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# Chemistry

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**Abstract**

**Full Text**

**Chemistry**

**T. I. Santalova, P. A. Konstantinov, and Ya. L. Gol' dfarb**

## **REDUCTIVE DESULFURIZATION OF SOME DIAMINES OF THE THIOPHENE SERIES**

*(Presented by Academician A. A. Balandin, December 18, 1959)*

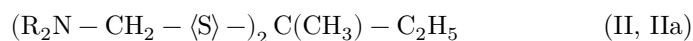
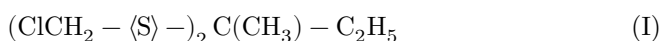
Earlier, one of us and M. B. Ibragimova showed that aliphatic amines <sup>(1)</sup> and amino alcohols <sup>(2)</sup> with a comparatively long chain of carbon atoms can be obtained from tertiary amines and amino alcohols of the thiophene series by the action of Raney nickel. It was of interest to extend the method of reductive desulfurization to ditertiary amines of the thiophene series, in order to arrive at higher alkylendiamines that could be used for the synthesis of the corresponding bis-ammonium salts with potential curare-like action. In a certain sense, a new type of such compounds, in comparison with decamethonium and similar salts <sup>(3)</sup>, would be the dihaloalkylates of diamines IV, IVa, distinguished by the presence of branching at the center of the chain. As far as we know, bis-ammonium salts of this type have not been described and, it seems to us, no accessible routes exist for their synthesis from derivatives of the aliphatic series. Meanwhile, the presence of branching has a definite effect on the activity of some compounds with curare-like action <sup>(4)</sup>.

The starting compound for obtaining the mentioned bases was 2,2-bis(2-thienyl)butane, which is readily formed in the interaction of thiophene with methyl ethyl ketone <sup>(5)</sup>. Chloromethylation of it gave the bischloromethyl derivative (I), which was usually used in "crude" form, since in vacuum it distills with considerable decomposition. Judging, however, from the fact that on interaction with amines the products are formed in a yield of about 60%, it may be assumed that the chloromethylation process proceeds quite satisfactorily. By the action of hexamethylenetetramine on compound I, the corresponding salt was obtained and, from it by the usual route, diamine II. Compound I reacts under rather mild conditions with diethylamine, piperidine, and morpholine, forming diamines IIa, III, IIIa, which with methyl iodide give diiodomethylates.

In view of the fact that hydrogenolysis of dialkylaminothiophenes had been achieved by the action of Raney nickel <sup>(1)</sup>, it seemed probable that this method would make it possible to arrive at the desired higher diamines. Under these conditions, however, mixtures were obtained that distilled over a wide range. This is possibly associated with the ability of skeletal nickel to cleave the C—N bond. We therefore decided to use skeletal cobalt, which for obtaining amines

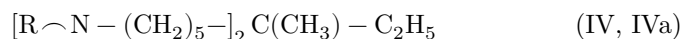
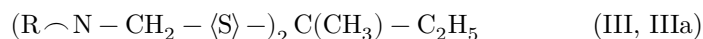
might prove more suitable than skeletal nickel, although in activity it is inferior to the latter <sup>(6,7)</sup>. Indeed, amines III and IIIa, when heated in methanol with a large excess of Co, slowly lose sulfur; after completion of the desulfurization process, diamines IV and IVa can be isolated by the usual route. The yield of the latter in the experiments described below did not exceed 30%, but we have reason to believe that by some change in the experimental conditions it can be increased. From the mentioned

diamines, diiodomethylates IV and IVa were obtained. The investigation is continuing.



II  $R = \text{H}$

IIa  $R = \text{C}_2\text{H}_5$



III, IV  $R = -(\text{CH}_2)_5 -$

IIIa, IVa  $R = -(\text{CH}_2)_2\text{O}(\text{CH}_2)_2 -$

## Experimental Part

**2,2-Bis(5-chloromethyl-2-thienyl)butane (I).** A mixture of 33.3 g of freshly distilled 2,2-bis(2-thienyl)butane, 50 ml of glacial acetic acid, and 35 g of chloromethyl ether was left for 16 h at 20°, and then heated for 2 h with stirring on a water bath at 40°. After cooling, it was washed twice with ice water, dissolved in 150 ml of benzene, washed with sodium bicarbonate solution and with water, and dried over calcium chloride. After removal of the solvent, compound I could be isolated by distillation in a yield not exceeding 27%, b.p. 183–185°/1 mm.

