

contain 30% inorganic material by trituration with ethanol. An analytical sample of VII was obtained as colorless needles from ethanol, m.p. 245–247°, dec., λ_{\max} 2.95, 3.17, 4.46, 6.04, 6.20 μ .

Anal. Calcd. for $C_7H_{12}N_4O$: C, 50.00; H, 7.14. Found: C, 49.85; H, 7.38.

The benzal derivative was obtained as colorless feathery needles in 66% yield by reaction with benzaldehyde in dilute aqueous hydrochloric acid. The compound was crystallized from 80% aqueous ethanol, m.p. 188–189°.

Anal. Calcd. for $C_{14}H_{16}N_4O$: C, 65.60; H, 6.25; N, 21.88. Found: C, 65.42; H, 6.03; N, 22.06.

The isopropylidene derivative was prepared similarly and obtained as colorless needles in 32% yield, m.p. 209–210° (from ethanol).

Anal. Calcd. for $C_{10}H_{16}N_4O$: C, 57.73; H, 7.69; N, 26.92. Found: C, 57.61; H, 7.78; N, 27.06.

1-Amino-2,6-dicarboxamidopiperidine (VIII). A reaction mixture identical to that described for the preparation of VII was allowed to stir at 25° for 3 days. During this time a granular precipitate replaced the original dense slurry of material. The product was collected by filtration, washed with a small amount of cold water, and dried to give 193 g. (52%) of colorless microcrystals, m.p. 247–253°, dec. An analytical sample was obtained as colorless needles, m.p. 246–250°, dec., after several crystallizations from water.

Anal. Calcd. for $C_7H_{14}N_4O_2$: C, 45.18; H, 7.52; N, 30.08. Found: C, 44.94; H, 7.61; N, 29.90.

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[CONTRIBUTION FROM THE KEDZIE CHEMICAL LABORATORIES, MICHIGAN STATE UNIVERSITY]

A New Synthesis of Thiophene- and Thianaphthenethiols

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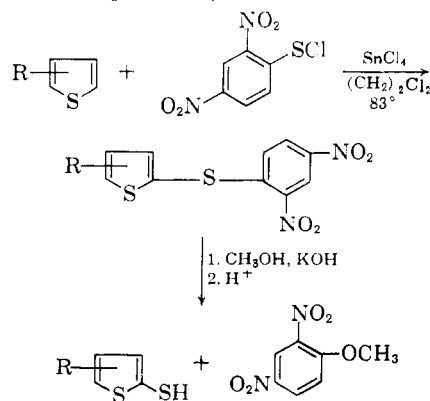
The thiols, 2-thiophenethiol, 5-methyl-2-thiophenethiol, 2,5-dimethyl-3-thiophenethiol, and 2-methyl-3-thianaphthenethiol were prepared by a simple synthesis involving the Friedel-Craft reaction of 2,4-dinitrobenzenesulfonyl chloride with the sulfur heterocyclic nucleus followed by basic cleavage of the resulting sulfide to obtain the heterocyclic mercaptan. The mercaptan, 2-thianaphthenethiol was also prepared by a reaction in which 2-methylthiirane was desulfurized by interaction with 2-thianaphthyllithium.

Relatively few thiophene- and thianaphthenethiols have been reported in the literature. Challenger and Harrison² prepared 2-ethyl-3-thiophenethiol by reducing thieno[3,2-*b*]thiophene with sodium in alcohol. Caesar and Branton³ obtained 3-thiophenethiol by treating 3-thienylmagnesium iodide with sulfur followed by acid hydrolysis. This thiol was also obtained by these investigators through the destructive distillation *in vacuo* of the tarry material produced during the commercial production of thiophene from the dehydrogenation and cyclization of butane with sulfur at high temperatures. More recently, Schuetz and Houff⁴ obtained 2-thiophenethiol by the zinc dust-sulfuric acid reduction of 2-thiophenesulfonyl chloride. Schuetz and Fawcett⁵ reported the preparation of 2,5-dimethyl-3-thiophenethiol by the lithium aluminum hydride reduction of the corresponding sulfonyl chloride. These same investigators also prepared 5-(1'-cyclohexenyl)-2-thiophenethiol by reduction of the corresponding disulfide with

lithium aluminum hydride. Schuetz and Heyd⁶ reported the synthesis of both the 2- and 3-thianaphthenethiols. The former was obtained by treating 2-benzo[*b*]thienyllithium with sulfur followed by acidification, and the 3 isomer by interaction of 3-benzo[*b*]thienylmagnesium bromide with sulfur and acidification of the organometallic complex.

