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RESEARCH IN THE FIELD OF UNSATURATED DERIVATIVES OF AZOLES.

11.* REACTION OF BENZIMIDAZOLE-2-THIONE WITH 1,2,3-TRIBROMOPROPANE

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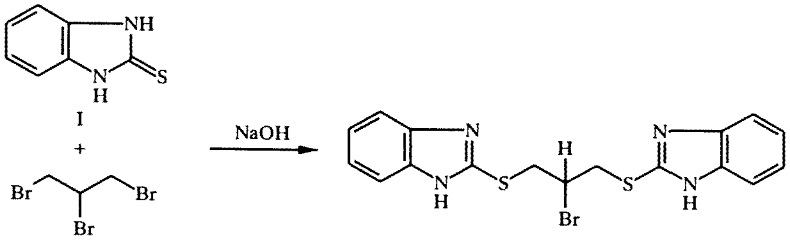
In the interaction of benzimidazole-2-thione with 1,2,3-tribromopropane under conditions of interfacial catalysis in an alkaline medium, 2-(2-bromo-2-propenylthio)benzimidazole is formed; debromination of this compound affords 3-methylthiazolo[3,2-a]benzimidazole, which is subsequently converted as a result of thermolysis to 2-propadienylthio)benzimidazole.

Benzimidazole-2-thione (I) in an alkaline medium is alkylated in steps, initially forming S-alkyl derivatives [2]. This offers the possibility of using the reaction of the thione I with dihaloalkanes for the synthesis of macrocyclic compounds — coronands and podands (compare [3]).

The reaction of the thione I with 1,2,3-tribromopropane in a two-phase aqueous system (40-50% NaOH, DMSO, TEBAC) proceeds with participation of the terminal bromomethyl groups (compare [4]), forming the podand II; in the debromination of this compound by the action of KOH in DMSO, large amounts of tar are formed, with decomposition of the reaction product.



II

In the PMR spectrum of compound II there are signals of the methine proton at 6.7 ppm and methylene protons at 2.5 ppm; in the IR spectrum there are absorption bands of the associated NH group at 3200-3400 cm^{-1}; in the mass spectrum there is a weak signal of the molecular ion M_{II}^+ 419 (0.6), fragmentation of which leads to the unstable cations *m/z* 392 (I), 329, and 325, subsequently forming the base alkylthiobenzylimidazolium ion with *m/z* 271 and fragment ions with *m/z* 311, 189, 150, and 122 (see Table 2).

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*For communication 10, see [1].

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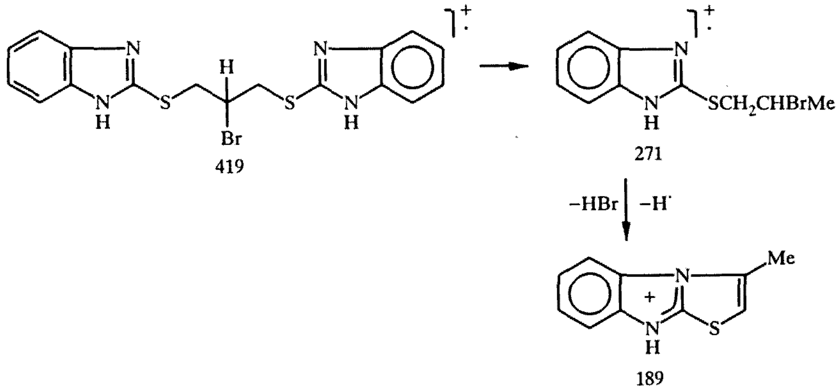
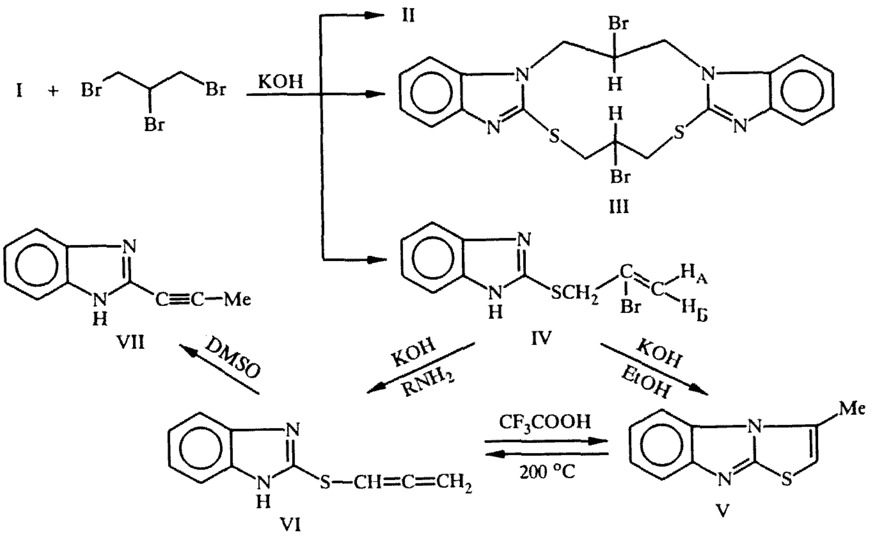


Interaction of the thione I with 1,2,3-tribromopropane in aprotic dipolar solvents [5] is accompanied by the formation of large amounts of tar in the reaction mixture; the main product of the reaction is the thioether IV; byproducts are compounds II and III. Thus, in the mass spectrum of the reaction product, even after three crystallizations from alcohol, there are still weak signals from the cation radicals of compounds II and III with *m/z* 419 (0.6) and 538 (1). The severe tarring of the reaction mixture is apparently due to decomposition of the disulfide II in the superbasic medium KOH—DMSO.



