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INVESTIGATION OF THE HALOCYCLIZATION OF S- AND N-ALLYL DERIVATIVES OF 2-BENZOTHIAZOLETHIONE

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3-Allyl-2-benzothiazolethione reacts with iodine regiospecifically with annelation of the five-membered ring, while with bromine a mixture of the five- and six-membered rings are formed. 2-Allylthiobenzothiazole reacts with halogens with annelation of the five- and six-membered rings, while 2-(2-methyl-2-propenyl)thiobenzothiazole is annelated at the five-membered ring.

Keywords: 2- and 3-halomethyl-2,3-dihydrothiazolo[2,3-*b*]benzothiazolium halides, 3-halo-3,4-dihydro-2H-[1,3]thiazino[2,3-*b*][1,3]benzothiazolium, halocyclization, X-ray crystallography.

Contradictory results on the bromocyclization of 2-allylthiobenzothiazole (**1a**) are described in the literature. For example, according to [1] 3-bromomethyl-2,3-dihydro[1,3]thiazolo[2,3-*b*][1,3]benzothiazolium bromide (**2a**) is formed, whereas according to [2] – 3-bromo-3,4-dihydro-2H[1,3]thiazino[2,3-*b*][1,3]benzothiazolium bromide (**3a**), and according to [3] – a mixture of compound **2a** and 2-bromomethyl-2,3-dihydro[1,3]thiazolo[2,3-*b*]-[1,3]benzothiazolium bromide (**4a**).

It should be noted that the ^{1}H NMR spectrum of compound **2a** obtained in [1] does not correspond to the structure. Thus, a multiplet in the region of 6 ppm, characteristic for proton H-3 in the structures of the similar compounds (3-halomethyl-2,3-dihydrothiazolo[3,2-*a*]pyridinium halides) is missing [4–6]. The structure of compound **3a** was confirmed by ^{1}H NMR data and independent synthesis, but the yield was only 52% which indicates the formation of other reaction products.

With the objective of investigating the direction of the halocyclization reaction, we have studied the interaction of bromine and iodine with compounds **1a**, 2-(2-methylprop-2-en-1-yl)thiobenzothiazole (**1b**), and 3-allylbenzothiazol-2(3H)-thione (**5**).

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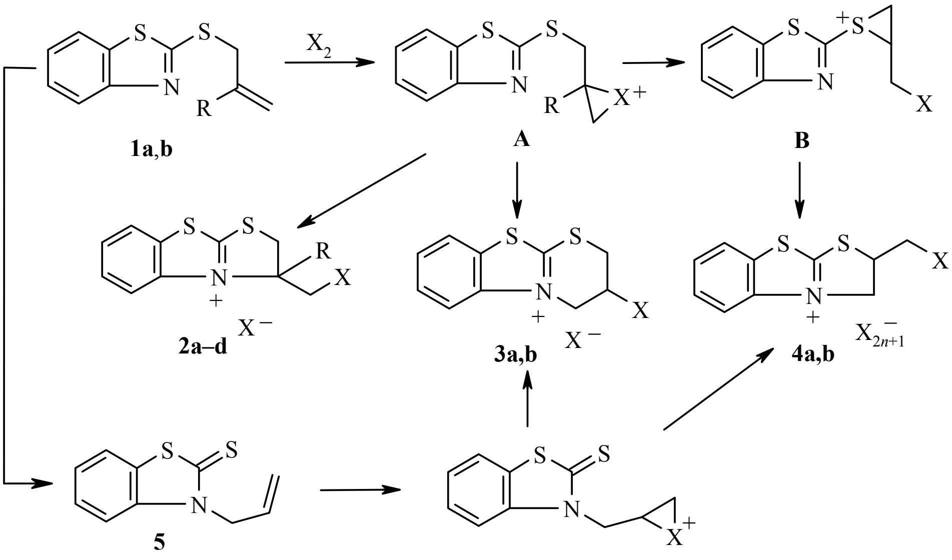

1a, **2a**,**b** R = H, 1b, **2c**,**d** R = Me; **2a,c, 3a**, **4a** X = Br, **2b**,**d, 3b**, **4b** X = I; **4 a** $n = 0$, **b** $n = 1$

Iodocyclization of compound **5** occurred regioselectivity to give a single reaction product, 2-iodomethyl-2,3-dihydro[1,3]-thiazolo[2,3-*b*][1,3]benzothiazolium triiodide (**4b**), the structure of which was established by X-ray crystallography and ^{1}H NMR spectroscopy. According to the X-ray results (Fig. 1) the compound crystallizes in the centrosymmetric space group of the monoclinic class. The deviation of the atoms of the benzothiazole ring from the mean squared plane is less than 0.02 Å. The dihydrothiazole ring of the cation has the *pseudoenvelope* conformation, with atoms C(8), C(1), N(1), and S(2) lying practically in a single plain (deviation less than 0.02Å), while atom C(9) lies 0.354 Å out of the plane. Atom S(2) is involved in the π-conjugation system which appears as more then 0.14 Å length difference between the formally single bonds C(1)–S(2) and S(2)–C(9) (Table 1) and the leveling of the C(1)–S(1), C(1)–S(2), and S(1)–C(7) bond lengths. The I–I bond lengths in the I_3^- anion are practically the same, and the bond angle is close to 180°. The molecular crystal packing is characterized by the presence of a shortened I(4)…I(1) contact (3.845(1) Å).

