benzoate (100 ml.) and finely divided sodium metal (5 g.). The reaction mixture was refluxed on an oil bath (180–200°) for 6 hr. The reaction mixture was then cooled and treated with methyl alcohol (10 ml.) to remove any unchanged sodium, acidified with acetic acid, and left overnight. It was steam-distilled until all the ethyl benzoate was removed and the reaction mixture assumed a yellow color. It was then extracted with ether and worked up as usual. The ether was driven off and a yellow oil was obtained, b.p. 220–225°/2 mm., (yield 8 g.).

The above condensation product (3 g.) was mixed with hydriodic acid (sp. gr. 1.71, 30 ml.) and glacial acetic acid (30 ml.). The reaction mixture was refluxed for 10 hr. It was then poured on ice, extracted with ether, and the ethereal layer was dried (sodium sulfate). The ether was driven off and the remaining oil was triturated with petroleum ether (b.p. 60–80°) until it solidified to an amorphous powder. It was sublimed to give VIII, m.p. 245°, (yield 2.2 g.).

Anal. Calcd. for $C_{15}H_{10}O_3$: C, 75.62; H, 4.23. Found: C, 75.28; H, 4.22.

ABBASSIA, CAIRO, U.A.R.

[CONTRIBUTION FROM THE ORGANIC CHEMICALS DIVISION, NITRO RESEARCH DEPARTMENT, MONSANTO CHEMICAL CO.]

Thiazolethiols and Their Derivatives

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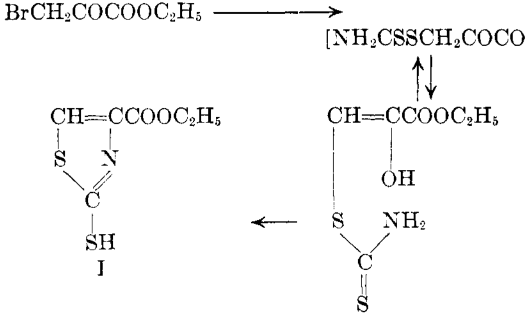
Ammonium dithiocarbamate and ethyl bromopyruvate reacted to give ethyl 2-mercapto-4-thiazolecarboxylate (I). Saponification of I gave 2-mercapto-4-thiazolecarboxylic acid. Thirty-four derivatives of I and related thiazolethiols were prepared. Oxidation of I, ethyl-2-mercapto-4-methyl-5-thiazolecarboxylate, or 2-mercapto-4-methyl-5-thiazolecarboxylic acid with hydrogen peroxide under acidic conditions gave the corresponding 4- or 5-substituted thiazoles.

Thiazolethiols and their derivatives have long been established as fundamentally important accelerators for the vlucanization of rubber with sulfur. Among the many derivatives prepared and screened, the thiazolesulfenamides, in particular, 2-(2,6-dimethylmorpholinothio)benzothiazole,[1] *N*-cyclohexyl-2-benzothiazolesulfenamide[2] and *N*-tert-butyl-2-benzothiazolesulfenamide,[3] have shown merit because of their delayed action. As thiazolethiols and their derivatives containing substituents, other than hydrocarbon radicals, in the 4-position have been prepared only in a limited number of examples,[4] it was desirable to prepare the unknown ethyl 2-mercapto-4-thiazolecarboxylate (I) and its derivatives. In addition, our objectives were: 1) the preparation of new derivatives of 5-substituted thiazolethiols and 2-mercaptobenzothiazole and 2) the synthesis of the 4- and 5-substituted thiazoles from the corresponding thiazolethiols. The accelerator activity for these new compounds will be reported in forthcoming patents.

Ammonium dithiocarbamate reacted with ethyl bromopyruvate to give I. The reaction may be represented as:



Saponification of I gave 2-mercapto-4-thiazolecarboxylic acid.

Diethyl 2,2′-dithiobis(4-thiazolecarboxylate) and 2,2′-dithiobis(4-thiazolecarboxylic acid) were prepared by the reaction of I or 2-mercapto-4-thiazolecarboxylic acid with an aqueous solution of ammonium persulfate.

The thiazolesulfenamides II, III, and IV were prepared by the oxidative condensation of I with *tert*-butylamine, cyclohexylamine, or morpholine.

The reaction of an aqueous solution of the sodium salt of I with zinc chloride or cadmium sulfate furnished the corresponding zinc and cadmium salt of I.

The reaction of an acetone solution of the potassium salt of I with β-dimethylaminoethyl chloride gave the desired ethyl 2-(2-dimethylaminoethylthio)-4-thiazolecarboxylate.

4-Ethoxycarbonyl-2-thiazolyl diethyldithiocarbamate was prepared by the reaction of the potassium salt of I with *N*,*N*-diethylthiocarbamoyl chloride.

The reaction of the potassium salt of I with 3-chloro-2,4-pentanedione, ethyl α-chloroacetoacetate, or chloroacetone gave ethyl 2-(1-acetyl acetonylthio)-4-thiazolecarboxylate (V), ethyl 2-(1-ethoxycarbonylacetonylthio)-4-thiazolecarboxylate (VI), and ethyl 2-acetonylthio-4-thiazolecarboxylate (VI), and ethyl 2-acetonylthio-4-thiazolecarboxylate (VII), respectively.

