

87°, together with some lower melting product, possibly geometric isomers.

Anal. Calcd. for $C_{12}H_{18}N_2O_2S$: C, 56.7; H, 7.10. Found: C, 56.82, 57.20, 57.17; H, 7.08, 7.15, 7.18.

2,5-bis-(3'-Aminobutyl)-thiophene (XVI).—The dioxime XIV (14 g.) was hydrogenated (1500 p.s.i.) in methanol at 80° using 10 g. of Raney nickel catalyst. The product was filtered from the catalyst, which was rinsed with purified dioxane, and the filtrate and washings combined. The product (XVI) boiled at 133–135° (2 mm.), yield, 6 g.

Anal. Calcd. for $C_{12}H_{22}N_2S$: N, 12.38. Found: N, 12.29, 12.02.

Acknowledgment.—The analytical data reported here were determined by the Analytical Division, Chemical Department, E. I. du Pont de Nemours & Co., Inc.

Summary

The preparation and properties of 2,5-bis-(chloromethyl)-thiophene and a number of compounds derived therefrom are described.

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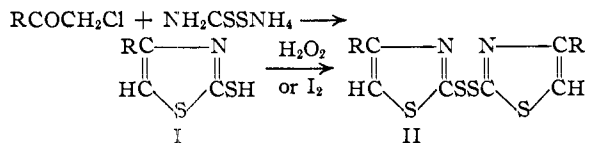
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

The Preparation of Certain Mercaptothiazoles and Thiazyl Disulfides¹

BY JOHN J. RITTER AND H. SOKOL

During the early stages of the Government Synthetic Rubber Program the need was felt for an elucidation of the mechanism of modifier action in the emulsion copolymerization of butadiene and styrene to produce GR-S. Several recent publications² have described the use of *n*-dodecyl mercaptan, thioglycolic acid, ethyl thioglycolate and diisopropyl xanthogen disulfide as modifiers and the effect of such modifiers in controlling polymer molecular weight has been demonstrated. In connection with this program it was thought desirable to synthesize certain other types of mercaptans and disulfides for evaluation as modifiers. This paper describes the preparation of a series of 2-mercaptothiazoles (I) and bis-(thiazyl-2) disulfides (II); the testing of these compounds for modifier activity was performed elsewhere.

Miolati,³ Levi⁴ and Buchman⁵ have previously described the preparation of 4-methyl-, 4-ethyl-, 4-carbomethoxymethyl-, 4-phenyl- and 4,5-dimethyl-2-mercaptothiazoles by the condensation of the corresponding halomethyl ketones with ammonium dithiocarbamate. The disulfides were ob-



tained by oxidation with hydrogen peroxide or iodine. In a more recent investigation,⁶ done in association with this project, there were prepared 4-dodecyl- and 4-tetradecyl-2-mercaptothiazoles.

(1) Abstracted from a portion of the thesis submitted by H. Sokol to the Graduate School of New York University in partial fulfillment of the requirements for the degree of Doctor of Philosophy. This work was done under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the Government Synthetic Rubber Program.

(2) Snyder, Stewart, Allen and Dearborn, *THIS JOURNAL*, **68**, 1422 (1946); Wall, Banes and Sands, *ibid.*, **68**, 1429 (1946).

(3) Miolati, *Gazz. chim. ital.*, **23**, I, 575 (1893).

(4) Levi, *ibid.*, **61**, 719 (1931).

(5) Buchman, Reims and Sargent, *J. Org. Chem.*, **6**, 764 (1941).

(6) Bunnett and Tarbell, *THIS JOURNAL*, **67**, 1945 (1945).

Using this same general reaction we have prepared a series of 2-mercaptothiazoles and bis-(thiazyl-2) disulfides bearing in the 4-position *n*-alkyl and *p*-substituted aryl substituents. *n*-Alkyl chloromethyl ketones were conveniently prepared in excellent yields (Table I) from the corresponding acid chlorides and ethereal diazomethane followed by treatment with dry hydrogen chloride. *p*-Alkylphenacyl chlorides were synthesized from alkylbenzenes and chloroacetyl chloride in the presence of an aluminum chloride catalyst. Both types of chloromethyl ketones were found to react readily at room temperature with ammonium dithiocarbamate. These condensations were carried out by slowly adding the chloromethyl ketone to a 50% molar excess of the dithiocarbamate in order to prevent the formation of 2-ketonylthiothiazoles. The 2-mercaptothiazoles were readily crystallized and melted sharply. They were found to be insoluble in cold 10% hydrochloric acid and potassium hydroxide solutions. Treatment with boiling 10% potassium hydroxide solution generally caused decomposition with the formation of ammonia. Attempts to form hydrochlorides of these mercaptothiazoles by saturation of their ethereal solutions with dry hydrogen chloride were unsuccessful; nor did they appear to form picrates readily. Although they gave insoluble salts by treatment with lead acetate and mercuric chloride, the compositions of these precipitates were not uniform and they could not be used for characterization. The reaction of 5% silver nitrate solution with an alcohol-pyridine solution of the mercaptothiazole occurred quantitatively to precipitate the silver salt of the mercaptothiazole and liberate an equivalent quantity of nitric acid. Titration of the nitric acid with 0.1 *N* sodium hydroxide served as an accurate and convenient method for the determination of per cent. mercaptan.⁷ The silver salts thus produced,

