Benzothiazoline Derivatives. IV. Comment on the Mechanism of Reaction of 2-Benzothiazolinethione with Ethylene Oxide in Acetic Acid

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Treatment of 2,3-dihydrothiazolo[2,3-*b*]benzothiazolium bromide with sodium acetate in acetic acid gave predominantly 3-(2-acetoxyethyl)-2-benzothiazolinethione and the minor product 3-(2-acetylthioethyl)-2-benzothiazolinone. The mechanistic implications of this and previous results are discussed in terms of the reaction of 2-benzothiazolinethione and its derivatives with ethylene oxide in acetic acid.

In the first paper of this series (1) it was shown that treatment of 2-benzothiazolinethione (1) with excess ethylene oxide in the presence of acetic acid gave 3-(2-hydroxyethyl)-2-benzothiazolinone (2) as an unexpected reaction product.
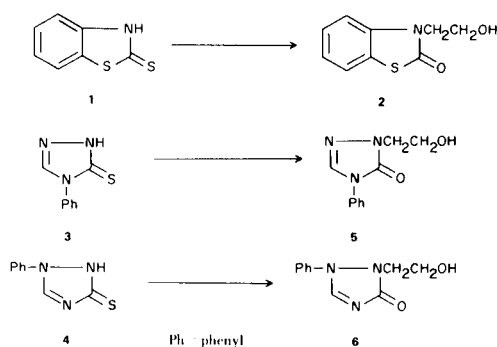
Vlasova, *et al.* (2) recently reported analogous transformations in which 4-phenyl-1,2,4-triazoline-3-thione (3) and its 1-phenyl isomer (4) were seen to undergo *N*-hydroxyethylation accompanied by replacement of sulfur by oxygen to give compounds 5 and 6, respectively, under the same conditions. In connection with their observations they have proposed a mechanism in which ethylene sulfide may be extruded from an intermediate as illustrated below.
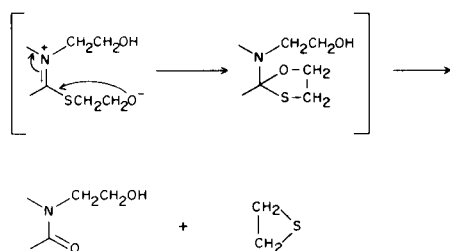

The mechanism whereby thiocarbonyl is replaced by carbonyl under these conditions was not considered in our original publication, but subsequent observations (3) now permit certain conclusions to be drawn. For example, we found that methoxide ion could effect a similar desulfurization with subsequent formation of a thioether possibly through a rearrangement as shown below. An ionized intermediate having a negative charge on sulfur is a possibility, but the intramolecular reactivity of such a
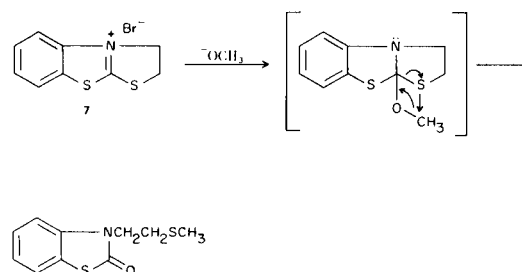

nucleophilic species in the ethylene oxide-acetic acid reaction mixture would be greatly exceeded by the rate of its protonation. We instead propose that the acetate ion enters the reaction leading to the formation of an intermediate which undergoes rearrangement analogous to that shown above followed by loss of an acetylthiol ester. Such a scheme would have the advantage of being applicable to the reactions of either *N*- or *S*-substituted isomers of 2-benzothiazolinethione, conforming to experimental evidence (1) (types A and B as summarized below). It would also explain why desulfurization does not proceed with ethylene oxide in other solvents such as methanol or acetone.

In our original experiments with ethylene oxide and acetic acid we did not detect or look for the critical

Type A (N-substituted):

R = H, CH₂CH₂OH, or alkyl
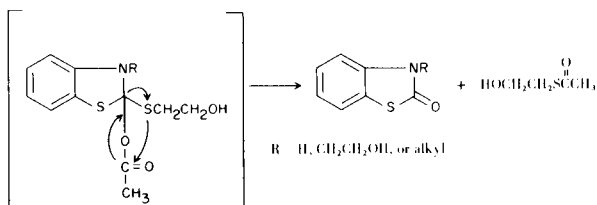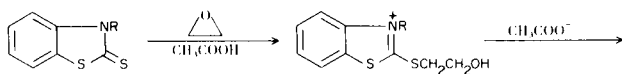
Type B (S-substituted):

R = alkyl or CH₂CH₂OH
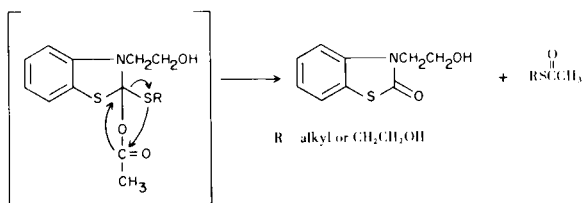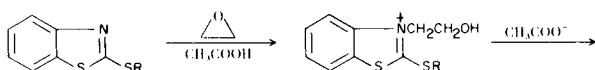
thiolester elimination products. In order to test the validity of the proposed route we decided to study the effect of acetate ion on the benzothiazolium salt **7**, which allows an easy isolation of the sulfur-containing leaving group in whatever form it assumes since it would be still attached to the parent molecule.

