FORMATION OF BICYCLIC COMPOUNDS IN THE REACTION OF 3-METHYL-2,3-EPOXYSULFOLANE WITH THIOCYANIC ACID

L. A. Mukhamedova, L. I. Kursheva,
K. M. Enikeev, and A. V. Il'yasov

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In the presence of an equivalent amount of sulfuric acid 3-methyl-2,3-epoxysulfolane reacts with sodium thiocyanate with primary opening of the oxy ring at the $C_{(3)}$—O bond to give, as the principal product, 5-methyl-3-oxo-2-oxa-4,8-dithiabicyclo[3.3.0]octane 8,8-dioxide.

We have shown previously [1] that the reaction of 3,4-epoxysulfolanes with thiocyanates in an acetic medium proceeds stereospecifically with cleavage of the $C_{(3)}$—O bond to give products of trans opening of the oxy ring, viz., hydroxythiocyanatosulfolanes.

In this connection, it seemed of interest to investigate, in the reaction with thiocyanates, the behavior of 3-methyl-2,3-epoxysulfolane in order to ascertain the effect of a sulfonyl group adjacent to the oxy ring on the direction and stereochemistry of the opening of the latter.

In contrast to 3,4-epoxysulfolanes, which, under the influence of potassium thiocyanate, undergo isomerization to unsaturated alcohols [1], 3-methyl-2,3-epoxysulfolane (I) does not react under similar conditions. According to the results of TLC, the reaction mixture contained only the starting epoxide and products of its resinification.

The reaction of epoxide I with sodium thiocyanate in the presence of an equivalent amount of sulfuric acid proceeds in a more complex manner than in the case of 3,4-epoxysulfolanes and leads to a mixture of products. From the reaction mixture we isolated three compounds, the IR spectra of which do not contain the absorption bands due to the vibrations of SCN and OH groups that are characteristic for thiocyanohydrins [1]. At the same time, the characteristic absorption frequencies of the sulfonyl group are retained in their spectra. In addition, absorption bands due to the vibrations of carbonyl or imino groups appear in the spectra. On the basis of these results, as well as the known properties of thiocyanohydrins [2-4] or amides [5] to undergo cyclization reactions, we assumed that, in our case, the following bicyclic compounds were formed: 5-methyl-3-oxo-2-oxa-4,8-dithiabicyclo[3.3.0]octane 8,8-dioxide (IV), 3-imino-1-methyl-2-oxa-4,6-dithiabicyclo[3.3.0]octane 6,6-dioxide (VII), and 5-methyl-3-oxo-4-4aza-2,8-dithiabicyclo[3.3.0]octane 8,8-dioxide (X), the structures of which were established by IR and NMR spectroscopy.

The principal product is thiocarbonate IV. In its IR spectrum one observes intense absorption of a carbonyl group at 1755 cm^{-1}, together with absorption bands at 1040 and 1340 cm^{-1}, which are due to the vibrations of the C—O—C bond. In the PMR spectrum of this product the signal of the methylidyne proton attached to the $C_{(3)}$ is shifted to the low-field region (5.60 ppm) as compared with the analogous signal in the spectrum of the starting epoxide (4.65 ppm). The formation of a cyclic thiocarbonate is also confirmed by a positive reaction in the presence of sulfide sulfur [6].

To the second reaction product we assigned a cyclic imine VII structure, as attested to by the presence in the IR spectrum of an intense absorption band at 3345 cm^{-1} (C=NH), as well as bands at 1490 and 1520 cm^{-1}, which can be assigned to vibrations of C=N and N—H bonds. The decrease of the latter two frequencies as compared with the values that are usually ascribed to these groupings [7] is evidently due to the effect of a five-membered sulfolane ring in conjunction with a cyclic imine structure.

A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Branch, Academy of Sciences of the USSR, Kazan 420083. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 331-335, March, 1985. Original article submitted March 26, 1984; revision submitted July 13, 1984.