(7) Private communication to Office of Rubber Reserve, Reconstruction Finance Corp., by Willard P. Tyler, B. F. Goodrich Company, Research Laboratories.

TABLE I
 2-MERCAPTHIAZOLES

$$\begin{array}{c} \text{R}-\text{C}=\text{N} \\ \diagdown \quad \diagup \\ \text{H}-\text{C} \quad \text{C}-\text{SH} \\ \diagup \quad \diagdown \\ \text{S} \end{array}$$

CHLOROMETHYL KETONES, RCOCH₂Cl

Substituent (R-)	M. p., °C.	Yield, %	Formula	% Mercaptan S		M. p., °C.	Yield, %	Formula	% Chlorine	
				Calcd.	Found				Calcd.	Found
Pentyl-	62	81	C ₈ H ₁₂ NS ₂	17.11	17.20	83-84 ^{a,e}	90	C ₇ H ₁₃ OCl	23.89	24.02
Hexyl-	59	78	C ₉ H ₁₅ NS ₂	15.90	15.75	102-103 ^e	92	C ₈ H ₁₅ OCl	21.82	21.97
Undecyl-	83	65	C ₁₄ H ₂₆ NS ₂	11.81	11.75	46 ^b	95	C ₁₃ H ₂₅ OCl	15.17	15.39
Tridecyl-	78 ^f	58	C ₁₆ H ₂₉ NS ₂	10.70	10.51	53-54 ^e	94	C ₁₅ H ₂₉ OCl	13.65	13.51
Pentadecyl-	85 ^f	55	C ₁₈ H ₃₃ NS ₂	9.78	9.59	57 ^e	90	C ₁₇ H ₃₃ OCl	12.04	11.89
<i>p-t</i> -Butylphenyl-	205	72	C ₁₃ H ₁₅ NS ₂	12.85	12.80	36 ^b	55	C ₁₂ H ₁₅ OCl	16.85	16.57
<i>p</i> -Cetylphenyl-	95-6	40	C ₂₅ H ₃₉ NS ₂	7.66	7.85	72 ^d	37	C ₂₄ H ₃₉ OCl	9.38	9.63
<i>p</i> -Phenylphenyl-	260 ^g	82	C ₁₅ H ₁₁ NS ₂	11.89	11.74					
4,5-Diphenyl	224	80	C ₁₅ H ₁₁ NS ₂	11.89	11.75					

^a McCusker and Vogt, THIS JOURNAL, 59 1307 (1937). ^b Recrystallized from ethanol. ^c Recrystallized from methanol. ^d Recrystallized from ether. ^e B. p. at 16 mm. ^f Recrystallized from ether. ^g Recrystallized from pyridine. S-methyl thioether, m. p. 114°. Anal. Calcd. for C₁₆H₁₃NS₂: N, 4.94. Found: N, 4.90.

TABLE II
 THIAZYL DISULFIDES

$$\begin{array}{c} \text{R}-\text{C}=\text{N} \\ \diagdown \quad \diagup \\ \text{H}-\text{C} \quad \text{C}-\text{S}-\text{S}-\text{C} \\ \diagup \quad \diagdown \quad \diagup \quad \diagdown \\ \text{S} \quad \text{S} \quad \text{C}=\text{N} \\ \diagdown \quad \diagup \\ \text{H} \end{array}$$