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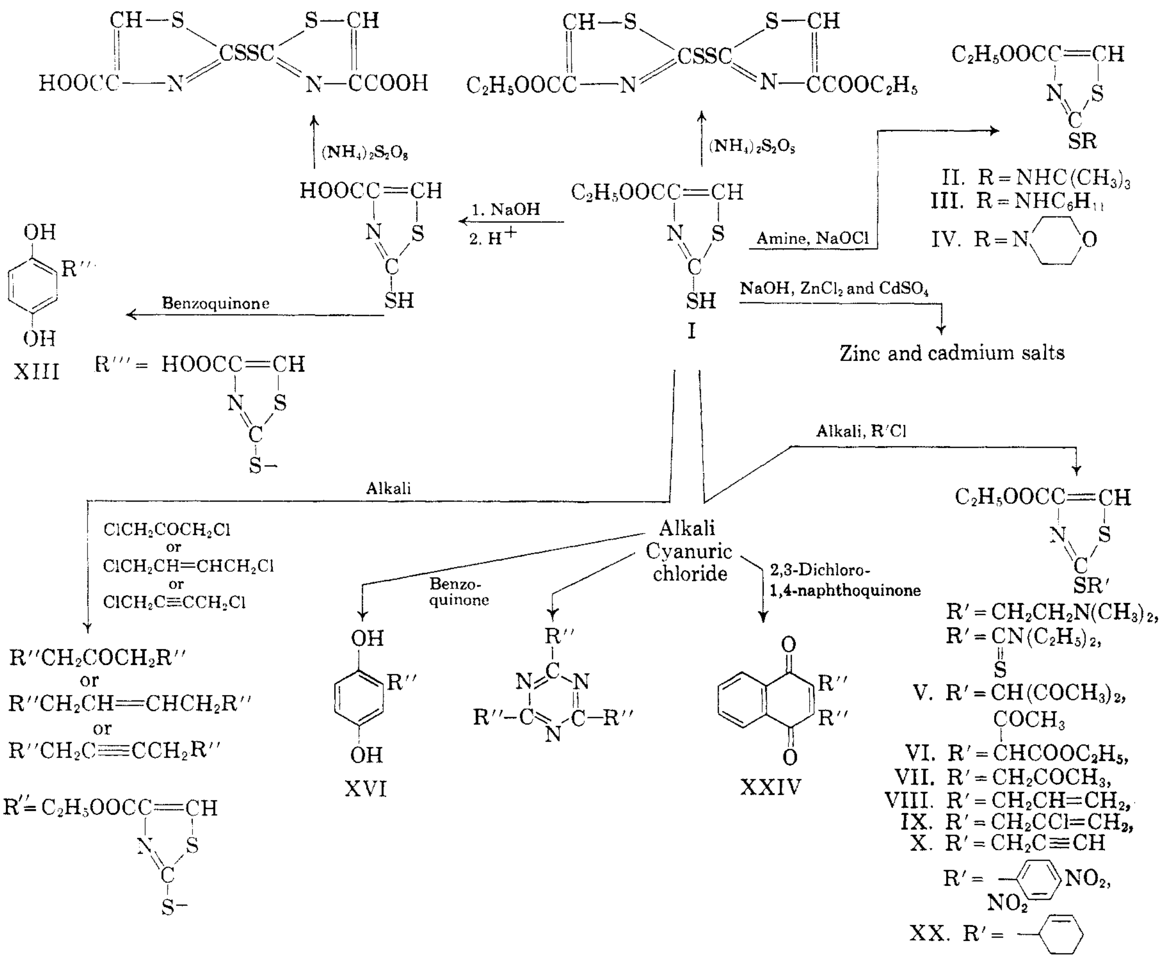
[1] J. J. D'Amico, M. W. Harman, and R. H. Cooper, *J. Am. Chem. Soc.*, **79**, 5270 (1957); U. S. Patent **2,871,239**.

[2] M. W. Harman, *Ind. Eng. Chem.* **29**, 205 (1937); U. S. Patent **2,191,656**.

[3] R. H. Cooper and J. J. D'Amico, U. S. Patent **2,807,620**.

[4] J. J. D'Amico, *J. Am. Chem. Soc.*, **77**, 476 (1955).



Diethyl 2,2′-(2-oxotrimethylene)dithiobis(4-thiazolecarboxylate) was prepared by the reaction of an acetone solution of the potassium of I with 1,3-dichloro-2-propanone.

The reaction of the sodium salt of I with allyl chloride, 2,3-dichloro-1-propene, or 3-bromo-1-propyne furnished ethyl 2-allylthio-4-thiazolecarboxylate (VIII), ethyl 2-(2-chloroallylthio)-4-thiazolecarboxylate (IX), and ethyl 2-(2-propynylthio)-4-thiazolecarboxylate (X), respectively.

Ethyl 2-(2,4-dinitrophenylthio)-4-thiazolecarboxylate was obtained by the reaction of the potassium salt of I with 2,4-dinitrochlorobenzene.

Diethyl 2,2′-(2-butenylene)dithiobis(4-thiazolecarboxylate) and diethyl 2,2′-(2-butynylene)dithiobis(4-thiazolecarboxylate) were prepared by the reaction of the potassium salt of I with 1,4-dichloro-2-butene or 1,4-dichloro-2-butyne.

