SYNTHESIS AND SOME REACTIONS OF SULFIDES OF THE THIOPHENE SERIES

XIV. The Action of Bromine and N-Bromosuccinimide on some Chelates of Mercaptoaldimines of the Thiophene Series

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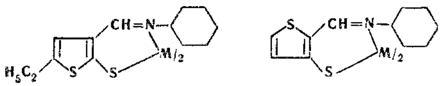
The bromination of metal complexes of mercaptothenylideneimines of types I and II with bromine and N-bromosuccinimide leads to the cleavage of the chelate ring and the formation of the corresponding thieno [3, 2-d]-and thieno [2, 3-d]isothiazolium bromides (IIIa, b).

In investigations of recent years devoted to the reactions of chelate compounds, two directions can be distinguished: 1) a study of the reactivity of the chelate ring and 2) a study of the influence of coordination on the reactivity of the organic part of the ligand containing the external donor atom. This relates, in particular, to the broad series of investigations by Collman et al. [1] and other authors [2] who have studied electrophilic substitution reactions of metal acetylacetonates considered as pseudoaromatic systems. From investigations in the second direction [3, 4], Jones has drawn the following conclusion in its most general form: coordination does not change the orientation of the substituents entering the organic part of the ligand but, by showing a definite influence on the nature of the transition state, may cause considerable changes in the reaction rate. For example, a number of electrophilic substitution reactions of bis(8-hydroxyquinolinato) copper take place more readily with the complex than with the free ligand [3].

In the present paper we give the first results of our experiments on the action of bromine and N-bromosuccinamide (NBS) on the internally complex compounds of types I and II that we have synthesized previously. These compounds can formally be regarded as systems forming condensed heterocyclic nuclei, one of which contains a metal.



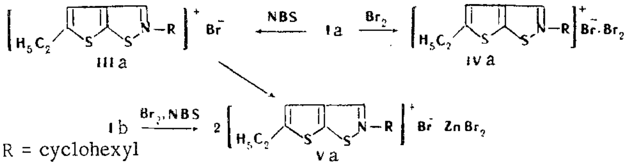
I a M = Ni II

As far as we are aware, the reactivity of chelates of this type has not been studied previously. Nevertheless, the question of the behavior of such compounds containing a "hyperaromatic" (thiophene) ring with respect to electrophilic agents is of considerable interest. In a certain sense, this system is analogous to bis(N-butylsalicyliminato)nickel, on which the action of NBS gave a product of the substitution of two hydrogen atoms by bromine [7]; unfortunately, the author did not give the structure of the bromination product.

Of course, the question of the relative capacity for substitution of each of the rings is impossible to answer if the chelate ring decomposes under the reaction conditions. In this connection we may mention that Collman was able to obtain substitution products of the chelate ring by the direct action of bromine on metal acetylacetonates only in the case of the most stable complexes of chromium and cobalt [8]. NBS proved to be a more suitable reagent for introducing bromine into a chelate ring, since in this case no highly acidic by-products are formed [7, 9].

We first studied the action of bromine and NBS on chelates of type I in which the possibility of substitution in the thiophene ring is limited by the unsuitable arrangement of the substituents. Because of this, study of the behavior of the chelate ring with the electrophilic agent was made possible.

With 2 moles bromine in chloroform, the nickel chelate **Ia** gave 2-cyclohexyl-5-ethylthieno [3, 2-d] isothiazolium bromide (**IIIa**), which was isolated from the reaction mixture in the form of the perbromide **IVa**. We had obtained the same compound previously [10] by the direct action of bromine on the corresponding ligand, (5-ethyl-2-mercapto-3-thenylidene)-cyclohexylamine. Similar results were obtained when NBS was used as the brominating agent. The isothiazolium bromide (**IIIa**) was obtained again with a yield of 83%.



