ice–acetone mixture. After removing the alcohol from the final filtrate the whole process was repeated several times. The collected higher melting fractions were recrystallized from toluene–petroleum ether and the collected lower melting fractions were recrystallized from alcohol.

Ortho isomer: m. p. 115–116°. *Anal.* Calcd. for $C_{13}H_{13}O_3N$: N, 6.06. Found: N, 6.02.

Para isomer: m. p. 89–90°. *Anal.* Calcd. for $C_{13}H_{13}O_3N$: N, 6.06. Found: N, 5.95.

The esters were hydrolyzed to the tolylacetic acids by refluxing with aqueous potassium hydroxide, and the acids were then converted to the amides. The ester (m. p. 115–116°) gave *o*-tolylacetamide (m. p. 161–163°) and the ester (m. p. 89–90°) gave *p*-tolylacetamide (m. p. 185°). One gram of the ortho amide was dissolved by refluxing with a solution of potassium hydroxide and then oxidized in the usual way with potassium permanganate. The acid after extraction with ether and crystallization from a minimum of hot water proved to be *o*-phthalic acid. This acid was also obtained directly from the higher melting ester by hydrolysis and oxidation; m. p. 208–210° (sealed tube). An authentic sample of *o*-phthalic acid melted at the same temperature under the same conditions.

o-Tolylhydroxymaleimide was prepared by passing a current of hydrogen chloride into a mixture of 23.1 g. of cyano-*o*-tolylpyruvic ester, 2.3 g. of water and 44 cc. of absolute alcohol for one hour at 70°. The yield of crude product (m. p. 183–187°) obtained by filtration and concentration of the mother liquor was 17.6 g. (87%). The recrystallized product melted at 186–187°.

Anal. Calcd. for $C_{11}H_9O_3N$: N, 6.89. Found: N, 6.98.

Bromination of 23.1 g. of ethyl cyano-*o*-tolylpyruvate according to the procedure employed for ethyl cyanophenylpyruvate gave 16.6 g. of yellow crystals, which precipitated from the chloroform, and 9.0 g. of very soluble material. The precipitate was dissolved in the minimum amount of cold alcohol, and the solution was diluted with an equal volume of water. Gradual concentration of the filtrate and recrystallization of the fractions yielded a total of 8.4 g. of the expected 4-bromo-*o*-tolylmaleimide, m. p. 237.5–238.5°.

Anal. Calcd. for $C_{11}H_8O_3NBr$: N, 4.97. Found: N, 4.93.

This imide (4.2 g.) was dissolved in 30 cc. of a 10% solution of potassium hydroxide and heated rapidly to boiling. Upon cooling, 1.5 g. of 4-bromo-*o*-tolylacetamide separated. The process of heating the filtrate was repeated twice in the same way to effect complete hydrolysis of the imide, total yield 3.2 g., m. p. 176–178°.

Anal. Calcd. for $C_9H_{10}ONBr$: N, 6.14. Found: N, 6.02.

The amide was very insoluble and was hydrolyzed by long refluxing with dilute potassium hydroxide to the acid which was oxidized by hot permanganate to 4-bromo-*o*-phthalic acid, m. p. 176–178°. This very soluble acid was isolated by extraction with ether and crystallization from water.

The remainder of the product of the reaction of bromine on cyano-*o*-tolylpyruvic ester is a mixture containing *o*-tolylmaleimide and unstable products. This material is being further investigated.

The reaction product from 23.1 g. of ethyl cyano-*p*-tolylpyruvate did not set to a solid mass and the bromine disappeared more slowly. The suspended needle-like yellow crystals were filtered and washed with cold chloroform; yield 16.5 g., m. p. 255–261°. One crystallization from absolute alcohol gave 10.4 g. of the unbrominated imide, m. p. 263–264°. This imide is much less soluble in alcohol than the imide from the ortho isomer.

Anal. Calcd. for $C_{11}H_9O_3N$: N, 6.90. Found: N, 6.87.