The present study was undertaken to determine the feasibility of preparing thiophene- and thianaphthenethiols via preparation and subsequent basic hydrolysis of thienyl and thianaphthyl (2,4-dinitrophenyl) sulfides.

The reaction sequence is,



(6) R. D. Schuetz and C. E. Heyd, Abstracts of Papers, Am. Chem. Soc. Meeting, Miami, Fla., April 7–12, 1957, p. 84-O.

(1) Abstracted in part from the Masters thesis of W. L. Fredericks, 1959.

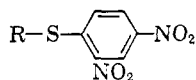
(2) F. Challenger and J. B. Harrison, *J. Inst. Petroleum Technol.*, **21**, 135 (1935).

(3) P. D. Caesar and P. D. Branton, *Ind. Eng. Chem.*, **44**, 122 (1952).

(4) R. D. Schuetz and W. H. Houff, *J. Am. Chem. Soc.*, **75**, 6316 (1953).

(5) R. D. Schuetz and R. J. Fawcett, Abstracts of Papers, Am. Chem. Soc. Meeting, San Francisco, Calif., April 13–18, 1958, p. 48-N.

TABLE I
THIENYL AND THIANAPHTHYL 2,4-DINITROPHENYL SULFIDES^d



R	Formula	M. P.	Yield, %	Carbon, %		Hydrogen, %		Nitrogen, %		Sulfur, % ^c	
				Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
	C ₁₀ H ₆ N ₂ O ₄ S ₂	119-120 ^a	89	42.55		2.13				22.70	
	C ₁₁ H ₈ N ₂ O ₄ S ₂	105-106	65	44.58	44.60	2.72	2.96			21.64	21.70
	C ₁₁ H ₈ N ₂ O ₄ S ₂	120-120 ₁₆	63	44.58	44.84	2.72	2.89			21.64	21.78
	C ₁₂ H ₁₀ N ₂ O ₄ S ₂	115-115 ₁₆ ^b	92	46.44	46.67	3.25	3.46			20.66	20.54
	C ₁₅ H ₁₀ N ₂ O ₄ S ₂	176-177	73	52.01	51.93	2.91	3.01	8.09	8.17		

^a See ref. 7, prep. from 2-thiophenethiol and 2,4-dinitrochlorobenzene, m.p. 119°. ^b See ref. 5. ^c Analysis by Micro-Tech Laboratories, Skokie, Ill. ^d Recrystallized from isopropyl alcohol.

This procedure when applied to the synthesis of thiophenols⁷ is reported to give good yields of easily purified products.

The necessary thienyl and thianaphthyl 2,4-dinitrophenyl sulfides were prepared by the interaction of 2,4-dinitrobenzenesulfonyl chloride with the sulfur heterocyclic nucleus in ethylene chloride as a reaction medium at its reflux temperature, using stannic chloride as a catalyst. An excess of the heterocyclic compound was employed to compensate its loss through the formation of polymeric material. In the case of 2,5-dichlorothiophene only a yellow-colored, polymeric material could be isolated. With alkylthiophenes, the sulfide yields ranged from 63% with 3-methylthiophene to 92% in the case of 2,5-dimethylthiophene. Thus alkyl substitution, which left open *alpha* positions, activated the heterocyclic nucleus toward greater polymerization. The thianaphthene was less susceptible to polymerization by the stannic chloride catalyst than the thiophenes. The product obtained from thianaphthene melted over a temperature range (146-152°) indicating it to be a mixture of the 2- and 3-substituted isomeric sulfides. This was indicated by melting point comparisons with the melting points of the pure isomers 2- (159-160°), 3- (163-164°) prepared from 2- and 3-thianaphthenethiols with 2,4-dinitrochlorobenzene.⁶ The thienyl and thianaphthyl 2,4-dinitrophenyl sulfides and some of their properties are given in Table I.

In addition to stannic chloride, two other catalysts were investigated for obtaining the sulfides. It was found that even when small amounts of anhydrous aluminum chloride were employed at temperatures as low as -25°, tar formation was excessive and very low yields of the products were isolated. An attempt to employ anhydrous

ferric chloride caused extreme tar formation and identifiable products could not be isolated. Further, anhydrous stannic chloride was found to be ineffective as a catalyst at temperatures below the boiling point of ethylene chloride.

