SYNTHESIS AND SOME TRANSFORMATIONS OF THIOPHENE SERIES SULFIDES

XIII. Structure of the Compound of Formula $C_{10}H_7NS_4$ Obtained from Sodium 2-Diethoxymethyl-3-Thienylmercaptide*

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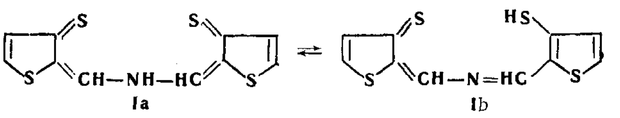
The compound of formula $C_{10}H_7N8_4$, formed by the reaction of sodium-2-diethoxymethyl-3-thienylmercaptide with ammonia followed by acidification to pH 8 [1], is evidently bis(3-thiono-2-thienylidene)-dimethylamine (Ia). The action of primary amines on the thienylidenamine Ia gives N-substituted 3-mercapto-2-thienylidenimines (XIIa–c). With nickel acetate the azomethine XIIa forms an intramolecular complex (XIII).

The preceding paper [1] described a compound of the formula $C_{10}H_7NS_4$ melting point 179° (I), formed by adding acid in the presence of ammonia to an aqueous solution of the product of reaction of 3-ethylmercapto-2-thiophenaldehyde acetal with sodium in liquid ammonia.



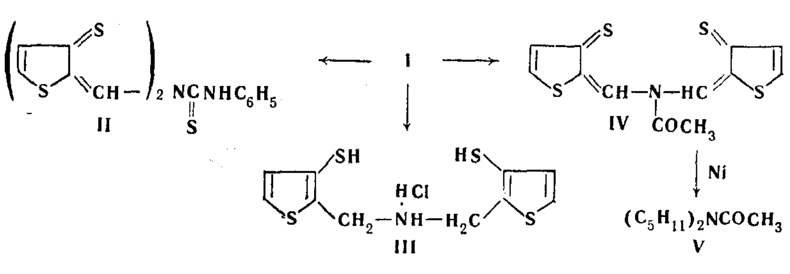
Ia Ib

The structure of this compound can best be represented by the symmetric formula Ia, though this does not exclude the possibility of the tautomeric equilibrium Ia ⇄ Ib in solution. The experimental results serving as a basis for this conclusion are given below.

The molecule of compound I contains one active hydrogen atom. Its IR absorption spectrum has bands in the 1135–1157 cm^{-1} region characteristic of the group—C=C—C= S [2], and a band in the 3300 cm^{-1} region, assignable to valence vibrations of the secondary amino group, but there is no band corresponding to > C=N group. (Fig. 1). The UV spectra of I in dioxane and in dioxane containing hydrochloric acid are alike, further the character of the spectrum changes somewhat if alkali is added to the dioxane solution (Fig. 2).

The PMR spectrum observed in dimethysulfoxide with a JNM-C60 instrument (operating frequency 60 megacycles), corresponds more to a structure bis (3-thiono-2-thienylidene) dimethylamine* (Ia) than to Ib, though tautomeric equilibrium between the two forms is not excluded. The spectrum consists of a group of lines forming a quartet of the AB type in weak fields, and having δ_A 7.15 ppm (also shifts measured from the TMS line), δ_B 6.4 ppm, and $J_{AB} \simeq \simeq 4.5$-5 cycles, belonging to four protons of the dihydrothiophene ring, a line δ 5.9 ppm having an integral intensity of the order of half the intensity of the AB spectrum and due to two =CH protons (these protons being chemically equivalent). Finally the line δ 3.7 ppm belongs to one proton, and shows the broadening of a proton directly linked to nitrogen (Fig. 3).

Compound I adds one molecule of phenylisothiocyanate, and the IR spectrum of II, the addition product, also lacks a band characteristc of the $\rangle$C=N group, confirming that the molecule contains the NH group and not a SH one. Lithium aluminum hydride reduction of compound I gives the mercaptoamine III, as its hydrochloride, so that this is formed by addition of four hydrogen atoms to the Ia molecule. Results obtained when acylating I also agree with formula Ia. The monoacetyl derivative IV obtained actually has its acetyl group linked directly to nitrogen, since reductive desulfurization of the acetylation product with Raney nickel gives N, N-diamylacetamide (V).



