A NEW SYNTHESIS OF THIOPHENE AND THIANAPHTHENE THIOLS

Thesis for the Degree of M. S.

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Wayne Leroy Frederick

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A NEW SYNTHESIS OF THIOPHENE AND THIANAPHTHENE THIOLS

By

WAYNE L. FREDERICK

A THESIS

Submitted to the College of Science and Arts
of Michigan State University of Agriculture
and Applied Science in partial fulfillment
of the requirements for the degree of

MASTER OF SCIENCE

Department of Chemistry

1959

ACKNOWLEDGMENT

The author wishes to express his appreciation to Professor Robert D. Schuetz for his guidance and counsel throughout the course of this work. The author is also grateful to his wife for her support and understanding during the course of this work.

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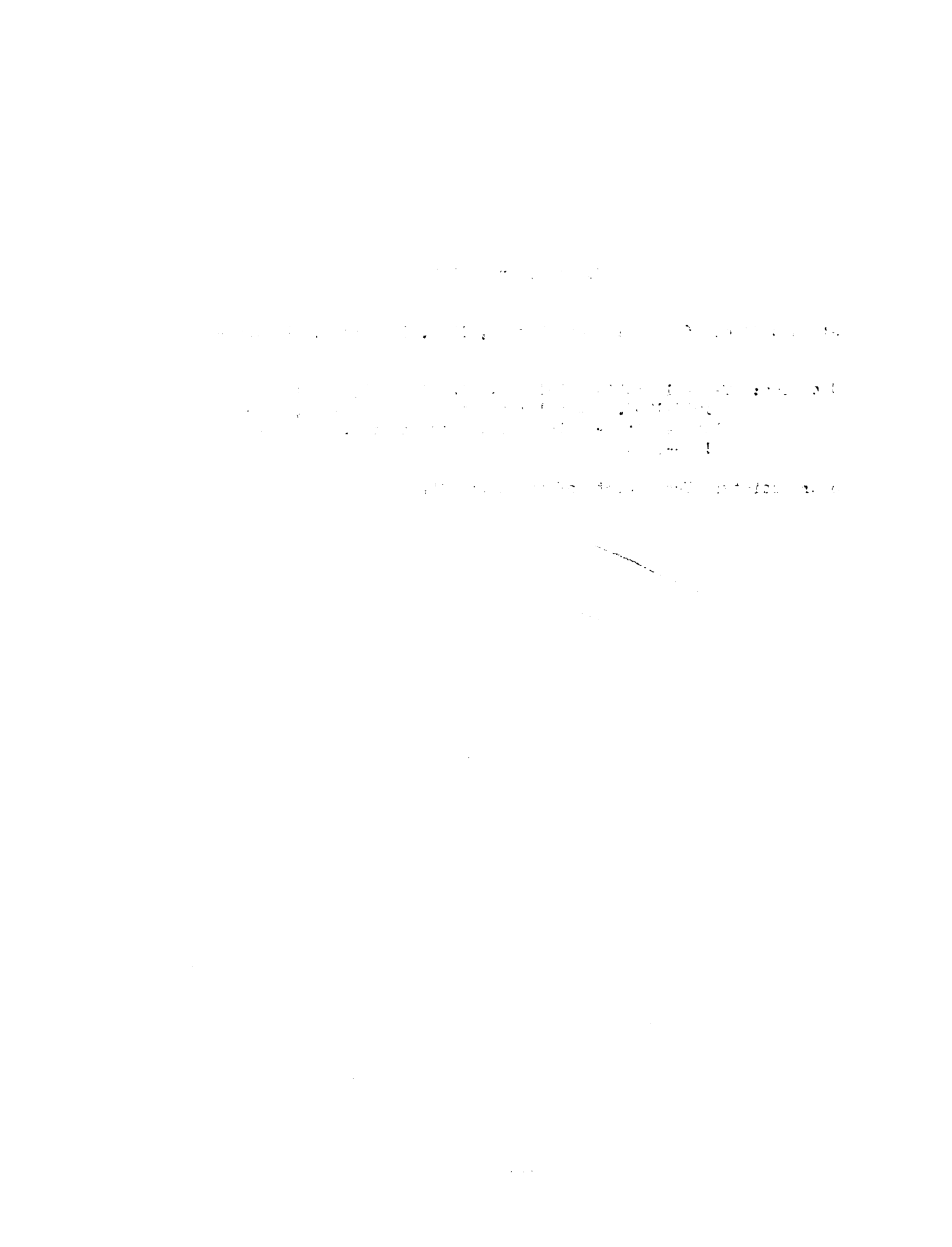

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AN ABSTRACT

Submitted to the College of Science and Arts of Michigan State University of Agriculture and Applied Science in partial fulfillment of the requirements for the degree of

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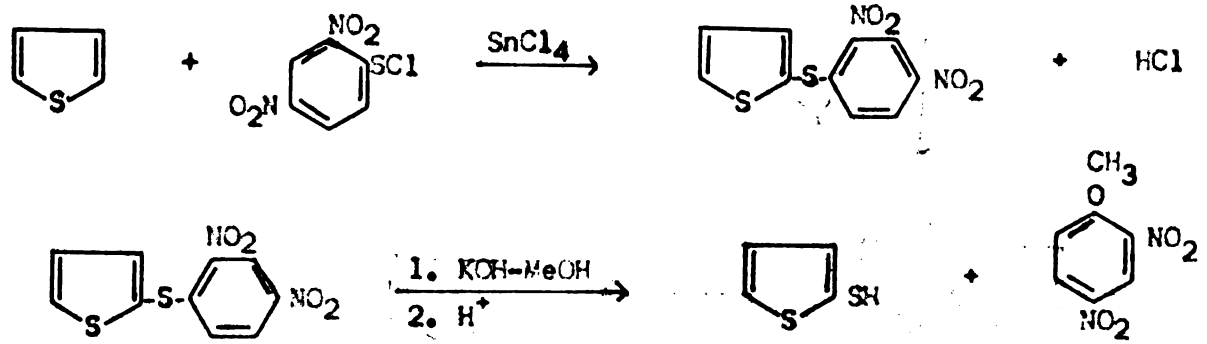
Approved _____

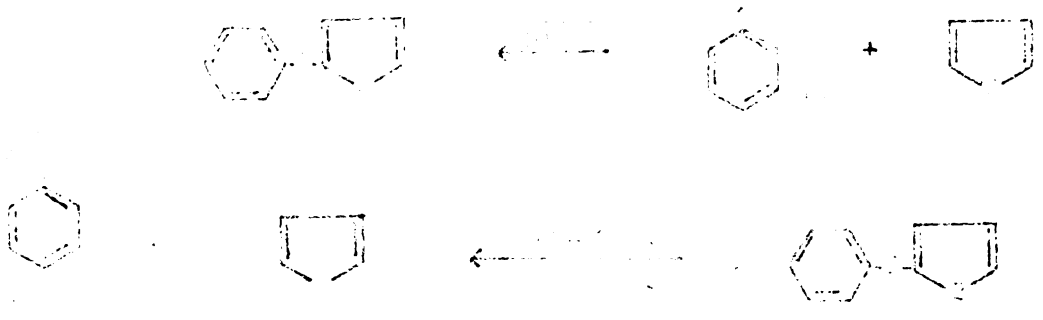
ABSTRACT

The present investigation was undertaken to determine whether and in what manner a two step synthesis involving the Friedel-Craft Reaction of 2,4-dinitrophenylsulfenyl chloride with an aromatic nucleus followed by basic cleavage of the resulting sulfide to obtain aryl mercaptans could be extended to heterocyclic compounds, particularly to the preparation of thiophene and thianaphthene thiols. The reaction sequence can be illustrated by the following equations, using thiophene as a specific example.



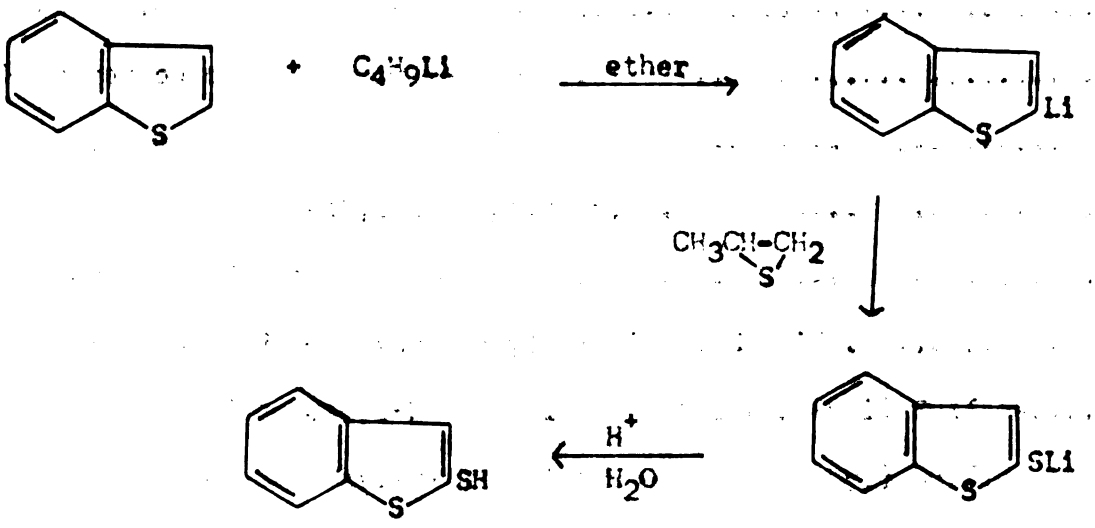
The thiols, 2-thiophenethiol, 5-methyl-2-thiophenethiol, 2,5-dimethyl-3-thiophenethiol, and 2-methyl-3-thianaphthenethiol were prepared and isolated as their mercuric or mercuric chloride salts. Two mercaptans, 2-thiophenethiol, and 5-methyl-2-thiophenethiol, were prepared and isolated as pure heterocyclic mercaptans.

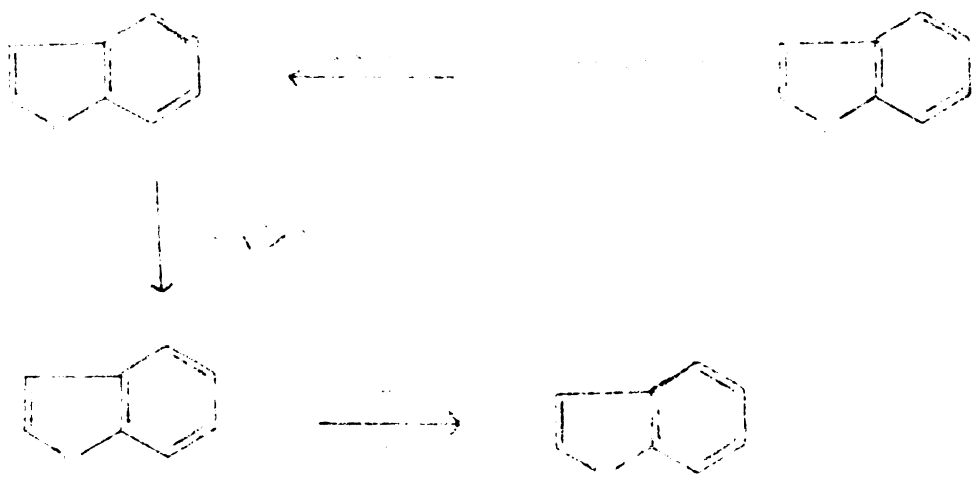
The thiol derivatives, 2-piperidinoethyl-2-thienyl sulfide hydrochloride and 3-methyl-2-thienyl methyl sulfide were prepared



without isolating the intermediate mercaptans to show the utility of the synthetic sequence of reactions in the preparation of derivatives of heterocyclic mercaptans.

The heterocyclic mercaptan, 2-thianaphthenethiol was also prepared by a reaction in which propylene sulfide was desulfurized by interaction with 2-thianaphthyllithium. This is the first example of the extension of this method, which was originally developed with aromatic compounds, to prepare heterocyclic mercaptans.





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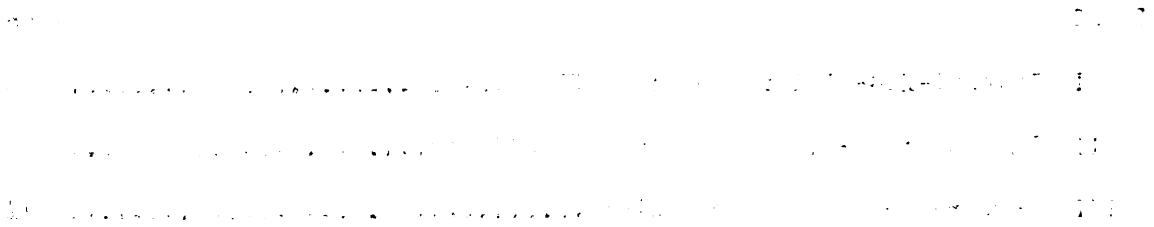


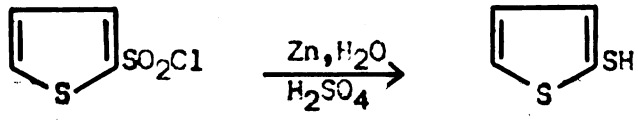
INTRODUCTION

The present study was undertaken to determine the feasibility of preparing thiophene and thianaphthene thiols via preparation and subsequent basic hydrolysis of thienyl and thianaphthyl (2,4-dinitrophenyl) sulfides. This sequence of reactions was reported to give good yields of easily purified products when applied to the synthesis of a series of thiophenols (17). The intermediate sulfides were prepared by reaction of the sulfur heterocyclics with 2,4-dinitrophenylsulfenyl chloride under Friedel-Crafts acylation conditions.

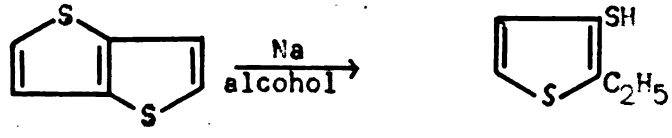
Previously reported methods for the preparation of thiophene and thianaphthene thiols usually had rather limited applicability and did not, in general, give good yields. It was hoped that a more general method, giving better yields of pure products could be developed. It was found convenient to isolate most of the thiols prepared in the course of this investigation as their mercury or mercuric chloride salts.

HISTORICAL

Relatively few thiophene and thianaphthene thiols have been reported in the literature. At present, six thiophenethiols and six thianaphthenethiols are known. The general methods used in obtaining these heterocyclic mercaptans can be best illustrated by several specific syntheses. Schuetz and Houff (7) prepared 2-thiophenethiol by the zinc dust-sulfuric acid reduction of 2-thiophenesulfonyl chloride. The latter material was obtained by the chlorosulfonation of thiophene.

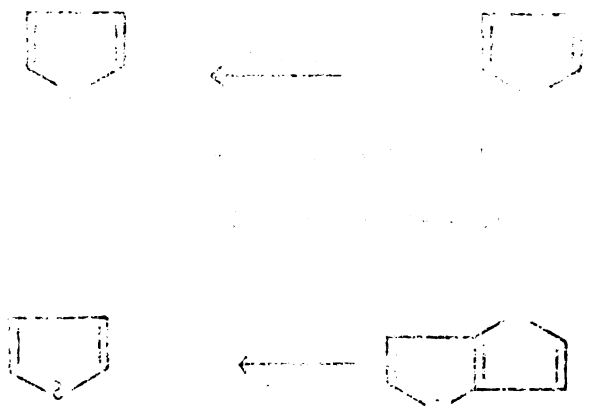


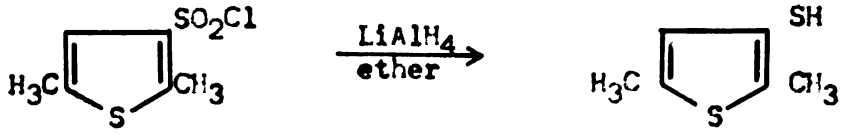
Challenger and Harrison (18) prepared 2 ethyl-3-thiophenethiol by reducing thieno-3,2-b-thiophene with metallic sodium in alcohol.



