# FUNCTIONAL THIOPHENE DERIVATIVES

## IX.* THIOCYANATION OF 2-ACYLAMINOTHIOPHENES AND SYNTHESIS OF THIENO[2,3-d]THIAZOLES

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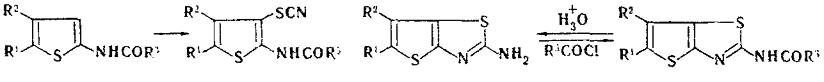
The thiocyanation of 5-acylaminothiophenes gives 4-thiocyanato derivatives, the intramolecular cyclization of which gives 2-acylaminothieno[2,3-d]thiazoles.

$\alpha$-Acylaminothiophene derivatives readily undergo electrophilic substitution [1, 2]. We have found that the thiocyanation of 5-acylamino-2,3-dialkylthiophenes (Ia-d) proceeds under mild conditions by the action of thiocyanate salts and bromine [3] to give $\alpha$-acylamino-$\beta$-thiocyanatothiophenes (IIa-d) in 80-90% yields. The structures of IIa-d were confirmed by spectral data: the IR spectra of these compounds contain an absorption band at 2160 $cm^{-1}$ that characterizes the stretching vibrations of the SCN group, and the 4H signal, which was observed in the PMR spectra of the starting Ia-d, is absent in the PMR spectra of the products; this indicates that the thiocyanato group enters the 4-position. Thiocyanatothiophenes IIa-d contain two functional groups – an acylamino group and a thiocyanato group – in the ortho position relative to one another, and this makes it possible to use them for the synthesis of thiene[2,3-d]thiazole derivatives. Thiocyanatothiophenes IIa-d undergo intramolecular cyclization when they are heated in ethyl benzoate solution; 2-acylaminothieno[2,3-d)thiazoles (IIIa-d) were obtained in 66-84% yields [4]. One might also have expected the formation of 2-imino-3-acylthieno[2,3-d]thiazoline derivatives as a result of cyclization of IIa-d. However, two absorption bands at 1535-1580 and 1650-1685 $cm^{-1}$, which are characteristic for thiazoles, are observed in the IR spectra of the compounds obtained; this confirms the formation of IIIa-d [5, 6]. Hydrolysis of 2-acetamidothieno[2,3-d]thiazoles (IIIa, c) gave aminothienothiazoles IV and V in 64-77% yields; the IR spectra of IV and V contain two absorption bands at 1520 and 1625 $cm^{-1}$. It is known that the acylation of 2-aminobenzothiazole derivatives proceeds at the exocyclic nitrogen atom [7], and this made it possible to expect that the acylation of V would lead to 2-acylaminothieno[2,3-d]thiazole derivatives. In fact, compounds that were identical with respect to spectral data, melting points, and thin-layer-chromatography (TLC) data to IIIc, d, which were obtained by intramolecular cyclization, were isolated in the acylation of amines V with acetic anhydride and benzoyl chloride.



I a-d    II a-d    IV, V    III a-d

I–III a $R^1=R^2=R^3=CH_3$; b $R^1=R^2=CH_3$, $R^3=C_6H_5$; c $R^1+R^2=(CH_2)_4$, $R^3=CH_3$; d $R^1+R^2=(CH_2)_4$, $R^3=C_6H_5$; IV $R^1=R^2=CH_3$; V $R^1+R^2=(CH_2)_4$

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* See [1] for communication VIII.

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TABLE 1. Characteristics of the Compounds Obtained

