mm.), n^{25}_D 1.4562. Solid ammonium dithiocarbamate[10] was used without purification.

4-Hydroxythiazolidine-2-thiones (I, VII, and XIII).—These substances were found to be the intermediate products isolated from the reactions of ammonium dithiocarbamate with chloroacetone, phenacyl bromide, and chloroacetaldehyde, respectively, under the conditions of procedures previously described.[3,4]

4-Hydroxythiazolidine-2-thiones (IV, X, XIV, and XV).—In a typical preparation, 27.9 g. (0.253 mole, 10% excess) of freshly prepared ammonium dithiocarbamate was suspended in 250 ml. of acetone in a 1-l. suction flask and stirred, with cooling, in an ice-brine bath. A solution of 37.9 g. (0.23 mole) of ethyl γ-chloroacetoacetate in 100 ml. of acetone was added dropwise over a 30-min. period, the temperature of the reaction mixture being kept below 10°. After the solution had been stirred for 45 min. longer, the minimum volume of water to cause solution was added and the cold solution was stirred for 15 min. longer. Removal of acetone *in vacuo* without letting the reaction mixture become warm resulted in separation of a colorless oil. Crystallization was induced by stirring a small portion of the oil in a little ether. Crude 4-carbethoxymethyl-4-hydroxythiazolidine-2-thione (XV) amounted to 45.0 g. and melted at 90°.

4-Hydroxy-3-methylthiazolidine-2-thiones (II, V, VIII, and XI).—An example of the general procedure used to prepare these compounds is the synthesis of 4-hydroxy-3,4,5,5-tetramethylthiazolidine-2-thione (V). Potassium acetate (43.2 g., 0.44 mole) was dissolved in 250 ml. of methanol. The solution was cooled in an ice-brine bath, and 34.2 g. (0.44 mole) of 40% methylamine was added. The temperature was maintained below 10° throughout the remainder of the reaction. To the stirred solution was added dropwise 26.5 ml. (0.44 mole) of carbon disulfide mixed with an equal volume of methanol during 15 min. The resulting solution stood for 2.5 hr. A solution of 36.3 g. (0.22 mole) of 3-bromo-3-methyl-2-butanone in 50 ml. of methanol was added over 15 min., with stirring. After standing for 3 hr., 150 ml. of water was added. To isolate the product, methanol was removed *in vacuo*, the reaction mixture being kept cold. Crude product separated as a white solid weighing 27.3 g., m.p. 96°.

Substituted Dithiocarbamates (III, VI, IX, and XII).—In a typical synthesis employing largely the method just described, a solution of 20.2 g. (0.206 mole) of potassium acetate, 37.1 g. (0.206 mole) of 25% dimethylamine and 12.4 ml. (0.206 mole) of carbon disulfide in 175 ml. of methanol was treated with 23.4 g. (0.103 mole) of α-bromoisobutyrophenone in 50 ml. of methanol. Standing overnight at room temperature afforded glistening, white crystals. After the solids had been collected by filtration and washed with cold water to separate a little potassium chloride, the crude α-(N,N-dimethylthiocarbamoylthio)isobutyrophenone (XII) amounted to 25 g., m.p. 113–114°.

An oxime and 2,4-dinitrophenylhydrazone of III and IX were made (see Table I). The hindered ketones VI and XII failed to form these carbonyl derivatives under similar conditions.

4-Thiazoline-2-thiones.—The 4-hydroxythiazolidine-2-thiones were dehydrated readily either by boiling in water for 1–2 hr. or in 0.5% hydrochloric acid for a few minutes. Methanol can be added to aid solution and then boiled off. In this way there was obtained the known derivative, 4-thiazoline-2-thione, λ_{max} 313 mμ (ε 12,500), m.p. 79–80°, lit.[3] m.p. 79–80°. Also afforded were the 4-methyl, λ_{max} mμ 318 (ε 15,700), m.p. 87.5–88.5°, lit.[4] m.p. 87°; 3,4-dimethyl, 315 mμ (ε 15,000), m.p. 117°, lit.[11] m.p. 119°; 4-phenyl, 236 and 318 mμ (ε 16,800 and 14,300), m.p. 173–174°, lit.[12] m.p. 173–174°; and 5-carbethoxy-4-methyl, 340 mμ (ε 21,800), m.p. 144–145°, lit.[8] m.p. 143–144°, homologs.