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 1100° F. produces 3-thiophenethiol (19) in yields of 30-40%.

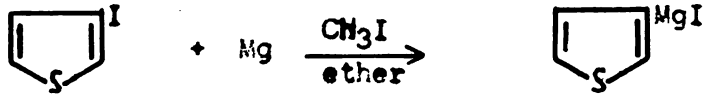
Fawcett (20) prepared 2,5-dimethyl-3-thiophenethiol by the lithium aluminum hydride reduction of 2,5-dimethyl-3-thiophenesulfonyl chloride.

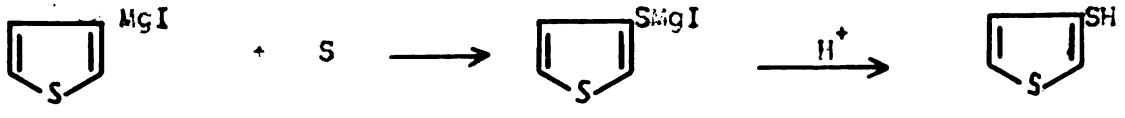




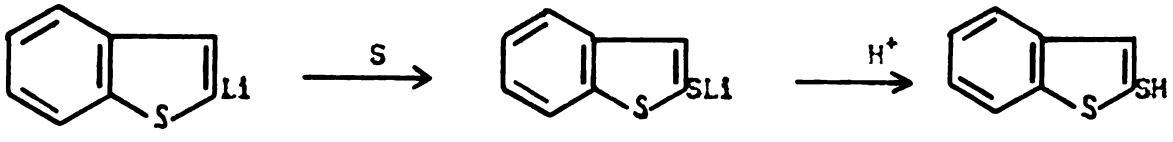
This same investigator also prepared 5-(1'-cyclohexenyl)-2-thiophenethiol by the lithium aluminum hydride reduction of the corresponding disulfide.

Caesar and Branton (19) prepared 3-thiophenethiol by adding sulfur to 3-thienylmagnesium iodide.

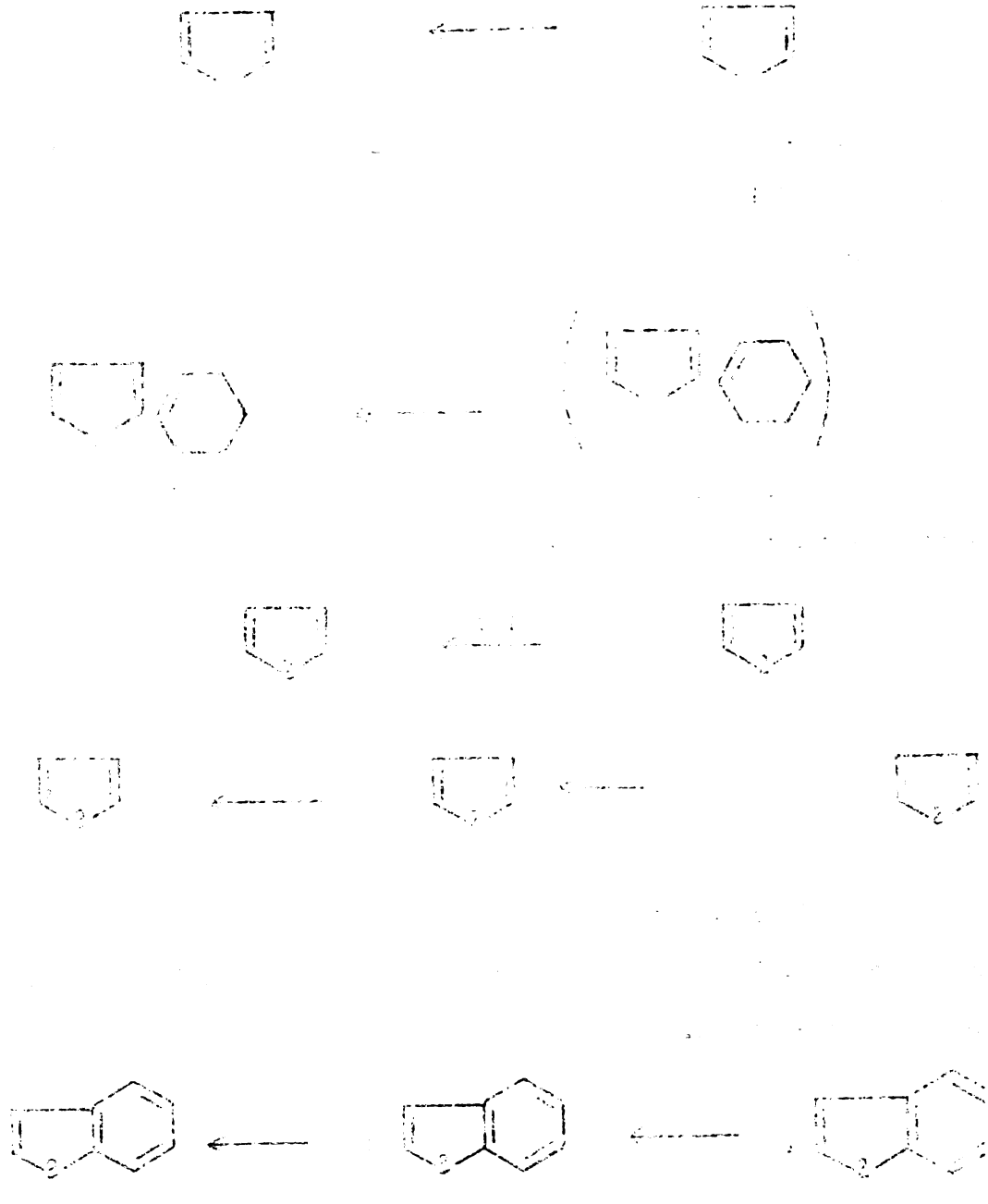


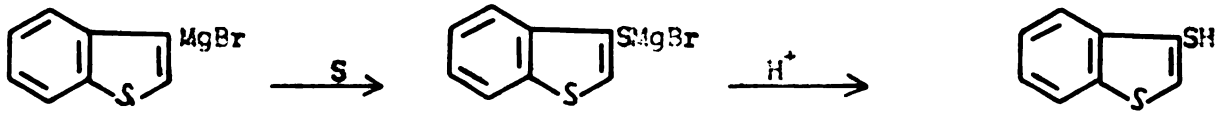


Heyd (21) prepared 2-thianaphthenethiol by adding sulfur to 2-thianaphthyllithium and acidifying the resulting lithium salt of 2-thianaphthenethiol.

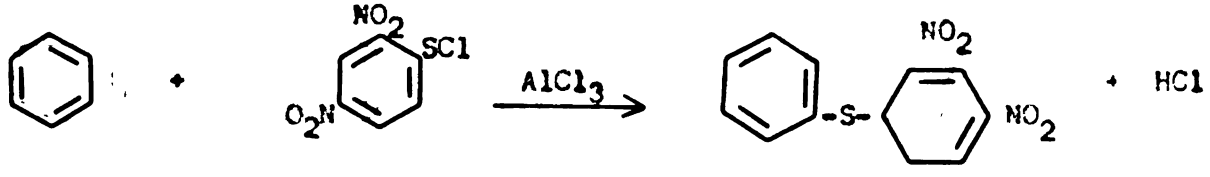


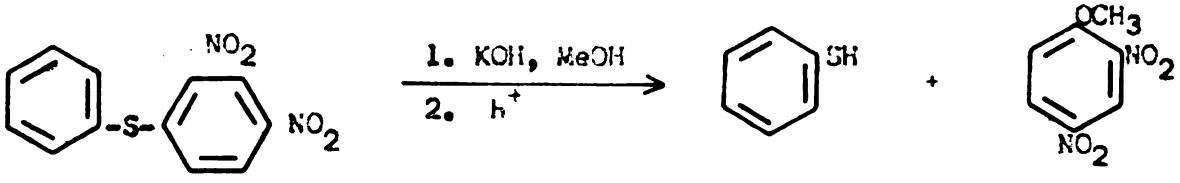
Heyd (21) also obtained the isomeric 3-thianaphthenethiol by treating 3-thianaphthylmagnesium bromide with sulfur followed by acid hydrolysis.





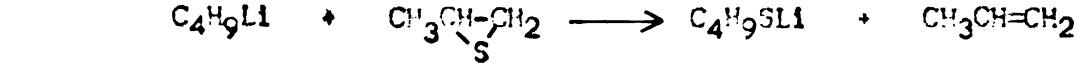
Kharasch (17) has recently introduced a new and somewhat novel method for the synthesis of aryl mercaptans involving basic cleavage of aryl-2, 4-dinitrophenyl sulfides. This procedure can be illustrated by the following equations.

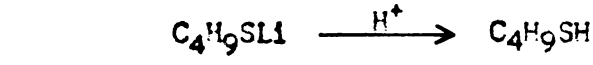




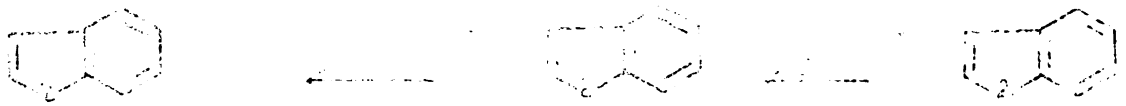
The present investigation dealt with the feasibility of developing a similar reaction sequence for the preparation of thiophene and thianaphthene thiols.

Bordwell (22) has reported a rather unique reaction of organolithium compounds with thiiranes in which the sulfur is abstracted from cyclic sulfides to yield lithium salts of mercaptans.



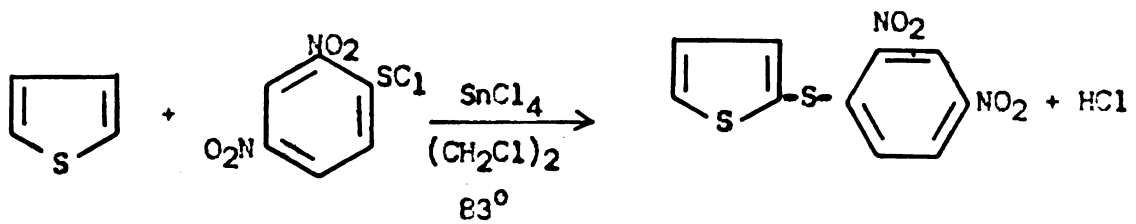


This desulfurization was successfully used to prepare 2-thianaphthenethiol in the present study.



DISCUSSION

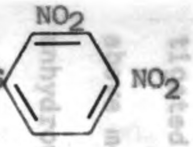
The necessary thienyl and thianaphthyl 2, 4-dinitrophenyl sulfides were prepared by the interaction of 2, 4-dinitrophenyl-sulfenyl chloride with the heterocyclic nucleus in ethylene chloride as a reaction media at its reflux temperature, using anhydrous stannic chloride as a catalyst. This reaction is illustrated by the following equations, using thiophene as a specific example.

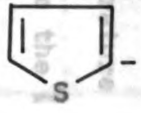
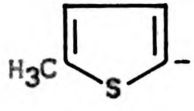
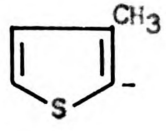
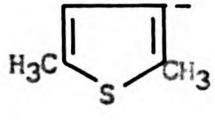


An excess of the heterocyclic compound was employed to reduce its loss through the formation of polymeric material. In the case of 2, 5-dichlorothiophene, only a yellow material, which appeared to be polymeric, could be isolated. With alkylthiophenes, the sulfide yields ranged from 63% in the case of 3-methylthiophene to 92% in the case of 2, 5-dimethylthiophene. Alkyl substitution, which left an open alpha position, activated the heterocyclic nucleus toward polymerization to a greater degree than toward substitution. The thienyl-2, 4-dinitrophenyl sulfides, two of which are prepared here for the first time, and some of their properties are summarized in Table I.

The thianaphthenes were less susceptible to polymerization by the stannic chloride catalyst than the thiophenes. The thianaphthenes, on reaction with 2, 4-dinitrophenyl-sulfenyl chloride, took on just a slight dark coloration and only a small amount of tarry material was

TABLE I

THIENYL 2, 4-DINITROPHENYL SULFIDES 

R(d)	M. P.° C	Yield %	Formula	Percent Calculated C	H	S	Percent Found(c) C	H	S
	119 (a)	89	$C_{10}H_6N_2O_4S_2$	42.55	2.13	22.70	-	-	-
	105	65	$C_{11}H_8N_2O_4S_2$	44.58	2.72	21.64	44.60	2.96	21.70
	120-120.5	63	$C_{11}H_8N_2O_4S_2$	44.58	2.72	21.64	44.84	2.89	21.78
	115-115.5(b)	92	$C_{12}H_{10}N_2O_4S_2$	46.44	3.25	20.66	46.67	3.46	20.54

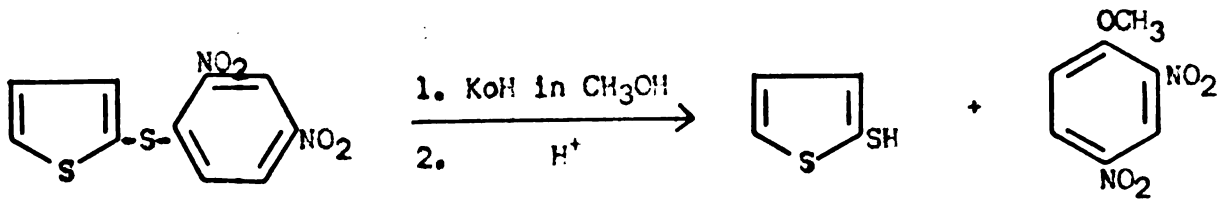
(a) Kharasch (1) reports m.p. 119°
(b) Fawcett (2) reports m.p. 104.5-105°
(c) Analyses by Micro-Tech Laboratory, Skokie, Illinois.

(d) Solvent for recrystallization, isopropyl alcohol.

formed. The product obtained from thianaphthene melted over a wide temperature range indicating it to be a mixture of the 2- and 3- substituted isomeric sulfides. The thianaphthyl-2, 4-dinitrophenyl sulfides and some of their properties are given in Table II.

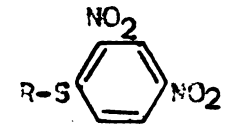
In addition to stannic chloride, two other catalysts were investigated during the development of preparative methods for obtaining the above mentioned sulfides. It was found that even when small amounts of anhydrous aluminum chloride were employed at temperatures as low as -25°, tar formation was excessive and very low yields of the products were isolated. An attempt to employ anhydrous ferric chloride resulted in extreme tar formation and identifiable product could not be isolated. Anhydrous stannic chloride was found to be ineffective as a catalyst at temperatures below the boiling point of ethylene chloride.

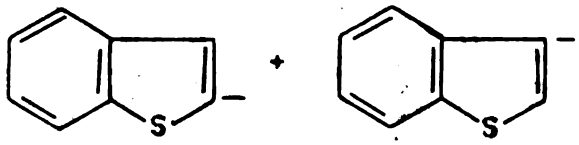
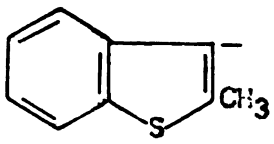
The heterocyclic -2, 4-dinitrophenyl sulfides could be cleaved by methanolic potassium hydroxide, or sodium methoxide in methanol (1). Since sodium methoxide offered no particular advantages and required additional effort in its preparation, methanolic potassium hydroxide was used throughout most of the work described here.