The heterocyclic 2,4-dinitrophenyl sulfides could be cleaved by methanolic potassium hydroxide or sodium methoxide in methanol.⁸ Since the latter reagent offered no particular advantages and required additional effort in its preparation, methanolic potassium hydroxide was used throughout most of the work described here.

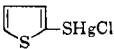
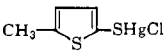
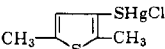
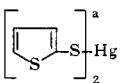
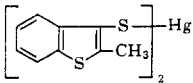
Initially, the sulfides were cleaved by refluxing them for an hour in methanolic potassium hydroxide. Isolation of the mercaptan after removal of the methanol by distillation at atmospheric pressure, resulted in a 17% yield of 2-thiophenethiol. However, bis(2-thienyl) sulfide, in good yields, was separated from the other expected basic cleavage product, 2,4-dinitrophenylanisole. The latter was recovered by filtration of the reaction mixture and from the residue remaining from the distillation of the mercaptan. Under similar experimental conditions, 2-methyl-2-thiophenethiol was obtained in only a 7% yield, and 2,5-dimethylthiophenethiol in less than 1%. In the latter case, however, a 90% yield of bis(2,5-dimethyl-3-thienyl) sulfide was obtained. When the basic cleavage reaction period was reduced to a third of an hour, and conducted in a nitrogen atmosphere to reduce decomposition and oxidative attack of the mercaptide ion, followed by vacuum removal of the solvent, the yield of 2-thiophenethiol obtainable was increased to 48%.

The apparent decomposition of the thiols occurring during their preparation and isolation suggested that these compounds might best be

(7) N. Kharasch, *J. Org. Chem.*, 19, 1704 (1954).

(8) C. M. Buess and N. Kharasch, *J. Am. Chem. Soc.*, 72, 3529 (1950).

TABLE II
 MERCURY DERIVATIVES OF THIOPHENE AND THIANAPHTHENE THIOLS

Salts	Formula	M. P.	Yield, %	Carbon, % ^b		Hydrogen, %		Mercury, %	
				Calcd.	Found	Calcd.	Found	Calcd.	Found
	C ₄ H ₄ S ₂ ClHg	173-174 dec.	75	13.70	14.06	0.86	1.52	57.11	57.16
	C ₅ H ₆ S ₂ ClHg	156-157 dec.	47	16.44	16.60	1.38	1.63	54.92	54.72
	C ₆ H ₇ S ₂ ClHg	175-176 dec.	19	19.00	19.28	1.86	2.11	52.89	53.11
	C ₈ H ₈ S ₄ Hg	126-127	79	22.29	22.42	1.40	1.58	46.55	46.18
	C ₁₈ H ₁₄ S ₄ Hg	214-216	58	38.66	37.85	2.52	2.35	35.88	35.89

^a Prepared from 2-thiophenethiol. ^b Analysis by Micro-Tech Laboratory, Skokie, Ill.; Hg analysis by one of authors W.L.F.

isolated as their mercuric or mercuric chloride salts. When the heterocyclic 2,4-dinitrophenyl sulfides were cleaved by methanolic potassium hydroxide in a nitrogen atmosphere and the solvent removed under vacuum, to minimize heating, the yields of the thiols, isolated, ranged from 19% for 2,5-dimethyl-3-thiophenethiol to 75% for 2-thiophenethiol. The previously undescribed mercury salts and some of their properties are summarized in Table II.

The isolation of satisfactory yields of the mercury derivatives of the sulfur heterocyclic thiols indicated that the synthetic route used in their preparation would be useful in obtaining thiol derivatives if the potassium mercaptide were used directly as obtained from the basic cleavage of the sulfur heterocyclic 2,4-dinitrophenyl sulfide. Such a procedure would avoid losses by decomposition during isolation and purification of the thiols.

Derivatives of two of the heterocyclic thiols were thus prepared by treating the alkaline aqueous solution of the potassium mercaptide directly with an organic halide after removal of the 2,4-dinitroanisole by-product. The amine salt, 2-piperidinoethyl-2-thienyl sulfide hydrochloride⁴ was obtained in a 71% yield by this procedure.