Summary

1. A method has been devised for the separation of a mixture of *o*- and *p*-tolylcyanopyruvates.

2. A comparison of the reactions of bromine with *o*-tolyl-, *p*-tolyl-, mesityl- and α-naphthylcyanopyruvates has been made.

NEWARK, DELAWARE RECEIVED JULY 6, 1948

[CONTRIBUTION FROM SOCONY-VACUUM LABORATORIES, A DIVISION OF SOCONY-VACUUM OIL CO., INC., RESEARCH AND DEVELOPMENT DEPARTMENT]

Aminomethylation of Thiophene. II. The Intermediate N-(2-Thenyl)-formaldimines and their Reactions

BY HOWARD D. HARTOUGH, SEYMOUR L. MEISEL, EMIL KOFT AND JOHN W. SCHICK

In the original article of this series[1] it was reported that 2-thenylamine, I, and di-(2-thenyl)-amine, II, were the primary reaction products of thiophene, formaldehyde and ammonium chloride.

Further investigation has led to the isolation of new intermediates, the N-(2-thenyl)-formaldiamines, which can be formed as the primary reaction products to the exclusion of I and II. The formation of these products is consistent with the previously reported basic molar ratios[1] of this reaction.

It has also been noted that the mixing of neutral solutions of formaldehyde and ammonium chloride immediately produced solutions of *p*H of about 1. The high acidity of ammonium chloride-formaldehyde solutions has been previously noted by Werner[2] who postulated the existence of formaldimine, $CH_2{=}NH$, from this observation.

These observations, in conjunction with the isolation of N-(2-thenyl)-formaldimine (2-methyleneiminomethylthiophene), III, from the reaction of formaldehyde, ammonium chloride and thiophene, now make possible a fairly accurate summation of the over-all reaction.

Equation (1) represents an equilibrium reaction and the hypothetical $CH_2{=}NH$ reacts rapidly with thiophene (2) at 65° to form IV. This in turn is quantitatively converted to V, the hydrochloride salt of III, as is represented in equation (2a). This latter step (3) has been carried out in 95% yields from authentic I to substantiate this theory. Equation (4) indicates the course of reaction, as previously reported, for the production of I and II by refluxing the reaction mixture at

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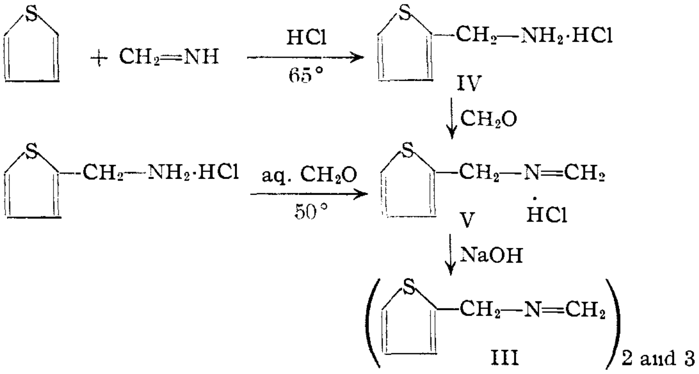
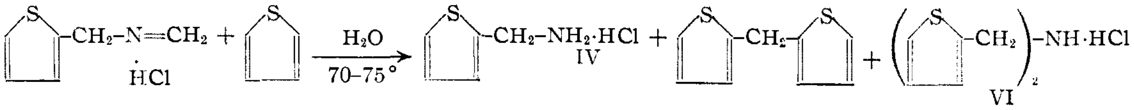
[1] Hartough, Lukasiewicz and Murray, THIS JOURNAL, **70**, 1146 (1948).

[2] Werner, *J. Chem. Soc.*, **111**, 844 (1917).

$$CH_2O + NH_4Cl \rightleftharpoons CH_2{=}NH + HCl + H_2O \quad (1)$$



(2) (2a) (3) (3a)



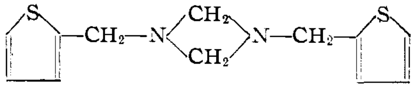
(4)

70–75° for a period of time. The mechanism of the formation of side products, the dithienylmethanes, is also clarified.