Compound IV, in contrast to the disulfide II, reacts smoothly with caustic in DMSO or alcohol solution, forming the intermediate allene derivative VI, which, in the same manner as 1-alkyl-3-propadienyl-2-iminobenzimidazolines [6], is cyclized under the conditions of reaction, forming 3-methylthiazolo[3,2-a]benzimidazole (V). The PMR spectrum of compound IV contains a singlet of the methylene group at 3.8 ppm and two doublets at 5.4 and 5.1 ppm with J = 2 Hz, which is characteristic for geminal vinyl protons. In the mass spectrum of compound IV there is an intense signal of the molecular ion M^+ (*m/z* 269) and the fragment ions 189, 150, and 119 that are repeated with the spectrum of II.

It should be noted that high yields of compound V are also obtained by the interaction of the thione I with 1,2,3-dibromopropane in DMSO in the presence of excess KOH. In this case, apparently, the thione I is alkylated by the 2,3-dibromopropene that is formed as a result of debromination of the 1,2,3-tribromopropane under the conditions of reaction.

Attempts to carry out the substitution of bromine in compound IV by an ethylenediamine or o-phenylenediamine group in the KOH/DMSO or K_2CO_3/DMF system produced compound VI in both cases. Apparently, the presence of these amines in the reaction medium has a stabilizing effect on the allene derivative VI, preventing its rearrangement to compound V. Along with this, the allene derivative VI was obtained unexpectedly in an attempt to distill compound V under vacuum (boiling at 200°C): In this case, the thermal rearrangement apparently proceeds with rupture of the C—N bond of the diazole fragment through a homolytic mechanism. This conversion is a rare case of thermal synthesis of an allene derivative.

TABLE 1. Characteristics of Compounds II and IV-VI

Compound	mp, °C	PMR spectrum, δ, ppm	Yield, %
II	98	7.2 (8H, m, arom.); 6.5 (1H, m, CHBr); 2.5 (4H, m, CH_2)	12
IV	150	7.1 (4H, m, arom.); 5.4, 5.1 (2H, dd, $=CH_2$, J = 2); 3.8 (2H, s, CH_2)	65
V	135	7.6-7.2 (4H, m, arom.); 6.7 (1H, s, 2-H); 2.5 (3H, s, CH_3)	95
VI	163...165	8.7-7.4 (4H, m, arom.); 4.6 (1H, s, =CH); 2.1 (2H, s, CH_2)	80

TABLE 2. Mass Spectra of Compounds II-VI*

Compound	Values of *m/z* (and relative intensity, %)
II	327 (5), 325 (7), 312 (35), 311 (50), 309 (28), 307 (10), 273 (10), 272 (19), 271 (100), 269 (93), 192 (5), 191 (15), 190 (35), 189 (79), 151 (19), 122 (10)
IV	272 (19), 271 (100), 269 (93), 150 (8), 149 (7)
V	190 (19), 189 (45), 188 (100), 187 (20), 155 (10), 144 (10), 143 (44), 117 (6), 116 (5), 103 (7), 102 (33), 94 (8), 90 (12), 77 (7), 76 (14), 75 (17), 74 (5), 71 (10), 64 (10), 50 (13)
VI	190 (12), 189 (48), 188 (100), 143 (16), 102 (8), 75 (5), 63 (5)

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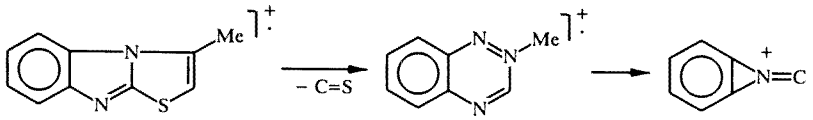
*The peaks that are listed are for ions with intensity more than 5% of the maximum.

The PMR spectrum of compound V contains a singlet of methyl-group protons at 2.5 ppm and a singlet of the proton in position 2 at 6.7 ppm, which stands apart from the overall aromatic multiplet. In the PMR spectrum of the allene derivative VI, the position of the signals of the methine and methylene protons is changed upon protonation, from 3.5 and 2.8 ppm to 4.6 and 2.1 ppm, respectively. The mass spectra of the isomeric compounds V and VI differ in the character of fragmentation of the molecular ions. Along with this, both compounds, under conditions of electron impact, form a molecular ion M^+ with *m/z* 188 and fragment ions with *m/z* 155, 144, 143, and 134 (2) (see Table 2).



