub>9</sub> NS	8.58	8.32
C <sub>6</sub> H <sub>5</sub>	14 <sup>c</sup>	..	..	86	174-174.5						
C <sub>6</sub> H <sub>5</sub>	13 <sup>b</sup>	..	..	93							
<i>o</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	34	A	1.0	81	177.5	16	1.101	1.5725	C <sub>10</sub> H <sub>11</sub> NS	7.90	8.04
<i>m</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	15	B	0.84	97	177.5	18	1.085	1.5673	C <sub>10</sub> H <sub>11</sub> NS	7.90	8.40
<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	37	B	.57	95	178.5	17	1.079	1.5635	C <sub>10</sub> H <sub>11</sub> NS <sup>m</sup>	7.90	8.20
C <sub>6</sub> H <sub>4</sub> -N=C   O	15 <sup>e,g</sup>	B	.70	88	m. p. 173-173.5 <sup>i</sup>	..	..	..	C <sub>10</sub> H <sub>8</sub> N <sub>2</sub> OS <sup>t</sup>	13.72	13.91
	3 <sup>d,g</sup>	B	1.8	88							
C <sub>6</sub> H <sub>4</sub> -N=C   S	7	B	1.37	87	m. p. 167 <sup>i</sup>	..	..	..	C <sub>10</sub> H <sub>8</sub> N <sub>2</sub> S <sub>2</sub>	12.72	13.04

<sup>a</sup> CH<sub>2</sub>ONa, A; 35% Triton B solution, B. <sup>b</sup> Dissolved in 127 g. of benzene at 0°, and kept at 0° for the first hour of reaction. A different synthesis of CH<sub>3</sub>SCH<sub>2</sub>CH<sub>2</sub>CN is reported in ref. 8. <sup>c</sup> Experiment of one-hour duration. <sup>d</sup> Experiment of half-hour duration. <sup>e</sup> Experiment of forty hours duration. <sup>f</sup> Experiment of five hours duration, and reactants heated on steam-bath. <sup>g</sup> Preliminary heating (five minutes) to dissolve reactants using 4-8 molar amounts of acrylonitrile, but large crusts of crystals separated on cooling. <sup>h</sup> Experiment of three hours duration. <sup>i</sup> Recrystallized in the form of rhombs from benzene. <sup>j</sup> White crystals from benzene. <sup>k</sup> After preliminary mixing at 0°, duration was one hour on the steam-bath. <sup>l</sup> *Anal.* Calcd. for S: 15.68. Found: S, 15.19. <sup>m</sup> *Anal.* Calcd. for C, 67.74; H, 6.25. Found: C, 67.66; H, 6.18. <sup>n</sup> The 61.4 g. of β-butylmercaptopropionitrile was combined with similar fractions from other runs and redistilled into two cuts: (1) b. p. 126-126.5° (14 mm.) as listed, and (2) b. p. 127° (14 mm.), *d*<sub>20</sub><sup>20</sup> 0.958, *n*<sub>D</sub><sup>20</sup> 1.4753.

### Experimental

**Materials.**—Methanethiol, acrolein and sodium acrylate were synthesized. Both ethyl mercaptoacetate, which was prepared by esterification of the Eastman Kodak Co. acid as well as an 80% grade from Evans Chemetics, Inc., and 2-hydroxyethyl sulfide ("Kromfax Solvent," Carbide and Carbon Chemicals Corporation) were freshly distilled before use. 2-Methyl-2-propanethiol of 97.6% purity was used as received from Phillips Petroleum Co. Aside from 2-mercaptobenzothiazole (industrial grade), other reagents were obtained from Eastman Kodak Company. Inhibitors in the unsaturated compounds were removed before use by distillation.

**Reactions with Acrylonitrile.**—The general procedure followed involved the dropwise addition of excess acrylonitrile to the chilled compound containing a small amount of basic catalyst. The excess of nitrile, almost completely recoverable at the end of the experiment by distillation, was an effective solvent. Aside from 2-mercaptobenzoxazole and 2-mercaptobenzothiazole, which were fairly insoluble in acrylonitrile, exothermic reactions were invariably encountered. The temperature was not permitted to rise above 45°.

The catalysts selected comprised commercial powdered sodium methoxide, a 35% aqueous solution of trimethylbenzylammonium hydroxide (Triton B from Röhm and Haas), or alcoholic sodium hydroxide. As some experiments were performed without added catalyst and since only traces of alkali can bring about a marked increase in yield, it was found expedient to rinse the reaction vessels

with mineral acid followed by water to insure the absence of alkali in the uncatalyzed runs.

The mixtures were stirred or shaken if non-homogeneous, a condition prevalent in experiments employing sodium methoxide catalyst or using 2-mercaptobenzoxazole and 2-mercaptobenzothiazole as reactants. At the end of the run most of the sodium methoxide was filtered off. The soluble basic catalysts were neutralized (dilute hydrochloric acid) before distilling the mixture, or, if solid, before crystallizing the product. To remove traces of unreacted thiophenols and higher boiling mercaptans, an alkali wash was introduced in some of the runs.

Conditions and results of selected experiments are presented in Table I. Except as otherwise stated, experiments were performed at room temperature for an overnight period of about sixteen hours, and 1.3-2.7 molar portions of acrylonitrile used in each experiment. Yields were calculated on the basis of the original sulfur compound. Some of the experiments call for special comments.

**β-*t*-Butylmercaptopropionitrile.**—Since an earlier run showed that an inhibition period occurred in this reaction, 38 g. of acrylonitrile was added dropwise to 19.4 g. (0.22 mole) of 2-methyl-2-propanethiol containing 0.20 g. of sodium methoxide over a period of thirty minutes, some heat being applied at the start. Intermittent cooling served to control the reaction. The contents were then stirred at 25° for thirty minutes, after which time the decanted product was rid of unreacted nitrile under reduced pressure. Distillation of the product yielded 29 g. of sulfide, b. p. 108-113° (15 mm.). This, on redistilla-

tion, gave the pure  $\beta$ -*t*-butylmercaptpropionitrile at 113.5–114° (17 mm.).