Caustic neutralization of the aqueous reaction mixtures followed by distillation gives a III whose molecular weight corresponds to a dimer. Redistillation of this material to remove any last traces of I gives a crystalline trimer of III. Presumably this compound contains a triazine ring.[3] While the monomer of this material has not been isolated as the free base some of the reactions to be reported in subsequent papers can be accounted for only if a monomer is present. In further reference to these compounds the monomer will be IIIA, the dimer, IIIB and the trimer, IIIC.

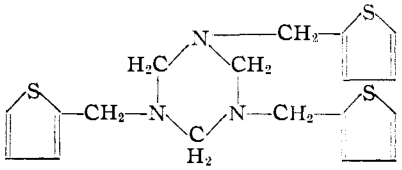
The unique properties of IIIB require some discussion. When III is obtained through equations (2) and (2a) or (3), only IIIB is obtained by caustic neutralization. In order to distill IIIB, which distills at a temperature consistent with a dimer, the material must be heated to 170–180° before any distillation takes place at pressures as low as 0.5 mm. The product boils at about 100° at this pressure. Even at 2 to 5 mm. the same still temperature is necessary. Superheating must be avoided as much as possible since further polymerization takes place at 200–225°. The distillate has no constant boiling point from a Claisen flask and apparently the product is not consistent in structure since products of consistent analysis vary in refractive index, $n^{20}D$ from 1.59 to 1.62. Molecular weight determinations indicate a dimer. Redistillation of this material, in which the same superheating is necessary, and removal of a foreshot fraction that contains a trace of I, gives a crystalline form, IIIC. One redistillation of IIIB gave a product that polymerized after a few minutes to a clear glass-like product with evolution of considerable heat. Fortunately this polymerization was observed on a refractometer and the refractive index, $n^{20}D$, was followed during the polymerization from greater than 1.61 down to approximately 1.58. This glass-like resin was stored in a half empty clear glass bottle and after a few weeks the material had depolymerized to a fluid.

Several attempts were made to obtain IIIC from IIIB by seeding a saturated alcohol solution of IIIB with IIIC but no growth of IIIC crystals could be obtained. This still does not refute an argument that IIIB is a mixture of IIIA and IIIC, but molecular weight determinations by freezing and boiling point methods over a period of several months are consistent with the dimer. These considerations and a study of the reactions of IIIB under hydrolytic conditions whereupon 2-thiophenealdehyde and N-methyl-2-thenylamine are produced (to be described in detail in a later paper) lead us to predict the following structures for IIIB[4] and IIIC.[3]



IIIB

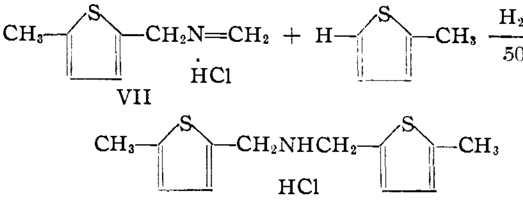
bis-N,N′-(2-Thenyl)-1,3-diazocyclobutane



IIIC

tris-N,N′,N″-(2-Thenyl)-hexahydro-1,3,5-triazine

The aminoalkylation reaction with 2-methylthiophene was reinvestigated and the N-(5-methyl-2-thenyl)-formaldimine, VII, was isolated in 30–60% yields along with 40–60% yield of di-(5-methyl-2-thenyl)-amine hydrochloride, VIII. VII obtained in this manner is trimeric and is probably tris-N,N′,N″-(5-methyl-2-thenyl)-hexa-



(5)

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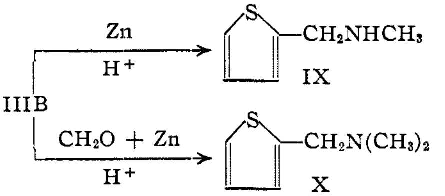
[3] Morton, "The Chemistry of Heterocyclic Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1946, p. 513.

[4] Hale and Lange, This Journal, **41**, 376, 380 (1919), list the basic ring as uretidine. Existence of this ring system in derivatives of urea appears to be established.

hydro-1,3,5-triazine. VII has not been observed in the dimeric form. To account for the high yield of VIII at temperatures as low as 35°, VII and 2-methylthiophene were found to give a good yield of VIII.