$\text{C}_{14}\text{H}_{16}\text{Cl}_2\text{S}_2$	Found, %:	C 52.73; 52.91;	H 4.97; 5.20
	Calculated, %:	C 52.66;	H 5.04

**2,2-Bis(5-aminomethyl-2-thienyl)butane (II).** The salt of I with hexamethylenetetramine, obtained from 12 g of distilled compound I and 10.3 g of urotropine in 100 ml of chloroform (2 days' standing at 20°), was heated for 3

h on a water bath with 30 g of conc. hydrochloric acid in 200 ml of ethanol. The crystalline hydrochloride II that separated on evaporation of the solvent was treated with 40% NaOH solution until alkaline. The mixture was extracted with ether and benzene, and the extracts were dried with potassium carbonate. After removal of the solvents from the extracts, about 8 g of compound II was obtained, b.p. 200–215°/1 mm and 210–225°/3–4 mm. On redistillation, 5.1 g (49%) of compound II was obtained, b.p. 210–215°/1 mm.

$C_{14}H_{20}N_2S_2$	Found, %:	C 60.30; 60.43;	H 7.38; 7.32;	N 9.93
	Calculated, %:	C 59.95;	H 7.19;	N 9.99

**2,2-Bis(5-diethylaminomethyl-2-thienyl)butane (IIa).** To a benzene solution of compound I, prepared from 33.3 g of 2,2-(2-thienyl)butane, 51 g of diethylamine was added; after standing for 16 h at 20° the mixture was heated for 2 h at 60°. The precipitated crystals of diethylamine hydrochloride were filtered off and washed with benzene. The benzene solution of the amine was dried over BaO. After removal of benzene and excess diethylamine, the residue was distilled in vacuo (2 mm): fraction 1 up to 198°, a few drops; fraction 2, 198–201°, 37 g. Repeated fractionation of fraction 2 gave 34.8 g of product, b.p. 194–195°/2 mm; yield 60%, based on the initial 2,2-bis(2-thienyl)butane;  $n_D^{20}$  1.5400;  $d_4^{20}$  1.0241;  $MR_D$  found 120.28; calculated 119.93.

$C_{22}H_{36}N_2S_2$	Found, %:	C 67.21; 67.34;	H 9.43; 9.39;	S 16.24; 16.24
	Calculated, %:	C 67.29;	H 9.24;	S 16.33

The dihydrochloride IIa, purified by precipitation with absolute ether from a methanol-acetone solution, melts at 155–156° (in a sealed capillary).

$C_{22}H_{38}N_2S_2Cl_2$	Found, %:	N 6.06; 6.07
	Calculated, %:	N 6.02

**2,2-Bis(5-piperidinomethyl-2-thienyl)butane (III).** To a benzene solution of I, prepared from 22.2 g of 2,2-bis(2-thienyl)butane and 27 g of chloroform ether, 34.0 g of piperidine was added; the mixture was left for 16 h. Then the contents of the flask were boiled for 2 h with a reflux condenser. Further treatment was as in the preceding experiment. On distillation of the product in vacuo (2 mm), fractions were obtained: fraction 1 up to 235°, 1.1 g; fraction 2, 235–237°, 27.3 g. Redistillation of fraction 2 at 2 mm gave 26.1 g of a colorless viscous product with b.p. 245–246°; yield 63%, calculated on the initial 2,2-bis(2-thienyl)butane;  $n_D^{20}$  1.5653;  $d_4^{20}$  1.0864;  $MR_D$  found 124.98; calculated 124.76.

$C_{24}H_{36}N_2S_2$ . Found %: C 69.19; 69.42; H 8.84; 8.92; S 15.43; 15.32  
 Calculated %: C 69.18; H 8.71; S 15.39

The **diiodomethylate**\* of III, purified by twice reprecipitating with abs. ether from a methanolic solution, melts at 192.5–193.5°.

$C_{26}H_{42}I_2N_2S_2$ . Found %: C 44.45; 44.43; H 5.94; 5.93; I 35.22; 35.53  
 Calculated %: C 44.57; H 6.07; I 36.23

The **picrate** of III\*\*, recrystallized from an acetone–heptane mixture (1:1), melts at 185–186°.

$C_{36}H_{42}N_8O_{14}S_2$ . Found %: C 49.66; 49.60; H 5.00; 4.95; S 7.10; 7.28  
 Calculated %: C 49.41; H 4.83; S 7.31

**2,2-Bis(5-morpholinomethyl-2-thienyl)butane (IIIa)** was obtained from 35 g of morpholine and a benzene solution of I, prepared from 22.2 g of 2,2-bis(2-thienyl)butane. After removal of the solvent the diamine was fractionated in vacuo (2 mm): fraction 1 up to 245°, 0.93 g; fraction 2, 245–246°, 28.9 g. On redistillation of fraction 2, 26.2 g (62%) of a viscous liquid with b.p. 243–244°/2 mm was obtained. On storage the product crystallizes, m.p. 60–63°. After recrystallization from heptane, m.p. 65–66°.

$C_{22}H_{32}N_2O_2S_2$ . Found %: C 62.68; 62.76; H 7.74; 7.91; S 15.20; 15.38  
 Calculated %: C 62.82; H 7.67; S 15.24

The **diiodomethylate** of IIIa, after two recrystallizations from methanol, melts at 195–197° (with decomp., in a sealed capillary).