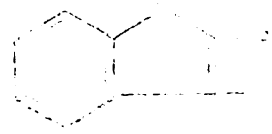
The sulfides were easily cleaved in approximately ten minutes at the reflux temperature of methanol. The reaction time was kept as short as possible since the initially formed mercaptide ion was found to decompose during the remainder of the cleavage reaction and during the

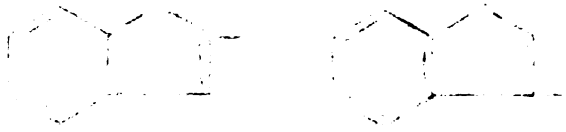
TABLE II

THIANAPHTHENE-2,4-DINITROPHENYL SULFIDES 

R	M. P.° C	% Yield	M. P.° C
	146-152	58	159-160 - 163-164[a]
	176	73	179-180[a]

(a) C. Heyd, Ph. D. Thesis, Michigan State University, 1956, pp. 48-51.





subsequent solvent removal operation. The cleavage step in the experimental procedure was carried out in a nitrogen atmosphere and the solvent was removed by vacuum distillation with minimum heating to minimize decomposition and side reactions. The crude thiols also suffered considerable decomposition during their vacuum distillation.

Employing a reaction period of an hour at the reflux temperature of methanol and removing the major part of the methanol solvent at atmospheric pressure, resulted in a 17% yield of 2-thiophenethiol. Bis (2-thienyl) disulfide was isolated as a byproduct from the crude 2, 4-dinitroanisole, the latter being recovered by filtration of the reaction mixture following the basic cleavage of the sulfide, and also from the distillation residue remaining after the purification of the mercaptan. Under similar experimental conditions, 5-methyl-2-thiophenethiol was isolated in only a 7% yield, and 2,5-dimethyl-3-thiophenethiol could not be isolated. In the latter case, however, a 90% yield of bis (2,5-dimethyl-3-thienyl) disulfide was isolated from the crude 2,4-dinitroanisole which was removed by filtration of the reaction mixture following the basic cleavage of the sulfide. When the basic cleavage reaction period was reduced to twenty minutes and the solvent was removed by vacuum distillation with minimum heating, the yield of 2-thiophenethiol isolated was increased to 48%.

The apparent decomposition of the thiols occurring during their preparation and isolation suggested that the mildest experimental conditions possible should be used during the basic cleavage of the intermediate sulfides and that the thiols be isolated as mercuric or mercuric chloride salts. When the heterocyclic-2,4-dinitrophenyl sulfides were

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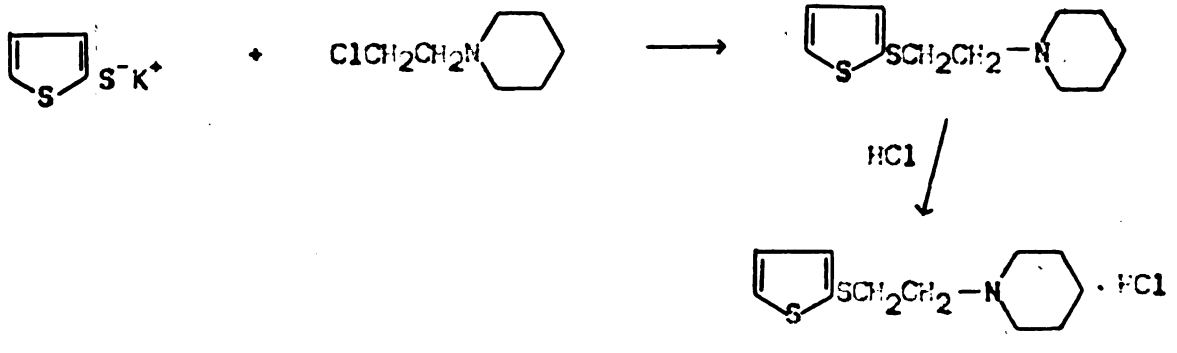
cleaved by methanolic potassium hydroxide, using short reaction periods, and the methanol solvent was removed by vacuum distillation with minimum heating, the yields of thiols, isolated as mercuric salts, ranged from 19% for 2,5-dimethyl-3-thiophenethiol to 75% for 2-thiophenethiol. The previously undescribed mercury salts and some of their properties are summarized in Table III.

The isolation of satisfactory yields of the mercury derivatives of the thiols indicated that the synthetic route used in their preparation would be useful in obtaining thiol derivatives if the potassium mercaptides were used directly as obtained from the reaction mixture. 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 the appropriate alkyl halide after removal of the 2,4-dinitroanisole byproduct. A 71% yield of 2-piperidinoethyl-2-thienyl sulfide hydrochloride was obtained by this experimental procedure.



The preparation of a second derivative, 3-methyl-2-thienyl methyl sulfide (32% yield), presented the possibility of either of two isomers or

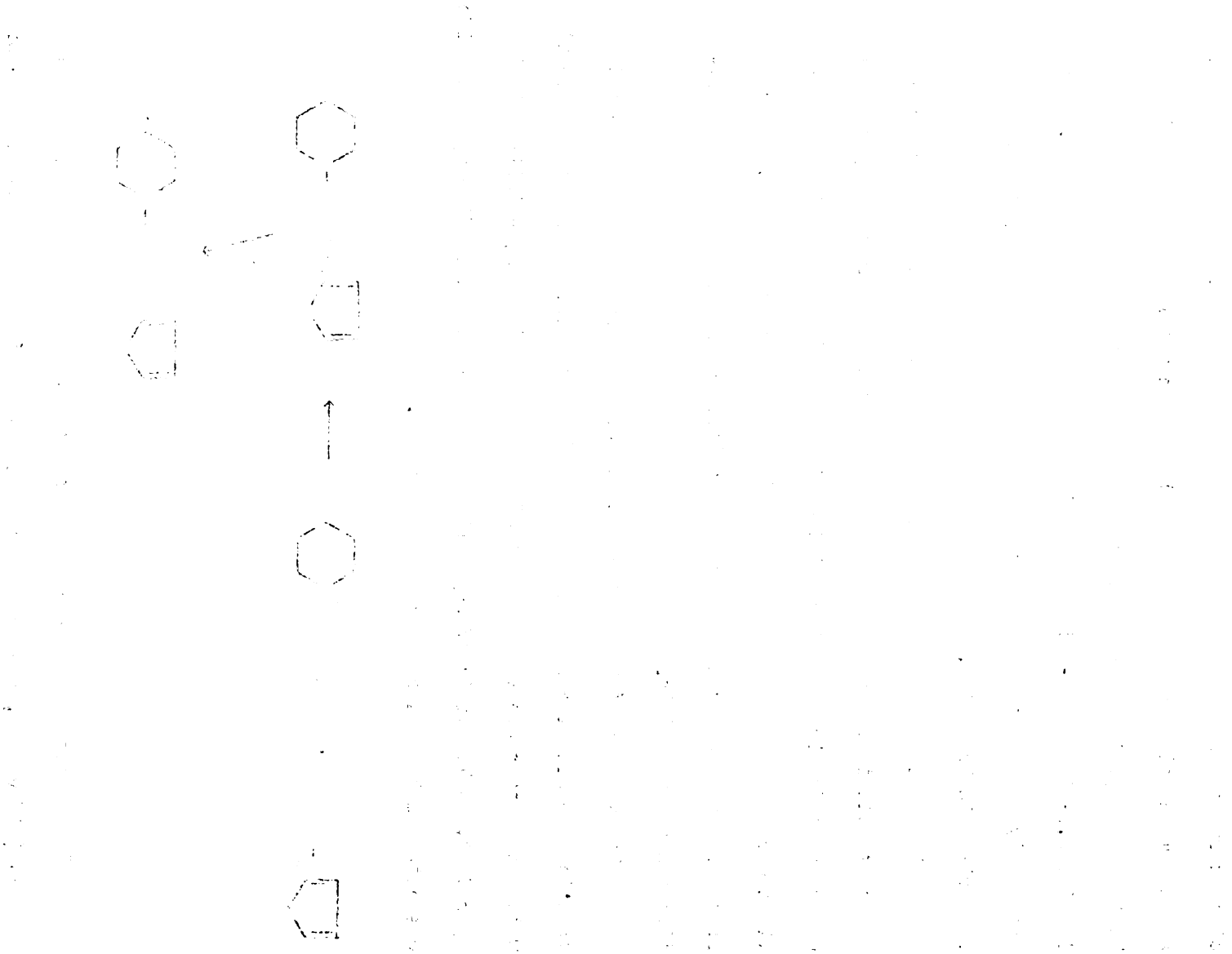
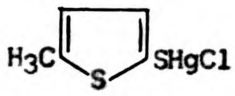
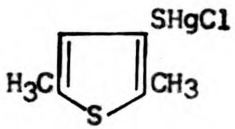
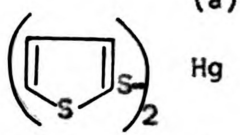
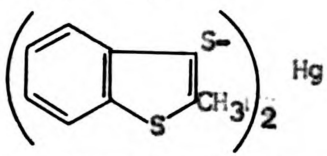


TABLE III

MERCURY DERIVATIVES OF THIOLS

TABLE III

MERCURY DERIVATIVES OF THIOLS

	M. P.° C.	Yield %	Formula	Percent Calculated C	H	Hg	Percent Found C	H	Hg
	dec. 173-174	75	$C_4H_3S_2ClHg$	13.70	0.86	57.11	14.06	1.52	57.16
	dec. 156-157	47	$C_5H_5S_2ClHg$	16.44	1.38	54.92	16.60	1.63	54.74
	dec. 175-176	19	$C_6H_7S_2ClHg$	19.00	1.86	52.89	19.28	2.11	53.11
(a) 	126	79	$C_8H_6S_4Hg$	22.29	1.40	46.55	22.42	1.58	46.18
	214-216	58	$C_{18}H_{14}S_4Hg$	38.66	2.52	35.88	37.85	2.35	35.89

(a) Prepared from a previously isolated sample of 2-thiophenethiol.

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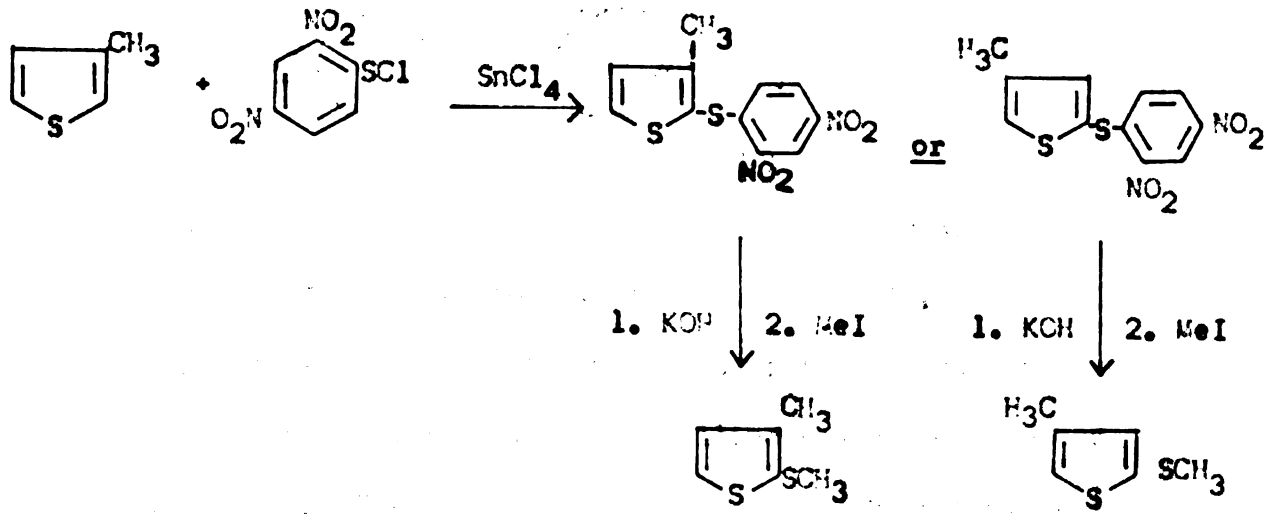
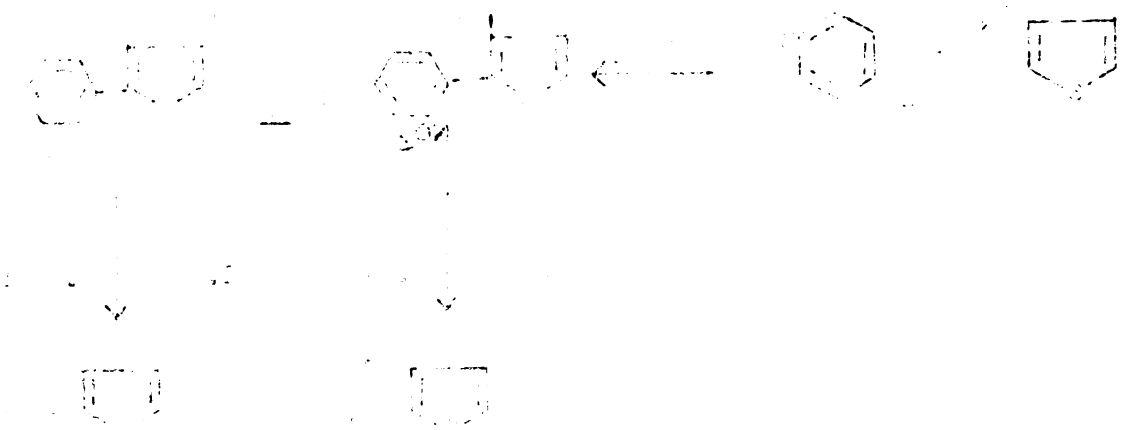
a mixture of isomers being formed. The 2,3-isomer was expected over the 2,4-isomer.



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 published spectra (23) of other 2,3-substituted thiophenes and this definitely indicated that the 2,3-substituted product had been obtained.



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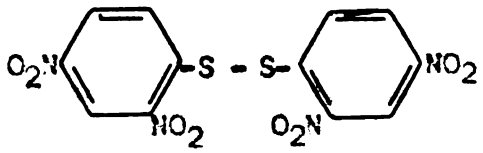
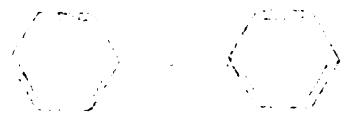
Preparation of Bis (2,4-dinitrophenyl) Disulfide



This compound was prepared using a procedure described for the preparation of bis (o-nitrophenyl) disulfide (24).

In a 3 l. round bottom flask fitted with a reflux condenser were placed 360 g. (1.5 moles) of crystalline sodium sulfide and 1.5 l. of ethanol. The reaction flask was heated on a steam bath until the sulfide completely dissolved. Then the quantity 48 g. (1.5 g. atoms) of powdered sulfur were added to the hot sulfide solution and heating was continued until the sulfur dissolved forming a reddish colored solution of sodium disulfide. A solution containing 404 g. (2.0 moles) of 2,4-dinitrochlorobenzene dissolved in the minimum amount of alcohol was prepared in a 5 l. three neck flask equipped with a stirrer and a reflux condenser. The sodium disulfide solution was added slowly to the 2,4-dinitrochlorobenzene solution through a funnel placed in the top of the reflux condenser. The reaction mixture was then stirred and heated on a steam bath, gently at first, and then at its reflux temperature for two hours. After cooling, the reaction mixture was vacuum filtered. The mixture of organic disulfide and sodium chloride was transferred to a 2 l. beaker and well stirred with 800 ml. of water to remove sodium chloride. The disulfide was recovered by vacuum filtration and washed on the filter with 100-150 ml.