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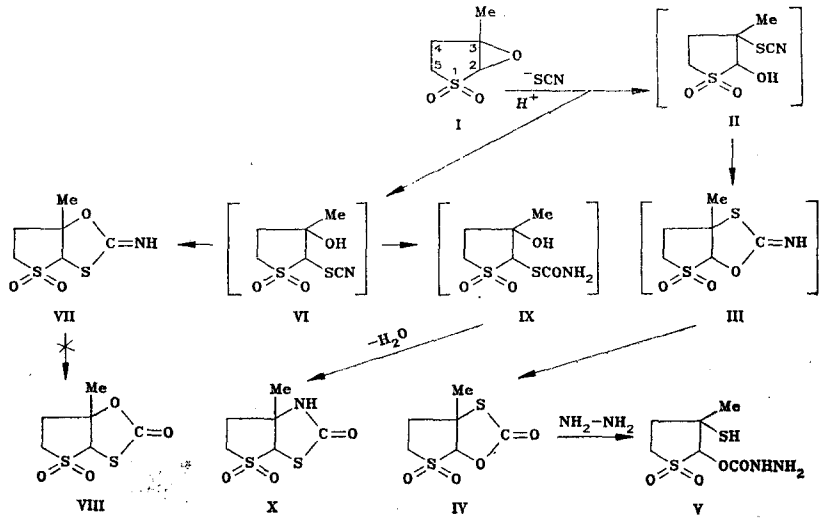


The position of the sulfide sulfur in IV and VII attached to the $C_{(3)}$ or $C_{(2)}$ atoms was determined by ^{13}C NMR spectroscopy. As model compounds we used the following compounds that we previously obtained: 3-methyl-3-thiocyanato-4-hydroxysulfolane (XI) [1], 3-methyl-3-ethoxy-4-hydroxysulfolane (XII) [8], 3-methyl-2,3-dimethoxysulfolane (XIII) [9], and 5-methyl-2,4-dioxa-3,8-dithiabicyclo[3.3.0]octane 3,3,8,8-tetroxide (XIV), which was specially synthesized from epoxide I and sulfuric acid, in analogy to the cyclophosphate steroid series [13] (see Table 1).

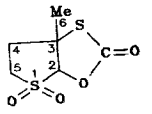
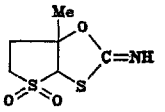
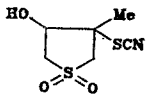
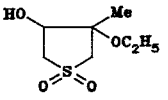
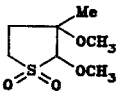
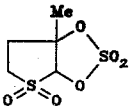
A comparison of the chemical shifts of the signals of the $C_{(2)}$—$C_{(5)}$ nuclei in thiocarbonate IV and imine VII with the $C_{(2)}$—$C_{(5)}$ shifts in model compounds XI-XIV showed that in the thiocarbonate the sulfur atom is attached to the carbon atom in the 3 position, whereas in the imine it is attached to the carbon atom in the 2 position.

A third product was isolated in very small amounts. In its IR spectrum, along with the absorption of a carbonyl group at 1715 cm^{-1}, one observes a band at 3370 cm^{-1}, which is due to the stretching vibrations of the NH bond. In the PMR spectrum of this substance the broad signal at 4.63 ppm corresponds to the proton of the NH group, whereas the position of the signal of the methylidyne proton attached to the $C_{(2)}$ atom is close in magnitude (4.86 ppm) to the chemical shift of this proton in imine VII (5.10 ppm). This makes it possible to propose structure X for this compound.