At first sight, the picture of the action of bromine on the zinc chelate **Ib** differs from that just considered. In this case, a white crystalline substance whose composition corresponded to the product of the addition of 2 moles of bromine to the molecule of the initial complex was isolated in quantitative yield. Its IR spectrum did not have the absorption band for the C=N bond that was present in the IR spectrum of the initial chelate **Ib**. This could be regarded as an indication of the addition of bromine to the C=N bond [11]. However, it was found that the UV absorption curves of the compound obtained and of 2-cyclohexyl-5-ethylthieno [3, 2-d] isothiazolium bromide (**IIIa**) were completely identical in nature, the only difference being that the molar extinction coefficients were in a ratio of ~2:1, in agreement with the composition of the bromination product and the isothiazolium bromide **IIIa** (Fig. 1, 1 and 2). These results permitted the conclusion that the action of bromine on the chelate **Ib** leads to the formation of a complex of the thienoisothiazolium bromide with zinc bromide of composition **Va** analogous to the complexes

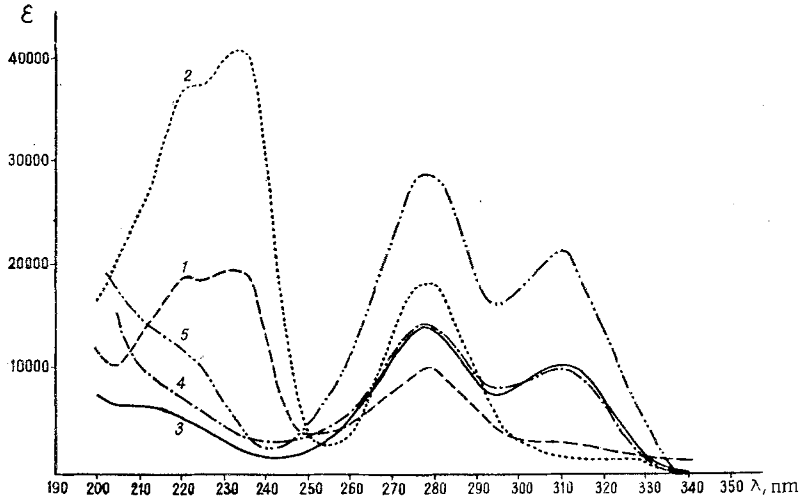
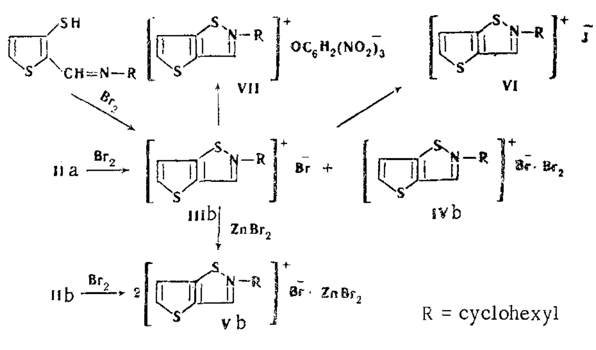


Fig. 1. UV spectra in ethanol: 1) 2-cyclohexyl-5-ethylthieno [3, 2-d]-isothiazolium bromide (IIIa); 2) complex of cyclohexyl-5-ethylthieno [3, 2-d] isothiazolium bromide with zinc bromide (Va); 3) 2-cyclohexylthieno [2, 3-d] isothiazolium bromide (IIIb); 4) 2-cyclohexyltheno [2, 3-d] isothiazolium bromide perbromide (IVb); 5) complex of 2-cyclohexyltheno [2, 3-d] isothiazolium bromide with zinc bromide (Vb).

of quaternary ammonium salts with zinc halides [12]. Such a complex is actually formed by the reaction of the isothiazolium bromide IIIa with zinc bromide in ethanol, as an experiment that we performed showed. The nature of the IR spectrum of the complex Va (Fig. 2) indicates that complex formation with zinc bromide takes place with some modification of the spectrum of the isothiazolium bromide IIIa. Thus, it can be stated that under the conditions of halogenation with bromine or NBS the chelate rings of both the nickel and the zinc complexes Ia and Ib are unstable.

In complexes of type II unlike I, two atoms of hydrogen capable of replacement by electrophilic agents are present in each thiophene ring. Consequently, in this case the formation of products of bromination of the thiophene ring might be expected if the rate of subsitution in the latter exceeded the rate of reaction of the electrophilic agent with the chelate ring. In actual fact, however, the action of 2 moles of bromine in chloroform or of NBS on the nickel chelate IIa led, just as in the case of the type I systems, to the cleavage of the chelate ring with the formation of 2-cyclohexylthieno [2, 3-d] isothiazolium bromide (IIIb) in admixture with its perbromide IVb.



We synthesized compound IIIb independently from (3-mercapto-2-thenylidene)-cyclohexylamine as described earlier for thieno [3, 2-d] isothiazolium bromides [10].