The potassium salt of I reacted with cyanuric chloride to form 2,4,6-tris(4-ethoxycarbonyl-2-thiazolylthio)*S*-triazine.

Employing the elegant procedure described by Newby[5] *p*-benzoquinone was allowed to react with the appropriate thiazolethiol to give XI through XVI.

5-Chloro-2-mercaptobenzothiazole, 2-mercaptobenzothiazole, 6-ethoxy-2-mercaptobenzothiazole, or I reacted with 3-bromocyclohexene to form 5-chloro-2-(2-cyclohexenylthio)benzothiazole (XVII), 2-(2-cyclohexenylthio)benzothiazole (XVIII), 6-ethoxy-2-(2-cyclohexenylthio) benzothiazole (XIX), and ethyl 2-(2-cyclohexenylthio)-4-thiazolecarboxylate (XX), respectively.

The reaction of 2,3-dichloro-1,4-naphthoquinone with the appropriate thiazolethiol furnished 2,3-bis(2-benzothiazolylthio)-1,4-naphthoquinone (XXI), 2,3-bis(5-chloro-2-benzothiazolylthio)-1,4-naphthoquinone (XXII), 2,3-(6-ethoxy-2-benzothiazolylthio)-1,4-naphthoquinone (XXIII), and diethyl 2,2′-(1,4-dihydro-1,4-dioxo-2,3-naphthylenedithio)bis(4-thiazolecarboxylate)(XXIV), respectively.

Following the procedure described by Buchman,[6] ethyl 4-methyl-5-thiazolecarboxylate (XXV), ethyl 4-thiazolecarboxylate (XXVI), and 4-methyl-5-thiazolecarboxylic acid (XXVII) were prepared by the oxidation of the corresponding thiazolethiols with hydrogen peroxide. H. T. Clarke[7] reported the preparation of XXV by the reaction of thioform-

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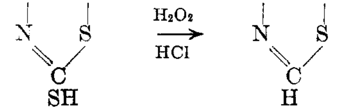
[5] T. H. Newby, U. S. Patent 2,616,871.

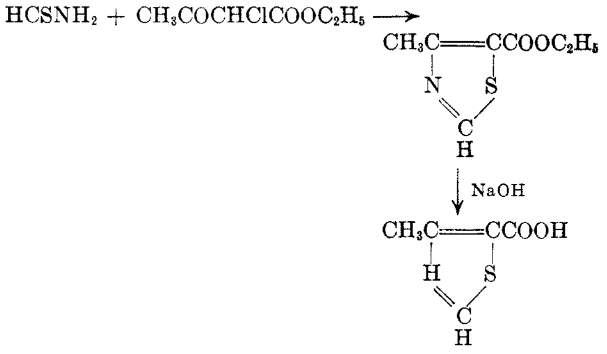
[6] E. R. Buchman, A. O. Reims, and H. Sargent, *J. Org. Chem.* 6, 764 (1941).

[7] H. T. Clarke and S. Gurin, *J. Am. Chem. Soc.*, 57, 1876 (1935).

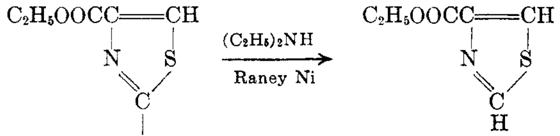
amide with ethyl α-chloroacetoacetate; and upon saponification of XXV obtained XXVII. H. Erlenmeyer[8] obtained XXVI by the reduction of ethyl 2-bromo-4-thiazolecarboxylate. These reactions may be represented as:



XXV. R = CH_3, R' = $COOC_2H_5$
XXVI. R = $COOC_2H_5$, R'=H
XXVII. R = CH_3, R' = COOH



XXVII



XXVI

EXPERIMENTAL[9]

Ethyl 2-mercapto-4-thiazolecarboxylate (I). To a stirred slurry containing 27.6 g. (0.25 mole) of ammonium dithiocarbamate and 150 ml. of ethyl alcohol was added 48.8g. (0.25 mole) of ethyl bromopyruvate[10]; the temperature rose immediately from 22 to 62°. The reaction mixture was stirred for 18 hr. and then heated at 70–80° for 2 hr. After the addition of 300 ml. of water and cooling to 10°, the precipitate was collected by filtration, washed with 200 ml. of cold water, and air-dried at 25–30°. The product, a light tan colored solid, m.p. 117–121°, was obtained in 65.7% yield, m.p. after recrystallization from ethyl alcohol 131–132°.

Anal. Calcd. for $C_6H_7NO_2S_2$: N, 7.40; S, 33.88. Found: N, 7.38; S, 33.98.

2-Mercapto-4-thiazolecarboxylic acid. A solution containing 44 g. (0.23 mole) of I, 74 g. (0.46 mole) of 25% aqueous sodium hydroxide solution and 100 ml. of water was stirred at 70–80° for 2 hr. After cooling to 15°, the solution was made acidic with concd. hydrochloric acid, the precipitate was collected by filtration, washed with 100 ml. of cold water, and air dried at 50°. The product, m.p. 246–250°, was obtained in 93.4% yield. After recrystallization from water it melted at 253–254°.