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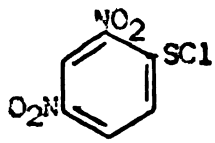
of alcohol to remove 2,4-dinitrochlorobenzene. A 320 g. quantity (80% yield) of the disulfide, decomposing above 240°, was obtained. Literature value, d. 240-280° (5).

Preparation of 2,4-Dinitrophenylsulfenyl Chloride



A suspension of 40 g. (0.10 mole) of bis (2,4-dinitrophenyl) disulfide in 500 ml. of ethylene bromide was prepared in a 1 l. three neck flask equipped with a stirrer, reflux condenser, thermometer, and chlorine gas inlet tube. A crystal of iodine was added to the stirred suspension which was then heated to a temperature of 122-126°. A stream of chlorine gas, dried by bubbling it through sulfuric acid, was passed into the hot reaction mixture until a clear dark red colored solution resulted, which required about ten hours. The solution was cooled and filtered, using celite, to remove some insoluble material. The major part of the solvent was removed by vacuum distillation, keeping the temperature below 80° to prevent decomposition of the product. The product crystallized after prolonged cooling in an ice bath of the residual syrupy liquid. A 38% yield of yellow colored crystalline product was isolated by filtration. Following a single recrystallization from carbon tetrachloride the product melted at 96-97°. Literature value, m. p. 97° (5). Several additional preparations of this sulfenyl chloride, employing the procedure described above on a larger scale, resulted in yields falling in the range of 50 to 60%.

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Two additional preparations of 2,4-dinitrophenylsulfenyl chloride were made, employing anhydrous aluminum chloride as the catalyst. In a typical preparation, a slurry composed of 55 g. (0.138 mole) of bis (2,4-dinitrophenyl) disulfide and 140 ml. of dry ethylene chloride was prepared in a 500 ml. three neck flask equipped with a stirrer and a distillation head. The slurry was stirred while 40 ml. of solvent was distilled, the distillation head was removed and the flask was protected with a drying tube while it cooled to room temperature. One gram of freshly sublimed aluminum chloride was added to the flask and chlorine gas, dried by bubbling it through concentrated sulfuric acid, was passed into the stirred slurry for three and a half hours. The dark red colored reaction mixture was filtered through celite to remove some dark colored insoluble material. The filtrate was thoroughly mixed with 200 ml of anhydrous ethyl ether and set aside, in a refrigerator, over night. The dark red colored crystalline material which separated was isolated by filtration to obtain a 36% yield of a crude product which retained a slight red coloration after recrystallization from carbon tetrachloride, using norite.

Several attempts were made to prepare 2,4-dinitrophenylsulfenyl chloride using fuming sulfuric acid as a catalyst, instead of anhydrous aluminum chloride, in the above described experimental procedure. The reaction was reported to be complete in one hour by Kharasch, Buess, and Gleason (6). In this investigation, however, no appreciable evidence of reaction could be noted after periods of chlorination as long as eleven hours.

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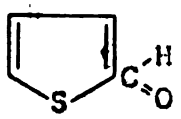
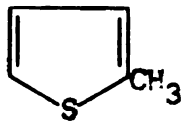
Preparation of 2-Thiophenealdehyde



To a mixture of 84 g. (1.0 mole) of thiophene and 92 g. (1.28 moles) of dimethylformamide, which was cooled and stirred in a 1 l. flask fitted with a reflux condenser, was slowly added, 192 g. (1.24 moles) of phosphorus oxychloride. The reaction flask was heated gently on a steam bath until the evolution of gas subsided and then at full steam flow for an hour and a half. The dark red colored reaction mixture was cooled in an ice bath and poured onto 1000 g. of cracked ice, with vigorous stirring. The aqueous mixture was partially neutralized with a concentrated solution of sodium hydroxide and the neutralization was completed by adding small portions of solid sodium carbonate. The red colored oil which separated was extracted into ether and the aqueous phase was washed twice with ether. The combined ether extracts were washed with water, dried in contact with anhydrous sodium sulfate, and the ether was removed on a steam bath. The residual red colored oil was vacuum distilled to obtain an 85% yield, 94.6 g. (0.85 mole) of a colorless product boiling at 52-53°/2-3 mm. A boiling point of 44-45°/1.1 mm is reported for 2-thiophenealdehyde (12). An additional preparation, using the experimental procedure described above, on a two mole scale gave an 84% yield of the heterocyclic aldehyde.

Preparation of 2-Methylthiophene



A 3 l. three neck flask fitted with a thermometer and a stirrer, and arranged for distillation, was charged with 94.6 g. (0.85 mole) of 2-thiophenealdehyde, 168 ml. of hydrazine hydrate (85%), and 672 ml. of ethylene glycol as a solvent. The stirred reaction mixture was kept in the temperature range of 130-160° for forty five minutes while water and excess hydrazine were removed by distillation. A small amount of water insoluble material was separated from the distillate and returned to the flask. The reaction mixture was cooled below 60°; an efficient reflux condenser was substituted for the distillation head, and a 168 g. (3.0 moles) quantity of potassium hydroxide was added to the flask. The stirred alkaline mixture was again heated. A vigorous reaction was initiated when the temperature of the reaction mixture reached 90-100°. When the initial reaction had subsided the mixture was heated at its reflux temperature for an additional hour and the product was isolated by distillation. The distillate was extracted with ether and the ether layer was washed with dilute hydrochloric acid and dried in contact with anhydrous calcium chloride. The drying agent was removed by filtration and the ether was removed by distillation. Fractionation of the residual liquid from metallic sodium resulted in an 80% yield of a colorless product boiling at 109-110°. The reported boiling point of 2-methylthiophene is 112-113° (13). An additional preparation of this material, using the experimental procedure described above, resulted in an 82% yield

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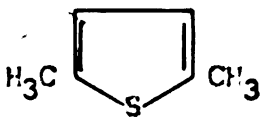
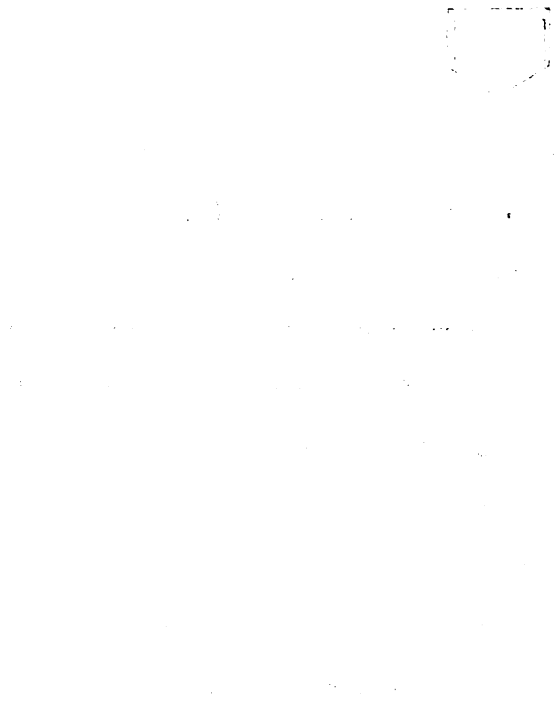
Preparation of 2,5-Dimethylthiophene



In a 3 l. three neck flask equipped with a stirrer, reflux condenser, and a dropping funnel, was placed a 250 g. (1.12 moles) quantity of phosphorus pentasulfide. A 300 g. (2.63 moles) quantity of 2,5-hexanedione was placed in the dropping funnel and a sufficient quantity of it was added to the reaction flask to slurry the stirred phosphorus pentasulfide. After the cyclization reaction had been initiated by heating the reaction mixture mildly with a bunsen burner flame, the remaining 2,5-hexanedione was added at a rate sufficient to maintain the reaction mixture at its reflux temperature. The reaction mixture was stirred at this temperature for an additional hour after adding all the 2,5-hexanedione. The product was isolated by distilling it from the stirred reaction mixture until the residue became very viscous. The crude product was extracted with 80 ml. of 3 N sodium hydroxide and washed with water. After drying it in contact with anhydrous magnesium sulfate it was redistilled to isolate a 71% yield of a colorless product boiling at 131-133°. Literature value, b.p. 134-135° (14).



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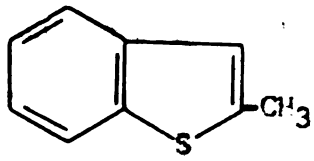
Preparation of 2-Methylthianaphthene



A three liter three neck flask fitted with a stirrer, dropping funnel, nitrogen inlet tube, and a thermometer was charged with 400 ml. of anhydrous ether and 25 g. (3.6 moles) of lithium metal chips. The reaction flask was cooled to -10° in a dry ice-isopropanol bath and a solution of 247 g. (1.8 moles) of redistilled n-butyl bromide dissolved in 250 ml. of dry ether was added during an hour. The reaction mixture was stirred for two hours following the addition of the bromide and then filtered under nitrogen through glass wool directly into a pre-chilled three liter flask. The filtered solution of n-butyl lithium was cooled to -10° and a solution of 215 g. (1.6 moles) of thianaphthene dissolved in 200 ml. of dry ether was added during a forty five minute period. The reaction mixture was stirred for an additional hour at a temperature between -5° and -10°, following the addition of the thianaphthene. A solution containing 279 g. (1.5 moles) of methyl-p-toluenesulfonate dissolved in 150 ml. of dry ether was then added to the thianaphthyl lithium solution during a one hour period. The reaction mixture was stirred for an additional hour, then allowed to warm to room temperature and poured onto 2000 g. of crushed ice. The ether layer was separated, washed with water, and dried in contact with anhydrous calcium chloride. The ether was removed on a steam bath and the residual syrupy liquid was fractionated at reduced pressure in an 80 cm. jacketed

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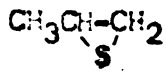
vigreaux column. The fraction which boiled at 74-76/2mm., and melted at 51-52° after distillation, corresponded to an 84% yield of 2-methylthianaphthene. Literature values, b. p. 73-74°/2mm. (9); m. p. 51.5-52° (10).

Preparation of Propylene Sulfide



A 1 l. three neck flask fitted with a stirrer and a thermometer was charged with 80 g. (1.0 mole) of thiourea, 350 ml. of water, and 30 ml. of concentrated sulfuric acid. The stirred solution was cooled, in an ice bath, to a temperature of 0-5° and 58 g. (1.0 mole) of propylene oxide was added to it during two hours. The cooled reaction mixture was stirred for ten minutes and allowed to warm to room temperature. The temperature of the reaction mixture was kept below 25° and a solution containing 106 g. (1.0 mole) of sodium carbonate dissolved in 300 ml. of water was added to it during a half hour. The oily product which separated was extracted into pentane and the aqueous phase was washed twice with additional quantities of pentane. The combined pentane extracts were dried in contact with anhydrous calcium sulfate and the pentane was removed by distillation. The residual liquid was distilled to obtain a 60% yield of a colorless product boiling at 72-73°. The boiling point of propylene sulfide is reported to be 72-75° (15).

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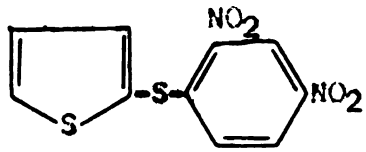
Preparation of 2,4-Dinitrophenyl-2-thienyl Sulfide



A 500 ml. three neck flask equipped with a stirrer and reflux condenser was charged with 325 ml. of dry ethylene chloride, 12 g. (0.051 mole) of 2,4-dinitrophenylsulfenyl chloride, 40 g. (0.154 mole) of anhydrous stannic chloride and 36 ml. (0.45 mole) of thiophene. The reaction mixture was stirred at its reflux temperature for two hours, during which the evolution of hydrogen chloride had become quite slow. The dark colored solution was cooled to room temperature and 30 ml. of ethanol was added to it. The reaction solution was extracted with two 100 ml. portions of dilute hydrochloric acid. The organic layer was separated and concentrated by an air stream on a steam bath until a viscous black residue remained. This solidified on the addition of 200 ml. of ethanol. The crystalline mass was broken up and boiled in the ethanol which was then decanted from it through a filter. The residue was boiled in 150 ml. of additional ethanol which dissolved all but a small amount of a black powdery material. The combined ethanol extracts were treated with Norite A and evaporated to isolate 12.9 g. (0.047 mole, 89% yield) of the crude sulfide melting at 118-118.5°. Literature value, m.p. 119° (1).

Two additional preparations of 2,4-dinitrophenyl-2-thienyl sulfide on a slightly smaller scale resulted in yields of 77% and 83%. In three additional preparations on an approximately 0.25 mole scale the yields decreased to 71%, 54%, and 60%, due to the formation of large amounts of

tarry material which complicated isolation of the product.

While carrying out the above preparation it was noted that although the reaction mixture began to darken immediately on addition of the stannic chloride catalyst, the evolution of hydrogen chloride did not become appreciable until the reaction mixture reached a temperature of approximately 75°. Further, the reaction mixture darkened considerably during the removal of the solvent on a steam bath. These observations prompted changes in the experimental procedure which resulted in considerably less tar formation and improved yields of the product.

In a typical modified preparation, a 1 l. three neck flask equipped with a stirrer and a reflux condenser was charged with 400 ml. of ethylene chloride, 20 g. (0.085 mole) of 2,4-dinitrophenylsulfenyl chloride, and 13.4 g. (0.16 mole) of thiophene. After heating the stirred reaction solution to a temperature of 65-70°, 63.5 g. (0.24 mole) of anhydrous stannic chloride was added during five minutes and the reaction mixture was then stirred at its reflux temperature for an additional hour and a half. The stirred reaction mixture was cooled to room temperature, 25 ml. of ethanol was added to it, and it was extracted with two 200 ml. portions of dilute hydrochloric acid. The organic layer was separated, filtered, and transferred to a 1 l. flask and the solvent was removed by vacuum distillation on a water bath at 70°. The gray residue was boiled in 400 ml. of ethanol and the solution was decanted from the undissolved solid. The residue was boiled in 150 ml. of additional ethanol and the solution was filtered to remove some insoluble gray powder. The ethanol extracts were treated separately with Norite

and cooled to precipitate the product, which was collected on a filter. The product which crystallized from the first ethanol extraction of the crude product was slightly brown in color while the crystalline material obtained from the second extraction had a bright yellow color. The combined ethanol filtrates were treated again with Norite and concentrated to yield an additional quantity of the crystalline product. The total yield of product, melting at 118.5-119°, was 17.4 g. (73% yield). A second preparation employing the same experimental procedure on a 0.106 mole scale resulted in an 80% yield of product.

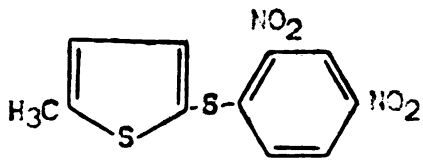
Several attempts were made to prepare 2,4-dinitrophenyl-2-thienyl sulfide using aluminum chloride as the catalyst. In a typical experiment, a 500 ml. three neck flask equipped with a stirrer and a thermometer was charged with 100 ml. of dry ethylene chloride, 42 g. (0.05 mole) of thiophene, and 9.4 g. (0.04 mole) of 2,4-dinitrophenylsulfenyl chloride. The reaction mixture was stirred at -10°, in an ice salt bath, and 12 g. of anhydrous aluminum chloride was added during a period of twenty minutes. The reaction mixture turned red in color and became very viscous and gummy. After a 5-10 minute period of stirring, 20 ml. of absolute ethanol was carefully added to the reaction mixture and it was then extracted with two 100 ml. portions of dilute hydrochloric acid. The organic layer was separated and concentrated to a volume of approximately 35 ml. by heating it under reduced pressure. The residual liquid was poured into 100 ml. of petroleum ether (b.p. 60-90°). The mixture was boiled on a steam bath and the petroleum ether solution was decanted from a layer of tarry material which had separated. The tarry material

was extracted with a second portion of boiling petroleum ether. Concentration and cooling of the combined petroleum ether extracts resulted in the precipitation of a very small amount of a yellow crystalline material melting at 116°, after a single recrystallization from ethanol. Additional preparations using as small a quantity as 5 g. of anhydrous aluminum chloride catalyst and a reaction temperature in the range -25 to 25° gave similar results.