The nature of IIIb as a salt-like compound is confirmed by the ionogenic nature of the halogen, which is capable of being replaced by a picric acid residue or by the iodide ion (compounds VI, VII).

A characteristic property of the isothiazolium bromide IIIb is its capacity for giving the perbromide IVb with an excess of bromine; in this process no substitution takes place in the thiophene ring. On treatment with ether in ethanolic solution, the perbromide IVb readily loses two atoms of bromine, being converted into the initial bromide. As was to be expected, the UV spectrum of the perbromide IVb in ethanol coincides completely with the spectrum of the isothiazolium salt IIIb (Fig. 1, curves 3 and 4), since the perbromide dissociates in solution.

The zinc chelate IIb reacts with bromine in a similar manner to Ib, forming a complex with the composition Vb, which proved to be identical with the complex obtained from 2-cyclohexylthieno [2, 3-d] isothiazolium bromide and zinc bromide. In the UV spectra of compounds Vb and IIIb (Fig. 1, curves 5 and 3), as in the case of compounds Va and IIIa, the ratio of the intensities of absorption is ~2:1. The IR spectra of IIIb and Vb are given in Fig. 2.

Thus, the bromination of complexes of mercaptothenylideneimines with zinc and nickel of types I and II both with bromine and with NBS leads to the decomposition of the chelate ring. It is likely that the fundamental driving factor of this reaction is the production of the stable heterocyclic system of the thienoisothiazolium bromides. The investigation is proceeding.