Anal. Calcd. for $C_4H_3NO_2S_2$: N, 8.69; S, 39.78. Found: N, 8.73; S, 39.64.

Diethyl 2,2'-dithiobis(4-thiazolecarboxylate) and 2,2'-dithiobis(4-thiazolecarboxylic acid). To an agitated suspension of 0.25 mole of either I or 2-mercapto-4-thiazolecarboxylic acid in 300 ml. of water was added dropwise a solution containing 63 g. (0.275 mole) of ammonium persulfate in 147 ml. of water over a 30-min. period at 25–30°. The reaction mixture was stirred for 2 additional hr. The precipitate was collected by filtration, washed with water until the wash water was neutral to litmus, and air-dried at 50°. The former product, m.p. 159–160° after recrystallization from ethyl alcohol, and the latter product, m.p. 267–268°, were obtained in 97.7 and 97.5% yields, respectively.

Anal. Calcd. for $C_{12}H_{12}N_2O_4S_4$: N, 7.44; S, 34.07. Found: N, 7.82; S, 33.78. Calcd. for $C_8H_4N_2O_4S_4$: N, 8.74. Found: N, 8.76.

Thiazolesulfenamides II, III, *and* IV. To an aqueous slurry containing 47.3 g. (0.25 mole) of I, 40 g. (0.25 mole) of 25% aqueous sodium hydroxide, and 50 ml. of water was added dropwise, with agitation, 1.5 to 2.0 moles of amine. After stirring for 15 min., 42 ml. of 25% sulfuric acid was added dropwise. To the resulting slurry was added dropwise at temperatures specified in Table I in 1.5 hr., 167 ml. (13.4 g./100 ml.) (0.30 mole) of aqueous sodium hypochlorite. The stirred reaction mixture was held at these temperatures for 1 hr. longer. The excess oxidizing agent was destroyed by the addition of 4 g. of sodium sulfite. For II the reaction mixture was extracted with 400 ml. of ethyl ether. The ether extract was washed with water until the washings were neutral to litmus and dried over sodium sulfate. Upon removal of the ether *in vacuo* a solid was obtained.

For III and IV the reaction mixture was cooled to 5°, the solid collected by filtration, washed with water until the wash water was neutral to litmus, and air-dried at 25–30°. The data are summarized in Table I.

Zinc and cadmium salts of I. To a stirred solution containing 47.3 g. (0.25 mole) of I, 40 g. (0.25 mole) of 25% aqueous sodium hydroxide, and 800 ml. of water was added in one portion 0.125 mole of zinc chloride or cadmium sulfate dissolved in 500 ml. of water. The reaction mixture was stirred for 2 hr., the resulting solid collected by filtration, washed with water until the washings were neutral to litmus, and air-dried at 50°. The zinc and cadmium salts were obtained in 88.8 and 84.7% yields, respectively.

Anal. Calcd. for $C_{12}H_{12}N_2O_4S_4Zn$: N, 6.34; S, 29.03; Zn, 14.80. Found: N, 6.35; S, 29.30; Zn, 14.25. Calcd. for $C_{12}H_{12}N_2O_4S_4Cd$: N, 5.73; S, 26.23; Cd, 22.99. Found: N, 5.58; S, 26.14; Cd, 22.10.

Ethyl 2-(2-dimethylaminoethylthio)-4-thiazolecarboxylate. To a stirred solution containing 47.3 g. (0.25 mole) of I, 32.2 g (0.50 mole) of 87% potassium hydroxide, and 400 ml. of acetone was added 36 g. (0.25 mole) of β-dimethylamino ethyl chloride hydrochloride. The reaction mixture was stirred at 25–30° for 24 hr. and filtered to remove potassium chloride. The acetone was removed *in vacuo* and the residue was filtered to remove a small amount of impurities. The product, an amber colored liquid, was obtained in 89.5% yield.

Anal. Calcd. for $C_{10}H_{16}N_2O_2S_2$: N, 10.76: S, 24.63. Found: N, 10.78; S, 24.34.

4-Ethoxycarbonyl-2-thiazolyl diethyldithiocarbamate. To a stirred solution containing 47.3 g. (0.25 mole) of I, 16.1 g. (0.25 mole) of 87% potassium hydroxide, and 400 ml. of acetone was added dropwise a solution containing 38 g. (0.25 mole) of *N*,*N*-diethylthiocarbamoyl chloride in 200 ml. of acetone. The reaction mixture was stirred for 4 hr. at 25–30° and filtered to remove the potassium chloride. The filtrate was added to 500 g. of ice water and stirred for 15 min. The resulting solid was collected by filtration, washed with water until free of chloride, and air-dried at 25–30°. The product, m.p. 100–105°, was obtained in 69.5% yield. After recrystallization from heptane it melted at 107–108°.

Anal. Calcd. for $C_{11}H_{16}N_2O_2S_3$: N, 9.20; S, 31.60. Found: 9.17: S, 31.63.

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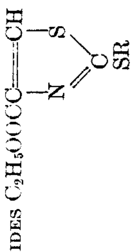
[8] H. Erlenmeyer and C. J. Morel, *Helv. chim. Acta*, **28**, 362 (1945).

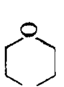
[9] All melting points were taken upon a Fisher-Johns block and are uncorrected.