| Compound | mp, °C* | Empirical formula | Found, % |  |  |  | Calc., % |  |  |  | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  | C | H | N | S | C | H | N | S |  |
| IIa | 181,5—182,5 | $C_9H_{10}N_2OS_2$ | 47,9 | 4,5 | 12,6 | 28,5 | 47,8 | 4,4 | 12,4 | 28,3 | 81,3 |
| IIb | 163.5—164,5 | $C_{14}H_{12}N_2OS_2$ | 58,3 | 4,4 | 9,6 | 22,3 | 58,3 | 4,2 | 9,7 | 22,2 | 90 |
| IIc | 163—163,5 | $C_{11}H_{12}N_2OS_2$ | 52,6 | 4,8 | 11,1 | 25,5 | 52,4 | 4,8 | 11,1 | 25,4 | 85,5 |
| IId | 180.5—181,5 | $C_{16}H_{14}N_2OS_2$ | 61,3 | 4,8 | 8,8 | 20,5 | 61,1 | 4,5 | 8,9 | 20,4 | 88,5 |
| IIIa | 281,5—282,5 | $C_9H_{10}N_2OS_2$ | 47,8 | 4,4 | — | 28,5 | 47,8 | 4,4 | — | 28,3 | 67,3 |
| IIIb | 239,5—240 | $C_{14}H_{12}N_2OS_2$ | 58,2 | 4,2 | 9,7 | 22,2 | 58,3 | 4,2 | 9,7 | 22,2 | 66,4 |
| IIIc | 271,5—273 | $C_{11}H_{13}N_2OS_2$† | 52,5 | 4,8 | 11,2 | 25,7 | 52,4 | 4,8 | 11,1 | 25,4 | 84 |
| IIId | 185—186 | $C_{16}H_{14}N_2OS_2$‡ | 61,2 | 4,4 | 8,8 | 20,4 | 61,1 | 4,5 | 8,9 | 20,4 | 60 |
| IV | 187—188 | $C_7H_8N_2S_2$ | 45,7 | 4,4 | 15,2 | 34,7 | 45,6 | 4,4 | 15,2 | 34,8 | 64,5 |
| V | 169—170 | $C_9H_{10}N_2S_2$ | 51,6 | 4,7 | 13,3 | — | 51,4 | 4,8 | 13,3 | — | 77 |

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*Compounds IIa, IIc, IIId, and V were recrystallized from methanol, IIb was recrystallized from methanol–acetone (1 : 2), IId was recrystallized from methanol–acetone (1 : 1), IIIa was recrystallized from dioxane, IIIb was recrystallized from dioxane–methanol (3 : 1), IIIc was recrystallized from acetone, and IV was recrystallized from 75% aqueous methanol.

†$R_f$ 0.69 on a Silufol plate with elution with benzene–methanol (1 : 1) and development with a 10% alcohol solution of phosphomolybdic acid.

‡$R_f$ 0.76 on a Silufol plate with elution by benzene–methanol (10 : 1) and development with a 10% alcohol solution of phosphomolybdic acid.

## EXPERIMENTAL

The IR spectra of the compounds were recorded with a UR-10 spectrometer. The PMR spectra were recorded with a JEOL-4H-100 spectrometer with hexamethyldisiloxane (HMDS) as the internal standard.

5-Acetamido-4-thiocyanato-2,3-dialkylthiophenes (IIa-d). A 0.12-mole sample of ammonium thiocyanate was added to a solution of 0.04 mole of thiophenes Ia-d in 500 ml of methanol, and the mixture was then cooled to 3-5°, after which a solution of 0.044 mole of bromine in 30 ml of methanol saturated with potassium bromide was added dropwise with stirring. The mixture was held at this temperature for 30 min, after which it was poured into 1.5 liters of water. The resulting precipitate was removed by filtration and dried (Table 1).

2-Acylamino-5,6-dialkylthieno[2,3-d]thiazoles (IIa-d). A mixture of 0.014 mole of IIa-d and 5 ml of ethyl benzoate was refluxed for 10 min, after which it was cooled, and the resulting precipitate was removed by filtration and washed with methanol (Table 1).

2-Amino-5,6-dimethylthieno[2,3-d]thiazole (IV) and 2-Amino-5,6-tetramethylenethieno[2,3-d]thiazole (V). Concentrated hydrochloric acid (40 ml) was added to a refluxing solution of 0.0084 mole of acylamines IIIa, c in 60 ml of dioxane, after which the mixture was refluxed for 1.5 h. It was then cooled, and the precipitate was removed by filtration and dried (Table 1).

Acylation of V with Acetic Anhydride. Fused sodium acetate (2 g) was added to a solution of 1.7 g (8.1 mmole) of amine IV in 20 ml of acetic anhydride, and the mixture was refluxed for 45 min. It was then poured into water, and the resulting precipitate was removed by filtration and dried to give 2.0 g (98%) of IIIc with mp 272-273° (from acetone). No melting point depression was observed for a mixture of this product with a sample of IIIc obtained from IIc. The product had $R_f$ 0.69 on Silufol in benzene–methanol (1 : 1) with development by a 10% alcohol solution of phosphomolybdic acid.

Acylation of V with Benzoyl Chloride. A 2-ml (11 mmole) sample of benzoyl chloride was added to a suspension of 0.8 g (3.8 mmole) of amine V in 30 ml of 10% sodium hydroxide solution, and the mixture was cooled and stirred for 1.5 h. The resulting precipitate was removed by filtration, washed with water, and recrystallized from methanol to give 0.7 g (57.7%) of IIId with mp 184.5-185.5° (from methanol).

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