3-Methyl-4-phenyl-4-thiazoline-2-thione.—This substance was obtained essentially quantitatively, m.p. 131–132°, by boiling 4-hydroxy-3-methyl-4-phenylthiazolidine-2-thione (VIII) in a solution of methanol and 0.5% hydrochloric acid. Recrystallization from ethanol gave white plates, m.p. 131–132°, λ_{max} 316 mμ (ε 15,600).

Anal. Calcd. for $C_{10}H_9NS_2$: C, 57.9; H, 4.4; N, 6.8; S, 30.9. Found: C, 57.7; H, 4.3; N, 6.9; S, 30.6.

2,2′-Dithiobis(4-phenylthiazole).—Oxidation of 4-phenyl-4-thiazoline-2-thione by the method using iodine[13] yielded the new disulfide in approximately quantitative yield, m.p. 158–159°. Recrystallization from chloroform-ethanol gave fine, white needles, m.p. 159.5–160.5°, λ_{max} 235 and 258 mμ (ε 33,800 and 30,700).

Anal. Calcd. for $C_{18}H_{12}N_2S_4$: C, 56.2; H, 3.2; N, 7.3; S, 33.3. Found: C, 55.9; H, 3.0; N, 6.9; S, 33.3.

5-Acetyl-4-methyl-4-thiazoline-2-thione Oxime.—Recrystallized from 80% ethanol, this derivative gave pale yellow needles, m.p. 215° dec.

Anal. Calcd. for $C_6H_8N_2OS_2$: C, 38.3; H, 4.3; N, 14.9. Found: C, 38.1; H, 4.5; N, 14.8.

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4-Thiazoline-2-thiones. II. Preparation of 4-Alkylsulfonylmethyl Derivatives

W. J. HUMPHLETT AND R. W. LAMON

Research Laboratories, Eastman Kodak Company, Rochester, New York 14650

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Syntheses and properties are described of the homologous series of 4-alkylsulfonylmethyl-4-thiazoline-2-thiones and disulfide derivatives obtained through intermediate 1-alkylsulfonyl-2-propanones, 1-alkylsulfonyl-3-bromo-2-propanones, and 4-alkylsulfonylmethyl-4-hydroxythiazolidine-2-thiones.

A series of 4-alkylsulfonylmethyl derivatives of 4-thiazoline-2-thiones has been obtained by reaction of ammonium dithiocarbamate and 1-alkylsulfonyl-3-bromo-2-propanones. This type of synthesis proceeds through an intermediate product which can be isolated and has been shown to be a substituted 4-hydroxythiazolidine-2-thione.[1] In a subsequent step, dehydration forms a 4-thiazoline ring. Required 1-alkylsulfonyl-3-bromo-2-propanones were obtained by reactions in the over-all scheme of synthesis, at the left. Use of these methods afforded the 1-alkylsulfonyl-2-propanones described in Table I. These ketones are characterized by 2,4-dinitrophenylhydrazones. Bromination of 1-butylsulfonyl-2-propanone in acetic acid has been reported to occur at C-3, and the site of reaction has been determined by unequivocal synthesis.[2]