[10] P. F. Kruse, Jr., N. Geurkink, and K. L. Gust, *J. Am. Chem. Soc.*, **76**, 5796 (1954).

TABLE I

THIAZOLESULFENAMIDES



No.	R	Amine	Mole Ratio, Amine to Thiazole	Reaction Temp., °	% Yield, Crude	M.P. °	Empirical Formula	% N Calcd.	% N Found	% S Calcd.	% S Found
II	$—NHC(CH_3)_3$	*tert*-Butylamine	6:1	30–40	49.4	99–101	$C_{10}H_{16}N_2O_2S_2$	10.76	10.72	24.63	24.55
III	$—NHC_6H_{11}$	Cyclohexylamine	8:1	45–50	42.0	112[a]	$C_{12}H_{18}N_2O_2S_2$	9.78	9.50	22.39	22.36
IV		Morpholine	8:1	45–50	55.3	155–157[a]	$C_{10}H_{14}N_2O_3S_2$	10.21	10.02	23.38	23.50

[a] Recrystallization from heptane.

Ethyl 2-(1-acetylacetonylthio)-4-thiazolecarboxylate (V), *ethyl 2-(1-ethoxycarbonylacetonylthio)-4-thiazolecarboxylate* (VI) *and ethyl 2-acetonylthio-4-thiazolecarboxylate* (VII). To a stirred solution containing 47.3 g. (0.25 mole) of I, 16.5 g. (0.25 mole) of 85% potassium hydroxide, 300 ml. of acetone, and 25 ml. of water was added in one portion 0.25 mole of 3-chloro-2,4-pentanedione,[11] ethyl α-chloroacetoacetate,[12] or chloroacetone. An exothermic reaction set in causing the temperature to rise from 25° to 45° over a period of 5 min. The reaction mixture was stirred for 6 hr. and then added to 500 g. of ice water. After stirring for 0.5 hr. the resulting precipitate was collected by filtration, washed with water until the washings were neutral to litmus, and air-dried at 25–30°. The data are summarized in Table II.

Diethyl 2,2'-(2-oxotrimethylene)dithiobis(4-thiazolecarboxylate). The procedure was the same as described for compounds V, VI, and VII except that 15.8 g. (0.125 mole) of 1,3-dichloro-2-propanone was employed. The product, m.p. 90–95°, was obtained in 90.8% yield. After recrystallization from ethyl acetate it melted at 100–101°.

Anal. Calcd. for $C_{15}H_{16}N_2O_5S_4$: N, 6.48; S, 29.65. Found: N, 6.44; S, 29.72.

Ethyl 2-allylthio-4-thiazolecarboxylate (VIII), *ethyl 2-(2-chloroallylthio)-4-thiazolecarboxylate* (IX), *and ethyl 2-(2-propynylthio)-4-thiazolecarboxylate* (X). To a stirred solution containing 47.3 g. (0.25 mole) of I, 40 g. (0.25 mole) of 25% aqueous sodium hydroxide, and 300 ml. of water was added in one portion 0.25 mole of allyl chloride 2,3-dichloro-1-propene, or 3-bromo-1-propyne. The reaction mixture was stirred at 25–40° for 18 hr. For VIII and IX the reaction mixture was extracted with 400 ml. of ethyl ether. The ether solution was washed with water until the wash water was neutral to litmus and dried over sodium sulfate. The ether was removed *in vacuo*.

For X the stirred reaction mixture was cooled to 0°, the resulting solid was collected by filtration, washed with water until the washings were neutral to litmus, and air-dried at room temperature. The data are summarized in Table III.

Ethyl 2-(2,4-dinitrophenylthio)-4-thiazolecarboxylate. A solution of the potassium salt of I was prepared by mixing 27 g. (0.14 mole) of I, 200 ml. of acetone, 9.4 g. (0.14 mole) of 85% potassium hydroxide, and 5 ml. of water. To this solution at room temperature 28.8 g. (0.14 mole) of 2,4-dinitrochlorobenzene was added and stirred at 25–30° for 6 hr. The reaction mixture was poured into 500 g. of crushed ice. After stirring for 10 min. the solid was collected, washed with water until the washings were neutral to litmus, and air-dried at 25–30°. The product, m.p. 127–129°, was obtained in 95% yield.

Anal. Calcd. for $C_{12}H_9N_3O_6S_2$: S, 18.05. Found: S, 17.70.

Diethyl 2,2'-(2-butenylene)dithiobis(4-thiazolecarboxylate) and diethyl 2,2'-(2-butynylene)dithiobis(4-thiazolecarboxylate). To a stirred solution containing 47.3 g. (0.25 mole) of I, 300 ml. of acetone, 16.5 g. (0.25 mole) of 85% potassium hydroxide, and 25 ml. of water was added 0.125 mole of 1,4-dichloro-2-butene or 1,4-dichloro-2-butyne. An exothermic reaction set in causing the temperature to rise from 25 to 40°. The reaction mixture was stirred at 25–30° for 6 hr. The reaction mixture was added to 500 g. of crushed ice. After stirring for 15 min. the resulting precipitate was collected, washed with water until the wash water was neutral to litmus, and air-dried at 25–30°. The former compound, m.p. 122–123°, after recrystallization from ethyl acetate and the latter compound, m.p. 89–91° after recrystallization from ethyl alcohol, were obtained in yields of 96.6 and 95.5%, respectively.