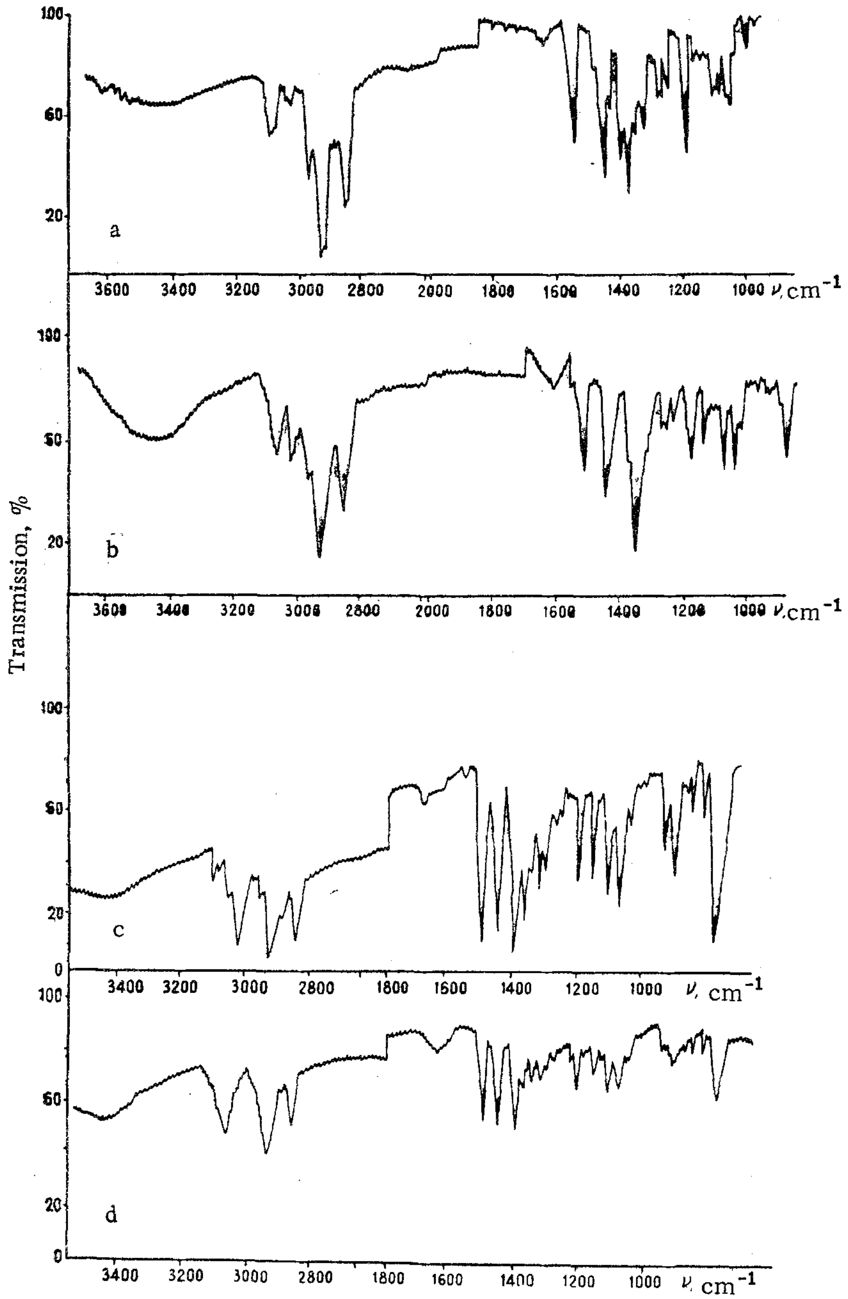


Fig. 2. IR spectra (compressed with KBr): a) 2-cyclohexyl-5-ethylthieno[3,2-d]isothiazolium bromide (**IIIa**); b) complex of 2-cyclohexyl-5-ethylthieno[3,2-d]isothiazolium bromide with $ZnBr_2$ (**Va**); c) 2-cyclohexylthieno[2,3-d]isothiazolium bromide (**IIIb**); d) complex of 2-cyclohexylthieno[2,3-d]isothiazolium bromide with $ZnBr_2$ (**Vb**).

EXPERIMENTAL

Action of bromine on bis[(5-ethyl-2-mercapto-3-thenylidene) cyclohexylaminato]-nickel (Ia). A solution of 0.75 g (1.3 mM) of the chelate **Ia** in 15 ml of chloroform was treated with 0.47 g (2.9 mM) of bromine in 2 ml of chloroform. The violet color of the solution rapidly disappeared and a yellow precipitate deposited. The mixture was heated at 50°-60° C for 30-40 min. The precipitate, which contained nickel, was filtered off and washed with chloroform. The chloroform was distilled off in vacuum and the residue was triturated in ethanol to give a yellow powder which, after recrystallization from ethanol containing ethyl acetate and from ethanol, melted at 124°-126° C. A mixture with a sample of 2-cyclohexyl-5-ethylthieno [3, 2-d] isothiazolium bromide perbromide obtained previously [10] gave no depression of the melting point. Yield of perbromide **IVa** 0.8 g (67%).

Action of NBS on bis[(5-ethyl-2-mercapto-3-thenylidene) cyclohexylaminato] nickel (Ia). A solution of 0.5 g (0.9 mM) of the chelate **Ia** in 20 ml of chloroform was treated with 0.32 g (1.8 mM) of NBS. The violet color of the solution rapidly disappeared giving a light green solution, which was stirred at 25°-35° C for 30 min and then at the boil for 20 min. The precipitate that deposited was filtered off and washed with chloroform. The chloroform was evaporated in vacuum. The residue, a viscous green oil, was triturated with ether to form a white powder containing 1.4% of inorganic impurities. The powder was heated with water to give 0.5 g (83%) of 2-cyclohexyl-5-ethylthieno [3, 2-d] isothiazolium bromide which, after being reprecipitated from ethanol with ether twice, had mp 167°-168° C. A mixture with a sample of the isothiazolium bromide obtained previously [10] gave no depression of the melting point. Found, %: C 47.25; 46.82; H 5.49; 5.40; Br 23.74; 23.65; S 19.05; 18.97. Calculated for $C_{13}H_{18}BrNS_2$, %: C 46.98; H 5.46; Br 24.05; S 19.34.

Action of bromine on bis[(5-ethyl-2-mercapto-3-thenylidene) cyclohexylaminato]-zinc (Ib). A solution of 0.32 g (1.8 mM) of bromine in chloroform was added to 0.5 g (0.9 mM) of the chelate **Ib** in 10 ml of chloroform. The solution became turbid and a yellow oil separated. The mixture was heated at 50°-60° C for 30 min, the chloroform was driven off in vacuum, and the residue was triturated in ethanol to give a white powder. In this way 1.1 g (88.5%) of the complex of 2-cyclohexyl-5-ethylthieno[3, 2-d] isothiazolium bromide with zinc bromide (**Va**) was obtained. After two recrystallizations from ethanol, mp 175°-176° C. On being heated, the complex dissolved in ethanol and methanol; it was insoluble in ether, chloroform, heptane, and ethyl acetate. Found, %: C 34.86; 34.73; H 4.17; 4.15; N 3.36; 3.46. Calculated for $2C_{13}H_{18}BrNS_2 \cdot ZnBr_2$, %: C 35.09; H 4.08; N 3.15.