$C_{24}H_{38}I_2N_2O_2S_2$ . Found %: C 40.79; 40.64; H 5.59; 5.43; I 35.39; 35.41  
 Calculated %: C 40.91; H 5.44; I 36.02

The **picrate** of IIIa, twice recrystallized from an alcohol–acetone mixture, melts at 198–199°.

$C_{34}H_{38}N_8O_{16}S_2$ . Found %: N 13.05; 13.22  
 Calculated %: N 12.82

**N-Oxide of 2,2-bis(5-morpholinomethyl-2-thienyl)butane.** A mixture of 1.34 g of IIIa and 20 ml of 25% H<sub>2</sub>O<sub>2</sub> solution was stirred for 28 h at 20°; water and excess hydrogen peroxide were distilled off on a water bath\*\*\* at 14 mm. The residue in the flask was dissolved in 50 ml of abs. alcohol, 0.5 g of manganese dioxide was added, and the mixture was boiled for 0.5 h with a reflux condenser. The MnO<sub>2</sub> was filtered off, 100 ml of benzene was added to the filtrate, and the solvents were distilled off. The solid remaining at the bottom of the flask

\* All iodomethylates were obtained by the action of an excess of methyl iodide on an ethereal solution of the base, except for the iodomethylate of IIIa, which was obtained by boiling an excess of methyl iodide and the diamine in acetone.

\*\* Picrates were obtained by mixing hot alcoholic solutions of picric acid and the corresponding diamine.

\*\*\* The temperature of the bath must not exceed 50°.

(a product that spreads out in air), after three recrystallizations from a mixture of absolute alcohol and benzene, melts at 152-153°.

$C_{22}H_{22}N_2O_4S_2$	Found, %:	N 6.00; 6.00
	Calculated, %:	N 6.19

**1,11-Dipiperidino-6-methyl-6-ethylundecane (IV).** A mixture of 12 g of compound III, 700 ml of methanol, and 180 g of skeletal cobalt\* was stirred for 5 h at 20°, and then refluxed for 40 h (until a negative test for sulfur was obtained). The cobalt was filtered off and washed with hot ethanol. After distillation of the alcohol, the residue was extracted with ether and dried over BaO. The ether was distilled off, and the residue was distilled in vacuo (4 mm): fraction 1, 152-201°, 2.6 g; fraction 2, 201-204°, 3.8 g. Redistillation of fraction 2 gave 3.6 g of a colorless viscous liquid with b.p. 199-202°/4 mm; yield 34%;  $n_D^{20}$  1.4836;  $d_4^{20}$  0.8991;  $MR_D$  found 115.94; calculated 116.51.

$C_{24}H_{48}N_2$	Found, %:	N 7.67; 7.77
	Calculated, %:	N 7.61

Mol. wt. found 369, calculated 364.6.

Diiodomethylate IV, m.p. 179.5-180.5° (from acetone).

$C_{26}H_{54}J_2N_2$	Found, %:	C 47.91; 47.74; H 8.14; 8.29; J 38.49; 38.43
	Calculated, %:	C 48.15; H 8.39; J 39.14

Picrate IV, m.p. 121.5-122.5° (from alcohol).

$C_{36}H_{54}N_8O_{14}$  Found, %: N 13.90; 13.93  
 Calculated, %: N 13.67

**1,11-Dimorpholino-6-methyl-6-ethylundecane (IVa)** was obtained analogously to compound IV from 12 g of compound IIIa in 600 ml of methanol by the action of 255 g of skeletal cobalt. The hydrogenolysis product was fractionated in vacuo (5 mm): fraction 1 up to 223°, 2.3 g; fraction 2, 223-226°, 3.6 g. Redistillation of fraction 2 gave 3.3 g of product with b.p. 202-206°/4 mm; yield 31%;  $n_D^{20}$  1.4830;  $d_4^{20}$  0.9487;  $MR_D$  found 110.56; calculated 110.97.

$C_{22}H_{44}N_2O_2$  Found, %: C 71.31; 71.60; H 11.99; 11.92  
 Calculated, %: C 71.74; H 12.03

Diiodomethylate IVa, recrystallized twice from acetone, has m.p. 193.5-196.5° (with decomp., in a sealed capillary).

$C_{24}H_{50}J_2N_2O_2$  Found, %: C 44.18; 43.85; H 7.67; 7.61; J 38.44; 38.34  
 Calculated, %: C 44.16; H 7.73; J 38.90

Picrate IVa, m.p. 135.5-136.5° (from methanol).

$C_{34}H_{50}N_8O_{16}$  Found, %: N 12.92; 13.14  
 Calculated, %: N 13.55

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\* Skeletal cobalt was prepared from a 50% alloy of cobalt with aluminum by the method proposed by Adkins and Billica (8) for preparing Raney nickel.

*Note: Figure translations are in progress. See original paper for figures.*

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