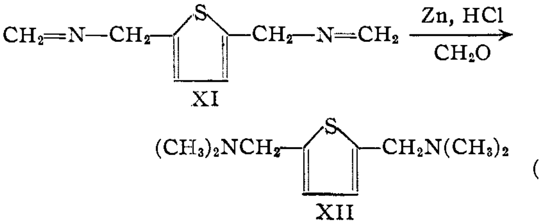
Further it was anticipated from this reaction that materials with active hydrogens in acidic media would condense with III. This was investigated to a minor extent and it was found that aniline and urea produced resins containing the thiophene radical.

IIIB can be reduced with zinc and hydrochloric acid to give the N-methyl-2-thenylamine, IX, or in the presence of formaldehyde to N,N-dimethyl-2-thenylamine, X.



(6)

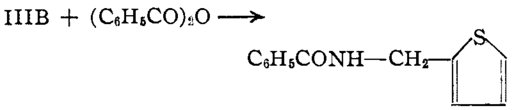
While the 2,5-bis-(methyleneiminomethyl)-thiophene, XI, has not been isolated from the aminoalkylation of thiophene its presence was detected by reduction of a reaction mixture containing excess formaldehyde wherein the corresponding 2,5-bis-(dimethylaminomethyl)-thiophene, XII, was formed.



(7)

Equation (4) demonstrates the tendency of the methylene radical to be removed from III. The following equations demonstrate the ease with which this reaction proceeds.

$$\text{IIIB} + H_2N\text{—}NHCONH_2 \longrightarrow CH_2\text{=}N\text{—}NHCONH_2 \qquad (8)$$



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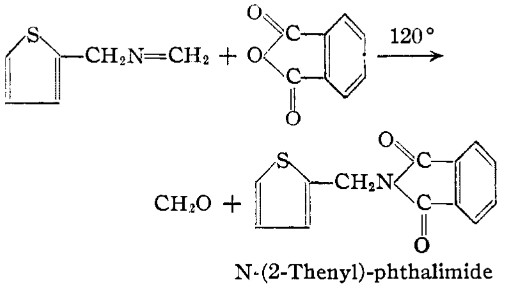

(10)

N-(2-Thenyl)-phthalimide

It would appear that the mechanisms of equations (9) and (10) differ somewhat. Otherwise, in (9) the dibenzamide would have formed. The other reaction products in (9) were not identified but they might have elucidated this reaction. Equation (10) proceeds with VII as well as IIIB but the yields are somewhat lower with the former.

During the course of many experiments it has been noted that solutions of ammonium chloride and formaldehyde, when warmed above 80°, fail to undergo the aminoalkylation reaction with thiophene. This further substantiates the theory of Werner[2] that CH_2=NH is an intermediate that reacts with more formaldehyde to form methylamines in the reaction between ammonium chloride and formaldehyde at higher temperatures.

The secondary reaction to form N-methylamines begins to occur only above about 80° since no N-methyl-2-thenylamines have ever been isolated at the operating temperature of 60–75°.

Experimental

Preparation of IIIB and IIIC.—A well-stirred mixture of 420 g. (5 moles) of thiophene, 540 g. (10 moles) of ammonium chloride and 1700 g. (20 moles) of 36% formaldehyde was warmed to 60° and the source of heat removed. The temperature was controlled at 64–67° by means of an ice-bath. After the temperature fell to 60° (thirty to sixty minutes) and all the thiophene had reacted, the reaction mixture was cooled to room temperature and ten moles of 20% sodium hydroxide added. The insoluble organic layer was taken up in benzene, filtered, and distilled to remove the benzene. About 350 g. (56%) of N-2-thenylformaldimine was obtained, b. p. 115–125 (3 mm.). The refractive index of several cuts varied from 1.603 to 1.589.

Molecular weight determinations were made by freezing point and boiling point methods of several samples of N-2-thenylformaldimine obtained from different runs and all indicated that the material was dimeric.