Action of NBS on bis[(5-ethyl-2-mercapto-3-thenylidene) cyclohexylaminato] zinc (Ib). 0.5 g (0.9 mM) of the chelate **Ib** in 10 ml of chloroform was treated with 0.3 g (1.7 mM) of NBS as described for chelate **Ia**. The viscous yellow oil which separated was washed with hot chloroform and triturated with ethanol and ether to give a white powder. The powder was filtered off and reprecipitated from ethanol with ether, mp 174°-175° C, yield 0.6 g (48%); it contained zinc. A mixture with the complex **Va** described above gave no depression of the melting point.

Complex of 2-cyclohexyl-5-ethylthieno[3, 2-d] isothiazolium bromide with zinc bromide (Va). An ethanolic solution of 0.1 g (0.4 mM) of zinc bromide was added to a solution of 0.2 g (0.6 mM) of **IIIa** in absolute ethanol. The white precipitate that separated was filtered off, washed with ethanol, and crystallized twice from ethanol. This gave 0.26 g (97%) of the complex **Va** with mp 175°-176.5° C. A mixture with a sample of the complex obtained by the bromination of the chelate **Ib** with bromine or NBS melted without depression. Found, %: C 35.43; H 4.10. Calculated for $2C_{13}H_{18}BrNS_2 \cdot ZnBr_2$, %: C 35.09; H 4.08.

Action of bromine on bis[(3-mercapto-2-thenylidene) cyclohexylaminato] nickel (IIa). A solution of 0.5 g (1 mM) of the chelate **IIa** in 10 ml of chloroform was treated with 0.3 g (~2 mM) of bromine in 1 ml of chloroform. The solution became lighter in color and a dark oil deposited. The chloroform was poured off and the oil was triturated with ethanol to form a powder, which was crystallized from ethanol. This gave 0.1 g of yellow crystals with mp 126°-128° C. A mixture with 2-cyclohexylthieno[2, 3-d] isothiazolium bromide perbromide (**IVb**) (see below) gave no depression of the melting point. Found, %: C 29.18; 29.11; H 3.36; 3.23; S 13.66; 13.60. Calculated for $C_{11}H_{14}BrNS_2 \cdot Br_2$, % C 28.47; H 3.04; S 13.82. From the filtrate was isolated 0.3 g (50%) of 2-cyclohexylthieno[2, 3-d] isothiazolium bromide, mp 185°-186° C (from ethanol). A mixture with a sample of the isothiazolium bromide **IIIb** (see below) gave no depression of the melting point. Found, %: C 43.85; 43.62; H 4.89; 4.70; Br 26.47; 26.42; S 21.26; 21.19%. Calculated for $C_{11}H_{14}BrNS_2$, %: C 43.42; H 4.64; Br 26.26; S 21.07%.

Action of NBS on bis[(3-mercapto-2-thenylidene) cyclohexylaminato] nickel (IIa). As described above for the chelate **Ia** 0.5 g (1 mM) of the chelate **IIa** in 20 ml of chloroform was treated with 0.34 g (~2 mM) of NBS. The precipitate that deposited, which contained nickel, was separated off, and from the filtrate was isolated 0.25 g (43%) of 2-cyclohexylthieno[2, 3-d] isothiazolium bromide with mp 184°-185° C (from ethanol). A mixture with a sample obtained by the bromination of 3-mercapto-2-thenylidenecyclohexylamine (see below) gave no depression of the melting point.

2-Cyclohexylthieno[2, 3-d] isothiazolium bromide (IIIb). A solution of 2.0 g (8.9 mM) of (3-mercapto-2-thenylidene) cyclohexylamine [6] in 40 ml of dry chloroform was treated gradually with 1.45 g (9.1 mM) of bromine in 5 ml of chloroform. As the bromine was added, a white precipitate appeared which then dissolved, and HBr was evolved. The solution was stirred at 40°-50° C for 30-40 min. The chloroform was distilled off in vacuum. The residue (dark oil) was triturated with alcohol and ether with cooling to give a white powder. The powder was filtered off and washed with ether. This gave 2.0 g (73.5%) of **IIIb**, which, after two recrystallizations from ethanol, had mp 184°-186° C. Found, %: C 43.34; 43.94; H 4.69; 4.74; Br 26.01; 26.09; S 20.86; 20.94. Calculated for $C_{11}H_{14}BrNS_2$, %: C 43.42; H 4.64; Br 26.26; S 21.07.