An interesting transformation of I occurs when it is treated with methyl iodide in methanolic potassium

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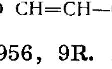
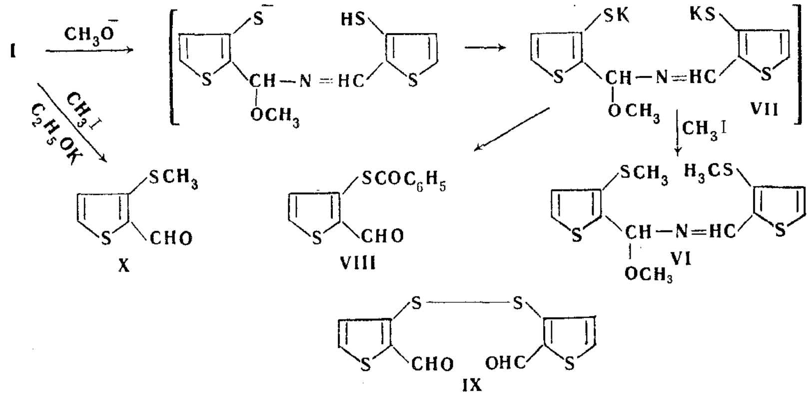
*For Part XII see [1].

*We used the name thienylidene by analogy with the name furylidene for the group  $\overbrace{\mathrm{CH{=}CH{-}\underset{\|}{C}{-}CH_2}}^{O}$ used in C. A. Subject Indexes 1947–1956, 9R. In what follows I will be called thienylidenamine for short.

hydroxide and it is one which confirms that the I molecule contains an α,β-unsaturated thioketo group, able to react in the tautomeric form Ib. The elementary analytical data and the molecular weight show that the compound can be assigned the structure (3-methylmercapto-2-thenylidene) [(α-methoxy)-3-methylmercapto-2-thienyl]-amine (VI). This conclusion is confirmed by estimation of methoxyl groups and the compound's IR spectrum, which has an intense absorption band of the C=N bond in the 1670 cm^{-1} region. Formation of compound VI can be explained by 1,4 addition of methanol to the C=C—C=S part of the molecule, such as obtains when nucleophilic reagents (alcohols, amines, Grignard compounds, etc) act on α,β unsaturated carbonyl componds or quinonemethides [3]. In the present case, as with quinonemethides, an added driving force is the aromatization of the initial system.



An attempt by us to isolate the intermediate bismercaptan VII as its dibenzoyl derivative, did not give the desired results, because there was hydrolytic scission leading to formation of the benzomercaptoaldehyde VIII, identical with that previously [1] prepared. The molecule I is hydrolyzed under the conditions used when oxidizing it with iodine in acetic acid, and bis(2-formyl-3-thienyl) disulfide IX is formed.

The addition reaction of I involving methanol and methyl iodide in alkaline solution is selective. If the methanol is replaced by ethanol, there is no formation of a derivative analogous to VI. Instead, under the [5] 3-methylmercapto-2-thiophene carboxylic acid.

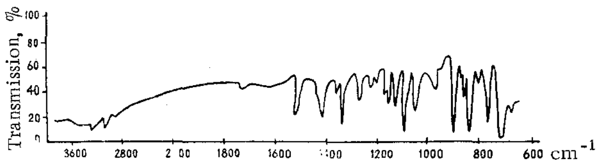
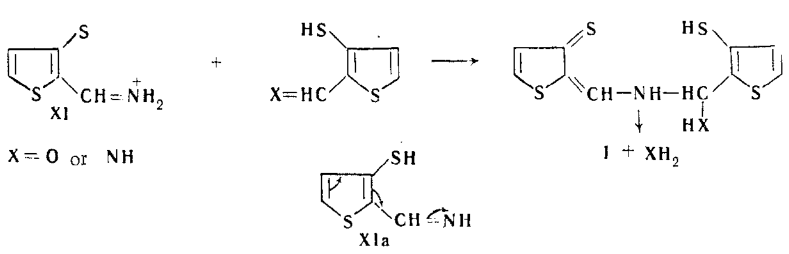


Fig. 1. IR spectrum of bis(3-thiono-2-thienylidene) dimethylamine I. Tabletted with KBr.