Anal. Calcd. for $(C_6H_7NS)_2$: S, 25.60; N, 11.20; mol. wt., 250. Found: S, 24.85; N, 10.97; mol. wt., 276, 262, 245.

A sample of N-2-thenylformaldimine was redistilled twice and allowed to stand. On standing it became hard and appeared to be glassy. It was crystallized from absolute alcohol and a white crystalline material was obtained (yield, 70%). After the third recrystallization from alcohol, the product melted at 55.5–56°. Analysis definitely indicated this material to be the N-(2-thenyl)-formaldimine trimer, presumably the tris-N,N′,N″(2-thenyl)-hexahydro-1,3,5-triazine.

Anal. Calcd. for $(C_6H_7NS)_3$: C, 57.60; H, 5.60; N, 11.20; S, 25.60; mol. wt., 375. Found: C, 57.65; H, 5.87; N, 10.98; S, 25.63; mol. wt. (f. p.), 381; mol. wt. (b. p.), 368.

Preparation of the N-(5-Methyl-2-thenyl)-formaldimine Trimer, VII.—Two moles each of 2-methylthiophene, 36% formaldehyde, and ammonium chloride were vigorously stirred. The temperature fell to about 15° and then began to rise slowly to 35°. The reaction temperature was controlled at 35–36° by means of an ice-bath until the temperature failed to rise above 36°. The mixture was stirred until the temperature fell to 30°, cooled to 15°, and filtered to remove the di-(5-methyl-2-thenyl)-amine hydrochloride, VIII (110 g. 40%), and after recrystallizing from water it melted at 218–219°.[5] Before recrystallization from water the crystals were washed with benzene and 11 g. of material was thus extracted therefrom. This extract contains di-(5-methyl-2-thienyl)-methane[1] and a few grams of an alcohol, presumably 5-methyl-2-thenyl alcohol, which has not been fully characterized. Neutrali-

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[5] Ref. 1 lists m. p. 218–219°.

zation of the filtrate gave an oily layer that was dissolved in ether, dried over sodium sulfate, and filtered. About 90% of the ether was distilled off. Enough alcohol was added to produce a mixture that would not separate an oil in an ice-bath. The trimer of N-(5-methyl-2-thenyl)-formaldimine (42 g.) crystallized slowly over a period of several hours. After filtering, the alcohol and ether were evaporated, the residue taken up in alcohol and stored in a refrigerator for several days whereupon further crystallization took place. Repeated treatment of the residue yielded 44 g. more of product (total yield, 86 g.). Recrystallization from absolute alcohol gave a pure white trimer of N-(5-methyl-2-thenyl)-formaldimine, presumably tris-N,N',N" (5-methyl-2-thenyl)-hexahydro-1,3,-5-triazine, m. p. 87–88°.

Anal. Calcd. for $C_{21}H_{27}S_3N_3$: C, 60.44; H, 6.47; N, 10.07; S, 23.02; mol. wt., 417. Found: C, 61.02; H, 6.32; N, 10.07; S, 22.73; mol. wt. (f. p.), 401.

By an alternate procedure, the product can be obtained by distillation, b. p. 128–133° at 4 mm. The product becomes quite warm after distillation, thickens on cooling and slowly solidifies. The yield is lower by this method since the product thermally polymerizes during the distillation and only about 50% is distillable.

Preparation of IIIB from 2-Thenylamine.—To a solution of 0.1 mole of 2-thenylamine hydrochloride, IV, in 20 ml. of water was added 0.15 mole of 36% formaldehyde. The mixture was stirred at 25° for two hours and then at 40° for thirty minutes. The product was obtained by neutralization and distilled to produce the IIIB in 95% yield.

