SYNTHESIS IN THE 2-MERCAPTOBENZOTHIAZOLE SERIES

VII. The Products of the Reduction of Benzothiazolium Salts with Sodium Borohydride*

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The reduction of some dihydrothiazolobenzothiazolium salts with sodium borohydride may take place in two directions: with the formation of thiazolidino[2, 3-b]benzothiazolines and with the cleavage of the C–S bond to give N-(β-mercaptoethyl)benzothiazolines. The behavior of thiazolidino[2, 3-b]benzothiazoline under the conditions of acid and alkaline hydrolysis has been studied.

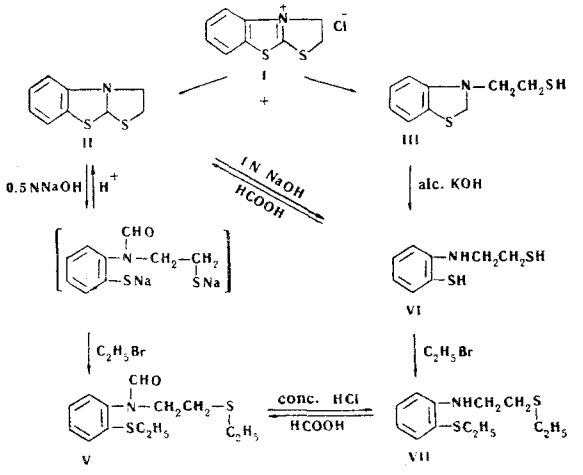
We have previously described the synthesis of a new tricyclic system, thiazolidino[2,3-b]benzothiazoline with substituents in the thiazole and benzene rings, and have shown that in the majority of cases the reduction of the corresponding salts with sodium borohydride takes place in one direction and with good yields [2]. For unsubstituted 2,3-dihydrothiazolo[2,3-b]benzothiazolium chloride (**I**), however, a hydrogenolysis product **III** was isolated in addition to the product of normal reduction, thiazolidino[2,3-b]benzothiazoline (**II**). The separation of the mixture made use of the different basicities of the nitrogen in these compounds; while the hydrochloride of **II** is stable and is readily soluble in water, the hydrochloride of **III** hydrolyzes easily with the liberation of the free base.

The IR spectrum of compound **III** exhibits absorption at 2550 cm^{-1} which is characteristic for the stretching vibrations of the –SH group. On the basis of this and the results of elementary analysis, the structure of N-(β-mercaptoethyl)benzothiazoline was proposed for **III**, and this was confirmed by independent synthesis; the reaction of benzothiazole and β-bromoethyl mercaptan gave an oily quaternary salt which, without isolation, was reduced with sodium borohydride in an aqueous medium to **III** with a yield of about 20%.

The reduction of 2-methyl-2,3-dihydrothiazolo[2,3-b]benzothiazolium chloride took place analogously. Here, also, two substances were obtained: one of them, 2-methylthiazolidino[2,3-b]benzothiazoline, we have described previously [2]. The structure of the hydrogenolysis product, N-(β-mercaptopropyl)benzothiazoline, was assumed by analogy with **III** on the basis of its properties and the results of elementary analysis.

In the case of 7-acetamido-2,3-dihydrothiazolo[2,3-b]benzothiazolium chloride (**IV**), only 6-acetamido-N-(β-mercaptoethyl)benzothiazoline in the form of the hydrochloride could be isolated from the reaction mixture. We were unable to purify the base, since even during recrystallization from aqueous ethanol it underwent oxidation.

Since there is no information on the new tricyclic system **II** in the literature, it was of interest to study its properties and some reactions. In the present work we have studied the stability of the rings of compound **II** to acid and alkaline hydrolysis. It is known from the literature that mercaptals of N-substituted amides readily undergo hydrolysis and oxidation and readily react with alcohols, amines, etc. [3]. The structure of system **II** is similar to that of cyclic amidomercaptals, and therefore a similarity of their chemical properties could have been expected. This was confirmed in relation to their alkaline hydrolysis. It was found that system **II** is extremely stable to the action of strong acids even on heating. At the same time, **II** decomposes even on standing in an alkaline medium. The brief heating (~30 min) of **II** in 0.5 N sodium hydroxide leads to its complete dissolution due to the opening of the ring system. On acidification, cyclization takes place again to give the initial **II**. For a more detailed knowledge of this process, we carried out a number of chemical reactions.



In order to exclude recyclization on acidification, it was necessary to block the mercapto group. For this purpose we used the alkylation reaction. After a suspension of **II** in aqueous sodium hydroxide had been dissolved (by boiling for ~30 min), ethyl bromide was added to the reaction mixture and the reaction product was isolated in the usual way. The IR spectrum of the substance obtained had strong absorption at 1680 cm^{-1}, which corresponds to the stretching vibrations of the N–C=O group. Consequently we assigned to the substance the structure o-ethylthio-N-(β-ethylthioethyl)-formanilide (**V**). Thus, the first stage of the alkaline hydrolysis of **II** was the formation of the N-formyl de-

*For communication VI, see [1].

o-Ethylthio-N-(β-ethylthioethyl)aniline (VII). a) 5.55 g (0.03 mole) of the dimercaptan **VI** was dissolved in 50 ml of water containing 2.8 g (0.07 mole) of sodium hydroxide. The turbid solution was extracted with ether. The aqueous layer was heated to 50° C and to it 11.0 g (0.10 mole) of ethyl bromide in 20 ml of ethanol was added in drops. Stirring was continued for another 3 hr at 50–60° C and then the mixture was diluted with water and the oil was extracted with ether. This gave 6.1 g (85%) of substance **VII**. Bp 138–139° C (1 mm); n_D^{20} 1.5892. Found, %: N 6.08, 5.87; S 26.49, 26.78. Calculated for $C_{12}H_{19}NS_2$, %: N 5.81; S 26.55.

b) A mixture of 3.2 g (0.012 mole) of the formanilide **V** and 15 ml of concentrated HCl was boiled for 1.5 hr, diluted with water, and extracted with chloroform. The chloroform extract was washed with water, sodium hydrogen carbonate solution, and water again, and was evaporated. The yield of **VII** was 1.9 g (68%). Bp 144° C (1.3 mm); n_D^{19} 1.5882.

Thiazolidino[2, 3-b]benzothiazoline (II). A solution of 2.5 g (0.0013 mole) of the dimercaptan **VI** in 15 ml of 98% formic acid was boiled for 4 hr. After cooling it was poured into ~150 ml of water, the turbid solution was extracted with chloroform, and the aqueous layer was made alkaline with sodium bicarbonate to give 2 g (76%) of **II** with mp 88–89° C (from ethanol). The mixture with the substance obtained by the other method gave no depression of the melting point.

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