Upon heating **7** in acetic acid and sodium acetate, however, not one but two major components were detected in the crude reaction mixture. The nmr spectrum showed the presence of both acetate and acetylthiol esters (about 3:1), while the uv spectrum indicated both the 2-carbonyl and the 2-thiocarbonyl forms of the benzothiazoline ring. Following separation by preparative-scale thin-layer chromatography, the two products were identified as the predicted rearrangement product 3-(2-acetylthioethyl)-2-benzothiazolinone (**8**) and its isomer 3-(2-acetoxyethyl)-2-benzothiazolinone (**9**), a compound previously prepared by the thiation of the corresponding 2-carbonyl compound (4). Identification of **8** was substantiated by independent synthesis from 3-(2-mercaptoethyl)-2-benzo-thiazolinone and acetic anhydride (5).
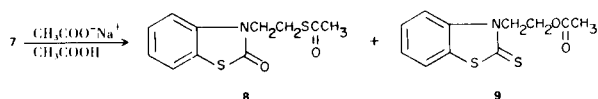
The formation of compound **8** in this experiment establishes the role of acetate ion in the desulfurization reactions. In addition, the other isomer provides an

example of the involvement of the α-carbon of the 2,3-dihydrothiazolo ring in the reaction which we were unable to detect or to prove previously. The preponderance of the latter reaction in the case of the cyclic benzothiazolium salt **7** may be explained by the more hindered environment of the carbon atom of the dithiocarbamate moiety and the increased reactivity of the methylene group in the 2,3-dihydrothiazolo ring.

EXPERIMENTAL (7)

A solution of 2.74 g. (0.01 mole) of 2,3-dihydrothiazolo-[2,3-b]benzothiazolium bromide (3) (**7**) and 8.2 g. (0.1 mole) of anhydrous sodium acetate in 50 ml. of acetic acid was heated at reflux overnight. The residue obtained by concentration in vacuo was suspended in 100 ml. of water and extracted with three 50-ml. portions of chloroform. The combined extracts were washed with sodium bicarbonate solution and dried over sodium sulfate. After the removal of the solvent 2.4 g. of thick oil was obtained which on silica gel tlc showed two spots at R_f 0.7 and R_f 0.5 (ether-petroleum ether, 1:1). For purification 0.8 g. of the total mixture was chromatographed on four silica gel preparative-scale tlc plates (E. Merck) with the same solvent system. On isolation the slower moving band (R_f 0.5) gave 0.31 g. (37%, crystallized from ether) of 3-(2-acetoxyethyl)-2-benzothiazolinethione (**9**) which was identified by comparison of ir spectra and melting point with authentic material (4). The faster moving band yielded 0.09 g. of crystalline material after isolation and crystallization from petroleum ether; m.p. 76-78°. Spectral and elemental analysis data confirmed the structure as that of 3-(2-acetylthioethyl)-2-benzothiazolinone (**8**); nmr (deuteriochloroform): δ 7.0-7.5 (m, 4, C₆H₄), 3.9-4.3 (m, 2, NCH₂), 2.9-3.3 (m, 2, SCH₂) and 2.36 ppm (s, 3, S-acetyl); λ max (methanol) (nm): (ε x 10⁻³); 290 (2.76), 282.5 (2.68), and 215 (39.9); mass spectrum: M⁺ at m/e 253.

Anal. Calcd. for $C_{11}H_{11}NO_2S_2$ (253.3): C, 52.15; H, 4.38; N, 5.53. Found: C, 52.09; H, 4.29; N, 5.34.

REFERENCES

(1) P. Sohar, G. H. Denny and R. D. Babson, J. Heterocyclic Chem., 5, 769 (1968).

(2) L. A. Vlasova and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., 700 (1971).

(3) P. Sohar, G. H. Denny and R. D. Babson, J. Heterocyclic Chem., 7, 1369 (1970).

(4) P. Sohar, G. H. Denny and R. D. Babson, ibid., 6, 163 (1969).

(5) Alternative preparation of **8** was performed by treating 3-(2-mercaptoethyl)-2-benzothiazolinone (1.1 g.), prepared as described in reference 6, in pyridine (50 ml.) with 10.2 g. of acetic anhydride. The solution was stirred for 18 hours at room temperature and pure **8** (yield, 72%) was precipitated by pouring the reaction mixture into water (300 ml.). The product was shown to be identical to that obtained from **7** by mixture melting point determination and spectral comparisons (uv, ir and nmr).

(6) E. A. Kuznetsova, V. A. Bogolyubskii, L. T. Bogolyubskaya, T. N. Stepanova and S. V. Zhuravlev, Khim. Geterotsikl. Soedin., 834 (1967).

(7) Petroleum ether refers to that fraction boiling from 30-60°.