Reaction of IIIB with Thiophene.—To 100 g. of IIIB in 200 g. of acetic acid were added 100 g. of thiophene and 70 g. of concd. hydrochloric acid. The mixture was heated for one hour at 75–78°, cooled, neutralized with 30% sodium hydroxide, extracted three times with benzene and the benzene was removed by distillation. Vacuum distillation yielded 42 g. of 2-thenylamine,[6] I, b. p. 61° (4 mm.), $n^{20}\text{D}$ 1.5618; 13 g. of a fraction, b. p. 92–138°, that contained about 50% of di-(2-thenyl)-amine, XIV, and 50% di-(2-thienyl)-methane, XV, 25 g. of XIV, b. p. 138–142 (2 mm.), $n^{20}\text{D}$ 1.6050[6]; 10 g. of a fraction, b. p. 148–158° (2 mm.), $n^{20}\text{D}$ 1.6238, that contained some XIV and an unidentified product that hydrolyzed to 2-thiophenealdehyde in cold concentrated hydrochloric acid (further discussion of the conversion of these materials to aldehydes will follow in a subsequent paper); and 36 g. of a residue that appeared to be a thiophene–formaldehyde polymer similar to that described by Caesar and Sachenen.[7]

Without acetic acid as solvent, the only products isolated were I and XIV.

Reaction of VII with 2-Methylthiopene.—Seven grams of VII was dissolved in 5 ml. of concd. hydrochloric acid in 15 ml. of water and stirred vigorously at 70–75° for fifteen minutes with 5 g. of 2-methylthiophene. After cooling, the crystalline di-(5-methyl-2-thenyl)-amine hydrochloride, VIII, (6 g.), separated and after crystallizing from water melted at 218–219°. A mixed melting point with an authentic sample[1] showed no depression.

Reaction of III with Urea.—To 75 g. of an aqueous reaction mixture prepared from one mole each of thiophene and ammonium chloride and two moles of formaldehyde (the unreacted thiophene was recovered) was added 10 g. of urea. The clear solution was warmed thirty minutes on a steam-bath and the insoluble crystalline material was filtered off. The product, insoluble in water, alcohol, benzene and chloroform, was digested with hot alcohol, filtered, and dried, m. p. 242° (uncor., block method). An analysis of this semi-pure product gave S, 9.28; N, 33.35; Cl, 3.7. These analyses indicate a compound containing eight nitrogen atoms to one sulfur. The chlorine content of the product probably indicates impurity since the product could not be recrystallized.

Reaction of III with Aniline.—To 75 g. of the aqueous solution of III as the hydrochloride, described directly above, was added 10 g. of aniline. A precipitate formed immediately and a vigorous heat of reaction was noted. The light red, resinous precipitate could not be dissolved in common solvents and was digested first with 10% caustic and then with water. After drying, analyses indicated 6.4% sulfur and 5.2% nitrogen or a nitrogen-sulfur ratio of 2:1. This indicates a combination of III and aniline in equimolar proportions.

Reaction of III B with Semicarbazide.—IIIB (5 g.) was dissolved in 100 ml. of hot absolute alcohol and 5 g. of semicarbazide hydrochloride was added. A yellow color immediately developed. Addition of water to dissolve the semicarbazide hydrochloride at this point did not cause separation of III (III is immediately separated by addition of 5 g. of water before the reaction). The reaction mixture was neutralized with 7.5 g. of sodium acetate, 150 ml. of water was added, and the mixture was concentrated on a steam-bath to 50 ml. Cooling gave 1.0 g. of the semicarbazone of formaldehyde; m. p. and mixed m. p., 210–211°.

Preparation of N-(2-Thenyl)-benzamide.—To 0.03 mole of IIIB was added 0.03 mole of benzoic anhydride. The mixture was warmed fifteen minutes on a steam-bath and then dissolved in alcohol. Careful dilution of the cold alcohol solution with water gave a white crystalline product. Recrystallization from 75% alcohol gave 1.5 g. of N-(2-thenyl)-benzamide, m. p. 123–124°. A mixed melting point with an authentic sample[1] showed no depression.

Preparation of N-(2-Thenyl)-phthalimide.—Phthalic anhydride (15 g.) and 10 g. of IIIB were refluxed in toluene for two hours. Paraformaldehyde formed in the reflux condenser and this was scraped out and identified as the 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 166–167°. After removal of the toluene the mixture was distilled *in vacuo* and 2 g. of III was recovered. The brown residue crystallized and after recrystallization from alcohol 20 g. (83%) of crude product was obtained. After three recrystallizations from alcohol, the pure white product melted at 125–127°. A mixed m. p. with an authentic sample[1] showed no depression.