The preparation of a second thiol derivative, 3-methyl-2-thienyl methyl sulfide, in a 32% yield, presented the possibility of either of two isomers or a mixture of isomers being formed; the 2,3-isomer was expected over the 2,4-isomer. The sulfide obtained in the first step melted sharply at 120-120.5°, indicating that a single isomer had been obtained. An infrared spectrum of the methyl sulfide obtained in the second step was compared with spectra⁹ of other 2,3-substituted thiophenes and this definitely indicated that the 2,3-substituted product had been obtained.

(9) H. D. Hartaugh, *Thiophene and Its Derivatives*, Interscience, New York, 1952, p. 10.

The heterocyclic mercaptan, 2-thianaphthene-thiol, was also prepared by conversion of thianaphthene to its lithium salt with *n*-butyllithium and treatment of alkali metal salt with 2-methylthiirane followed by acidification to obtain the mercaptan. This mercaptan synthesis was developed for aromatic compounds.¹⁰

EXPERIMENTAL

Intermediates. The intermediates bis(2,4-dinitrophenyl) disulfide,¹¹ 2,4-dinitrophenylsulfenyl chloride,¹² 2-methylthiophene,¹³ 2,5-dimethylthiophene,¹⁴ 2-methylthianaphthene,¹⁵ and propylene sulfide,¹⁶ were prepared by methods described in the literature.

Thienyl and thianaphthyl 2,4-dinitrophenyl sulfides. In a typical experiment 13.4 g. (0.16 mole) of thiophene, and 20.0 g. (0.085 mole) of 2,4-dinitrophenylsulfenyl chloride were added to 400 ml. of ethylene chloride. The solution was heated to 65-70°; 63.5 g. (0.24 mole) of anhydrous stannic chloride was added during 5 min. and the reaction mixture was then kept at its reflux temperature for 1.5 hrs. It was cooled, 25 ml. of ethanol was added and it was extracted with two 200-ml. portions of dilute hydrochloric acid. The organic layer was separated, filtered and the solvent removed by vacuum distillation on a water bath (70°). The gray residue was boiled in 400 ml. of ethanol and the solution decanted from undissolved solid. The second residue was boiled in an additional 150 ml. of ethanol and filtered to remove a small amount of insolubles. The ethanol extracts were treated separately with Norit and cooled to precipitate the product. The material crystallizing from the initial ethanol extraction was slightly brown in color, while that obtained from the second ethanol extraction had a bright

(10) F. G. Bordwell and H. M. Anderson, *J. Am. Chem. Soc.*, **75**, 4959 (1953).

(11) H. Gilman and A. H. Blatt, *Org. Synthesis*, Coll. Vol. I, 220 (1941).

(12) N. Kharasch, H. L. Wehrmeister, and H. Tigerman, *J. Am. Chem. Soc.*, **69**, 1612 (1947).

(13) E. Campaigne and W. L. Archer, *J. Am. Chem. Soc.*, **75**, 989 (1953).

(14) C. Paal, *Ber.*, **18**, 2251 (1885).

(15) D. A. Shirley and M. D. Cameron, *J. Am. Chem. Soc.*, **74**, 664 (1952).

(16) F. G. Bordwell and H. M. Anderson, *J. Am. Chem. Soc.*, **75**, 4959 (1953).

yellow color. The combined ethanol filtrates were treated again with Norit and concentrated (ca. 50%) to yield additional product.

Thiophenethiols and thianaphthenethiols. In a typical experiment, a solution containing 6 g. (0.12 mole) of potassium dissolved in 300 ml. of methanol was prepared by stirring the warm alkali methoxide solution with a stream of nitrogen. A 17-g. (0.06 mole) quantity of 2-thienyl-2,4-dinitrophenyl sulfide was added to the alkaline solution and it was heated at its reflux temperature for 20 min. in a nitrogen atmosphere. The majority of the solvent was removed by vacuum distillation in a water bath (30–35°). The residue was poured onto cracked ice and sufficient water added to bring the final volume to 400 ml. The cold aqueous suspension was stirred and filtered to remove a light orange solid (2,4-dinitroanisole and 2,2'-dithienyl sulfide). The filtrate was acidified with concentrated hydrochloric acid, and extracted with three portions of ether. The combined extracts were dried (calcium chloride), filtered and the ether was removed by distillation on a steam bath. The residual dark red colored oil was vacuum distilled to obtain the thiol.