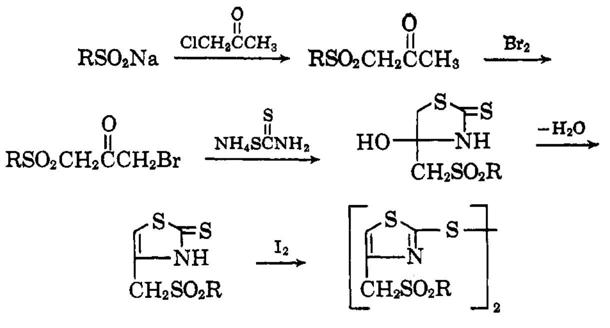

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TABLE I

ALKYLSULFONYL-2-PROPANONES

$CH_3(CH_2)_nSO_2CH_2COCH_3$

									2,4-Dinitrophenylhydrazones[a]			
	Yield,	B.p., °C.			Calcd., %		Found, %				Calcd., %	Found, %
n	%	(mm.)	$n^{25}D$	Formula	C	H	C	H	M.p., °C.	Formula	N	N
1	23	152–154 (11)	1.4630	$C_5H_{10}O_3S$	40.0	6.7	39.9	6.6	134–135	$C_{11}H_{14}N_4O_6S$	17.0	16.7
2	28	146–147 (10)	1.4618	$C_6H_{12}O_3S$	43.9	7.3	43.8	7.4	148–149	$C_{12}H_{16}N_4O_6S$	16.3	16.0
3		146–147[b] (6)	1.4628						143–144	$C_{13}H_{18}N_4O_6S$	15.6	15.4
4	43	165–167 (7)	1.4633	$C_8H_{18}O_3S$	50.0	8.4	49.7	8.4	149–150	$C_{14}H_{20}N_4O_6S$	15.1	14.9
5	34	121–123 (0.5)	1.4623	$C_9H_{18}O_3S$	52.4	8.8	52.1	9.0	118–119	$C_{15}H_{22}N_4O_6S$	14.5	14.3
6	50	121–122 (0.1)	1.4616	$C_{10}H_{20}O_3S$	54.5	9.2	54.6	9.3	90–91	$C_{16}H_{24}N_4O_6S$	14.0	13.9

[a] Recrystallized from ethanol. [b] Lit.[4] b.p. 147–150° (7 mm.).

TABLE II

1-ALKYLSULFONYL-3-BROMO-2-PROPANONES

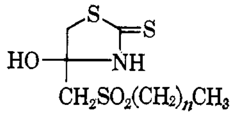
$CH_3(CH_2)_nSO_2CH_2COCH_2Br$

	Yield,			Calcd., %			Found, %		
n	%	M.p., °C.[a]	Formula	C	H	Br	C	H	Br
1	87	84–85	$C_5H_9BrO_3S$	26.2	4.0	34.9	26.3	4.0	34.8
2	89	112–113	$C_6H_{11}BrO_3S$	29.6	4.6	32.9	29.7	4.6	33.1
3		119–120[b]							
4	100	116–117	$C_8H_{15}BrO_3S$	35.4	5.6	29.5	35.4	5.7	29.8
5	86	108–109	$C_9H_{17}BrO_3S$	37.9	6.0	28.0	38.0	6.0	28.1
6	95	99–100	$C_{10}H_{19}BrO_3S$	40.1	6.4	26.8	39.9	6.4	27.0

[a] Recrystallized from ethanol. [b] Lit.[2] m.p. 119°.

TABLE III

4-ALKYLSULFONYLMETHYL-4-HYDROXYTHIAZOLIDINE-2-THIONES[a]



	Yield,				Calcd., %		Found, %	
n^b	%	M.p., °C.	Recrystn. solvent	Formula	C	H	C	H
2	98	128–129	Chloroform–ethanol–petr. ether	$C_7H_{13}NO_3S_3$	32.9	5.1	33.1	5.3
3	94	119	Ether	$C_8H_{15}NO_3S_3$	35.7	5.6	35.3	5.5
4	89	128–129	Chloroform–ethanol	$C_9H_{17}NO_3S_3$	38.1	6.1	38.1	6.2
5	94	138–139	Chloroform–ethanol	$C_{10}H_{19}NO_3S_3$	40.6	6.4	40.6	6.4
6	89	141–142	Chloroform–ethanol–petr. ether	$C_{11}H_{21}NO_3S_3$	42.4	6.8	42.3	6.9

[a] Generally very soluble in alcohol or acetone, slightly soluble in ether, insoluble in water. [b] Attempts to isolate the pure homolog, $n = 1$, were unsuccessful.

Bromination in acetic acid of the ketones listed in Table I yielded the corresponding 1-alkylsulfonyl-3-bromo-2-propanones (Table II). Reaction of ammonium dithiocarbamate with the α-bromo ketones produced the 4-alkylsulfonylmethyl-4-hydroxythiazolidine-2-thiones listed in Table III.