In considering the question of the reaction paths involved in formation of compound I, it is necessary to take into consideration the formation of 2-mercapto—conditions used, the molecule is observed to split, to give 3-methylmercapto-2-thiophenaldehyde (X), whose structure was confirmed by oxidizing it to the known 5-alkyl-2-thenylidenimine [6] from 2-alkylmercapto-5-alkyl-3-thiophenaldehyde acetal under comparable conditions. If it is assumed that the analogous structure XI also arises as an intermediate product when sodium in liquid ammonia acts on 3-ethylmercapto-2-thiophenaldehyde, one can imagine that the compound described is formed by reaction of the molecule XI with a like molecule, or with a molecule of the corresponding aldehyde:



Possibly the reason why reaction does not stop at the stage of mercaptoaldimine XI formation is due to a stronger base being involved here, due to possible propagation of a conjugation effect along the entire system of the bonds of the thiophene ring XIa.

One of the characteristic properties of compound I is its ability to add to amines to give azomethines,

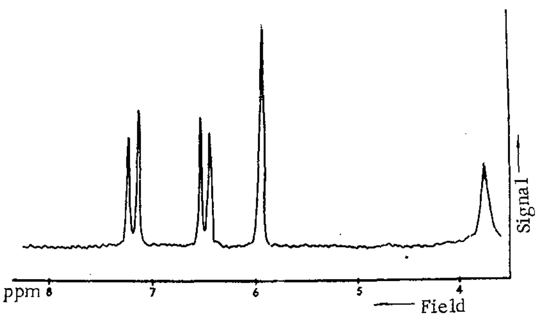
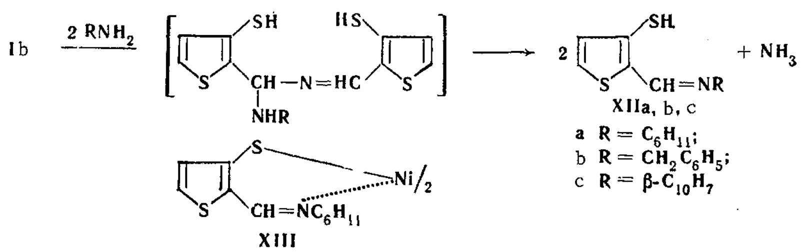


Fig. 3. PMR spectrum of bis (3-thiono-2-thienylidene) dimethylamine I in dimethysulfoxide.

one molecule of I giving two molecules of the new base. This reaction can be variously interpreted. For example it can be considered as an ammonolysis of Schiff's base Ib, proceeding through a stage of addition at a C=N bond [6], or through 1, 4 addition, by analogy with methanol:



These azomethines XII, differing from those previously described [5] by reversal of the positions of the —SH and —CH=NR groups with respect to one another, also give internal complexes with ions of metal. For example with nickel acetate the azomethine XIIa gives the chelate XIII, where the metal: ligand ratio is 1:2. Its IR spectrum has an intense absorption band in the 1580–1590 cm^{-1} region (in starting axomethine at 1630–1640 cm^{-1}), assignable to valence vibrations of the coordinated C=N group [7].

The authors thank V. F. Bystrova for determining the PMR spectrum.

EXPERIMENTAL

N, N-bis(3-thiono-2-thienylidene)-N'-phenylthiourea (II). 0.15 g thienylidinamine I, 0.2 ml phenylisothiocyanate, and 5 ml EtOH were refluxed together for a few minutes on a water-bath. On cooling white crystals of N, N-bis(3-thiono-2-thienylidene)-N'-phenylthiourea (0.2 g, yield 89%) separated, mp 145°–146° C (ex EtOH). Found: C 50.41; 50.57; H 3.12; 3.16%. Calculated for $C_{17}H_{12}N_2S_5$: C 50.45; H 2.99%. The IR spectrum of the compound did not have a band characteristic of the C=N bond.

Reduction of bis(3-thiono-2-thienylidene)dimethylamine (I). 0.5 g (0.0019 mole) thienylidenamine I was gradually added to a suspension of 0.3 g (0.0077 mole) $LiAlH_4$ in 25 ml dry ether. The mixture was stirred for 1 hr at room temperature, then for 30 min while refluxing, the products were cooled and treated with 5 ml water and 10 ml HCl (1:1). The precipitate was filtered off, and twice reprecipitated from EtOH with dry ether. Yield 0.25 g (43.5%) di(3-mercapto-2-thenyl) amine hydrochloride III, mp 129°–131° C. Found: C 38.99; 38.97; H 3.81; 3.77; N 4.54; 4.43%. Calculated for $C_{10}H_{12}ClNS_4$: C 38.75; H 3.90; N 4.52%.