Substituent (R-)	M. p., °C.	Yield, %	Conditions of oxidation		Recrystallized from	Formula	Nitrogen, %		Sulfur, %	
			Solvent	Temp., °C.			Calcd.	Found	Calcd.	Found
4-Pentyl-	33	78	H ₂ O	60-80	C ₂ H ₅ OH	C ₁₆ H ₂₄ N ₂ S ₄	7.53	7.39		
4-Hexyl-	39	81	H ₂ O	60-80	C ₂ H ₅ OH	C ₁₈ H ₂₈ N ₂ S ₄	7.00	6.87	32.00	32.16
4-Undecyl-	61	75	H ₂ O	60-80	C ₂ H ₅ OH	C ₂₈ H ₄₈ N ₂ S ₄	5.18	5.37	23.70	23.92
4-Dodecyl- ^a	60	71	H ₂ O	60-80	C ₂ H ₅ OH	C ₃₀ H ₅₂ N ₂ S ₄	4.92	4.81	22.53	22.70
4-Tridecyl-	66	50	H ₂ O	60-80	CHCl ₃ -C ₂ H ₅ OH	C ₃₂ H ₅₆ N ₂ S ₄	4.69	4.84		
4- <i>p-t</i> -Butylphenyl-	159	76	H ₂ O	65-95	C ₂ H ₅ OH	C ₂₆ H ₂₈ N ₂ S ₄	5.65	5.66		
4- <i>p</i> -Phenylphenyl-	220	54	C ₆ H ₅ N	50-80	C ₆ H ₅ N	C ₃₀ H ₂₀ N ₂ S ₄	5.21	5.24	23.88	23.69
4,5-Diphenyl-	125	62	C ₂ H ₅ OH	60-70	CHCl ₃	C ₃₀ H ₂₀ N ₂ S ₄	5.21	5.08	23.88	23.90

^a The preparation of 2-mercapto-4-dodecylthiazole has been previously described.⁵

when dried, were found to be unstable in light and darkened rapidly. Methylation of the thiol group with methyl iodide and sodium hydroxide proceeded readily. The S-methyl derivatives of the 2-mercapto-4-alkylthiazoles were oils.

An attempt to prepare bis-(thiazyl-2) disulfides by the direct condensation of halomethyl ketones with thiuram disulfide was unsuccessful; with phenacyl bromides there were obtained 2-phenacylthio-4-arylthiazoles.⁸ The disulfides described in Table II were all prepared by the oxidation of the corresponding mercaptothiazoles with neutral 30% hydrogen peroxide.⁵ Oxidation of 2-mercapto-4-*p*-phenylphenylthiazole and 2-mercapto-4,5-diphenylthiazole did not proceed satisfactorily in aqueous suspension. The use of pyridine for the former and ethanol for the latter gave smooth conversions to the disulfides. The melting points were in every case lower than those of the corresponding mercaptothiazoles. Absence of the thiol group was demonstrated by the silver nitrate titration method.

Experimental⁹

n-Alkyl Chloromethylketones.—Aliphatic acid chlorides were obtained from Eastman Kodak Co. and redistilled.

(8) Ritter and Sokol, THIS JOURNAL, 69, 2069 (1947).

(9) Melting and boiling points uncorrected.

Diazomethane was prepared according to the method of Arndt.¹⁰ The acid chlorides and diazomethane in a molar ratio of 1 to 2.5 were allowed to react in cold ether according to the general procedure of Walker.¹¹ The diazomethane was not isolated, but was converted directly to chloromethyl ketones by saturating their ethereal solutions with anhydrous hydrogen chloride over a period of two hours. The ether was removed by distillation and the residual chloromethyl ketones were purified by distillation or recrystallization. The six *n*-alkyl chloromethyl ketones prepared in this manner are described in Table I.

p-Alkylphenacyl Chlorides.—*t*-Butylbenzene was obtained from Eastman Kodak Co. and redistilled. Cetylbenzene was prepared from cetyl bromide and benzene via the Friedel-Crafts synthesis run in the usual manner, yield 57%, b. p. 212-215° at 10 mm.¹² The *p*-alkyl phenacyl chlorides were prepared from equimolar quantities of alkyl benzenes, chloroacetyl chloride and anhydrous aluminum chloride in cold carbon disulfide according to the general procedure of Kunckell.¹³ These compounds are described in Table I. Permanganate oxidation of these phenacyl chlorides gave only terephthalic acid, identified as its diethyl ester, m. p. 44°. ¹⁴

Desyl chloride was prepared from benzoin and thionyl chloride in pyridine.¹⁵ *p*-Phenylphenacyl bromide was

(10) Arndt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 165, 461.

(11) Walker, J. Chem. Soc., 1304 (1940).

(12) Kraft, Ber., 19, 2983 (1886).

(13) Kunckell, *ibid.*, 30, 577 (1897).

(14) Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1940, p. 164.

(15) Ward, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 159.

obtained from Eastman Kodak Co. and used without purification.