#### Monocyanoethylation of 2-Mercaptoethanol

**Sodium Methoxide.**—Into a stirred, chilled mixture of 20 g. of 2-mercaptoethanol and 0.30 g. of sodium methoxide was added 38 g. of acrylonitrile over a thirty-minute period, then 15 g. more to make a total of 53 g. Stirring was maintained overnight at room temperature, or for two and one-half hours on a steam-bath. The orange-red mixture was filtered, the excess of acrylonitrile stripped off, and a small quantity (under 5%) of water-insoluble, sulfur-containing distillate was collected in advance of the main fraction of b. p. 160–162° at 4 mm. The latter (28 g. or 82%) contained some polymeric, gelatinous substance which separated on standing for a few days. This white flocculent material which contained both sulfur and nitrogen (2.5%) and amounting to less than 1 g. was filtered off and the filtrate (19.1 g.) redistilled. The  $\beta$ -(2-hydroxyethylmercapto)-propionitrile (14.0 g.) now boiled at 163.5–164.5° (8 mm.);  $d_{20}^{20}$  1.140,  $n_D^{20}$  1.5120. The fraction, which possessed a mild sulfide odor, was miscible with water, acetone or alcohol, but was less soluble in ether. It reacted vigorously with acetyl chloride and metallic sodium and was inert toward lead acetate. Although the  $\alpha$ -naphthylcarbamic and 3,5-dinitrobenzoic esters appeared as oils, they resisted attempts at crystallization.

*Anal.* Calcd. for  $C_5H_9NOS$ : C, 45.77; H, 6.91; N, 10.68. Found: C, 45.32; H, 6.80; N, 9.89.

**No Catalyst.**—Acrylonitrile (32 g.) was added all at once to 19.5 g. of 2-mercaptoethanol. After about five minutes the mixture was cooled because of the liberated heat. The contents were left at 25° for sixteen hours, then distilled at 183–185° (21 mm.); yield, 91% (29.7 g.). No other product was formed.

#### Dicyanoethylation of 2-Mercaptoethanol

**Triton B.**—A cooled mixture of 20 g. of 2-mercaptoethanol and 0.50 g. of Triton B was gradually treated with 47 g. of acrylonitrile. After an overnight period at 25°, the contents were washed with water and dilute hydrochloric acid, dried over anhydrous sodium sulfate, and rid of solvent under reduced pressure. A viscous fraction weighing 41.6 g. (93.6%) was collected at 197–203° (3 mm.). On redistillation it boiled at 225° (9 mm.) or 208° (3 mm.). Virtually no lower boiling monocyanoethylated product was formed. This was also true in analogous experiments which omitted the scrubbing with water. The 4-oxa-7-thiadedecanedinitrile was a liquid not very soluble in water, ether or ethanol. It is soluble in acetone or benzene. The OH and SH groups were absent as shown by test with the usual reagents. The liquid possessed a somewhat foul odor:  $d_{20}^{20}$  1.111,  $n_D^{20}$  1.4946.

*Anal.* Calcd. for  $C_8H_{12}N_2OS$ : N, 15.21. Found: N, 15.27.

**Alcoholic Sodium Hydroxide.**—When 23.4 g. of 2-mercaptoethanol and 0.15 g. of sodium hydroxide in 5 ml. of ethanol was treated in the cold with 42 g. of acrylonitrile, and the mixture allowed to stand at 25° for sixteen hours, a total yield of 54.3 g. (98.3%) of 4-oxa-7-thiadedecanedinitrile, b. p. 218–219° (7 mm.), resulted. The forerun contained some  $\beta$ -ethoxypropionitrile.

**Cyanoethylation of  $\beta$ -(2-Hydroxyethylmercapto)-propionitrile (II).**—Cooling was maintained while 7.1 g. of acrylonitrile was added to a mixture of 7.40 g. of (II) and 0.07 g. of Triton B solution. When the orange-red mixture was worked up after sixteen hours at 25°, it yielded 9.15 g. (88%) of colorless 4-oxa-7-thiadedecanedinitrile, b. p. 224–225° (9 mm.).

#### Other Factors Affecting Cyanoethylation

**Thiophenol.**—Several experiments were performed at room temperature wherein the effect of irradiation, peroxide, mercuric acetate, hydroquinone or hydrochloric acid was tested on the reaction of thiophenol and acrylonitrile. Seven typical runs are listed in Table II. Con-

trol experiments (no catalysts) for one, three and sixteen-hour periods in runs otherwise comparable to those listed in Table II were 86, 93, 97%, respectively.

Except for the irradiation experiments, closed systems were employed. The reaction flasks were rinsed initially with concd. hydrochloric acid, then water, to minimize basic impurities. Small amounts of heat were liberated in all cases except where the inhibitory effect was very great. The light source in the irradiation experiments was an 100-watt Mazda lamp. The product formed was always  $\beta$ -phenylmercaptpropionitrile, as judged both by boiling point and by melting point and mixed melting point of the sulfone derivative (see below).

TABLE II

EFFECT OF VARIOUS AGENTS ON THE CYANOETHYLATION OF THIOPHENOL

Thiophenol, g.	Acrylonitrile, g.	Added agent	Duration, hr.	Yield of sulfide, %
18.9	20	Irradiation	1	84.3
20.25	16	Irradiation	3	96.0
6.4	12	0.05 g. benzoyl peroxide	4	65.6
20.0	16	0.10 g. benzoyl peroxide, and irradiation	3	61.9
7.85	12	0.07 g. pyrogallol	4	80
15.2	20	0.10 g. hydroquinone	3	88.4
14.2	16	0.10 g. conc. hydrochloric acid	3	28.1
10.0	8	0.07 g. conc. hydrochloric acid	16	19.9
9.0	10	0.05 g. mercuric acetate	16	<4.5

**Alkanethiols.**—Irradiation, benzoyl peroxide, both peroxide and irradiation, or mercuric acetate were all ineffective in initiating reaction between acrylonitrile and either 2-propanethiol (0.1–0.25 molar quantities taken) or ethyl mercaptoacetate. Only a trace of sulfide was formed, comparable to the yield when no catalyst was present. There was non-reaction when acrylonitrile was stirred for sixteen hours at 25° with a mixture of 1 part of sodium mercaptoacetate and 6 parts of mercaptoacetic acid.