Thus the reaction of 3-methyl-2,3-epoxysulfolane with thiocyanic acid can be conceived of by means of the scheme presented above. Attack by the thiocyanate ion on the tertiary $C_{(3)}$ atom of the reaction center leads to a product of opening of the oxy ring at the $C_{(3)}$—O bond, viz., intermediate thiocyanohydrin II, the rapid intramolecular cyclization of which to imine III and subsequent hydrolysis give cyclic thiocarbonate IV — the principal reaction product. In addition to this process, although to a lesser extent, one observes nucleophilic attack at the alternative $C_{(2)}$—O bond, as evidenced by the isolation of cyclic imine VII, along with a very small amount of X. Product X is evidently formed as a result of hydrolysis of the nitrile fragment of the SCN group in intermediate thiocyanohydrin VI with subsequent dehydration and cyclization. We were unable to detect the cyclic thiocarbonate with alternative structure VIII in the reaction products.

One should note the extreme stability of thiocarbonate IV with respect to chemical transformations. An attempt to subject it to resinification by means of alcoholic potassium hydroxide by refluxing for several hours was unsuccessful. Repeated attempts to accomplish desulfuration over Raney nickel were also unsuccessful. According to the data in [10], cleavage of the thiocarbonate bond is observed under the influence of hydrazines on thiocarbonates with noncyclic structures. The action of hydrazine hydrate on thiocarbonate IV was accompanied by a vigorous exothermic reaction and led to cleavage of the thiocarbonate ring to give 2-hydrazinocarbonyl-3-mercapto-3-methylsulfolane (V). The data from the IR spectrum are in agreement with the structure assigned to it. The observed cyclization with the formation of stable bicyclic products in the reaction of 3-methyl-2,3-epoxysulfolane I with thiocyanic acid constitutes evidence for the stereoselectivity of the reaction, which leads to cis opening of the oxy ring, which is under the influence of the SO_2 electronegative

TABLE 1. ^{13}C NMR Spectra of IV, VII, and XI-XIV in d_6-Acetone

Compound	Chemical shift, δ, ppm				
	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$
IV 	95,6	62,4	31,4	50,9	29,5
VII 	78,5	94,7	33,4	49,1	25,2
XI 	59,1	59,4	74,7	61,9	22,2
XII 	58,6	84,3	75,9	60,9	18,6
XIII 	98,3	82,0	32,6	51,1	18,3
XIV 	91,5	94,5	31,9	47,2	23,7

grouping. It is known that a bicyclic system from two trans-fused five-membered rings is sterically hindered [11]. A similar stereochemical outcome has also been noted in the opening of the oxy ring in steroid keto epoxides [3, 12].

EXPERIMENTAL

The IR spectra were recorded between KBr plates with a UR-20 spectrometer. The PMR spectra were recorded with a Varian T-60 spectrometer with d_6-dimethyl sulfoxide and pyridine as the solvents and tetramethylsilane (TMS) as the internal standard. The ^{13}C NMR spectra were recorded with a Bruker WM-250 spectrometer in d_6-acetone. The chemical shifts were measured relative to TMS. Column chromatography on silica gel (0.16-0.1 mesh) with benzene and ethyl acetate as the eluents was used for the separation and identification of the products. The purity of the compounds obtained was monitored by TLC on Silufol UV-254 plates in a benzene–ethyl acetate system (13:10) with development by iodine vapors.

3-Methyl-2,3-epoxysulfolane (I) with mp 74-75°C, and 3-methyl-2,3-dimethoxysulfolane (XIII), with mp 76-78°C, were obtained by the method in [9], whereas 3-methyl-3-ethoxy-4-hydroxysulfolane (XII), with mp 87-88.5°C, was obtained by the method in [8]. No melting-point depressions were observed for mixtures of these products with the previously described compounds [1, 8, 9].

Action of Thiocyanic Acid on Epoxide I. An 8-g (54 mmoles) sample of epoxide I was added to a solution of 5 g (61 mmoles) of NaSCN and 3.02 g (30 mmoles) of H_2SO_4 in 20 ml of water, and the mixture was stirred at 55-70°C for 1.5-2 h. The precipitate that formed from the reaction mixture was removed by filtration and washed with water to give 8 g (71%) of a product with mp 135-138°C (R_f 0.56 and R_f 0.28). The liquid portion of the reaction mixture was concentrated to give 3.63 g of a precipitate, which consisted of inorganic and organic parts.