Ammonium Dithiocarbamate.—The procedure previously described employing butyl or amyl alcohol as solvent was used.³

2-Mercaptothiazoles.—The same general method was used in the preparation of all the 2-mercaptothiazoles described in Table I. To a stirred suspension of 16.5 g. (0.15 mole) of ammonium dithiocarbamate in 100 ml. of absolute ethanol, at room temperature, was added over a period of fifteen minutes, 0.10 mole of purified halo-methyl ketone. During this addition period the temperature of the reaction mixture generally rose to 35–40°. When all the ketone was added, the mixture was stirred for one-half hour, then heated on a water-bath at 60–65° for two hours and finally allowed to cool to room temperature. Alcohol-soluble mercaptothiazoles were isolated by filtering the reaction mixture, washing the solid with two 10-ml. portions of absolute ethanol, evaporating the combined filtrate and washings to dryness and recrystallizing the residue. Alcohol-insoluble mercaptothiazoles were isolated by pouring the reaction mixture, with stirring, into one liter of water containing 200 g. of cracked ice. The mixture was allowed to come to room temperature, the solid separated by filtration and washed on

the filter with three 50-ml. portions of water. After air-drying, the material was recrystallized from ethanol.

bis-(Thiazyl-2) Disulfides.—Oxidation of the 2-mercaptothiazoles to the corresponding disulfides was carried out using neutral 30% hydrogen peroxide according to the general directions given by Buchman⁵ for the preparation of bis-(4,5-dimethylthiazyl-2) disulfide. The compounds prepared are described in Table II.

Summary

1. Four new *n*-alkyl chloromethyl ketones and two new *p*-alkylphenacyl chlorides have been prepared and described.

2. A series of nine new 2-mercaptothiazoles substituted in the 4-position with *n*-alkyl, aryl and *p*-alkaryl groups has been prepared for evaluation as synthetic rubber modifiers. The properties of these compounds are described.

3. The preparation of eight new bis-(thiazyl-2) disulfides by oxidation of mercaptothiazoles is described.

NEW YORK, N. Y.

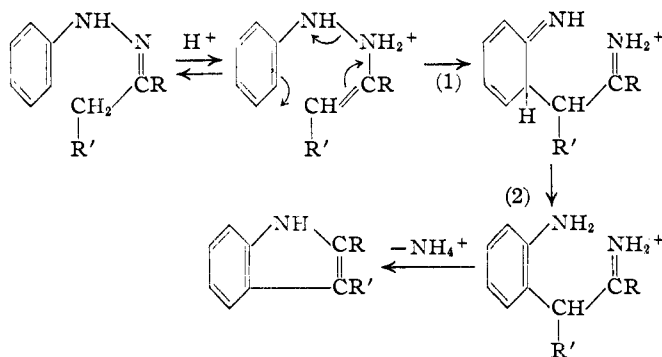
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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

Studies on the Fischer Indole Synthesis. I

BY ROBERT B. CARLIN AND E. E. FISHER¹

The mechanism proposed by Robinson and Robinson² for the Fischer indole synthesis has been supported by the more recent work of Allen and Wilson.³ The Robinsons observed that the reaction may be considered to be a particular type of "ortho benzidine" rearrangement. If the Robinsons' mechanism for the Fischer indole synthesis is written in the following manner



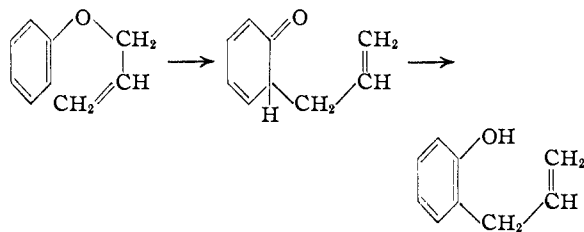
it is clear that a formal analogy exists between steps 1 and 2 and the two steps which have been proposed to explain the Claisen rearrangement to the ortho-position⁴

(1) Institute Graduate Fellow in Organic Chemistry, 1947–1948.

(2) Robinson and Robinson, *J. Chem. Soc.*, **113**, 639 (1918); 827 (1924).

(3) Allen and Wilson, *THIS JOURNAL*, **65**, 611 (1943).

(4) Cf. Tarbell, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 16.



Investigations of the Claisen rearrangement have revealed that 2,6-disubstituted phenyl allyl ethers, in which the ortho positions are blocked, often undergo para migration of the allylic group, although the mechanism of the para rearrangement is apparently different from that of the ortho rearrangement.⁵ Certain 2,6-dibromo⁶ and 2,6-dichlorophenyl allyl ethers⁷ have been shown to undergo both ortho rearrangement, with displacement of a halogen atom, and para rearrangement. The ortho benzidine rearrangement also has its para analog; in fact, many more examples of para benzidine rearrangement than of the ortho rearrangement appear in the literature. The Robinsons recognized that their mechanism for the Fischer indole synthesis suggested the possible occurrence of some para rearrangement concurrently with the normal reaction, but they pointed

(5) Tarbell, *Chem. Rev.*, **27**, 495 (1940).

(6) Hurd and Webb, *THIS JOURNAL*, **58**, 2190 (1936).

(7) Tarbell and Wilson, *ibid.*, **64**, 1066 (1942).