**Dimerization Effects with Thiophenol and Acrylonitrile.**—To a mixture of 13.4 g. of thiophenol and 0.10 g. of concentrated hydrochloric acid was added 16 g. of acrylonitrile. After a week these products were separated by distillation: 5.3 g. of thiophenol at 81–91° (37 mm.); 5.2 g. of  $\beta$ -phenylmercaptpropionitrile at 183–187° (26 mm.); 0.70 g. of fraction A,  $n_D^{20}$  1.5650, at 217–220° (4 mm.); 0.70 g. of fraction B,  $n_D^{20}$  1.5605, at 220–225° (4 mm.); then 2 g. chiefly of thiophenol at 234–237° (4 mm.) caused by pyrolysis of the residue. Fraction B contained a little thiophenol, since it gave a small precipitate with 5% lead acetate solution. Fraction A gave no such precipitate.

*Anal.* Calcd. for  $C_{12}H_{12}N_2S$ : C, 66.62; H, 5.59; N, 12.95. Found, Fraction A: C, 65.98; H, 5.48; N, 11.17. Found, fraction B: N, 9.75.

Similar high boiling material was obtained by refluxing for about ten hours a mixture of 18.2 g. of thiophenol, 0.10 g. of concentrated hydrochloric acid, and 28 g. of acrylonitrile. The yellow liquid was decanted from resin formed in the flask and distilled, yielding 1.2 g. thiophenol, and 10.3 g. of  $\beta$ -phenylmercaptpropionitrile at 182–189° (30 mm.). A 1.4-g. fraction,  $n_D^{20}$  1.5698, was then collected up to 216° (4 mm.); 3.6 g. of  $n_D^{20}$  1.5633 at 218–219° (4 mm.); and finally 10.8 g. of product containing much thiophenol through decomposition.

**3-Methylmercaptopropanal via Stephen Reaction.**—The general procedure of Williams<sup>14</sup> was followed. From 20 g. of  $\beta$ -methylmercaptpropionitrile, after reaction with stannous chloride (76 g.) and hydrogen chloride in ether, was isolated 7 g. of viscid sirup from which 1 g. (5%) of 3-methylmercaptopropanal was isolated by distillation,

(14) Williams, "Organic Syntheses," **23**, 63 (1943).

TABLE III  
 AROMATIC  $\beta$ -SULFONYLPROPIONIC ACIDS, NITRILES AND AMIDES

Ar	M. p., °C.	Acids, $\text{ArSO}_2\text{CH}_2\text{CH}_2\text{COOH}$				Nitriles, $\text{ArSO}_2\text{CH}_2\text{CH}_2\text{CN}$			Amides, $\text{ArSO}_2\text{CH}_2\text{CH}_2\text{CONH}_2$		
		Analyses, %		Analyses, % N		M. p., °C.	Analyses, % N		M. p., °C.	Analyses, % N	
		Calcd.	Found	Calcd.	Found		Calcd.	Found		Calcd.	Found
$\text{C}_6\text{H}_5^b$	125.5-126	50.47	4.71	50.50	4.95	95.5-96	7.18	7.30	126.5 <sup>f</sup>	6.57	6.57
$\text{C}_6\text{H}_5\text{CH}_2^c$	174.5-176	52.61	5.30	53.39	5.58	117-117.5	6.69	7.06	190-191 (dec.) <sup>e</sup>	6.16	6.07
<i>o</i> - $\text{CH}_3\text{C}_6\text{H}_4$	.....	.....	.....	.....	.....	72	6.69	6.40	162-162.5	6.16	5.93
<i>m</i> - $\text{CH}_3\text{C}_6\text{H}_4$	95-95.5	52.61	5.30	52.40	5.39	50.5-51	6.69	6.35	134.5	6.16	5.80
<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4^d$	112.5-113.5 <sup>e</sup>	52.61	5.30	52.60	5.18	93.5-94	6.69	6.53	177-177.5	6.16	6.09

<sup>a</sup> Rods (from water). <sup>b</sup> Different synthesis of this acid reported in ref. 2, 13. <sup>c</sup> Different synthesis: ref. 2, 15. <sup>d</sup> Different synthesis: Kohler and Reimer, *Am. Chem. J.*, **31**, 175 (1904). Carothers, *THIS JOURNAL*, **55**, 2011 (1933). <sup>e</sup> Small compact crystals; all the others are acicular. <sup>f</sup> Previously made by a different method (ref. 13), the m. p. being listed as 123-124°.

b. p. 90-105° (40 mm.). Its orange-colored 2,4-dinitrophenylhydrazone derivative, after crystallization from ethanol, melted at 118.5-119.5°.

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_{12}\text{N}_4\text{O}_4\text{S}$ : N, 19.72. Found: N, 19.46.

**Aromatic  $\beta$ -Sulfonylpropionitriles.**—Several substituted mercaptopropionitriles were oxidized to the corresponding sulfones by adding a 50% excess of hydrogen peroxide to a solution of the mercapto compound in acetic acid. The flask was first cooled to avoid excessive heat of reaction, then heated at 100° for about four hours, a procedure which also produced about 7% of the corresponding amide,  $\text{RSO}_2\text{CH}_2\text{CH}_2\text{CONH}_2$ . An alternate procedure was to allow the mixture to stand at 25° for one week. Both procedures gave about the same yield, and both gave rise to 4-7% concurrent hydrolysis to the sulfonylpropionamide,  $\text{RSO}_2\text{CH}_2\text{CH}_2\text{CONH}_2$ , and a trace of the corresponding acid. The details of the experiment with  $\beta$ -*p*-tolylmercaptpropionitrile are typical.