It should be noted that in this case the "dimeric III" has reacted almost totally as a monomer.

Preparation of N-(5-Methyl-2-thenyl)-phthalimide.—In an effort to prepare a phthalimide derivative of the formaldimines in a rapid manner with little regard to the yield, the following method was developed. Three grams each of the trimeric VII and phthalic anhydride were placed in a test-tube and fused while stirring with a glass rod in an oil-bath (130–140°) until the melt darkened to a red color. The mixture was cooled and dissolved in absolute alcohol. Careful dilution with water while cooling gave the crystalline N-(5-methyl-2-thenyl)-phthalimide, which melted after two recrystallizations from alcohol at 123–124°.

Anal. Calcd. for $C_{14}H_{11}NO_2S$: N, 5.45. Found: N, 5.32.

Reduction of III B with Zinc and Hydrochloric Acid.—To a well-stirred mixture of 50 g. (0.4 mole) of IIIB, 200 ml. of water and 40 g. of zinc dust warmed to 45° was added 110 ml. of concd. hydrochloric acid diluted with 150 ml. of water over a period of one hundred minutes. The reaction was then warmed to the reflux temperature for seven hours or until all the zinc had reacted. Neutralization with 40% sodium hydroxide was followed by suction filtration of the zinc hydroxide. A filter-aid (Hi-flo) was necessary to speed the filtration. The filter cake was thoroughly washed with benzene and the filtrate further extracted with benzene. Removal of the benzene by distillation gave 14 g. (28%) of N-methyl-2-thenylamine, IX, b. p. 67° (11 mm.), $n^{20}\text{D}$ 1.5371, and 7 g. of unreacted IIIB.

The product was contaminated with some I which is very difficult to remove because of the proximity of boiling points. A phenylthiourea (XVI) of this mixture melted, after two recrystallizations from dilute alcohol, at 113.5–114.5°. A supposed sample of authentic IX prepared from I and methyl iodide, gave a phenylthiourea of the

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(6) Ref. 1 lists b. p. 82° (17 mm.), $n^{20}\text{D}$ 1.5615 for I and b. p. 134–135 (3 mm.), $n^{20}\text{D}$ 1.6032 for XIV.

(7) Caesar and Sachenen, *Ind. Eng. Chem.*, **40**, 922 (1948).

same m. p. and mixed m. p. However, an authentic sample prepared by the method of Blicke and Burckhalter[8] gave the N'-phenyl-N-methyl-N-2-thenylthiourea, XVII, m. p. 127–128°.

Anal. Calcd. for $C_{13}H_{14}N_2S_2$: N, 10.68; S, 24.40. Found: N, 10.52; S, 24.26.

A mixture of XVI with XVII melted at 114–115°. A mixed melting point of XVI with an authentic sample of N-phenyl-N'-2-thenylthiourea, XVIII, m. p. 123.5–124°,[1] melted at 113–114°. A mixed m. p. of XVIII with XVII melted at 112–114°. This latter melting point was not nearly as sharp as that obtained when a phenylthiourea was made of the mixture. Until these tests were made it was thought that the phenylthiourea of the mixture was a pure compound.

Reduction of III with Zinc and Hydrochloric Acid in the Presence of Formaldehyde.—(A) The prior example was repeated in the presence of 33 g. of 36% formaldehyde with double the amount of zinc dust and acid. Only 6 g. of N,N-dimethyl-2-thenylamine, X, was obtained, b. p. 60–61° (10 mm.), $n^{20}D$ 1.5188. The methiodide melted at 152.5–153° after two recrystallizations from absolute alcohol.

Anal. Calcd. for $C_8H_{14}NSI$: N, 4.95; S, 11.32. Found N, 4.95; S, 11.12.

A mixed melting point with a methiodide of a sample prepared by treating I with methyl iodide in a two-step process gave no depression.