A single preparation was carried out, using this same general experimental procedure, with anhydrous ferric chloride as the catalyst. Tar formation was excessive in this case and no product could be isolated.

An attempt was made to employ 8 g. of anhydrous stannic chloride as a catalyst, using a reaction temperature of 0-5° in the above described experimental procedure, but this also resulted in failure to obtain any of the desired product.

Preparation of 5-Methyl-2-thienyl (2,4-dinitrophenyl) Sulfide



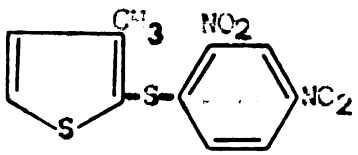
A solution containing 25 g. (0.106 mole) of 2,4-dinitrophenylsulfenyl chloride and 19.6 g. (0.20 mole) of 2-methylthiophene dissolved in 400 ml. of ethylene chloride was prepared in a 1 l. three neck flask equipped with a stirrer and a reflux condenser. This stirred solution was heated to a temperature of 70-75° and 79 g. of anhydrous stannic chloride were added to it during a five minute period. The reaction mixture was then kept at its reflux temperature for an additional hour.

After cooling to room temperature, 25 ml. of ethanol was added to the reaction mixture and it was extracted with two 200 ml. portions of dilute hydrochloric acid. The odor of hydrogen sulfide was detected during the extractions. The organic layer was separated and the solvent was removed under vacuum in a distillation flask on a water bath at 65°. The brown residual solid was boiled in 250 ml. of 2-propanol and the clear red colored solution was decanted from an insoluble gummy residue. The 2-propanol extract, on cooling, became cloudy immediately and a quantity of a dark red colored oil separated. This oil failed to completely dissolve on adding an additional 50 ml. of 2-propanol and boiling the solution. The 2-propanol solution was decanted from the insoluble residue, which was discarded. The gummy residue from the reaction mixture was extracted with an additional 150 ml. of boiling 2-propanol, but only a small portion dissolved. The combined 2-propanol extracts were treated with Norite and set aside in a refrigerator. A thin layer of light brown colored crystalline material precipitated and then a quantity of yellow colored crystals formed. The crystalline material was collected on a filter and washed with ethanol to isolate a 65% yield of a crude product melting at 99-101°. A single recrystallization from ethanol raised the melting point to 102-103°. Elemental analysis gave the following results. Calc'd. for $C_{11}H_8N_2O_4S_2$: C, 44.58; H, 2.72; S, 21.64. Found: C, 44.60; H, 2.96; S, 21.70.

In two additional preparations of this compound in which the stannic chloride catalyst was added at room temperature, prior to heating the reaction mixture at its reflux temperature, the yields decreased to

44% and 48%. One additional preparation in which a reaction temperature of 55-60° was used instead of the reflux temperature of the reaction mixture resulted in a 42% yield of the desired product.

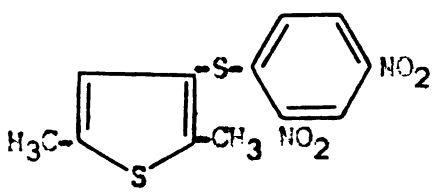
Preparation of 3-Methyl-2-thienyl-2,4-dinitrophenyl Sulfide



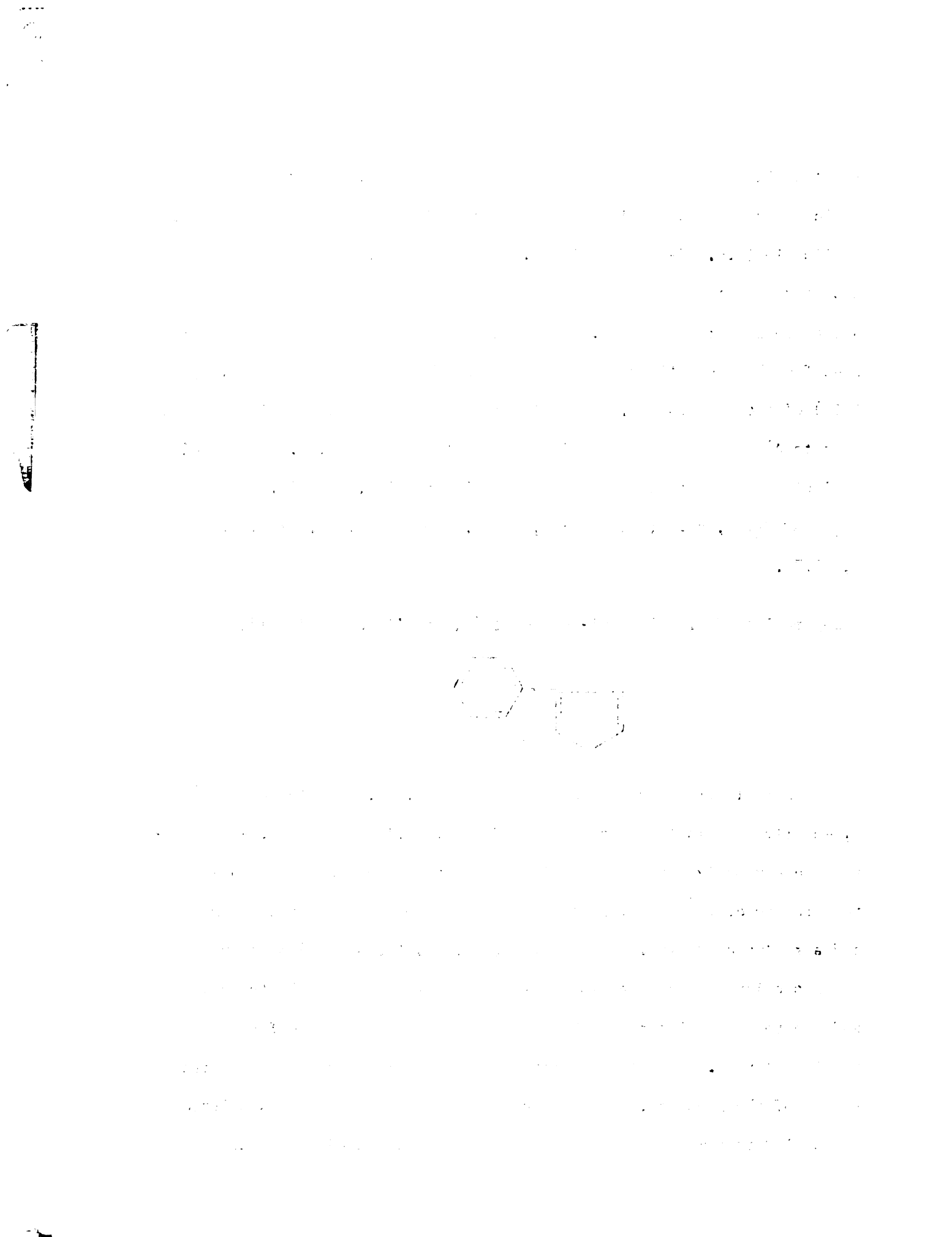
A stirred solution containing 20 g. (0.085 mole) of 2,4-dinitrophenylsulfenyl chloride and 15.7 g. (0.16 mole) of 3-methylthiophene dissolved in 350 ml. of ethylene chloride was heated to a temperature of 75° in a 500 ml. three neck flask equipped with a stirrer and reflux condenser. A 63.5 g. (0.24 mole) quantity of anhydrous stannic chloride was added to the reaction mixture during a five minute period, after which it was kept at its reflux temperature for an additional hour. The dark colored, stirred reaction mixture was cooled in a water bath, diluted with 30 ml. of ethanol, and extracted with two 150 ml. portions of dilute hydrochloric acid. The organic layer was separated and the solvent removed by vacuum distillation on a water bath at a temperature of 65°. The dark colored residual oil was extracted by boiling it in 250 ml. of isopropanol and decanting the alcohol solution from the tarry residue. A quantity of a dark colored oil separated as the alcohol solution cooled slightly. The solution was boiled on a steam bath and decanted, through a filter, from the undissolved material. Cooling during filtration caused additional quantities of dark colored oil and some crystalline material to collect on the filter. The filtrate was

treated with Norite and set aside in a refrigerator. The reaction residue and the fluted filter paper were boiled in a mixture of 200 ml. of ligroin (b.p. 60-90°) and 15 ml. of isopropanol. The solution was decanted from the undissolved tarry residue, treated with Norite, and set aside in a refrigerator. The yellow colored crystals which separated from both solutions were recovered by filtration to yield 15.9 g. (63%) of a crude product. After two recrystallizations from isopropanol (Norite A) the melting point of the product was 120-120.5°. Elemental analysis of the material gave the following results. Calc'd. for $C_{11}H_8N_2O_4S_2$; C, 44.58; H, 2.72; S, 21.64. Found: C, 44.84; H, 2.89; S, 21.78.

Preparation of 2,5-Dimethyl-3-thienyl (2,4-dinitrophenyl) Sulfide



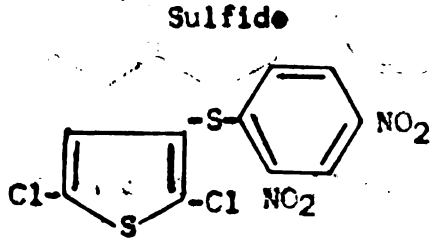
A well stirred solution containing 20 g. (0.085 mole) of 2,4-dinitrophenylsulfenyl chloride and 19 g. (0.17 mole) of 2,5-dimethylthiophene dissolved in 400 ml. of ethylene chloride was heated to a temperature of 70° in a 1 l. three neck flask equipped with a stirrer and a reflux condenser. The quantity, 63.5 g. (0.24 mole) of anhydrous stannic chloride was added to the solution during a five minute period and the reaction mixture was kept at its reflux temperature for an additional hour. Hydrogen chloride was evolved rapidly at the initial stages of the reaction. The dark colored reaction mixture was stirred and cooled in a water bath and 20 ml. of ethanol was added to it,



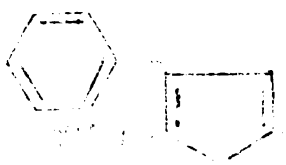
followed by an extraction with two 200 ml. portions of dilute hydrochloric acid. The organic layer was separated and the solvent was removed by vacuum distillation in a water bath at a temperature of 65°. The residual solid was extracted with 200 ml. of boiling 2-propanol and the extract was treated with Norite and filtered. The remaining yellow product was dissolved in boiling 2-propanol and the alcohol solution was filtered to remove a small amount of insoluble matter. The combined 2-propanol solutions were set aside in a refrigerator and the crystalline product which separated was isolated by filtration. The yield was 24.4 g. (92%) of yellow colored crystals which melted at 115-115.5°. Fawcett (2) reported a melting point of 104.5-105° for this compound. Elemental analysis gave the following results: Calc'd. for $C_{12}H_{10}N_2O_4S_2$: C, 46.44; H, 3.25; S, 20.66. Found: C, 46.67; H, 3.46; S, 20.54.

In a second preparation of this sulfide the stannic chloride catalyst was added at room temperature, prior to heating the reaction mixture at its reflux temperature, and the solvent was removed at atmospheric pressure. The yield, in this case, decreased to 74%.

Attempted Preparation of 2,5-Dichloro-3-thienyl-2,4-dinitrophenyl Sulfide

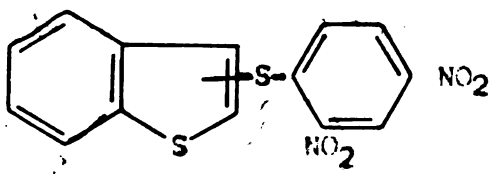


A 500 ml. three neck flask equipped with a stirrer and reflux condenser was charged with 250 ml. of ethylene chloride, 10 g. (0.043 mole)



of 2,4-dinitrophenylsulfenyl chloride, 15 ml. of 2,5-dichlorothiophene, and 33 g. of anhydrous stannic chloride. The reaction mixture was stirred at its reflux temperature for three and a half hours. Hydrogen chloride was slowly evolved throughout the reaction period. The stirred reaction mixture was cooled to room temperature and 25 ml. of ethanol was added to it. The dark colored reaction solution was then extracted with three 100 ml. portions of dilute hydrochloric acid. The solvent was removed from the organic layer by heating it in an air stream on a steam bath. The dark colored residue was boiled in 150 ml. of ethanol and the ethanol solution was decanted through a filter. The residue was extracted with a second portion of boiling ethanol, but only a small amount of the material dissolved. A yellow colored powdery material, which decomposed above 120°, without melting, was isolated on treating the combined ethanol extracts with charcoal and chilling the solution in an ice bath. Apparently, the only product obtained in the above reaction was a polymeric material. The desired sulfide is reported to be a crystalline solid melting at 136.5-137° (16).

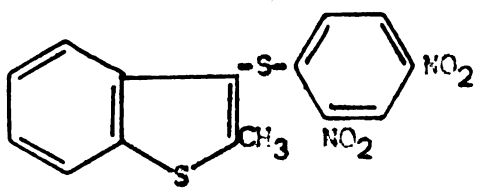
Preparation of Thianaphthyl-2,4-dinitrophenyl Sulfide



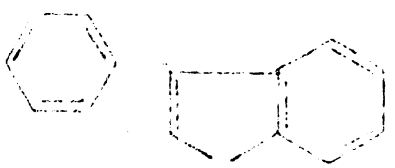
A stirred solution containing 10 g. (0.043 mole) of 2,4-dinitrophenylsulfenyl chloride and 8 g. (0.06 mole) of thianaphthene dissolved in 250 ml. of ethylene chloride was heated to a temperature of 70° in a 500 ml. three neck flask equipped with a stirrer and a reflux condenser.

A 33 g. (0.13 mole) quantity of anhydrous stannic chloride catalyst was added, during a five minute period, to the reaction mixture which was then stirred at its reflux temperature for an hour. The reaction mixture was cooled to room temperature, in a water bath, and 15 ml. of ethanol was added to it. The mixture was then extracted with two 100 ml. portions of dilute hydrochloric acid. The organic layer was separated and the solvent was removed by vacuum distillation on a water bath at a temperature of 65°. The yellow colored solid residue was dissolved in hot benzene and the solution was filtered to remove a small amount of insoluble matter. The filtrate was diluted with an equal volume of isopropanol, treated with Norite, and set aside to cool in a refrigerator. The yellow colored crystalline material which separated was collected on a filter and recrystallized from isopropanol containing a small amount of benzene. A 58% yield of product, melting in the temperature range 146-152°, was obtained. Based on this melting point range, the product was judged to be a mixture of the 2 and 3 substituted isomers. The literature values are: 2-thianaphthyl-2,4-dinitrophenyl sulfide, m.p. 159-160° (3); 3-thianaphthyl-2,4-dinitrophenyl sulfide, m.p. 163-164° (21).