N-acetylbis(3-thiono-2-thienylidene)dimethylamine (IV). 5 g thienylidenimine I was refluxed for 1 hr with 30 ml freshly distilled Ac_2O, the excess of the latter vacuum-distilled off, the residue washed with ether dissolved in EtOAc, and well boiled with decolorizing charcoal. After filtering the solution was evaporated under vacuum, to give 3.7 g (64% yield) of the acetyl derivative of IV, mp 190°–191.2° C (ex EtOAc). Found: C 46.37; 46.48; H 2.94; 2.86. Calculated for $C_{12}H_9NOS_4$: C 46.28; H 2.91%.

Reductive desulfurization of N-acetylbis(3-thiono-2-thienylidene) dimethylamine (IV). 3.0 g acetyl derivative IV in 150 ml dry benzene was stirred with about 30 g Raney nickel for 10 hr at 60° C, until a negative test for sulfur was obtained. The precipitate was filtered off, washed with benzene and ethanol, and the solvents distilled off; the residue was treated with dry ether, and the ether solution dried over $MgSO_4$. 1.4 g pale yellow oil (n_D^{20} 1.4555) was obtained. Two vacuum-distillations gave N, N-diamylacetamide (V) bp 170°–172° C (30 mm), n_D^{20} 1.4555. Found: C 72.03; 71.81; H 12.10; 12.18; N 7.00; 6.83%. Calculated for $C_{12}H_{25}NO$: C 72.30; H 12.64; N 7.03%.

Action of methyl iodide plus methanolic alkali on thienylidenamine I. A solution of 1.5 g thienylidenamine in 30 ml 10% methanolic KOH was mixed with 1.8 g MeI, and the mixture refluxed for 5 hr. The solvent was vacuum-distilled off, and water added to the residue. The precipitate was filtered off, washed with water, and dried. Yield 1.0 g (54.5%) (3-methylmercapto-2-thenylidene)[(α-methoxy)-3-methylmercapto-2-thenyl]-amine (VI) as a brown powder, mp about 50° C. After two recrystallizations from ethanol, using decolorizing charcoal, the amine had mp 55°–56.5° C. Found: C 47.03; 47.22; H 4.39; 4.49; N 4.21; 4.08; S 39.08; 38.91; OCH_3 10.13; 10.23%; M 314.3*. Calculated for $C_{13}H_{15}NOS_4$: C 47.38; H 4.59; N 4.25; S 39.08; OCH_3 9.45%.

Action of methyl iodide and ethanolic alkali on thienylidenamine I. 2.0 g thienylidenamine was dissolved in 30 ml 10% ethanolic KOH, the solution filtered, and refluxed for 5 hr with 2.3 g MeI. The products were evaporated to dryness, and water added to the residue. The oil which separated was extracted with ether, the ether solution washed with water, and dried over $MgSO_4$. The residue (after distilling off the ether) was 1.5 g mobile red oil, which crystallized on cooling. The crystals were filtered off, and washed with cold ethanol, to give 1.0 g 3-methylmercapto-2-thiophenaldehyde (X), mp 32°–33.5° C (ex 50–70% EtOH using decolorizing charcoal). Found: C 45.73; 45.74; H 3.97; 3.95; S 40.37; 40.30%. Calculated for $C_6H_6OS_2$: C 45.53; H 3.82; S 40.52%.

3-Methylmercapto-2-thiophene carboxylic acid. 0.5 g 3-methylmercapto-2-thiophenaldehyde was oxidized with silver oxide to 3-methylmercapto-2-thiopene carboxylic acid, which after being precipitated from 10% Na_2CO_3 solution by means of HCl, and then recrystallized from 50% EtOH, had mp 197° C (the literature gives [4] mp 201°–202° C). Found: C 41.24; 41.52; H 3.45; 3.47; S 36.64; 36.78%. Calculated for $C_6H_6O_2S_2$: C 41.35; H 3.45; S 36.81%.

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*Determined ebullioscopically in dioxane.