$\beta$ -*p*-Toluenesulfonylpropionitrile.—To 3.1 g. of  $\beta$ -*p*-tolylmercaptpropionitrile in 5 ml. of glacial acetic acid was added 5.2 g. of 30% hydrogen peroxide solution (Merck Superoxol). The exothermic reaction which developed within five minutes necessitated cooling by shaking the flask under the tap. At first there were two layers, but the content soon became homogeneous. After five hours on the steam-bath, the cooled colorless liquid was poured into 10 ml. of ice water. The resulting solid was filtered and dried; weight, 3.1 g. (85%), m. p. 90-92°. After recrystallization from dilute aqueous alcohol (or hot water), it melted at 93.5-94°.

Concentration of the filtrate yielded 0.3 g. of solid melting over a wide range. One crystallization from hot water brought the m. p. to 165-168° (m. p. of the pure amide, 177°). The acid contaminant in this amide was readily separated by aqueous sodium carbonate.

Physical constants and analytical data for these sulfones are listed in Table III. Melting points are uncorrected. *m*-Toluenesulfonylpropionitrile tended to be an oil but gradually crystallized when stored in a vacuum desiccator over sulfuric acid. It crystallized from 50% alcohol in the form of plates.  $\beta$ -(Phenylmethanesulfonyl)-propionitrile crystals were micaceous in appearance.

**Substituted  $\beta$ -Sulfonylpropionic Acids.**—These acids (Table III) were prepared from the corresponding nitriles by refluxing the latter with 70% sulfuric acid solution. Yields were 54-58%. The example cited below for  $\beta$ -benzenesulfonylpropionic acid is typical.

$\beta$ -Benzenesulfonylpropionic Acid.—A mixture of 1.0 g. of  $\beta$ -benzenesulfonylpropionitrile and 4 ml. of 70% sulfuric acid was heated under reflux for thirty-five minutes, and the resulting clear, light brown solution, after cooling, was taken up in 8 ml. of water, filtered, the solid dissolved in 5% aqueous sodium carbonate, and the acid reprecipitated by sulfuric acid. There resulted 0.61 g. (55%) of  $\beta$ -benzenesulfonylpropionic acid. Compact

white crystals were obtained on recrystallization from water; m. p. 125.5-126°.

**Amides.**—In these hydrolyses the respective sulfonylpropionitriles were treated with concentrated sulfuric acid, then the contents were poured into ice water. The benzene- and toluenesulfonylpropionitriles gave violet colored solutions at this point, whereas phenylmethanesulfonylpropionitrile produced a green colored solution. This procedure, as exemplified by the synthesis of  $\beta$ -*p*-toluenesulfonylpropionamide, was employed for the last four compounds in Table III. Benzenesulfonylpropionamide was made by treatment of  $\beta$ -benzenesulfonylpropionic acid with thionyl chloride, followed by reaction of the acid chloride with concentrated ammonium hydroxide.

$\beta$ -*p*-Toluenesulfonylpropionamide.— $\beta$ -*p*-Toluenesulfonylpropionitrile (0.37 g.) was dissolved in 1 ml. of concentrated sulfuric acid. After nineteen hours, the mixture was poured into 3 ml. of ice water. The product was filtered, washed, and dried. It weighed 0.39 g. (97%). After washing with a small amount of aqueous sodium carbonate and recrystallization from 9 ml. of hot water, the white needles (0.29 g.) melted at 177-177.5°.

**Reaction of Mercapto Compounds with Methyl Acrylate and Methyl Methacrylate.**—The experimental techniques employed in the reactions of alkanethiols and thiophenol with acrylic and methacrylic esters in the presence or absence of basic catalysts were similar to those outlined under the reactions with acrylonitrile. An excess of the acrylic ester was employed. No significant amount of polymeric product was produced.

The substituted mercaptopropionic and mercaptoisobutyric esters were mobile liquids, soluble in the usual organic solvents. The odors were mild and, in some cases, typically ester-like. Methyl  $\beta$ -isopropylmercaptpropionate and methyl  $\beta$ -*t*-butylmercaptpropionate possessed odors reminiscent of dill seed oil. The following examples are typical of the procedures employed:

**Methyl  $\beta$ -Phenylmercaptpropionate.**—A chilled mixture of 22 g. of thiophenol and 0.20 g. of sodium methoxide, after dropwise addition of 38 g. of methyl acrylate, was stirred for sixteen hours at 25°. The contents were filtered to remove base and a small amount of polymerized ester. After the unreacted ester was removed under reduced pressure, the residue was distilled to yield 38 g. (96%) of methyl  $\beta$ -phenylmercaptpropionate of b. p. 133-155.5° (13 mm.). On redistillation, it boiled exclusively at 153.5° (12 mm.).

**Methyl  $\beta$ -Carbomethoxymethylmercaptisobutyrate.**—Similar directions were followed. The reaction mixture was made up of 10 g. of ethyl mercaptoacetate, 0.10 g. of sodium methoxide, and 15 g. of methyl methacrylate. The mixture was stirred for thirty minutes at 25°, then rid of methyl methacrylate under diminished pressure. There resulted 16.0 g. (87.9%) of methyl  $\beta$ -carbomethoxymethylmercaptisobutyrate, b. p. 129.5-131° at 4 mm. The yield for a comparable seventeen-hour experiment, but employing twice these quantities, was 96%.

**Methyl  $\beta$ -Hydroxyethylmercaptpropionate.**—To a chilled, stirred mixture of 15.6 g. of 2-mercaptoethanol

(15) Holmberg, *Arkiv Kemi, Mineral Geol.*, **A14**, No. 8 (1940); *C. A.*, **35**, 2114 (1941).