5-Methyl-3-oxo-2-oxa-4,8-dithiabicyclo[3.3.0]octane 8,8-Dioxide (IV) and 5-Methyl-3-oxo-4-aza-2,8-dithiabicyclo[3.3.0]octane 8,8-Dioxide (X). A 4-g sample of the reaction product with mp 135-138°C was chromatographed with a 70 by 3.5 cm column by elution with benzene and ethyl acetate, as a result of which, in succession, 3.47 g (61.7%) of thiocarbonate IV [R_f 0.56; elution with benzene–ethyl acetate (19:4); mp 145-146°C (from ethyl acetate); found: C 34.7; H 3.6; S 30.6%. $C_6H_8O_4S_2$: calculated: C 34.6; H 3.9; S 30.8%] and 0.1 g (1.9%) of X [R_f 0.28; elution with benzene–ethyl acetate (18:7); mp 209-209.5°C (from ethyl acetate). Found: C 34.7; H 4.3; N 6.8%. $C_6H_9O_3NS_2$: calculated: C 34.8; H 4.4; N 6.8%] were isolated.

3-Imino-1-methyl-2-oxa-4,6-dithiabicyclo[3.3.0]octane 6,6-Dioxide (VII). A 3.63-g sample of the precipitate isolated from the liquid portion was refluxed in a solution of KOH (16 ml of 0.5 N KOH in 15 ml of ethanol), after which the inorganic portion was separated and the ethanolic filtrate was acidified with concentrated HCl (up to the point of turbidity). After 2 days, workup gave 0.5 g (14%) of VII with mp 207-212°C (from ethanol). Found: C 34.5; H 4.6; N 6.7; S 30.5%. $C_6H_9O_3NS_2$. Calculated: C 34.8; H 4.4; N 6.8; S 30.9%.

3-Hydrazinocarbonyl-3-mercapto-3-methylsulfolane (V). A 0.55-g (11 mmoles) sample of hydrazine hydrate was added to 2 g (9 mmoles) of thiocarbonate IV, during which we observed pronounced warming up of the reaction mixture and the development of an unpleasant odor. Cooling of the mixture yielded 0.62 g of a precipitate, with mp 135-143°C, which did not depress the melting point of starting IV. From the filtrate, after concentration, we isolated 0.38 g (20%) of V with mp 130.5-131°C (from ethanol). IR spectrum: 3200 (NH_2), 3320 (NH), 2660 (SH), 1755 (C=O), 1100 and 1330 cm^{-1} (SO_2). Found: C 29.6; H 5.1; N 11.2; S 27.2%. $C_6H_{12}O_3N_2S_2$. Calculated: C 29.9; H 5.0; N 11.6; S 26.7%.

5-Methyl-2,4-dioxa-3,8-dithiabicyclo[3.3.0]octane 3,3,8,8-Tetroxide (XIV). A 1.1-ml sample of 98% H_2SO_4 was added at 20°C to a solution of 1 g of epoxide I in 100 ml of CH_3CO_2H, which had been previously treated by refluxing in $(CH_3CO)_2O$ and fractionated. After 1 day at 20°C, the solution was diluted with water (1:1); however, no precipitation was observed. The aqueous solution of acetic acid was extracted with chloroform (six 30-ml portions), and the solvent was removed to give ∿ 0.1 g (15%) of cyclosulfate XIV with mp 151-155°C (from acetone). IR spectrum: 1155, 1340 (SO_2); 1290, 1390 cm^{-1} (covalent sulfate) [7]. Found: C 26.8; H 3.8%. $C_3H_8O_6S_2$. Calculated: C 26.3; H 3.5%.

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