(B) Two moles each of thiophene and ammonium chloride were reacted at 65° with four moles of formaldehyde. Stirring was continued until the temperature fell to 47° and addition of 200 g. of zinc dust was begun (seventy-five minutes required). The temperature was maintained at 40–45° by means of an ice-bath. To this mixture was slowly added (ninety minutes) 255 ml. of concd. hydrochloric acid in 300 ml. of water. Fifteen hours of stirring at 55–60° was required to completely dissolve the zinc dust. The mixture was processed in the usual manner and 47 g. of X and 15 g. of XII, b. p. 134–138 (10 mm.), $n^{20}D$ 1.5453, was obtained. The latter product was identified as the di-methiodide. After two recrystallizations from absolute alcohol it melted (block method) at 248–250° (dec.).

Anal. Calcd. for $C_{12}H_{24}N_2SI_2$: C, 29.93; H, 5.02; N, 5.81; S, 6.65. Found: C, 29.87; H, 5.59; N, 5.84; S, 6.89.

Aminoalkylation of IIIB.—To 35 g. of the IIIB were added 45 g. of 36% formaldehyde and 15 g. of ammonium chloride. The mixture was stirred for one hour at 70°, cooled to room temperature, and extracted with ether. Evaporation of the ether yielded 8 g. (26%) of 2-thiophenealdehyde which was identified as the semicarbazone, m. p. and mixed m. p. 223–224°.

Neutralization of the aqueous layer with 20% sodium hydroxide gave 31 g. of a light yellow oil. Analysis of this product showed 13.6% N and 21.2% S. This indicates a mixture of III and bis-2,5-(methyleneiminomethyl)-thiophene, XI, in about equal portions. Oxidation of this sample with alkaline permanganate gave a mixture[9] of 2-thiophenecarboxylic acid, XIX, m. p. 128–129°, and 2,5-thiophenedicarboxylic acid, XX, m. p. 358.5–359.5°. Each was identified by a mixed melting point with an authentic sample.[10]

Preparation of N-(5-Chloro-2-thenyl)-formaldimine, XXI.— Relatively impure XXI can be prepared from a mixture of one mole of 2-chlorothiophene, four moles of paraformaldehyde, and two moles of ammonium chloride in 100 ml. of acetic acid stirred at 70° for two hours. All of the 2-chlorothiophene reacts and the di-(5-chloro-2-thenyl)-amine hydrochloride, 43 g., m. p. 240–242° (dec.)[11] is removed by filtration and the water soluble products processed in the normal manner. Distillation yields an impure product boiling in the range of 123–135° (2 mm.), $n^{20}D$ 1.596, along with considerable decomposition products.

It was suitable to use the filtered reaction mixture containing XXI for further reactions some of which will be presented in the next paper of this series.

Preparation of N-(*t*-Butyl-2-thenyl)-formaldimine, XXII.—In a similar manner to XXI above, XXII was prepared from *t*-butylthiophene[12] by a modification of an aminoalkylation reaction previously described[1] using 100 ml. of acetic acid per mole of 2-*t*-butylthiophene and treating the materials at 70–75° for one hour. The organic layer contains the formaldimines and can be used directly in subsequent reactions.

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Summary

Further study of the aminoalkylation of thiophene with formaldehyde and ammonium chloride has led to the isolation of the intermediates, the N-(2-thenyl)-formaldimines. Their isolation and the study of some of their unique reactions has made possible a fairly accurate prediction of the mechanism of the reaction.

The physical properties of the N-(2-thenyl)-formaldimines indicate that they exist in the dimeric and trimeric forms as the free bases.

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[8] Blicke and Burckhalter, THIS JOURNAL, **64**, 478 (1942).

[9] These acids are conveniently separated by digestion in boiling benzene, XIX being completely soluble and XX very insoluble.

[10] See Hartough and Conley, THIS JOURNAL, **69**, 3096 (1947), for authentic sample of XIX, and Hartough, *ibid.*, **69**, 1355 (1947), for XX.

[11] Ref. 1 lists m. p. of 240–242° (dec.).

[12] Sample contains about equimolar quantities of the 2-*t*-butyl- and 3-*t*-butylthiophene.