Reactions of 2-cyclohexylthieno[2, 3-d] isothiazolium bromide (IIIb). The perbromide IVb. A suspension of 0.3 g (1 mM) of the isothiazolium bromide **IIIb** is 5 ml of chloroform was treated with 0.16 g (1 mM) of bromine and the mixture was boiled for a few minutes until the solid material had dissolved completely; on cooling, lustrous yellow crystals of the perbromide separated (yield 0.4 g, 86%), and after recrystallization from absolute ethanol these melted at 128° C. Found, %: C 28.20; 28.43; H 3.26; 3.15 Br 51.32; 51.49; S 13.72; 13.77. Calculated for $C_{11}H_{14}Br_3NS_2$, %: C 28.47; H 3.04; Br 51.66; S 13.82. An alcoholic solution of the perbromide was poured into ether. On standing, white crystals of 2-cyclohexylthieno[2, 3-d] isothiazolium bromide deposited; mp 185°-186° C; a mixture with the sample obtained previously gave no depression of the melting point.

The iodide VI. A mixture of ethanolic solutions of 0.3 g (1 mM) of the isothiazolium bromide **IIIb** and 0.4 g (2.7 mM) of sodium iodide in the minimum amount of solvent was boiled in the water bath for a few minutes. The yellow crystals that deposited were filtered off and recrystallized twice from ethanol. Mp 154°-156° C, yield 0.25 g (72%). Found, %: C 37.74; 37.56; H 4.21; 4.16; I 35.81; 35.74; S 18.10; 18.06. Calculated for $C_{11}H_{14}INS_2$, %: C 37.61; H 4.02; I 36.13; S 18.26.

The picrate VII. Alcoholic solutions of 0.3 g (1 mM) of isothiazolium bromide **IIIb** and 0.23 g (1 mM) of picric acid were mixed. On the following day the yellow precipitate was filtered off and was recrystallized from ethanol. Yield 0.35 g (74%), mp 180°-81.5° C. Found, %: C 44.98; 45.27; H 3.50; 3.73; S 14.21; 13.97. Calculated for $C_{17}H_{16}N_4O_7S_2$, %: C 45.12; H 3.56; S 14.17.

Bis[(3-mercapto-2-thenylidene) cyclohexylaminato] zinc (IIb). This was obtained from 0.5 (2.2 mM) of (3-mercapto-2-thenylidene) cyclohexylamine and 0.25 g (1.4 mM) of zinc acetate in methanol, as described previously [5]. The yield was quantitative, mp 226°-228° C (after reprecipitation from chloroform with methanol). Found, % C 51.69; 51.59; H 5.70; 5.39; Zn 12.88. Calculated for $C_{22}H_{28}N_2S_4Zn$, %: C 51.39; H 5.49; Zn 12.76.

Action of bromine on bis[(3-mercapto-2-thenylidene) cyclohexylaminato] zinc (IIb). As described for the chelate **Ib**, 1.5 g (2.9 mM) of the chelate **IIb** and 0.9 g (~5.8 mM) of bromine in chloroform gave

2.3 g (quantitative yield) of the complex of 2-cyclohexylthieno[2, 3-d] isothiazolium bromide with zinc bromide. Mp 173°-174.5° C (from ethanol). Found, %: C 31.38; 31.36; H 3.27; 3.13. Calculated for $2C_{11}H_{14}BrNS_2 \cdot ZnBr_2$, %: C 31.69; H 3.38.

Complex of 2-cyclohexylthieno[2, 3-d] isothiazolium bromide with zinc bromide (Vb). This was obtained with a yield of 88% from 0.5 g (1.6 mM) of (IIIb) and 0.2 g (0.9 mM) of zinc bromide in ethanolic solution as described above for the complex Va. After two recrystallizations from ethanol, mp 174°-174.5° C. A mixture with a sample of the complex obtained by brominating the chelate IIb (see above) gave no depression of the melting point. Found, %: C 31.88; H 3.14. Calculated for $2C_{11}H_{14}BrNS_2 \cdot ZnBr_2$, %: C 31.69; H 3.38.

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