The ^{1}H NMR spectrum of compound **4b** has proton signals of the groups CH_2I, $=NCH_2$, and SCH at 3.83, 4.93, and 5.05 ppm respectively.

According to the ^{1}H NMR spectrum, the reaction of compound **5** with bromine gave a mixture of two compounds in a 13:1 ratio. The principal product is 2-bromomethyl-2,3-dihydro[1,3]thiazolo[2,3-*b*][1,3]benzothiazolium bromide (**4a**), the ^{1}H NMR spectrum of which is close to that of compound **4a**. According to its ^{1}H NMR spectrum, the second compound is the bromide **3a**.

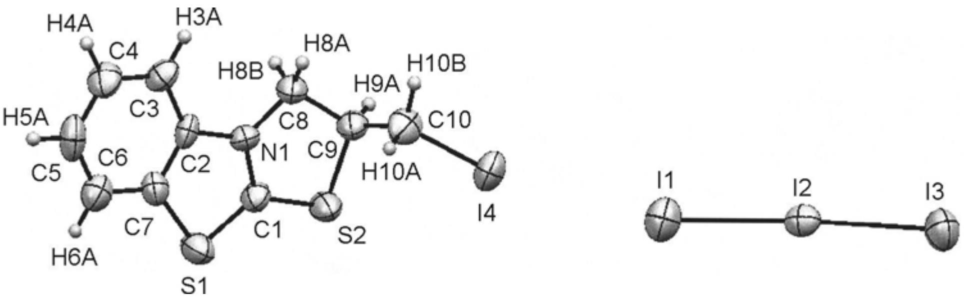

Fig. 1 Overall view of the molecule of compound **4b** from X-ray data.

TABLE 1. Chosen Bond Lengths (*d*) and Valence Angles (ω) of Compound **4b** from X-ray Data

Bond	*d*, Å	Angle	ω, deg
I(1)–I(2)	2.942(8)	I(1)–I(2)–I(3)	176.3(2)
I(2)–I(3)	2.944(8)	C(1)–S(2)–C(9)	91.7(3)
S(1)–C(7)	1.750(6)	C(1)–S(1)–C(7)	90.6(3)
S(1)–C(1)	1.688(6)	S(1)–C(1)–S(2)	131.6(4)
C(1)–S(2)	1.728(6)	C(2)–N(1)–C(8)	129.9(5)
S(2)–C(9)	1.869(6)	C(1)–N(1)–C(2)	114.3(5)
N(1)–C(1)	1.351(6)	C(9)–C(10)–I(4)	113.2(4)
N(1)–C(2)	1.408(7)	N(1)–C(1)–S(1)	113.2(4)
N(1)–C(8)	1.484(7)	N(1)–C(1)–S(2)	115.2(4)
I(4)–C(10)	2.136(6)	C(1)–N(1)–C(8)	115.7(5)

Comparison of the ^{1}H NMR spectra of compounds **3a**, **4a**, and **4b** allows us to establish the structures of the products of halocyclization of compound **1a**. The reaction of compound **1a** with iodine in ethanol gave a 6:1 mixture of 3-iodomethyl-2,3-dihydro[1,3]thiazolo[2,3-*b*][1,3]benzothiazolium iodide (**2b**) and 3-iodo-3,4-dihydro-2H-[1,3]thiazino[2,3-*b*][1,3]benzothiazolium iodide (**3b**). The ^{1}H NMR spectrum of compound **2b** contains a multiplet at 5.86 ppm, characteristic for proton H-3. It was suggested earlier that iodocyclization of compound **1a** gave compounds **2b** and **4b**.

On bromination of compound **1a** in CCl_4 a precipitate is formed immediately which consists of a mixture of the bromides **2a** and **4a**. The ^{1}H NMR spectrum includes a multiplet at 5.75 ppm of the proton H-3 of compound **2a**. Then a 7.5:1 mixture of bromides **3a** and **4a** precipitates from the reaction mixture. The ^{1}H NMR spectrum of compound **3a** coincides with the spectrum we had obtained earlier [3]. In our view compounds **2a** and **3a** are formed by bromination of ion **A** and compound **4a** from the thiiranium ion **B**.