Preparation of 2-Methyl-3-thianaphthyl-2,4-dinitrophenyl Sulfide

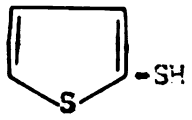


A 500 ml. three neck flask equipped with a stirrer and reflux condenser was charged with 300 ml. of ethylene chloride, 10 g. (0.043 mole)



of 2,4-dinitrophenylsulfenyl chloride, 8 g. (0.054 mole) of 2-methylthianaphthene, and 33 g. (0.13 mole) of anhydrous stannic chloride. The reaction mixture was stirred vigorously at its reflux temperature for an hour. Hydrogen chloride was rapidly evolved during the first half of the reaction period and the mixture took on a light yellow-brown coloration. After cooling the reaction mixture to room temperature, 15 ml. of ethanol was added to it and it was extracted with two 100 ml. portions of dilute hydrochloric acid. The organic layer was separated and the solvent removed by vacuum distillation on a water bath at a temperature of 70°. The yellow colored residual solid was dissolved in a boiling 2:1 ethanol-dioxane mixture, filtered, and set aside in a refrigerator. The crystalline material which separated was collected on a filter. The filtrate was concentrated to approximately one fourth its volume and treated with Norite. Water was added to the hot solution until a yellow crystalline solid began to separate, at which point the mixture was set aside in a refrigerator to precipitate an additional quantity of the crystalline product. A combined yield of 75% of product, melting at 176°, was obtained. Heyd (4) reported a melting point of 179-181° for this sulfide. Two additional preparations of this compound gave yields of 73% and 76% respectively.

Preparation of 2-Thiophenethiol



To a solution of sodium methoxide prepared by allowing 5 g. (0.22 g. atom) of sodium metal to react with 500 ml. of methanol was added 29 g. (0.1 mole) of 2-thienyl-2,4-dinitrophenyl sulfide. The stirred suspension was continuously flushed with nitrogen and held at its reflux temperature for a half hour. Approximately 260 ml. of methanol was then distilled from the reaction mixture. The residual liquid was poured onto cracked ice and the flask was rinsed with sufficient water to bring the final volume to approximately 800 ml. The resulting aqueous suspension was stirred for a few minutes and filtered to remove a quantity of a red solid. The dark red colored filtrate was acidified with 1:1 sulfuric acid and steam distilled until 400 ml. of distillate had been collected. The light yellow colored distillate was extracted with two 50 ml. portions of ether. The combined ether extracts were dried in contact with anhydrous sodium sulfate, filtered to remove the drying agent, and concentrated by distillation on a steam bath. The concentrated solution was transferred to a 50 ml. flask, using a small amount of ether, and the ether was removed by distillation. The residual red colored oil was vacuum distilled to isolate a 14% yield of a light yellow colored oil boiling at 53-54°/4-5 mm. Houff and Schuetz report a boiling point of 54°/5 mm. for 2-thiophenethiol(7).

A 2,4-dinitrophenyl sulfide derivative of the product was prepared and found to melt at 119° after a single recrystallization from ethanol. Literature value, m.p. 119° (1).

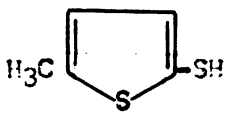
Two additional preparations of 2-thiophenethiol, employing the above experimental procedure, resulted in yields of 14% and 17% respectively.

Small amounts of 2,2'-dithienyl disulfide were isolated from the initial distillation residue and from the red colored precipitate isolated after pouring the residue from the basic cleavage onto ice. The distillation residue was thoroughly washed with warm water and recrystallized from aqueous ethanol to isolate a light yellow colored crystalline material melting at 57°. Challenger, Miller, and Gibson (8) reported a melting point of 56° for 2,2'-dithienyl disulfide. The red colored precipitate was recrystallized from methanol, using charcoal. The yellow colored crystalline material melted at 88° and was assumed to be 2,4-dinitroanisole. A melting point of 87-88° is reported (11) for 2,4-dinitroanisole. An additional quantity of this material was isolated by adding ethanol to the filtrate, and concentrating it on a steam bath. Isopropyl alcohol was added to the filtrate and it was again concentrated and set aside in a refrigerator. A small quantity of yellow colored crystalline material separated from solution. This melted at 42-44° and was assumed to be impure 2,2'-dithienyl disulfide.

Several modifications of the experimental procedure described above effected a considerable increase in the yield of 2-thiophenethiol obtainable. In the modified procedure, a solution containing 6 g.

(0.12 mole) of potassium hydroxide dissolved in 300 ml. of methanol was prepared by warming the components in a 500 ml. three neck flask while stirring the alkali methoxide solution with a stream of nitrogen. A reflux condenser was attached to the flask and 17 g. (0.06 mole) of 2-thienyl-2,4-dinitrophenyl sulfide were added to the reaction mixture, which was then heated at its reflux temperature for twenty minutes in a nitrogen atmosphere. The major share of the solvent was removed by vacuum distillation on a water bath at 30-35°. Care was necessary to prevent severe bumping during the later stages of solvent removal. The residue was poured onto cracked ice and the flask was rinsed with sufficient water to bring the final volume to 400 ml. The aqueous suspension was stirred until thoroughly chilled and then filtered to remove a light orange colored solid, which was washed with water. The filtrate was acidified with concentrated hydrochloric acid. The aqueous phase was extracted with three portions of ether, which were combined and dried in contact with anhydrous calcium chloride, and the ether was removed by distillation on a steam bath. The residual dark red colored oil was vacuum distilled to obtain a 48% yield of a light yellow colored oil boiling at 30-32°/1-2 mm.

Preparation of 5-Methyl-2-thiophenethiol

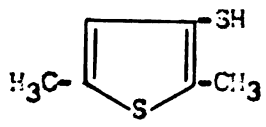


To a solution of sodium methoxide prepared by allowing 4.6 g. (0.21 g. atom) of sodium metal to react with 500 ml. of methanol in a

one liter three neck flask equipped with a stirrer and a distilling head was added 32 g. (0.108 mole) of 2,4-dinitrophenyl-5-methyl-2-thienyl sulfide. The stirred reaction mixture was heated at its reflux temperature until the sulfide disappeared and then 260 ml. of methanol was removed by distillation. The dark red colored solution was poured onto ice and the flask was rinsed with sufficient water to bring the volume to 800 ml. The aqueous suspension was stirred until thoroughly chilled and filtered to remove a quantity of a red colored solid. The filtrate was acidified with 1:1 concentrated sulfuric acid and extracted with two 35 ml. portions of ether. The combined ether extracts were dried in contact with anhydrous magnesium sulfate, filtered, and the ether removed by distillation on a steam bath. The residual red colored oil was vacuum distilled to isolate a 7% yield of a straw colored oil boiling at 50-53°/3 mm.

A 2,4-dinitrophenyl sulfide derivative was prepared. It melted at 103-103.5 as obtained directly from the reaction mixture. Two crystallizations from ethanol raised its melting point to 105°. Elemental analysis gave the following results. Calc'd for $C_{11}H_8N_2O_4S_2$: C, 44.58; H, 2.72; S, 2164. Found: C, 44.60; H, 2.96; S, 21.70.

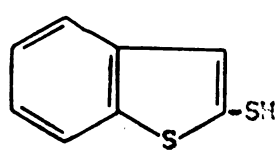
Attempted Preparation of 2,5-Dimethyl-3-thiophenethiol (Isolation of 2,5-Dimethyl-3-thienyl Disulfide)



To a solution composed of 11.2 g. (0.2 mole) of potassium hydroxide dissolved in 500 ml. of methanol contained in a 1 l. three neck flask

fitted with a stirrer, distillation head, and a nitrogen inlet tube, were added 30.6 g. (0.1 mole) of 2,5-dimethyl-3-thienyl-2,4-dinitrophenyl sulfide. The stirred reaction mixture was heated under a nitrogen atmosphere until 300 ml. of methanol had been removed by distillation. The dark red colored residue was poured onto cracked ice and the flask was rinsed with sufficient water to bring the volume of the mixture to 800 ml. An insoluble residue remained in the reaction flask. The aqueous suspension was stirred in an ice bath until thoroughly chilled and filtered through celite to remove a red colored gummy solid. The filtrate was acidified with concentrated hydrochloric acid but no material, solid or oil, separated from solution and only a faint odor of mercaptan was detected. The red colored gummy precipitate was extracted thoroughly with hot aqueous base to remove 2,4-dinitroanisole. The alkali insoluble residue was equivalent to an 89% recovery of 2,5-dimethyl-3-thienyl disulfide. After recrystallization from aqueous ethanol the light yellow colored disulfide melted at 58.5-59°. Elemental analysis gave the following results. Calc'd for $C_{12}H_{14}S_4$: C, 50.31; H, 4.93; S, 44.77. Found: C, 50.29; H, 5.07; S, 44.77.

Preparation of 2-Thianaphthenethiol



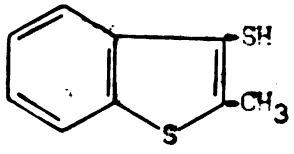
A 500 ml. three neck flask fitted with a stirrer, dropping funnel, nitrogen inlet tube, and a thermometer, was charged with 120 ml. of dry ether and 6.4 g. (0.90 g. atom) of lithium metal chips. The reaction

flask was cooled to -10° in a dry ice-isopropanol bath and a solution of 60 g. (0.44 mole) of redistilled n-butyl bromide dissolved in 60 ml. of dry ether was added during a half hour. The reaction mixture was stirred for an additional hour following the addition of the bromide and then filtered under nitrogen through glass wool directly into a precooled 500 ml. flask. The filtered solution of n-butyl lithium was cooled to -10° and a solution of 48 g. (0.36 mole) of thianaphthene dissolved in 25 ml. of ether was added during a fifteen minute period. The reaction mixture was stirred for an additional half hour at a temperature between -5° and -10° and then it was allowed to warm to room temperature. A solution containing 15 g. (0.22 mole) of propylene sulfide dissolved in 40 ml. of dry ether was then added to the thianaphthyl lithium solution during a fifteen minute period. No increase in temperature was noted during the addition of the propylene sulfide. The reaction mixture was stirred at its reflux temperature for one hour, during which the color changed from blue through green to light yellow. After being set aside overnight the reaction 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. The combined aqueous extracts were acidified with concentrated hydrochloric acid. A quantity of yellow colored oil separated. This was separated and the aqueous layer was extracted three times with pentane. The combined pentane extracts were dried in contact with anhydrous calcium sulfate and the pentane was removed by distillation to isolate 13 g. (36% yield) of a yellow colored oil. An attempt to

purify the product by vacuum distillation was discontinued when the material began to darken at a still head temperature of 160°/ 2 mm.

A 2,4-dinitrophenyl sulfide of the mercaptan was prepared and it melted at 159° after recrystallization from a 1:1 methanol dioxane mixture. Heyd (3) reports a melting point of 159-160° for this derivative of 2-thianaphthenethiol. Calculated for $C_{14}H_8O_4N_2S_2$: C, 50.59; H, 2.43; S, 19.30. Found: C, 50.62; H, 2.51; S, 19.46.

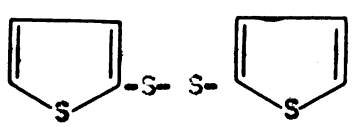
Attempted Preparation of 2-Methyl-3-thianaphthenethiol



To a solution containing 7.8 g. (0.14 mole) of potassium hydroxide dissolved in 370 ml. of a 1:1 methanol-dioxane mixture contained in a 500 ml. three neck flask was added 25 g. (0.072 mole) of 2-methyl-3-thianaphthyl-2,4-dinitrophenyl sulfide. A stream of nitrogen was led into the reaction mixture and it was heated at its reflux temperature for fifteen minutes. The major part of the solvent was removed by vacuum distillation. The residue was poured onto cracked ice and the flask was rinsed with sufficient water to bring the final volume of the mixture to approximately 400 ml. The aqueous suspension was stirred until thoroughly chilled and filtered to remove a quantity of a red colored solid. A red colored solid precipitated from the filtrate on acidification with concentrated hydrochloric acid. This was extracted into ether and the aqueous phase was washed twice with

ether. The combined ether extracts were dried in contact with anhydrous calcium chloride and the ether was removed by vacuum distillation. Vacuum distillation of the residue yielded 4.3 g. of red oil, distilling in the range 125-175°/2 mm., which solidified as an orange colored solid. This material melted in the range 90-100°. A considerable quantity of a dark colored residue remained in the distillation flask. An attempt was made to prepare a 2,4-dinitrophenyl sulfide derivative but the product obtained softened at 143° and melted above 153° even after recrystallization from methanol. A part of the product was found to be insoluble in ethanol or aqueous base during the attempted derivative preparation. The insoluble material melted at 153-154° after it was washed with water and alcohol and dried. It was assumed to be the disulfide of the desired thiol.

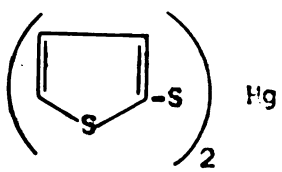
Attempted Preparation of 2,2'-Dithienyl Disulfide



A one liter three neck flask equipped with a stirrer, distillation head, and an air inlet tube was charged with a solution containing 17.0 g. (0.3 mole) of potassium hydroxide dissolved in 525 ml. of methanol, and 42.5 g. (0.15 mole) of 2-thienyl-2,4-dinitrophenyl sulfide. The reaction mixture was distilled, while flushing the system with a stream of air, until 390 ml. of methanol had been collected. The stirred reaction mixture was cooled in a water bath and 250 ml. of ether was added to it.

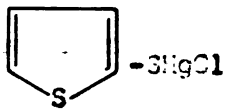
A quantity of a brown colored precipitate which formed was removed by filtration. The filtrate was extracted with two portions of cold water and the organic layer was separated and evaporated on a steam bath. The dark red colored aqueous extracts were discarded. The residue was dissolved in hot ethanol and the solution was acidified with concentrated hydrochloric acid. Treatment of the solution twice with Norite failed to remove its dark red coloration. A dark red colored oil separated on cooling the ethanol solution in a refrigerator overnight and it was discarded.