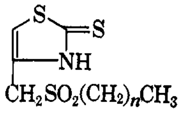
When 4-hydroxythiazolidine-2-thione was substituted by a 4-methyl group, the product became more reactive towards dehydration and was unstable at room temperature.[1] Substitution by a 4-alkylsulfonylmethyl group, however, resulted in increased stability. 4-Butylsulfonylmethyl-4-hydroxythiazolidine-2-thione was unchanged, for example, after storage for 18 months at room temperature. Infrared absorption spectra of the hydroxy intermediates showed major characteristic absorption bands near 3.0 (OH), 3.2 (NH), 14.2 (NHC=S), and 7.7 and 8.8 μ (SO_2). These hydroxy intermediates were dehydrated readily by boiling in water for 1 hr., forming 4-thiazoline-2-thiones (Table IV). The 4-alkylsulfonylmethyl-4-hydroxythiazolidine-2-thiones were characterized by ultraviolet absorption spectra having λ_{max} 245 and 277 mμ, whereas the 4-thiazoline-2-thiones absorbed at λ_{max} 319 mμ. Oxidation of the 4-thiazoline-2-thiones to disulfides (Table V) resulted in a shift in the ultraviolet spectra to a shorter wave length, λ_{max} 270 mμ.

Experimental

Melting points were determined in open, soft-glass capillaries and are corrected; boiling points are uncorrected. Infrared spectra were recorded on a Baird-Atomic spectrophotometer,

TABLE IV

4-ALKYLSULFONYLMETHYL-4-THIAZOLINE-2-THIONES[a]

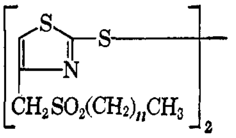


n	Yield, %	M.p., °C.	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N	$\lambda_{max.}^{EtOH}$, mμ	ε
1	100	183–184	$C_6H_9NO_2S_3$	32.3	4.1	6.3	32.0	4.0	6.2	319	14,700
2	91	153–154	$C_7H_{11}NO_2S_3$	35.4	4.7	5.9	35.6	4.6	5.9	319	13,400
3	89	164–165	$C_8H_{13}NO_2S_3$	38.2	5.2	5.6	38.4	5.3	5.6	319	12,600
4	74	164–165	$C_9H_{15}NO_2S_3$	40.7	5.8	5.3	40.6	5.7	5.2	319	15,200
5	62	160–161	$C_{10}H_{17}NO_2S_3$	43.0	6.1	5.0	42.8	6.3	5.0	319	14,500
6	24	152–153	$C_{11}H_{19}NO_2S_3$	45.0	6.5	4.8	44.8	6.3	4.6	318	14,000

[a] Generally insoluble in chloroform or ether; slightly soluble in hot water; soluble in hot ethanol, crystallizing on cooling as yellow needles.

TABLE V

2,2′-DITHIOBIS(4-ALKYLSULFONYLMETHYL)THIAZOLES[a]



n	Yield, %	M.p., °C.	Formula	Calcd., % N	Calcd., % S	Found, % N	Found, % S	$\lambda_{max.}^{CHCl_3}$ mμ	ε
1	83	160–161	$C_{12}H_{16}N_2O_4S_6$[b]	6.3		6.0		270	8600
2	84	159–160	$C_{14}H_{20}N_2O_4S_6$	5.9	40.7	5.6	40.8	270	11,000
3	97	169	$C_{16}H_{24}N_2O_4S_6$	5.6	38.4	5.8	38.1	270	9100
4	100	182	$C_{18}H_{28}N_2O_4S_6$[c]	5.3		5.0		270	9200
5	99	182–183	$C_{20}H_{32}N_2O_4S_6$	5.0	34.5	4.9	34.3	270	9200
6	100	169–171	$C_{22}H_{36}N_2O_4S_6$	4.8	32.9	4.6	32.8	270	9100

[a] Recrystallized from chloroform; soluble in pyridine; insoluble in alcohol, acetone, ethyl acetate, or water. [b] Calcd.: C, 32.4; H, 3.6. Found: C, 32.3; H, 3.6. [c] Calcd.: C, 40.9; H, 5.3. Found: C, 40.9; H, 5.5.