TABLE IV  
 DATA CONCERNING  $\text{RSCH}_2\text{CH}_2\text{COOCH}_3$ 

RSH	g.	Base <sup>a</sup>	Yield, %	B. p. (uncor.)				Formula	Analyses, %							
				°C.	Mm.	$d^{20}_{20}$	$n^{20}_D$		Calcd. C	Calcd. H	Found C	Found H	Sapn. equiv. Calcd.	Found		
$\text{CH}_3$	27 <sup>b</sup>	A	86 <sup>a</sup>	80.5	15	1.075	1.4646	.....	.....	.....	.....	.....	.....	.....	.....	
<i>i</i> - $\text{C}_3\text{H}_7$	16	A	97	94	13	1.012	1.4610	$\text{C}_7\text{H}_{14}\text{O}_2\text{S}$	51.83	8.70	52.03	8.71	162	158		
<i>i</i> - $\text{C}_3\text{H}_7$	12	..	5													
<i>i</i> - $\text{C}_3\text{H}_7$	11 <sup>d</sup>	..	9													
<i>t</i> - $\text{C}_4\text{H}_9$	19	A	96	102	17	0.986	1.4604	$\text{C}_8\text{H}_{16}\text{O}_2\text{S}$	54.50	9.15	54.70	9.09	176.3	180.9		
$\text{HOCH}_2\text{CH}_2$	35	A	60	138.5	9	1.163	1.4908	$\text{C}_6\text{H}_{12}\text{O}_3\text{S}$	43.88	7.37	43.54	7.55	164	161		
$\text{HOCH}_2\text{CH}_2$	16	B	89													
$\text{C}_2\text{H}_5\text{OOCCH}_2$	21	A	96	142	8	1.148	1.4700	$\text{C}_8\text{H}_{14}\text{O}_4\text{S}$	46.60	6.84	46.81	6.93	103	101		
$\text{C}_6\text{H}_5\text{CH}_2$	24	A	91	173	14	1.119	1.5414	$\text{C}_{11}\text{H}_{14}\text{O}_2\text{S}$	62.82	6.71	63.06	6.75	210	208		
$\text{C}_6\text{H}_5$	22	A	96	153.5	12	1.142	1.5510	$\text{C}_{10}\text{H}_{12}\text{O}_2\text{S}$	61.19	6.16	61.76	6.30	...	...		
$\text{C}_6\text{H}_5$	22	B	98													
$\text{C}_6\text{H}_5$	17 <sup>e</sup>	..	52 <sup>f</sup>													

<sup>a</sup> Same as Table (I), (a); 0.2–0.4 g. of base used. <sup>b</sup> Dissolved in 100 ml. of benzene at 2°. Reaction gradually raised to room temperature after the dropwise addition of methyl acrylate. <sup>c</sup> Method of Redemann and Lucas, *Ind. Eng. Chem., Anal. Ed.*, 9, 521 (1937). This method gave much lower than the calculated values for methyl  $\beta$ -phenylmercapto-propionate and methyl  $\beta$ -phenylmercaptoisobutyrate even under a longer saponification period. <sup>d</sup> Heated on steam-bath for five hours. <sup>e</sup> Recovered 3.65 g. (21.2%). After distilling off the 16.1 g. of product, there was collected about 6 g. of liquid, b. p. 184° (2 mm.);  $n^{20}_D$  1.5295,  $d^{20}_{20}$  1.161. It was probably methyl 2-phenylmercaptoadipate. <sup>f</sup> Or 66.0% yield, if based on unrecovered thiophenol. <sup>g</sup> Previously prepared by different method, ref. 5.

 TABLE V  
 DATA<sup>a</sup> CONCERNING  $\text{RSCH}_2\text{CH}(\text{CH}_3)\text{COOCH}_3$ 

RSH	g.	Yield, %	B. p. (uncor.)				Formula	Analyses, %							
			°C.	Mm.	$d^{20}_{20}$	$n^{20}_D$		Calcd. C	Calcd. H	Found C	Found H	Sapn. equiv. Calcd.	Found		
$\text{CH}_3$	35 <sup>b</sup>	62 <sup>c</sup>	79	12	1.039	1.4610	$\text{C}_8\text{H}_{12}\text{O}_2\text{S}$	48.62	8.16	48.95	8.64	148	150		
<i>i</i> - $\text{C}_3\text{H}_7$	20	98	91	10	0.988	1.4578	$\text{C}_8\text{H}_{16}\text{O}_2\text{S}$	54.50	9.15	54.32	9.42	176	175		
<i>i</i> - $\text{C}_3\text{H}_7$	7 <sup>d</sup>	0.7													
$\text{C}_2\text{H}_5\text{OOCCH}_2$	20	96	139	7	1.115	1.4667	$\text{C}_9\text{H}_{16}\text{O}_4\text{S}$	49.07	7.32	49.02	7.44	110	106		
$\text{C}_2\text{H}_5\text{OOCCH}_2$	10 <sup>e</sup>	89													
$\text{C}_6\text{H}_5\text{CH}_2$	21	96	169.5	13	1.091	1.5323	$\text{C}_{12}\text{H}_{16}\text{O}_2\text{S}$	64.24	7.19	64.64	7.40	224	217		
$\text{C}_6\text{H}_5$	22	97	154 <sup>f</sup>	13	1.111	1.5406	.....	.....	.....	.....	.....	.....	.....		
$\text{C}_6\text{H}_5$	16 <sup>g</sup>	51 <sup>h</sup>													

<sup>a</sup> No base employed in runs 3 and 8; 0.2–0.3 g. of sodium methoxide used in other runs. <sup>b</sup> Dissolved in 129 g. of benzene at 2°. <sup>c</sup> Same as Table IV, c. <sup>d</sup> Irradiated for sixteen hours at 25°. <sup>e</sup> Reaction time thirty minutes. <sup>f</sup> Jacobson, ref. 4, lists the b. p. as 129–130° (2.5 mm.);  $n^{20}_D$  1.5420. His preparation involved irradiation for a period of one week. <sup>g</sup> There was recovery of 3.3 g. <sup>h</sup> Based on 16.4 g. of thiophenol, or 64.5% based on 13.1 g. <sup>i</sup> This low yield is due to very large losses in handling the  $\text{CH}_3\text{SH}$ .

containing 0.15 g. of Triton B solution was added 35 g. of methyl acrylate with cooling. After sixteen hours at 25° the excess acrylate was removed under reduced pressure. A total of 29.9 g. (89%) of the sulfide resulted at 153–155° (19 mm.) together with 3 g. of still residue, which was water-soluble but quite dark and viscous. The sulfide was soluble in water and reacted vigorously with acetyl chloride. No mercaptide formed with aqueous lead acetate. Physical constants are given in Table IV.