Preparation of 2-Thienyl Mercury Mercaptide

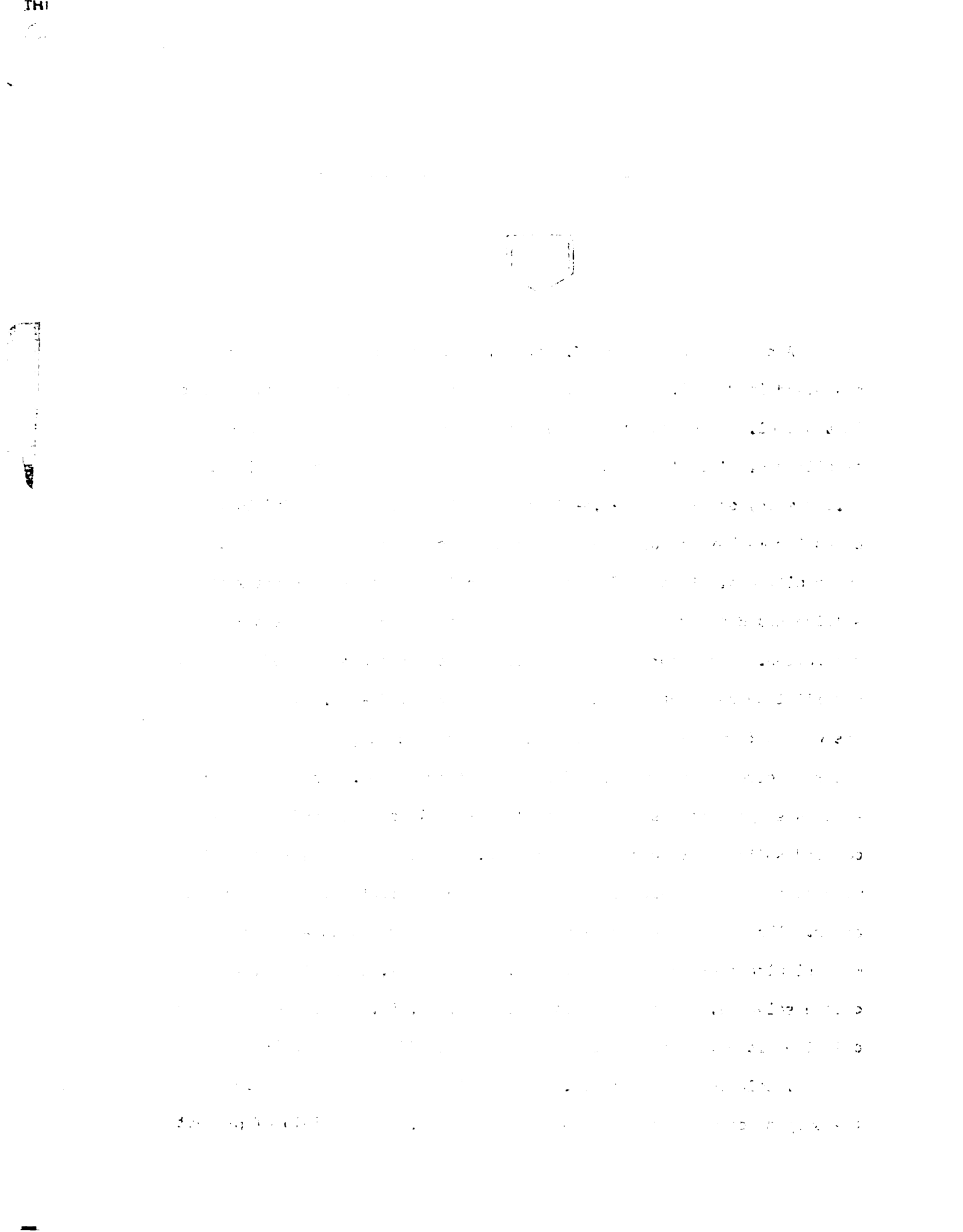


To a warm solution containing 1.6 g. (0.014 mole) of 2-thiophenethiol dissolved in 75 ml. of ethanol was added a solution containing 2.1 g. (0.0065 mole) of mercuric acetate dissolved in 20 ml. of ethanol. A yellow colored solid precipitated immediately. The mixture was stirred and set aside in a refrigerator. The product was isolated by filtration and washed with alcohol. A yield of 79% of a yellow colored solid in the form of needles, which melted at 126° after a single recrystallization from ethanol, was obtained. Elemental analysis gave the following results. Calc'd. for $C_8H_6S_4Hg$: C, 22.29; H, 1.40; Hg, 46.55. Found: C,22.42; H, 1.58; Hg, 46.18.

Preparation of 2-Thiophenemercaptomercuric Chloride

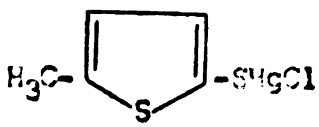


A solution containing 4.8 g. (0.086 mole) of potassium hydroxide dissolved in 250 ml. of methanol was prepared by warming the components in a 500 ml. three neck flask while stirring the methanol with a stream of nitrogen. A reflux condenser was attached to the flask and 12 g. (0.043 mole) of 2-thienyl-2,4-dinitrophenyl sulfide were added to the potassium methoxide solution. The resulting suspension was heated, under nitrogen, at its reflux temperature for eight minutes after the sulfide had dissolved and the reaction mixture had taken on a dark coloration. The major part of the alcohol solvent was removed by vacuum distillation on a water bath at a temperature of 30-35°. The residue was washed from the reaction flask, onto crushed ice, with sufficient water to give a final volume of approximately 400 ml. The resulting aqueous suspension was stirred until thoroughly chilled and a yellow colored solid was removed by filtration. The filtrate was acidified with concentrated hydrochloric acid and then extracted three times with ether. The combined ether extracts were concentrated on a steam bath with simultaneous addition of 150 ml. of methanol, in portions, to change solvents. A solution containing 16.3 g. (0.06 mole) of mercuric chloride dissolved in 50 ml. of methanol was added to the stirred methanol solution of the thiol. A precipitate formed immediately and the suspension was set aside in a refrigerator. A 75% yield of product



was isolated by filtration. After a single recrystallization from a 1:1 ethanol-ethyl acetate mixture the product was light yellow in color and decomposed at 173-174°. Elemental analysis gave the following results. Calculated for $C_4H_3S_2ClHg$: C, 13.70; H, 0.86; Hg, 57.11. Found: C, 14.06; H, 1.52; Hg, 57.16.

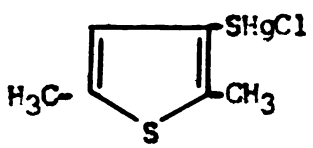
Preparation of 5-Methyl-2-thiophenemercaptomercuric Chloride



A solution containing 4.9 g. (0.0875 mole) of potassium hydroxide dissolved in 250 ml. of methanol was prepared by warming the base and the alcohol in a 500 ml. three neck flask while stirring the solution with a stream of nitrogen gas. A reflux condenser was attached to the flask and 13 g. (0.044 mole) of 5-methyl-2-thienyl-2,4-dinitrophenyl sulfide were added to the alkali methoxide solution. The reaction mixture was heated, under nitrogen, at its reflux temperature for twelve minutes. The major part of the solvent was removed by vacuum distillation on a water bath at a temperature of 30-35°. The residue was poured onto cracked ice and the flask was rinsed with sufficient water to bring the final volume of the mixture to approximately 300 ml. The aqueous suspension was stirred until thoroughly chilled and filtered to remove a quantity of orange colored solid, which was washed with water. The filtrate was acidified with concentrated hydrochloric acid and extracted three times with ether. The combined ether extracts were concentrated

on a steam bath with simultaneous addition of 150 ml. of methanol, in portions, to change solvents. A solution containing 16.3 g. (0.06 mole) of mercuric chloride dissolved in 50 ml. of methanol was added to the stirred solution of the mercaptan. A bulky precipitate formed and the suspension was set aside in a refrigerator. A 47% yield of the product was isolated by filtration of the chilled solution. After a single recrystallization from ethyl acetate-acetone the light yellow colored product decomposed at 156-157° on slow heating. Elemental analysis gave the following results. Calculated for $C_5H_5S_2ClHg$: C, 16.44; H, 1.38; Hg, 54.92. Found: C, 16.60; H, 1.63; Hg, 54.74.

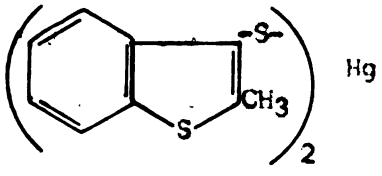
Preparation of 2,5-Dimethyl-3-thiophenemercaptomercuric Chloride



Employing the experimental procedures previously described for the synthesis of thiophenemercaptomercuric chlorides, 12 g. (0.039 mole) of 2,5-dimethyl-3-thienyl-2,4-dinitrophenyl sulfide was cleaved in a solution containing 4.8 g. (0.086 mole) of potassium hydroxide dissolved in 250 ml. of methanol. A solution containing 14.4 g (0.053 mole) of mercuric chloride dissolved in 35 ml. of methanol was added to the methanol solution of the mercaptan to precipitate the product. A 19% yield of a light yellow-gray colored product, which decomposed at 175-176° after a single recrystallization from a 1:1 ethyl acetate-ethanol mixture, was obtained. Elemental analysis gave the following results. Calculated

for C_6H_7SClHg: C, 19.00; H, 1.86; Hg, 52.89. Found: C, 19.28; H, 2.11; Hg, 53.11.

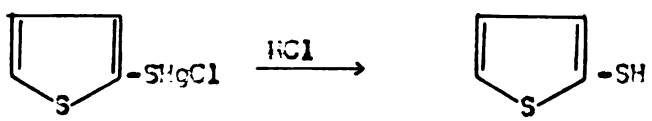
Preparation of 2-Methyl-3-thianaphthyl Mercury Mercaptide



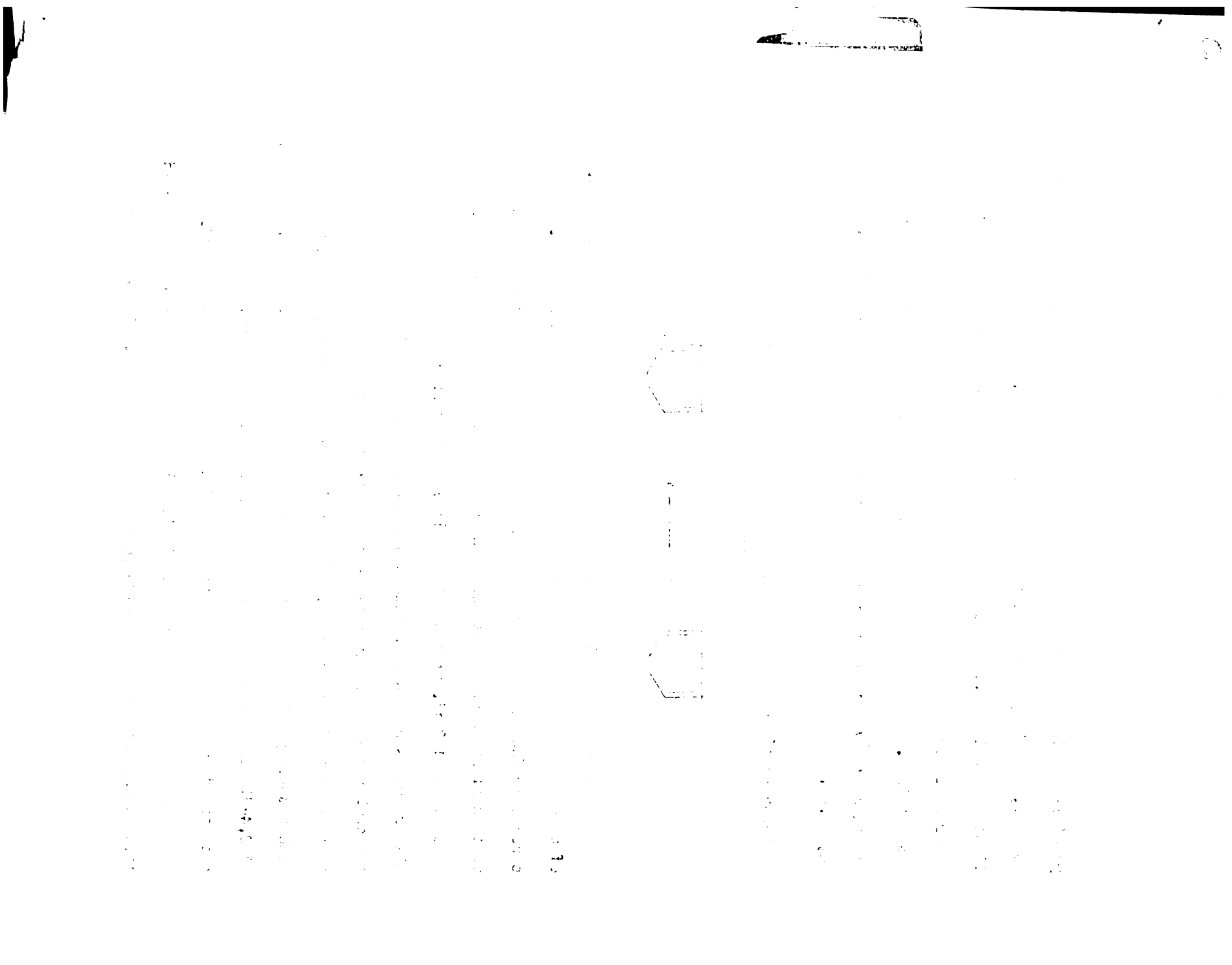
To a solution prepared from 2.8 g. (0.05 mole) of potassium hydroxide and 150 ml. of 1:1 methanol-dioxane, which was contained in a 500 ml. three neck flask fitted with a reflux condenser and a nitrogen gas inlet tube, was added 8.9 g. (0.026 mole) of 2-methyl-3-thianaphthyl-(2,4-dinitrophenyl) sulfide. The reaction mixture was heated at its reflux temperature for fifteen minutes, while a stream of nitrogen flushed the system. The major part of the solvent was removed by vacuum distillation on a water bath at a temperature of 35°. The residue was flushed from the reaction flask, onto ice, with sufficient water to bring the final volume of the mixture to approximately 400 ml. The aqueous suspension was stirred until thoroughly chilled and filtered to remove an orange solid, which was washed with water. The filtrate was acidified with concentrated hydrochloric acid and extracted three times with ether. The combined ether extracts were concentrated on a steam bath with simultaneous addition of 125 ml. of methanol, in portions, to change solvents. A solution containing 3.5 g. of mercuric chloride dissolved in 30 ml. of methanol was added, with stirring, to the warm solution of the mercaptan. The mercaptide

precipitated immediately; the suspension was set aside in a refrigerator to cool, and the product was collected on a filter. A 58% yield of a light gray colored product, which melted with decomposition at 214-216° after a single recrystallization from a 1:1 ethanol-ethyl acetate mixture, was obtained. Elemental analysis gave the following results: Calc'd for $C_{18}H_{14}S_4Hg$: C, 38.66; H, 2.52; Hg, 35.88. Found: C, 37.85; H, 2.35; Hg, 35.89.

Recovery of 2-Thiophenethiol from 2-Thiophenemercaptomercuric Chloride

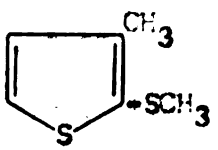


A 2 g. quantity of 2-thiophenemercaptomercuric chloride and 15 ml. of concentrated hydrochloric acid were shaken together in a 100 ml. separatory funnel for a few minutes. The slurry was extracted with a portion of pentane, the latter being decanted from the aqueous layer. An additional 3 ml. of concentrated hydrochloric acid was added and the mixture was shaken with a second portion of pentane, which was decanted and combined with the initial pentane extract. The aqueous phase was again extracted with pentane. The combined pentane extracts were washed with a small portion of water and added to a solution of 1.1 g. (0.005 mole) of 2,4-dinitrochlorobenzene dissolved in 20 ml. of alcohol. The mixture was warmed on a steam bath until most of the pentane had evaporated. The remaining solution was made alkaline by the addition of a concentrated solution of potassium hydroxide to the heated solution. The alkaline



solution took on a dark coloration and a precipitate formed after a few minutes of heating. The mixture was extracted with a portion of aqueous base to remove any 2,4-dinitrophenol. The alkali insoluble residue was acidified with concentrated hydrochloric acid and dissolved in hot isopropanol. The large yellow colored needles which precipitated on cooling the solution melted at 119-120°, and represented a 31% recovery of 2-thiophenethiol. Literature value, m.p. of 2-thienyl-2,4-dinitrophenyl sulfide, 119-119.5° (1).