TABLE 2. ^{1}H NMR Spectra of Compounds **1a,b, 2a–d, 3a,b, 4a,b,** and **5**

Compound	Chemical shifts, δ, ppm (*J*, Hz)
1a	7.90–7.30 (4H, m, H Ar); 6.02 (1H, m, =CH); 5.39 (1H, m, $=CH_2$); 5.21 (1H, m, $=CH_2$); 3.99 (2H, m, SCH_2)
1b	7.90–7.21 (4H, m, H Ar); 5.12 (1H, m, $=CH_2$); 4.96 (1H, m, $=CH_2$); 4.02 (2H, s, SCH_2); 1.89 (3H, s, CH_3)
2a	7.80–7.00 (4H, m, H Ar); 5.75 (1H, m, H-3); 4.50 (2H, m, CH_2Br); 3.80 (2H, m, SCH_2)
2b	8.35–7.70 (4H, m, H Ar); 5.86 (1H, m, H-3); 4.54 (1H, dd, *J* = 9.9, *J* = 12.2, CH_2I); 3.97 (2H, m, SCH_2); 3.81(1H, d. d, *J* = 2.4, *J* = 11.7, CH_2I)
2c	8.40–7.70 (4H, m, H Ar); 4.65 (1H, m, CH_2Br); 4.32 (1H, m, CH_2Br); 4.17 (2H, s, SCH_2); 2.12 (3H, s, CH_3)
2d	8.35–7.65 (4H, m, H Ar); 4.65 (1H, m, CH_2Br); 4.37 (1H, d, *J* = 11.7, SCH_2); 4.32 (1H, m, CH_2Br); 4.13 (1H, d, *J* = 11.8, SCH_2); 2.15 (3H, s, CH_3)
3a	8.40–7.80 (4H, m, H Ar); 5.42 (1H, m, CHBr); 5.00 (2H, m, NCH_2); 4.05 (2H, m, SCH_2)
3b	8.40–7.75 (4H, m, H Ar); 5.17 (1H, dd, *J* = 3.9, *J* =13.8, NCH_2); 5.07 (1H, m, CHI); 4.89 (1H, dd, *J* = 8.5, *J* = 13.8, NCH_2); 3.93–4.10 (2H, m, SCH_2)
4a	8.35–7.65 (4H, m, H Ar); 5.15 (1H, m, SCH); 5.05 (2H, m, NCH_2); 4.10 (2H, m, CH_2Br)
4b	8.30–7.65 (4H, m, H Ar); 5.05 (1H, m, SCH); 4.93 (1H, m, NCH_2); 3.83 (2H, m, CH_2I)
5	7.80–7.35 (4H, m, H Ar); 5.90 (1H, m, =CH); 5.22 (1H, m, $=CH_2$); 5.10 (2H, m, NCH_2); 5.08 (1H, m, $=CH_2$)

Compound **1b**, which has an electron-donor methyl group on the β-carbon atom of the allyl unit, reacts with bromine and iodine with annelation of the five-membered ring to give 3-bromomethyl-3-methyl-2,3-dihydro[1,3]thiazolo[2,3-*b*][1,3]benzothiazolium bromide (**2c**) and 3-iodomethyl-3-methyl-2,3-dihydro[1,3]thiazolo[2,3-*b*][1,3]benzothiazolium iodide (**2d**) respectively. According to paper [7], if two methyl groups are on the γ-carbon atom, halocyclization occurs with annelation of the six-membered ring.

EXPERIMENTAL

^{1}H NMR spectra were recorded using Bruker DRX-400 (400 MHz) spectrometer in DMSO-d$_6$ solutions with TMS as internal standard.

2-Allylthiobenzothiazole (**1a**) was obtained by method [10] and 3-allylbenzothiazole-2-thione (**5**) by method [11].