**Benzoate.**—Benzoylation of the above compound by benzoyl chloride and pyridine (100°, five minutes) gave rise to methyl  $\beta$ -(2-benzyloxyethylmercapto)-propionate in 85% yield; b. p. 200.5° (4.5 mm.);  $n^{20}_D$  1.5310.

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{16}\text{O}_4\text{S}$ : neutr. eq., 134.2. Found: neutr. eq., 134.6.

**Methyl 3-Thia-6-oxa-8-cyano-1-octanecarboxylate.**—No evidence of reaction was apparent when 20 g. of acrylonitrile was added to 27 g. of methyl  $\beta$ -hydroxyethylmercapto-propionate containing 0.12 g. of Triton B. After standing at 25° for sixteen hours, 87% of this ester was recovered. Even the small still residue gave positive alcohol tests. There was some reaction, however, (29% yield) when a similar mixture was heated on the steam-bath for twenty-four hours. The ester,  $\text{NCCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{SCH}_2\text{CH}_2\text{COOCH}_3$ , gave negative tests for hy-

droxyl and possessed these constants: b. p. 178.5–180° (2 mm.);  $n^{20}_D$  1.4874.

*Anal.* Calcd. for  $\text{C}_9\text{H}_{15}\text{O}_3\text{NS}$ : N, 6.45. Found: N, 6.58.

**Thiophenol and Methyl Acrylate.**—Twenty grams of methyl acrylate was added to 17 g. of thiophenol containing 0.10 g. of concentrated hydrochloric acid. The initial heat was counteracted by a cooling bath. After sixteen hours (25°) 3.1 g. of thiophenol was removed, then 16 g. of methyl  $\beta$ -phenylmercapto-propionate at 173–182° (27 mm.). Distillation of the residue at 4 mm. yielded 1.65 g. to 187°, 2.1 g. at 193–196° ( $n^{20}_D$  1.5350), 4.4 g. at 198–199° ( $n^{20}_D$  1.5300,  $d^{20}_{20}$  1.163). The last fraction contained S, but no SH group by the lead acetate test. The product was probably methyl 2-phenylmercaptoadipate.

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{18}\text{O}_4\text{S}$ : C, 59.55; H, 6.43. Found: C, 59.80; H, 6.72.

**Thiophenol and Methyl Methacrylate.**—A solution of thiophenol and 23.5 g. of methyl methacrylate was allowed to stand in the dark for a period of sixteen hours at 25° after which time the excess methacrylate was distilled off under reduced pressure. Aside from 3.3 g. of recovered thiophenol, the products included 16.1 g. of methyl  $\beta$ -

TABLE VI  
SULFONE ESTERS

Compound	M. p., °C.	Formula	Analyses, %			
			Calcd. C	Calcd. H	Found C	Found H
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> SO <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> COOCH <sub>3</sub>	104	C <sub>11</sub> H <sub>14</sub> O <sub>4</sub> S	54.52	5.82	54.94	5.94
C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> COOCH <sub>3</sub>	71.5-72.5 <sup>a</sup>	C <sub>10</sub> H <sub>12</sub> O <sub>4</sub> S	52.60	5.30	52.77	5.27
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> SO <sub>2</sub> CH <sub>2</sub> CH(CH <sub>3</sub> )COOCH <sub>3</sub>	50-50.5	C <sub>12</sub> H <sub>16</sub> O <sub>4</sub> S	56.22	6.29	55.69	6.52
C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> CH <sub>2</sub> CH(CH <sub>3</sub> )COOCH <sub>3</sub>	57 <sup>a</sup>	C <sub>11</sub> H <sub>14</sub> O <sub>4</sub> S	54.52	5.82	54.83	5.77

<sup>a</sup> Needles.

phenylmercaptpropionate, and a 9.1-g. fraction collected at 239-244 (29 mm.). Redistillation of the last fraction yielded 7.5 g. of light yellow and mild-odored liquid; b. p. 194-198° (3.5 mm.),  $n_{D}^{20}$  1.5272, agreeing in constants with the methyl 2-phenylmercapto-2,5-dimethylacipate reported by Jacobson<sup>4</sup> in irradiation experiments.

*Anal.* Calcd. for C<sub>16</sub>H<sub>22</sub>O<sub>4</sub>S: C, 61.92; H, 7.14. Found: C, 62.30; H, 7.21.

Data concerning substituted  $\beta$ -mercaptpropionic esters are presented in Table IV. The analogous isobutyric derivatives are treated in Table V. Duration of the runs are for overnight (sixteen hours) periods at room temperature unless otherwise stated. Each of the runs employed 1.4-2.5 molar amounts of methyl acrylate or methyl methacrylate, respectively.

**Aromatic  $\beta$ -Sulfonylpropionic and Isobutyric Esters.**—A number of  $\beta$ -mercaptpropionic and isobutyric esters were oxidized to the sulfones. The procedure comprised treatment of the chilled sulfide in glacial acetic acid with excess superoxol and allowing the mixture to stand at room temperature for four days. The resulting solution was then poured into water. If solid, the sulfone was filtered; when oily, the aqueous layer was evaporated at 25°. This procedure is exemplified by the following preparation.