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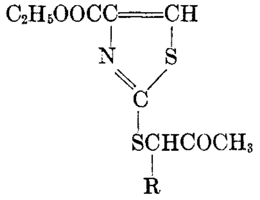
(11) E. R. Buchman and E. M. Richardson, *J. Am. Chem. Soc.*, **67**, 395 (1945).

(12) E. R. Buchman and E. M. Richardson, *J. Am. Chem. Soc.*, **61**, 891 (1939).

TABLE II

Ethyl 2-(1-acetylacetonylthio)-, Ethyl 2-(1-ethoxycarbonylacetonylthio), and Ethyl 2-acetonylthio-4-thiazolecarboxylate

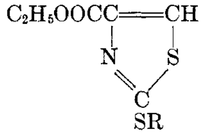


No.	R	% Yield, Crude	M.P., °	Empirical Formula	% N		% S	
					Calcd.	Found	Calcd.	Found
V	$COCH_3$	88.5	99–100[a]	$C_{11}H_{13}NO_4S_2$	4.87	4.88	22.30	22.02
VI	$COOC_2H_5$	86.0	85–86[a]	$C_{12}H_{15}NO_5S_2$	4.41	4.46	20.21	20.40
VII	H	81.9	103–105	$C_9H_{11}NO_3S_2$	5.71	5.69	26.14	25.83

[a] Recrystallization from heptane.

TABLE III

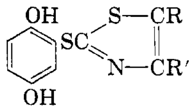
Ethyl 2-(allylthio)-, Ethyl 2-(2-chloroallylthio)-, and Ethyl 2-(2-propynylthio)-4-thiazolecarboxylates



No.	R	% Yield, Crude	M.P., °	Empirical Formula	% N		% S		% Cl	
					Calcd.	Found	Calcd.	Found	Calcd.	Found
VIII	$—CH_2CH{=}CH_2$	57.6	Liquid	$C_9H_{11}NO_2S_2$	6.11	6.22	27.97	28.28	—	—
IX	$—CH_2CCl{=}CH_2$	53.3	Liquid	$C_9H_{10}ClNO_2S_2$	5.31	5.38	24.31	24.72	13.44	12.92
X	$—CH_2C{\equiv}CH$	61.6	62	$C_9H_9NO_2S_2$	6.16	5.91	28.21	28.36	—	—

TABLE IV

Derivatives of *p*-Dihydroxybenzene



No.	R	R′	% Yield, Crude	M.P., °	Empirical Formula	% N		% S	
						Calcd.	Found	Calcd.	Found
XI	$COOC_2H_5$	CH_3	93.5	215–217[a]	$C_{13}H_{13}NO_4S_2$	4.50	4.46	20.60	20.38
XII	$COOCH_3$	CH_3	79.3	216–218[a]	$C_{12}H_{11}NO_4S_2$	4.71	4.72	—	—
XIII	COOH	CH_3	88.7	230–232	$C_{11}H_9NO_4S_2$	4.94	5.10	22.63	22.18
XIV	$CONHC_6H_5$	CH_3	48.0	128–130[a]	$C_{17}H_{14}N_2O_3S_2$	7.82	7.35	17.89	17.87
XV	$CONH_2$	CH_3	65.6	158–160	$C_{11}H_{10}N_2O_3S_2$	9.92	9.72	—	—
XVI	H	COOH	40.2	103–105	$C_{10}H_7NO_4S_2$	5.20	4.86	—	—

[a] Recrystallization from ethyl acetate.

Anal. Calcd. for $C_{16}H_{18}N_2O_4S_4$: N, 6.51; S, 29.79. Found: N, 6.45; S, 29.54. Calcd. for $C_{16}H_{16}N_2O_4S_4$: N, 6.54; S, 29.93. Found: N, 6.31; S, 29.88.

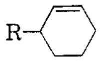
2,4,6-Tris(4-ethoxycarbonyl-2-thiazolylthio)-S-triazine. To a solution containing 47.3 g. (0.25 mole) of I, 400 ml. of acetone, and 16.5 g. (0.25 mole) of 85% potassium hydroxide was added dropwise 15.4 g. (0.083 mole) of cyanuric chloride dissolved in 100 ml. of acetone. After heating at 50–55° for 5 hr. the reaction mixture was added to 500 g. of ice water. After stirring for 15 min., the precipitate was collected, washed with water until free of chloride, and air-dried at 50°. The product, m.p. 217–218°, was obtained in 99% yield.

Anal. Calcd. for $C_{21}H_{18}N_6O_6S_6$: N, 13.08; S, 29.93. Found: N, 12.90; S, 29.40.