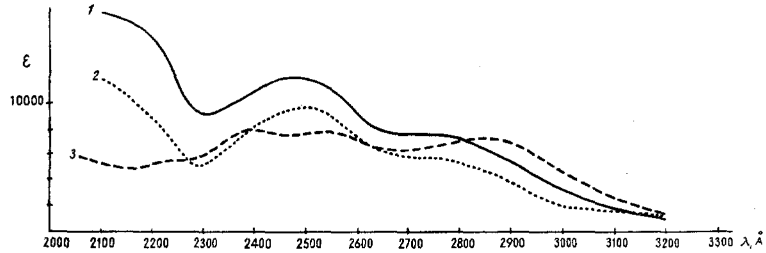

Fig. 2. UV spectra in dioxane. 1) Bis (3-thiono-2-thienylidene)dimethylamine (I); 2) thienylidenamine I in the presence of hydrochlorid acid; 3) thienylidenamine in the presence of sodium hydroxide.

Action of benzoyl chloride and methanolic alkali on thienylidenamine I. A solution of 0.5 g thienylideneamine in 5 ml 10% methanolic KOH was refluxed for 5 hr and the MeOH then vacuum-distilled off. When water was added the solid dissolved completely. 1.2 ml benzoyl chloride was gradually added to the aqueous solution, and the precipitate formed washed with water, then with EtOH, dried, and twice recrystallized from EtOH, using decolorizing charcoal. Yield 0.2 g (46%) 3-benzoyl-mercapto-2-thiophenaldehyde (VIII), mp 90°–90.5° C. Mixed mp with the 3-benzoylmercapto-2-thiophenaldehyde previously prepared [1], undepressed. Found: C 57.74; 57.85; H 3.21; 3.17; S 25.63; 25.52%; M 245.8*. Calculated for $C_{12}H_8O_2S_2$: C 58.03; H 3.25; S 25.82%; M 248.3.

Oxidation of bis-(3-thiono-2-thienylidene)dimethylamine (I). A solution of 0.15 g iodine in AcOH was dropped into a solution of 0.3 g thienyliden-amine in AcOH, the precipitate filtered off, and the filtrate poured into water. The yellow crystals of bis(2-formyl-3-thienyl)disulfide (X) were filtered off, and recrystallized from EtOH, mp 137°–138° C. Found: C 42.49; 42.22; H 2.23; 2.16; S 44.46; 44.35%. Calculated for $C_{10}H_6O_2S_4$: C 41.93; H 2.11; S 44.78%.

Azomethines from bis(3-thiono-2-thienylidene)dimethylamine (I). a) A solution of 0.3 g thienylidenamine and 0.2 g cyclohexylamine in 5 ml EtOH was heated for 10 min, when ammonia was evolved. On cooling 0.35 g of a yellow precipitate separated; it had mp about 110° C, yield 70%. After two recrystallizations from EtOH, (3-mercapto-2-thenylidene)cyclohexylamine (XIIa) had mp 114°–115°. The IR spectrum had a band at 1630–1640 cm^{-1} (C=N). Found: C 58.55; 58.77; H 6.76; 6.84; N 6.23; 6.29; S 28.14; 28.40%. Calculated for $C_{11}H_{15}NS_2$: C 58.62; H 6.84; N 6.21; S 28.46%.

b) 0.2 g thienylidenamine and 0.2 ml benzylamine in 3 ml EtOH gave, in the way described above, 0.2 g (85% yield) (3-mercapto-2-thenylidene)-benzylamine (XIIb), which after recrystallizing from EtOH and EtOAc had mp 107°–108° C. Found: C 61.75; 61.55; H 4.73; 4.57; S 27.21; 27.44%. Calculated for $C_{12}H_{11}NS_2$: C 61.76; H 4.75; S 27.52%.

c) A solution of 0.3 g β-naphthylamine in EtOH was added to a solution of 0.3 g thienylideneamine in $CHCl_3$, and the mixture refluxed for 10 min. The precipitate (0.15 g) proved to be the starting thienylidenamine. Evaporation of the filtrate gave 0.3 g red substance mp ~ 80° C, which after recrystallization from EtOH and benzene had mp 144°–145° C. Undepressed mixed mp with authentic (3-mercapto-2-thenylidene)-β-naphthylamine [1].

Ni chelate of 3-mercapto-2-thenylidenecyclohexylamine (XIII). This was prepared from 0.5 g Schiff's base XIIa and 0.2 g Ni acetate in methanol, yield 89%. Two precipitations from $CHCl_3$ with MeOH gave violet crystals, mp 204°–205° C. Found: C 52.04; 52.09; H 5.82; 5.73; Ni 11.98; 12.15%. Calculated for $C_{22}H_{28}N_2NiS_4$: C 52.07; H 5.56; Ni 11.57%.

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*Determined ebullioscopically in dioxane.