**Methyl  $\beta$ -(Phenylmethanesulfonyl)-propionate.**—A chilled solution of 7.8 g. of methyl  $\beta$ -benzylmercaptpropionate in 7 ml. of glacial acetic acid was treated with 14 g. of Superoxol, the contents being allowed to stand at 25° for four days. A thick crystalline slurry resulted, which was poured into 20 ml. of ice water. The resulting solid was filtered off and washed with 15 ml. of water. The dried solid (4.3 g.) melted at 98-100.5°. Development of the filtrate yielded another 3.7 g., m. p. 101-102.5°, making a total of 8.0 g. (88%). There was also separated (by sodium carbonate treatment) 0.6 g. of crude acid (m. p. 171-174°). Two recrystallizations from aqueous ethanol yielded the pure ester in plates of m. p. 104°.

The sulfone esters are presented in Table VI. Each run was comparable in size to the above. Yields ranged from 88-95%.

**$\beta$ -Methylmercaptpropionyl Chloride.**—Methyl  $\beta$ -methylmercaptpropionate (51 g.) was saponified (150 g. of 20% NaOH solution, 100°, one-half hour). The cooled solution was extracted with ether before acidification. The  $\beta$ -methylmercaptpropionic acid which separated from the aqueous solution on acidification was separated, dried (sodium sulfate) and distilled; yield 42 g., or 93%. It possessed these constants: b. p. 129.5-130° (14 mm.),  $n_{D}^{20}$  1.4898,  $d_{20}^{20}$  1.158, neut. equiv. 118 (calcd. 120).

When 36 g. of the acid was treated with 53 g. of thionyl chloride, an endothermic process took place, the flask becoming quite cold. Much hydrogen chloride was evolved. The reaction was completed by heating on the steam-bath for thirty-five minutes. Distillation brought over 35 g. (85%) of the acid chloride, b. p. 99.5-106° (40 mm.), possessing a very foul, piercing odor. On redistillation, it boiled at 98-101° (34 mm.),  $n_{D}^{20}$  1.500.

*Anal.* (Parr fusion) Calcd. for C<sub>4</sub>H<sub>7</sub>ClOS: Cl, 25.60. Found: Cl, 25.77.

**$\beta$ -Benzylmercaptpropionic Acid from Sodium Acrylate.**—A 2-layer system persisted for a considerable period after adding 26 g. of phenylmethanethiol to a solution of 19 g. of sodium acrylate and 50 ml. of water. After heating for four hours on the steam-bath, however, the mix-

ture became homogeneous. The unreacted phenylmethanethiol (2 g.) was separated. Evaporation of the water solution and drying at 120° left a residue of 40 g. This was dissolved in 60 ml. of water and acidified with sulfuric acid giving rise to an oil which soon crystallized<sup>16</sup>; yield, 33 g., m. p. 81-81.5°.

No reaction occurred at 25° when 19 g. of sodium acrylate was stirred for sixteen hours in suspension with 26 g. of phenylmethanethiol and 75 ml. of dioxane.

**3-Methylmercaptopropanal.**—A stirred, chilled mixture of 30 g. of methanethiol and 0.20 g. of sodium methoxide in 85 g. of anhydrous benzene was treated with 35 g. of freshly distilled acrolein over a period of thirty minutes. After nine hours at 25°, and ninety minutes at 55-60°, it was cooled, filtered and distilled; yield, 19 g. (31%) at 75-83° (24 mm.). The residue, when treated with a few drops of concentrated sulfuric acid and further heated at reduced pressure, gave another gram of product, but there was extensive carbonization. The 3-methylmercaptopropanal, on redistillation, boiled exclusively at 71-72° (23 mm.). It was identical with the material obtained in the Stephen reduction of  $\beta$ -methylmercaptpropionitrile, as judged by the m. p. and mixed m. p. of the 2,4-dinitrophenylhydrazine derivatives.

**3-Benzylmercaptobutanal.**—A mixture of 34.5 g. of freshly distilled crotonaldehyde, 0.20 g. of sodium methoxide and 46 g. of phenylmethanethiol after stirring at 25° for sixteen hours, was filtered and vacuum distilled. Aside from the recovery of 32 g. (69%) of phenylmethanethiol, fractionation yielded 19 g. (26%) of 3-benzylmercaptobutanal, b. p. 170-174° (21 mm.). On redistillation, it boiled at 171-172° (20 mm.); constants,  $n_{D}^{20}$  1.5519,  $d_{20}^{20}$  1.07. Its odor was mild but persistent. It gave no reaction with lead acetate. It was insoluble in water, soluble in alcohol or ether.

*Anal.* Calcd. for C<sub>11</sub>H<sub>14</sub>OS: C, 67.99; H, 7.26. Found: C, 68.13; H, 7.59.

**Semicarbazone.**—Reaction of this aldehyde with semicarbazide hydrochloride yielded a crystalline semicarbazone from aqueous alcohol, m. p. 109.5-110.5°.

*Anal.* Calcd. for C<sub>11</sub>H<sub>15</sub>N<sub>3</sub>OS: N, 17.7. Found: N, 17.0.

**Cyanoethylation of 2-Hydroxyethyl Sulfide.**—An induction period of fifteen minutes was observed before a mixture of 26 g. of 2-hydroxyethyl sulfide, 0.20 g. of 35% Triton B, and 49.5 g. of acrylonitrile displayed a vigorous exothermic reaction, necessitating cooling. The orange-red solution was then warmed four hours on the steam-bath and distilled thirty-six hours later. The forerun (3.9 g.) contained unreacted sulfide. Then a 40-g. fraction was collected at 189-234° at 5 to 3 mm. (some decomposition). The residue was about 4 g. and dark in color. Repeated fractionation yielded two components with the following properties:

(A) Monocyanoethylated product (13 g.) had a b. p. 198° (6.5 mm.),  $n_{D}^{20}$  1.4993,  $d_{20}^{20}$  1.133. It reacted with acetyl chloride, and was miscible with ethanol, acetone, benzene, water but only partially soluble in ether.

*Anal.* Calcd. for C<sub>7</sub>H<sub>13</sub>NO<sub>2</sub>S: C, 48.00; H, 7.43; N, 8.00. Found: C, 47.15; H, 7.34; N, 8.09.

(16) Previously synthesized by Mörner, *Z. physiol. Chem.*, **42**, 352 (1904); Schönberg and Iskander, *J. Chem. Soc.*, 93 (1942); also ref. 2, 15.