Model NK-1, with sodium chloride optics. Ultraviolet spectra were recorded on a Cary spectrophotometer, Model 11 MS.

Alkylsulfonyl-2-propanones (Table I).—Butylsulfonyl-2-propanone and higher homologs were prepared by a known method by reaction of sodium alkanesulfinates[3] with chloroacetone.[4]

Propylsulfonyl-2-propanone was prepared by the following modification. Gaseous sulfur dioxide was bubbled into a solution of 1 mole of propylmagnesium bromide in 800 ml. of ether, with cooling and stirring, until precipitation of magnesium propanesulfinate was complete. The suspension was stirred into 1500 g. of ice and water, heated under water-pump vacuum to remove ether, and filtered. To the filtrate was added 212 g. of sodium carbonate, and the mixture was boiled for a few minutes. After evaporation to dryness, the resulting solid was extracted by boiling and stirring with 2.3 l. of ethanol. Evaporation of the extract gave a weight of a white solid about equal to the theoretical yield of sodium propanesulfinate. The salt was used without further purification. A solution was made of 95 g. of crude sodium propanesulfinate and 67.7 g. (0.73 mole) of chloroacetone in 550 ml. of ethanol, and refluxed for 3 hr. Concentrated *in vacuo* and diluted with water, the separated organic layer was collected, and the residue was extracted with ether. The combined organic phases were dried over anhydrous sodium sulfate and fractionated through a 20-cm. column packed with glass helices, yielding 24 g. of product. Recovered chloroacetone amounted to 19 g.

Ethylsulfonyl-2-propanone was prepared similarly except that crude, solid sodium ethanesulfinate was used, without purification by extraction with alcohol.

1-Alkylsulfonyl-3-bromo-2-propanones (Table II).—All bromo ketones of this series were afforded by a known procedure[2] by bromination of alkylsulfonyl-2-propanones in acetic acid solution.

4-Alkylsulfonylmethyl-4-hydroxythiazolidine-2-thiones (Table III).—Preparation of 4-butylsulfonylmethyl-4-hydroxythiazolidine-2-thione by a procedure similar to that used to make 4-hydroxythiazolidine-2-thiones described in part I of this series[1] is typical of syntheses of compounds of Table III. Thus, 15.0 g. (0.058 mole) of 1-bromo-3-butylsulfonyl-2-propanone in an equal volume of acetone was added over 15 min. to a stirred suspension of 7.0 g. (0.064 mole, 10% excess) of ammonium dithiocarbamate in 150 ml. of acetone, cooled to 10°. After the mixture had been cooled and stirred for 45 min. longer, the crude product was isolated by adding 50 ml. of water and the acetone was removed *in vacuo* without allowing the product to become warm. The yield was 18 g. of white crystals, m.p. 119°. Recrystallization did not alter the melting point. Characteristic bands in the infrared spectrum appeared at 2.93 (OH), 3.18 (NH), 7.68 and 8.82 (SO_2), and 14.3 μ (NHC=S).

4-Alkylsulfonylmethyl-4-thiazoline-2-thiones (Table IV).—As an example of the general method of dehydration to form compounds of this class, a mixture of 13.5 g. (0.05 mole) of 4-butylsulfonylmethyl-4-hydroxythiazolidine-2-thione and 500 ml. of water was boiled for 1 hr. On cooling, crystals formed which were collected by filtration. The yield of crude 4-butylsulfonylmethyl-4-thiazoline-2-thione amounted to 11.2 g., m.p. 164–165°. After recrystallization from water or ethanol, the melting point remained unchanged.

Ethanol may be added to the reaction mixture to increase the solubility of higher homologs.

2,2′-Dithiobis(4-alkylsulfonylmethyl)thiazoles (Table V).—Oxidation of 4-alkylsulfonylmethyl-4-thiazoline-2-thiones by the method using iodine[5] gave the disulfides of this series.

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(4) A. A. Fehnel and M. Carmack, *J. Am. Chem. Soc.*, **71**, 237 (1949).

(5) E. M. Gibbs and F. A. Robinson, *J. Chem. Soc.*, 925 (1945).