188 144 102

Compound VI, under conditions of acid catalysis, is evidently very susceptible to either intramolecular cyclization to form compound V or acetylene—allene rearrangement to form compound VII. Thus, in the PMR spectrum of the allene derivative VI, taken in a 4:1 DMSO-d_6/CF_3COOH mixture at 90°C, there are no signals of allene protons at 3.5 ppm, and a signal of the methyl group of the acetylene derivative VII appears at 2.8 ppm. In CF_3COOH solution, over the course of a day, the allene derivative VI is cyclized, forming compound V, with the appearance of a proton signal at 6.7 ppm and a methyl-group signal at 2.5 ppm.

EXPERIMENTAL

The IR spectra were recorded in a UR-20 instrument in white mineral oil, the PMR spectra in a Tesla BS-487 instrument (80 MHz) in CF_3COOH, and the PMR spectrum of compound VI in a Tesla BS-567 instrument (100 MHz) in DMSO-d_6, internal standard HMDS. The mass spectra were obtained in a Finnigan 4021 spectrometer with an ionizing voltage of 70 eV, ionization chamber temperature 200-250°C. The chromatography was performed on Al_2O_3 (No. III Brockman activity). Compounds II-VI were crystallized from alcohol. The physicochemical characteristics and PMR spectrometric data are given in Table 1.

Elemental analyses for C, H, Br, N, and S matched the calculated values.

1,3-Bis(2-benzimidazolylthio)-2-bromopropane (II, $C_{17}H_{15}BrN_4S_2$). To a solution of 3 g of NaOH in 4 ml of water and 3 ml of DMSO, 3 g (0.02 mole) of the thione I and 0.3 g of TEBAC were added; then, 6 g (0.02 mole) of 1,2,3-tribromopropane was added dropwise with stirring. After 3 h, the reaction mixture was diluted with water. The precipitate was filtered off, dried, and chromatographed in chloroform solution in a column with aluminum oxide, taking the fraction containing a substance with R_f 0.7 in the first portions of the eluate. After driving off the solvent, obtained 0.5 g of compound II.

2-(2-Bromo-2-propenylthio)benzimidazole (IV, $C_{10}H_9BrN_2S$). To a suspension of 56 g of KOH in 100 ml of DMSO, 2 g of TEBAC and 30 g (0.2 mole) of the thione II were added. The mixture was heated for 0.5 h on a boiling water bath until the calcium salt of the thione I was formed; then, 70 g (0.25 mole) of freshly distilled 1,2,3-tribromopropane was added dropwise over the course of 3 h with stirring. As the reaction mixture thickened, 50 ml of THF and 50 ml of dioxane were added, after which the stirring was continued for 3 h at 60-80°C. The reaction mixture was diluted with 150 ml of water; the dark-colored precipitate was transferred to a filter, washed with alcohol, and dried. Obtained 23.4 g of compound IV. The mother liquor was refluxed with activated carbon, filtered, and cooled, obtaining an additional 5.3 g of compound IV. After driving off part of the solvent, another 6.3 g was recovered. Total yield of compound IV 35.0 g.

By reaction of the thione I with 1,2,3-tribromopropane under analogous conditions, using 60 g of KOH powder, obtained 32 g of compound V.

3-Methylthiazolo[3,2-a]benzimidazole (V, $C_{10}H_8N_2S$). To a suspension of 3 g of powdered KOH in 10 ml of DMSO, 0.1 g of TEBAC and 2.7 g (0.01 mole) of compound IV were added, and the mixture was heated while stirring on a boiling water bath for 3 h. The reaction mixture was diluted with water; the precipitate was separated, dissolved in 100 ml of 10% HCl with heating, refluxed with activated carbon, and filtered; the mother liquor was neutralized with ammonia, and the precipitate was transferred to the filter. Obtained 1.6 g of compound V.

2-(1,2-Propadienylthio)benzimidazole (VI, $C_{10}H_8N_2S$). A. A melt of 7.5 g (0.04 mole) of compound V was heated in a Claisen flask under vacuum (3 mm Hg), while raising the temperature gradually from 135°C to 205°C over the course of 0.5 h, until there was no more foaming or violent boiling of the liquid. After cooling, the melt was washed out with hot alcohol, the solution was refluxed with activated carbon and filtered, part of the solvent was driven off, and the precipitate that formed after cooling the solution was filtered. Yield 6 g.

B. A mixture of 2.7 g (0.01 mole) of compound IV, 3 g (0.01 mole) of ethylenediamine dihydrochloride or 1.1 g (0.01 mole) of o-phenylenediamine, 3 g of potassium carbonate, 0.1 g of TEBAC, and 10 ml of DMF was refluxed for 3 h, cooled, diluted with 20 ml of 5% HCl, refluxed with activated carbon, and filtered; the filtrate was neutralized with ammonia, and the precipitate of compound VI was filtered off. Yield 1.6 g.

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