(B) Dicyanoethylated product (25 g.) boiled mainly at 245–246° (6 mm.),  $n_D^{20}$  1.4900,  $d_4^{20}$  1.113. This water-insoluble product gave no reaction with acetyl chloride. It was miscible with acetone and benzene, soluble in ethanol, but much less so in ether.

*Anal.* Calcd. for  $C_{10}H_{16}N_2O_2S$ : C, 52.63; H, 7.02; N, 12.28. Found: C, 52.75; H, 6.61; N, 12.23.

**Behavior of 2-Hydroxyethyl Sulfide toward Methyl Acrylate.**—Over 85% of this sulfide was recovered when the reaction of 23.0 g. of it with 38 g. methyl acrylate in the presence of 0.13 g. Triton B solution was attempted. As in the above case, the mixture was heated for four hours on the steam-bath prior to distillation.

**Crystallographic Examination of  $\beta$ -Benzenesulfonylpropionic Acid and its Amide.**— $\beta$ -Benzenesulfonylpropionic acid is uniaxial and positive. It has a high birefringence:  $N_\omega$  (or  $n_\alpha$ ) 1.569,  $N_\epsilon$  (or  $n_\gamma$ ) 1.620. It seems to be tetragonal but may be hexagonal.

The amide is triclinic with these indices:  $n_\alpha$  1.530,  $n_\gamma$  1.640, indicating a high birefringence (0.110). Because

of the elongation of the crystal fragments, orientation to obtain  $n_\beta$  was not possible.

**Acknowledgments.**—Most of the micro combustion analyses (carbon, hydrogen, nitrogen) reported in this paper were performed by Mrs. M. M. Ledyard. A few were carried out by Miss W. A. Brandt, Miss Rita Pivan and Dr. T. S. Ma. We are indebted to M. D. Quigley of the Geology Department, Northwestern University for the crystallographic data.

#### Summary

The chemistry of the addition of alkanethiols and thiophenols to acrylic and methacrylic derivatives (nitrile, ester, salt, aldehyde) is presented. The role of catalysts is considered in some detail.

EVANSTON, ILLINOIS

RECEIVED JANUARY 11, 1947

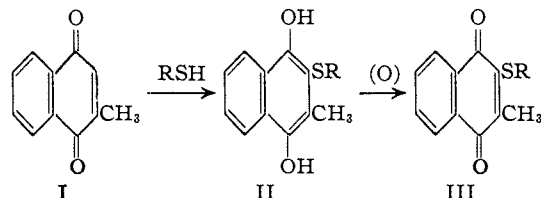
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

## The Addition of Sulfhydryl Derivatives to 2-Methyl-1,4-naphthoquinone<sup>1</sup>

BY LOUIS F. FIESER AND RICHARD B. TURNER

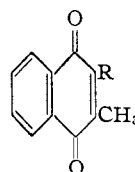
Although the alkyl substituent of 2-methyl-1,4-naphthoquinone prevents or greatly inhibits the addition of most reagents of the HA-type that add readily to unsubstituted quinones, it does not interfere markedly with the addition of sulfhydryl compounds.<sup>2</sup> This addition reaction has been utilized in the present investigation as a route to the synthesis of 2,3-disubstituted 1,4-naphthoquinones of types that seemed to offer some prospect of having antihemorrhagic or bacteriostatic activity<sup>3</sup> or of having application in chemotherapy.

The initial addition, usually conducted in alcoholic solution at room temperature, affords a thio-substituted methyl-naphthohydroquinone (II) that subsequently may become partially oxidized by interaction with the starting quinone. Usually it was found expedient to submit the total reaction mixture to oxidation with silver oxide in ether solution and to isolate the product in the oxidized form (III). Substituted derivatives of the type



III were obtained in reactions with thioglycolic acid, benzyl mercaptan,  $\alpha$ -mercaptostearic acid, and homocysteine.

S-(2-Methyl-1,4-naphthoquinonyl-3)-thioglycolic acid (IV) is a crystalline solid soluble in aqueous bicarbonate solution. Assays for vitamin K activity in the chick (eighteen hour method) were kindly carried out on this and other new compounds by Dr. W. L. Sampson of the Merck Institute for Therapeutic Research. The quinone IV was found to possess half the antihemorrhagic activity ( $ED = 2\gamma$ ) of vitamin  $K_1$ . Since this quinone, like  $K_1$ , is fully substituted and hence not subject to interfering side reactions with body constituents to be expected of administered 2-methyl-1,4-naphthoquinone,<sup>2</sup> and since it is more readily accessible than  $K_1$  and has the added feature of forming water-soluble salts, the substance may warrant consideration for application to vitamin K therapy. The quinone acid IV was conjugated with glycine through its acid



IV, R =  $-\text{SCH}_2\text{CO}_2\text{H}$   
V, R =  $-\text{SCH}_2\text{CH}_2\text{CHCO}_2\text{H}$

VI, R =  $-\text{SCHC}_6\text{H}_{13-n}$   
 $\text{CO}_2\text{H}$

chloride, but the conjugate has an ED value between 5 and 50 $\gamma$ . The amino acid derivative V, prepared from methyl-naphthoquinone and homocysteine, is practically insoluble in both water and organic solvents and it is likewise only weakly active in the chick assay ( $ED = 50\gamma$ ). The quinone resulting from the addition of *s*-butyl mercaptan is an oil but was obtained in a pure con-

(1) From the doctoral dissertation of Richard B. Turner, May 1, 1942. The research was assisted by a fellowship from the Allied Chemical and Dyestuff Corporation in 1941–1942.

(2) Preliminary qualitative observations: Fieser, *Ann. Internal Med.*, **15**, 648 (1941); the analogous addition of thioglycolic acid to trimethylbenzoquinone is described by Snell and Weissberger, *This Journal*, **61**, 450 (1939).

(3) See discussion of quinone acids by Fieser, Gates and Kilmer, *ibid.*, **62**, 2966 (1940).