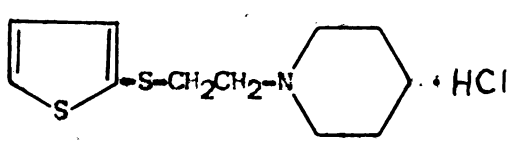
Preparation of 3-Methyl-2-thienyl Methyl Sulfide



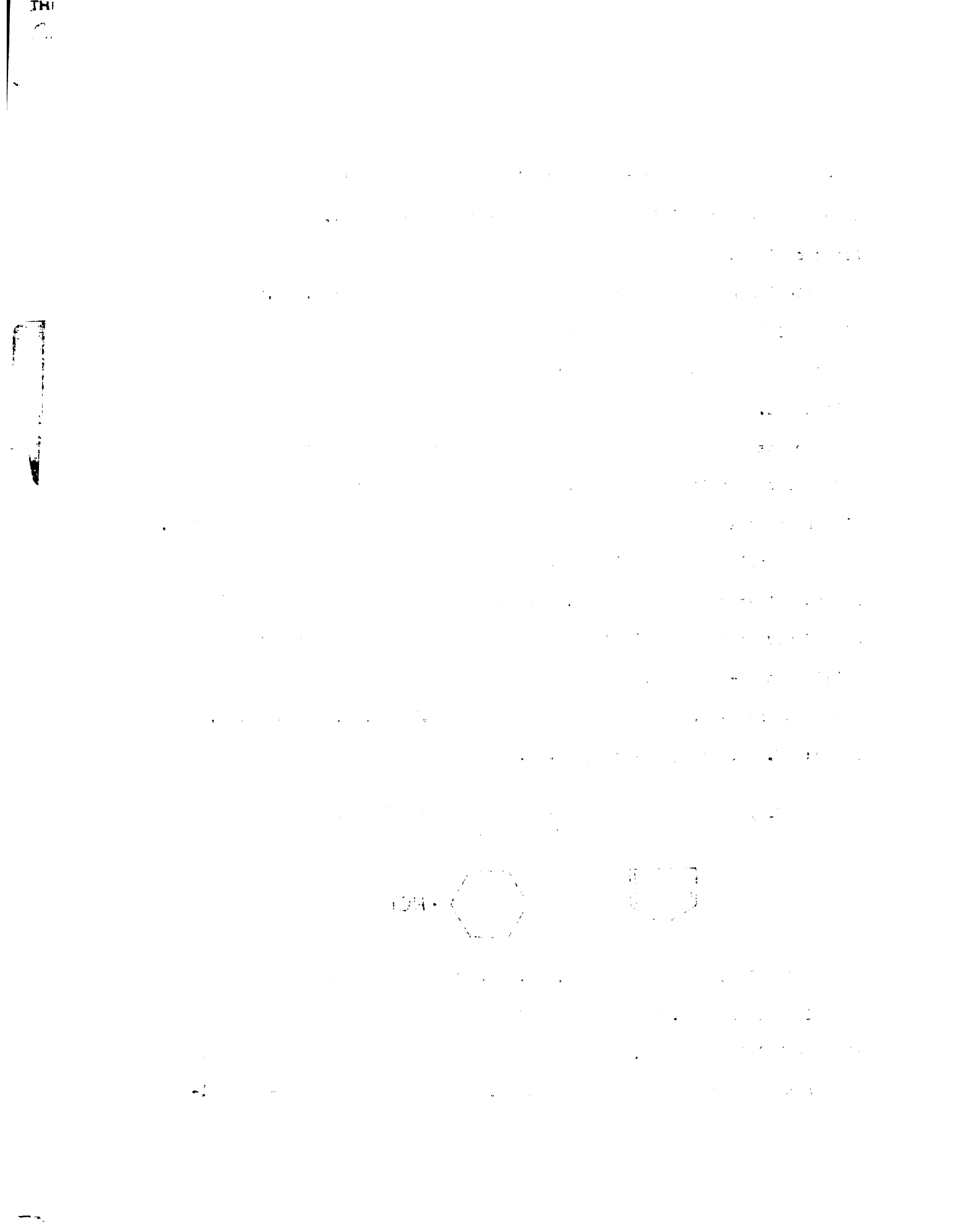
A solution containing 6.1 g. (0.11 mole) of potassium hydroxide dissolved in 285 ml. of methanol was prepared by warming the base and alcohol in a 500 ml. three neck flask while stirring the solution with a stream of nitrogen. A reflux condenser was attached to the flask and 15.9 g. (0.054 mole) of 3-methyl-2-thienyl-2,4-dinitrophenyl sulfide were added to the alkali methoxide solution. The reaction mixture was heated at its reflux temperature, under a nitrogen atmosphere, for twelve minutes. The major part of the solvent was removed by vacuum distillation on a water bath at a temperature of 30-35°. The residue was poured onto cracked ice and the flask was rinsed with sufficient water to bring the final volume of the mixture to approximately 300 ml. The aqueous suspension was stirred until thoroughly chilled and filtered

to remove an orange colored insoluble material. The latter was washed with water and the filtrate was transferred to a 500 ml. three neck flask equipped with a stirrer, reflux condenser, and a dropping funnel. The solution was warmed with an electric mantle and 6.1 g. (0.043 mole) of methyl iodide were added during a half hour. The reaction mixture was stirred at its reflux temperature for an additional three and a half hours. A red colored oil which separated on cooling the reaction mixture was extracted into ether and the aqueous layer was separated and extracted twice with ether. The combined ether extracts were washed with aqueous sodium hydroxide followed by three washings with cold water. The ether solution was dried in contact with anhydrous calcium chloride and the ether removed by distillation. The residual oil was fractionated at reduced pressure to isolate a 32% yield of a light yellow colored oil boiling at 67-68°/6 mm. Elemental analysis of the product gave the following results. Calc'd for $C_6H_8S_2$: C, 49.95; H, 5.59; S, 44.46. Found: C, 50.09; H, 5.78; S, 44.63.

Preparation of 2-Thienyl-2-piperidinoethyl Sulfide Hydrochloride



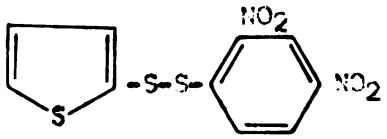
A solution composed of 5.6 g. (0.1 mole) of potassium hydroxide dissolved in 275 ml. of methanol was prepared by warming the base and the alcohol in a 500 ml. three neck flask while stirring the methanol with a stream of nitrogen. A 14 g. (0.05 mole) quantity of 2-thienyl-



2,4-dinitrophenyl sulfide was added to the alkali methoxide solution and the resulting mixture was heated, under nitrogen, at its reflux temperature for a ten minute period. The major part of the solvent was removed by vacuum distillation on a water bath at a temperature of 30-35°. The residue was poured onto ice and the flask was rinsed with sufficient water to bring the final volume of the mixture to approximately 300 ml. The aqueous suspension was stirred until thoroughly chilled and filtered to remove a quantity of orange colored solid. The filtrate was transferred to a 500 ml. three neck flask fitted with a stirrer, reflux condenser, and a dropping funnel. To the stirred, refluxing filtrate was added, during a half hour period, a solution of 5.5 g. (0.03 mole) of 2-piperidinoethyl chloride hydrochloride dissolved in 20 ml. of water. The reaction mixture was stirred at its reflux temperature for an additional two hours following the addition of the hydrochloride. A brown colored oil, which separated on cooling the reaction mixture, was extracted into ether and the aqueous layer was washed twice with ether. The combined ether extracts were washed once with aqueous sodium hydroxide and twice with cold water. After drying in contact with anhydrous magnesium sulfate the ether solution of the amine was cooled in ice water and treated with a gentle stream of hydrogen chloride gas. The precipitate was collected on a filter and the filtrate was again treated with hydrogen chloride to completely remove the amine. An excess of hydrogen chloride caused the product to become quite intractable. A 71% yield, 5.6 g. (0.021 mole), of a slightly red colored crude product was obtained. After recrystallization from isopropanol,

using charcoal, the white crystalline product melted at 150-150.5°. A melting point of 145-145.5° has been previously reported for this compound (7). Calc'd. for $C_{11}H_{18}NS_2Cl$: C, 50.07; H, 6.87; S, 24.30. Found: C, 49.98; H, 6.65; S, 24.12.

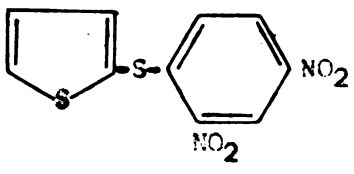
Preparation of 2-Thienyl (2,4-dinitrophenyl) Disulfide

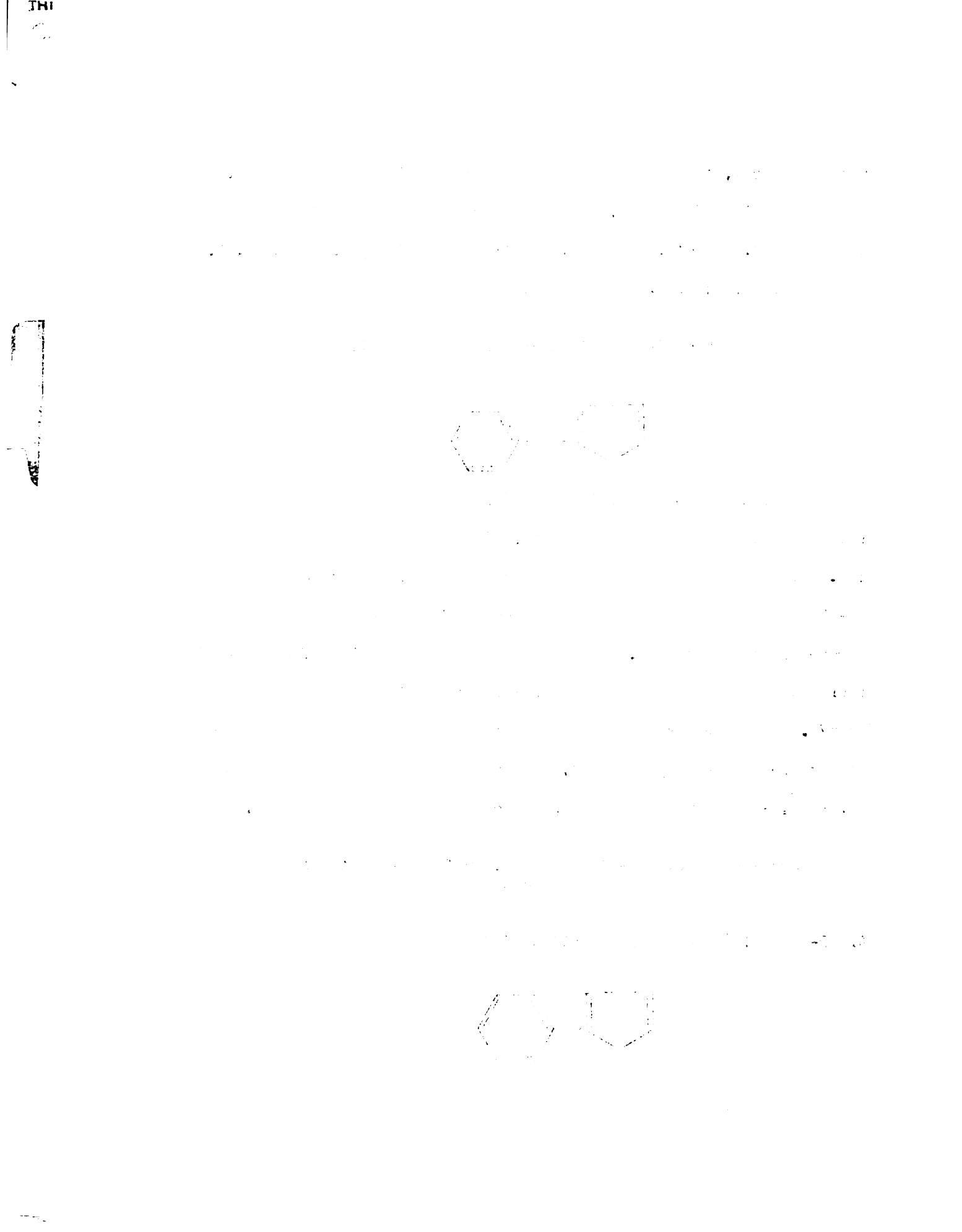


To a solution containing 1 g. (0.0043 mole) of 2,4-dinitrophenyl sulfenyl chloride dissolved in 10 ml. of carbon tetrachloride was added 1 g. (0.0086 mole) of authentic 2-thiophenethiol. The reaction mixture was heated on a steam bath for ten minutes and the solvent was then removed in an air stream. The residue was recrystallized from ethanol (Norite) twice to obtain a yellow colored crystalline disulfide melting at 57°. The above procedure was repeated using a sample of a research preparation of 2-thiophenethiol. The resulting derivative melted at 56.5-57°, and the mixed melting point of the two samples was 57°.

Preparation of 2,4-Dinitrophenyl Sulfide Derivatives of Thiols

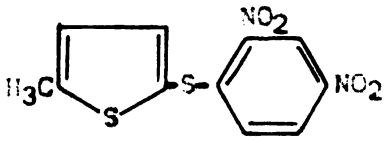
A. 2-thienyl (2,4-dinitrophenyl) sulfide





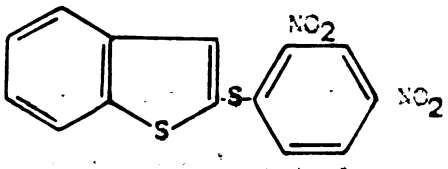
An ethanolic solution of the sodium salt of 2-thiophenethiol was prepared by treating 1.5 g. (0.013 mole) of the mercaptan, dissolved in 40 ml. of ethanol, with 0.52 g. (0.013 mole) of sodium hydroxide. The stirred solution was heated on a steam bath and a solution containing 2.63 g. (0.013 mole) of 2,4-dinitrochlorobenzene dissolved in 10 ml. of ethanol was added to it. The stirred reaction mixture was heated on a steam bath for an additional ten minutes, filtered hot, and set aside to cool at room temperature. The yellow crystalline sulfide which separated melted at 119° after a single recrystallization from ethanol. Literature value, m.p. 119° (1).

B. 5-methyl-2-thienyl (2,4-dinitrophenyl) sulfide

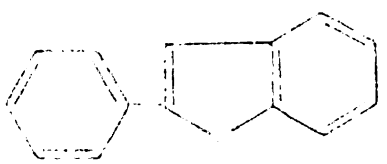


To a solution containing 0.9 g. (0.0069 mole) of 5-methyl-2-thiophenethiol dissolved in 20 ml. of methanol was added 1 ml. (20 drops) of 5N sodium hydroxide. The alkaline solution was stirred on a steam bath and a solution containing 1.2 g. (0.0059 mole) of 2,4-dinitrochlorobenzene dissolved in 15 ml. of methanol was added to it. The stirred reaction mixture was heated for an additional twenty minutes and set aside, at room temperature, overnight. The yellow crystalline sulfide which separated melted at 105° after being recrystallized twice from ethanol. Elemental analysis gave the following results. Calc'd. for $C_{11}H_8N_2O_4S_2$: C, 44.58; H, 2.72; N, 9.45; S, 21.64. Found: C, 44.60; H, 2.96; N, 9.57; S, 21.70.

C. 2-thianaphthyl (2,4-dinitrophenyl) sulfide



This derivative of 2-thianaphthenethiol was prepared employing the experimental procedure described above in the preparation of 2-thienyl (2,4-dinitrophenyl) sulfide. After recrystallization from a 1:1 methanol-dioxane mixture the yellow colored powdery sulfide melted at 159°. Literature value, m.p. 159-160° (3). Elemental analysis gave the following results. Calc'd. for $C_{14}H_8N_2O_4S_2$: C, 50.59; H, 2.43; S, 19.30. Found: C, 50.62; H, 2.51; S, 19.46.



SUMMARY

1. A two step synthesis involving the Friedel-Craft reaction of 2,4-dinitrophenylsulfenyl chloride with a heterocyclic nucleus followed by basic cleavage of the resulting sulfide was adapted to the synthesis of thiophene and thianaphthene thiols.

2. The previously unreported 5-methyl-2-thiophenethiol was prepared and characterized.

3. The previously unreported 3-methyl-2-thienyl methyl sulfide was prepared and characterized.

4. Two thiol derivatives, 5-methyl-2-thienyl-2,4-dinitrophenyl sulfide and 3-methyl-2-thienyl-2,4-dinitrophenyl sulfide, were prepared for the first time and characterized.

5. Five previously unreported mercury mercaptide and mercapto-mercuric chloride derivatives were prepared and characterized.

6. The mercaptan, 2-thianaphthenethiol, was prepared by a method not previously reported for the synthesis of this compound.

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