Ethyl 2-(2,5-dihydroxyphenylthio)-4-methyl-5-thiazolecarboxylate (XI), *methyl 2-(2,5-dihydroxyphenylthio)-4-methyl-5-thiazolecarboxylate* (XII), *2-(2,5-dihydroxyphenylthio)-4-methyl-5-thiazolecarboxylic acid* (XIII), *2-(2,5-dihydroxyphenylthio)-4-methyl-5-thiazolecarboxanilide* (XIV), *2-(2,5-dihydroxyphenylthio)-4-methyl-5-thiazolecarboxamide* (XV), *and 2-(2,5-dihydroxyphenylthio)-4-thiazolecarboxylic acid* (XVI). A suspension of 27 g. (0.25 mole) of benzoquinone and 185 ml. of methyl alcohol was heated to 50°. The resulting solution was cooled to 0° and to the recrystallized benzoquinone a suspension con-

TABLE V

2-(2-CYCLOHEXENYLTHIO)THIAZOLES



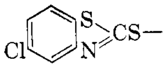
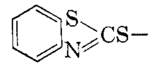
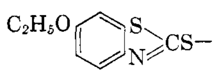
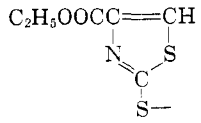
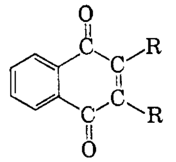
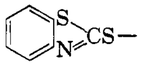
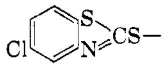
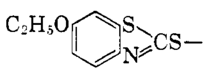
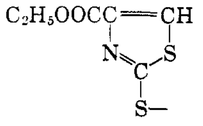
No.	R	State	% Yield, Crude	Empirical Formula	% N Calcd.	% N Found	% S Calcd.	% S Found
XVII		Amber liquid	81	$C_{13}H_{12}ClNS_2$	4.97	4.74	22.76	22.21
XVIII		Amber liquid	91	$C_{13}H_{13}NS_2$	5.66	5.55	25.93	25.39
XIX		Amber liquid	87	$C_{15}H_{17}NO_2S_2$	4.81	4.81	22.00	21.55
XX		Amber liquid	62	$C_{12}H_{15}NO_2S_2$	5.20	4.81	23.81	23.95

TABLE VI

2,3-BIS(2-THIAZOLYLTHIO)-1,4-NAPHTHOQUINONE



No.	R	M.P., °	% Yield, Crude	Empirical Formula	% N Calcd.	% N Found	% S Calcd.	% S Found
XXI		161–162[a]	96.5	$C_{24}H_{12}N_2O_2S_4$	5.73	5.60	26.25	25.85
XXII		223–225[a]	95.2	$C_{24}H_{10}Cl_2N_2O_2S_4$	5.03	5.26	23.00	23.18
XXIII		148–149[a]	97.1	$C_{28}H_{20}N_2O_4S_4$	4.86	4.55	22.24	22.08
XXIV		195–197	80.0	$C_{22}H_{16}N_2O_6S_4$	5.26	5.42	24.08	24.13

[a] Recrystallization from benzene.

taining 0.25 mole of alkyl 2-mercapto-4-methyl-5-thiazolecarboxylate,[13] 2-mercapto-4-methyl-5-thiazolecarboxylic acid,[13] 2-mercapto-4-methyl-5-thiazolecarboxanilide,[14] 2-mercapto-4-methyl-5-thiazolecarboxamide,[15] or 2-mercapto-4-thiazolecarboxylic acid in 300 ml. of methyl alcohol was added in one portion. The stirred reaction mixture was held at 0–10° for 2 hr. and then heated at 60–65° for 15 min. The reaction mixture was filtered at 65° to remove impurities. The filtrate was added to 1500 ml. of hot water and stirred at 60–70° for 1 hr. After cooling to 5° the solid was collected by filtration, washed with 1 l. of water, and air-dried at 25–30°. The data are summarized in Table IV.

5 - Chloro - 2 - (2 - cyclohexenylthio)benzothiazole (XVII), *2 - (2 - cyclohexenylthio)benzothiazole* (XVIII), *6-ethoxy - 2-(2-cyclohexenylthio)benzothiazole* (XIX), *and ethyl 2-(2-cyclohexenylthio)-4-thiazolecarboxylate* (XX). To a stirred solution containing 0.1 mole of 5-chloro-2-mercaptobenzothiazole, 2-mercaptobenzothiazole, or 6-ethoxy-2-mercaptobenzothiazole, 16 g. (0.1 mole) of 25% aqueous sodium hydroxide and 100 ml. of water was added in one portion 16.1 g. (0.1 mole) of 3-bromocyclohexene.[16] The stirred reaction mixture was heated at 80–90° for 8 hr.; and after cooling to 25° was extracted with 300 ml. of ethyl ether. The ether solution was washed with water until neutral to litmus and

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(13) J. J. D'Amico, *J. Am. Chem. Soc.*, **75**, 102 (1953).

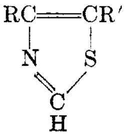
(14) R. A. Mathes, *U. S. Patent 2,402,066.*

(15) R. B. Hill and H. W. Kilbourne, U. S. Patent 2,758,046.

(16) F. L. Greenwood, *J. Am. Chem. Soc.*, **73**, 4495 (1951).