2-Thianaphthenethiol. In an alternative preparation of this thiol, an ether solution of *n*-butyllithium was prepared by adding 60 g. (0.44 mole) of redistilled *n*-butyl bromide dissolved in 60 ml. of ether, during 0.5 hr., at –10° to a suspension of 6.4 g. (0.90 g.-atom) of lithium chips in 120 ml. of ether. The reaction mixture was stirred for 1.0 hr. after adding the bromide and filtered under nitrogen through glass wool. The filtrate was cooled (–10°) and a solution of 48 g. (0.36 mole) of thianaphthene in 25 ml. of ether was added to it during 0.25 hr. The lithium thianaphthenate solution was stirred and cooled (–10°) for 0.5 hr., allowed to warm to room temperature and then 15 g. (0.22 mole) of propylene sulfide dissolved in 40 ml. of ether was added during 0.25 hr. The stirred reaction mixture was kept at its reflux temperature for 1.0 hr. during which its color changed from blue through green to light yellow. After being set aside overnight the mixture was poured into an equal volume of ice water; the aqueous layer was separated, and the ether layer was extracted twice with 2*N* potassium hydroxide. A yellow-colored oil separated from solution on acidification of the combined aqueous extracts. This was separated and the aqueous layer was extracted three times with pentane. The combined hydrocarbon extracts were dried (calcium chloride) and the pentane was removed to yield the crude thiol.

A 2,4-dinitrophenyl sulfide of the mercaptan was prepared and melted at 159° after recrystallization from a 1:1

methanol dioxane mixture in agreement with previous reports⁶ from these laboratories.

Thienylmercury mercaptides. In a typical preparation a warm solution containing 1.6 g. (0.014 mole) of 2-thiophenethiol dissolved in 75 ml. of ethanol was added to a solution containing 2.1 g. (0.0065 mole) of mercuric acetate dissolved in 20 ml. of ethanol. The product precipitated as a yellow colored solid and was recrystallized from ethanol.

2-Thienyl 2-piperidinoethyl sulfide. A solution containing 5.6 g. (0.1 mole) of potassium hydroxide dissolved in 275 ml. of methanol was prepared by warming the base and alcohol together while stirring the methanol with a stream of nitrogen. A 14-g. (0.05 mole) quantity of 2-thienyl 2,4-dinitrophenyl sulfide was added to the alkali methoxide solution which was then heated, under nitrogen at its reflux temperature for 10 min. The major share of the solvent was removed by vacuum distillation (water bath, 35°). The residue was poured onto ice, enough water was added to make the final volume 300 ml., and filtered. To the stirred filtrate, was added during 0.5 hr., a solution of 5.5 g. (0.30 mole) of 2-piperidinoethyl chloride hydrochloride dissolved in 20 ml. of water. The reaction mixture was kept at its reflux temperature for 2.0 hrs. and cooled. The brown oil which separated was extracted into ether and the aqueous layer was extracted twice with ether. The combined ether extracts were washed once with dilute sodium hydroxide and twice with water. After drying the ether solution (magnesium sulfate) it was treated with gaseous hydrogen chloride to precipitate the amine hydrochloride salt. After recrystallization from 2-propanol, its melting point was in agreement with that previously reported for this material.⁴

3-Methyl-2-thienyl methyl sulfide. An alkaline solution of the potassium salt of 3-methyl-2-thiophenethiol was prepared from 6.1 g. (0.11 mole) of potassium hydroxide, 285 ml. of methanol and 15.9 g. (0.054 mole) of 3-methyl-2-thienyl 2,4-dinitrophenyl sulfide using the preceding experimental procedure. To the alkali metal salt solution of 3-methyl-2-thiophenethiol kept at its reflux temperature was added 6.1 g. (0.043 mole) of methyl iodide during 0.50 hr. A red-colored oil separated on cooling the reaction mixture. This was extracted into ether and the aqueous layer was extracted twice with ether. The combined ether extracts were washed with dilute sodium hydroxide and three times with water, dried (calcium chloride) and the ether removed. The residual was fractionated under reduced pressure to isolate a light yellow oil, yield 32%, b.p. 67–68°/6 mm.

Anal. Calcd. for C₈H₈S₂: C, 49.95; H, 5.59; S, 44.46. Found: C, 50.09; H, 5.78; S, 44.63.

EAST LANSING, MICH.