TABLE VII

4- AND 5-SUBSTITUTED THIAZOLES



No.	R	R′	M.P., ° Obtained	M.P., ° Reported	% Yield, Crude	Empirical Formula	% N Calcd.	% N Found	% S Calcd.	% S Found
XXV	CH_3	$COOC_2H_5$	98–99°/3 mm.[a]	140°/12 mm.[7]	51.4	$C_7H_9NO_2S$	8.18	8.16	18.73	18.62
XXVI	$COOC_2H_5$	H	52–54[b]	57[8]	44.6	$C_6H_7NO_2S$	8.91	8.92	—	—
XXVII	CH_3	COOH	255[c]	255[7]	82.9	$C_5H_5NO_2S$	9.78	9.41	22.40	22.73

[a] Boiling point. [b] Recrystallization from heptane. [c] Recrystallization from water.

dried over sodium sulfate. The ether was removed *in vacuo* at a maximum temperature of 80–90°.

To a stirred solution containing 32 g. (0.17 mole) of I, 200 ml. of ethyl alcohol, and 11.1 g. (0.17 mole) of 85% potassium hydroxide was added 27.2 g. (0.17 mole) of 3-bromocyclohexene. An exothermic reaction set in causing the temperature to rise from 25 to 48°. After stirring at 25–30° for 24 hr., 200 ml. of water and 300 ml. of ethyl ether were added. The ether solution was separated, washed with water until the wash water was neutral to litmus, and dried over sodium sulfate. The ether was removed *in vacuo* at a maximum temperature of 80–90°. The data are summarized in Table V.

2,3 - Bis(2 - benzothiazolylthio) - 1,4 - naphthoquinone (XXI), *2,3 - bis(5 - chloro - 2 - benzothiazolylthio) - 1,4 - naphthoquinone* (XXII), *2,3 - bis(6 - ethoxy - 2 - benzothiazolylthio) - 1,4 - naphthoquinone* (XXIII) *and diethyl 2,2′ - (1,4-dihydro - 1,4 - dioxo - 2,3 - naphthylenedithio)bis(4 - thiazolecarboxylate* (XXIV). To a stirred solution containing 0.2 mole of 2-mercaptobenzothiazole, 5-chloro-2-mercaptobenzothiazole, 6-ethoxy-2-mercaptobenzothiazole, or I, 13.2 g. (0.2 mole) of 85% potassium hydroxide, and 400 ml. of acetone, was added in one portion 23.7 g. (0.1 mole) of 2,3-dichloro-1,4-naphthoquinone.

The stirred reaction mixture was heated at 50–56° for 4 hr. and then added to 1500 g. of ice water. After stirring for 15 min., the solid was collected by filtration, washed with water until the washings were neutral to litmus, and air-dried at 25–30°. The data are summarized in Table VI.

Ethyl 4 - methyl - 5 - thiazolecarboxylate (XXV); *ethyl-4 - thiazolecarboxylate* (XXVI) *and 4 - methyl - 5 - thiazolecarboxylic acid* (XXVII). To a stirred slurry containing 0.5 mole of ethyl-2-mercapto-4-methyl-5-thiazolecarboxylate,[13] I or 2-mercapto-4-methyl-5-thiazolecarboxylic acid,[13] and 300 ml. of concd. hydrochloric acid at 50° was added dropwise 170 g. of 30% hydrogen peroxide over a 2-hr. period. During this addition an exothermic reaction set in and the temperature of the stirred reaction mixture was maintained at 50–75° by occasional cooling. The reaction mixture was stirred for an additional hour. For XXV and XXVI the stirred reaction mixture was cooled to 25° and filtered to remove the disulfides. To the stirred filtrate 245 g. of sodium carbonate was added in small portions until the *p*H of 8 was obtained. The stirred reaction mixture was extracted with 700 ml. of ethyl ether. The ether solution was dried over sodium sulfate and the ether was removed *in vacuo*. XXV was purified by distillation *in vacuo* and XXVI was recrystallized from heptane.

For XXVII the reaction mixture was added to 1000 g. of ice water. To this stirred slurry sodium carbonate was added in small portions until a *p*H 3.5 was obtained. The resulting solid was collected by filtration, washed with 400 ml. of water, and air-dried at 50°. The data are summarized in Table VII.

Acknowledgment. The writers wish to acknowledge their indebtness to R. O. Zerbe and D. D. Mullins for assistance rendered during the course of this investigation.

NITRO, W. VA.

[CONTRIBUTION FROM THE CHEMISTRY RESEARCH LABORATORY OF THE DEPARTMENT OF SURGERY,
UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE]

Derivatives of Fluorene. X. Fluorofluorenes. III[1]

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Received December 31, 1959

Preparation of further monofluoro-2-acetamidofluorenes is described, completing the series for biological testing (carcinogenicity), together with new substances obtained in the course of this work. A further example of monodemethylation in the Schiemann decomposition of a dimethylamino-substituted molecule is observed.

In this paper we describe preparation of the two remaining monofluoro-(6- and 3-)-2-acetamidofluorenes and related compounds. These two, together with the four new isomers already reported, the 1-, 4-, 5- and 8-fluoro-2-acetamidofluorenes,[1,2] have been tested for toxicity and carcinogenicity

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[1] *Fluorofluorenes. II., J. Org. Chem.*, **25**, 996 (1960). This work has been aided in part by a research grant (C-1744) from the National Cancer Institute, U.S.P.H.S. Part of this material was presented at the Chicago meeting of the American Chemical Society in September, 1958.

[2] T. L. Fletcher, W. H. Wetzel, M. J. Namkung, and H. L. Pan, *J. Am. Chem. Soc.* **81**, 1092 (1959).