X-ray Crystallographic Analysis of Compound 4b, which was obtained by crystallization from ethanol, was carried out with an Xcalibur 3 automatic four-circle diffractometer using standard procedures (MoKα radiation, graphite monochromator, 295(2) K, ω/2θ scanning). A fragment of a brown prismatic crystal with the dimensions 0.147 × 0.093 × 0.025 mm was used for the analysis. The crystal was monoclinic, space group $P2_1/c$, parameters of the unit cell a = 14.955(2), b = 7.6846(11), c = 15.426(2) Å, β = 96.999(11)°, V = 1759.6(4) Å^3, for the empirical formula $C_{10}H_9I_4NS_2$, $Z = 4$, d_{calc} = 2.699 g/cm^3, μ = 7.303 mm^{-1}. In the range 2.74 < θ < 28.41°, 9313 reflections were collected, of which 4347 (R_{int} = 0.0402) were independent, and 2821 had $I > 2\sigma(I)$, complexity for θ = 28.41° (98.3%). Errors for adsorption were introduced analytically [8] using the multigrain crystal model. The structure was solved and refined using the SHELX complex of programs [9]. All non-hydrogen atoms were refined in the anisotropic approximation, hydrogen atoms were placed in geometrically calculated positions and refined in the "rider" model with depend isotropic thermal parameters. The final parameters of the refined structure were R_1 = 0.0339, wR_2 = 0.0544 (with reflections $I > 2\sigma(I)$ R_1 = 0.0943, wR_2 = 0.0564) (with all reflections at S = 0.993). The peaks of maxima and minima in the final electronic density were Δρ = 1.249 and –0.901 e/Å^3. The results of the X-ray analysis in the form of a cif-file have been registered in the Cambridge Structural Database (deposit CCDC 819767). These data are freely accessible and may be requested at the address *www.ccdc.cam.ac.uk/data_request/cif* or from the authors.

2-(2-Methylprop-2-en-1-yl)thiobenzothiazole (1b). 2-Benzothiazole (1.67 g, 10 mmol) and 3-chloro-2-methylpropene (0.96 g, 10 mmol) were added to a solution of sodium (0.23 g, 10 mmol) in 2-propanol (15 ml). The mixture was boiled for 3 h. After cooling it was filtered, the ethanol was evaporated, the residue was treated with ether to give compound **1b** as a yellow oil. Yield 1.75 g (79%). Found, %: C 59.35; H 4.91; N 6.48; S 28.10. $C_{11}H_{11}NS_2$. Calculated, %: C 59.69; H 5.01; N 6.33; S 28.97.

A Mixture of 3-Bromomethyl-2,3-dihydro[1,3]thiazolo[2,3-*b*][1,3]benzothiazolium (2a), 3-Bromo-3,4-dihydro-2H-[1,3]thiazino[2,3-*b*][1,3]benzothiazolium (3a) and 2-Bromomethyl-2,3-dihydro[1,3]thiazolo[2,3-*b*][1,3]benzothiazolium (4a) Bromides were prepared by method [3].

A Mixture of 2-Bromomethyl-2,3-dihydro[1,3]thiazolo[2,3-*b*][1,3]benzothiazolium (4a) and 3-Bromo-3,4-dihydro-2H-[1,3]thiazino[2,3-*b*][1,3]benzothiazolium (3a) Bromides. A solution of Br_2 (0.1 ml, 2 mmol) in CH_2Cl_2 (3 ml) was added dropwise to a solution of compound **5** (0.21 g, 1 mmol) in CH_2Cl_2 (2 ml) with cooling in ice. After 24 h, the CH_2Cl_2 was evaporated, the residue was treated with acetone and filtered off. Yield 0.24 g (66 %).

3-Bromomethyl-3-methyl-2,3-dihydro[1,3]thiazolo[2,3-*b*][1,3]benzothiazolium Bromide (2c). A solution of Br_2 (0.1 ml, 2 mmol) in $CHCl_3$ (3 ml) was added dropwise to a solution of compound **1b** (0.22 g, 1 mmol) in $CHCl_3$ (2 ml) with cooling in ice. After 24 h, the $CHCl_3$ was evaporated, the residue was treated with acetone, and filtered off to give a yellow residue. Yield 0.23 g (60%); mp 152–155°C. Found, %: Br 42.52; S 16.79. $C_{11}H_{11}Br_2NS_2$. Calculated, %: Br 41.93; S 16.83.

2-Iodomethyl-2,3-dihydro[1,3]thiazolo[2,3-*b*][1,3]benzothiazolium Triiodide (4b). Iodine (0.06 g, 0.1 mmol) in ethanol (3 ml) was added to a solution of compound **5** (0.022 g, 0.1 mmol) in ethanol (2 ml). The brownish crystals (0.30 g, 65%), mp 150°C, were filtered off after 24 h. Found, %: I 71.25; S 8.84. $C_{10}H_9I_4NS_2$ Calculated, %: I 71.00; S 8.97.

Preparation of Compounds 2b,d, 3b (General Method). Iodine (0.5 g, 2 mmol) in ethanol (5 ml) was added to a solution of compound **1a,b** (1 mmol) in ethanol (3 ml). After 48 h, the solution was decanted, the precipitate was dissolved in acetone (3 ml) and a solution of $NaI \cdot 2H_2O$ (0.37 g, 2 mmol) in acetone (3 ml) was added. The yellow precipitate formed was filtered off.

A Mixture of 3-Iodomethyl-2,3-dihydro[1,2]thiazolo[2,3-*b*][1,3]benzothiazolium (2b) and 3-Iodo-3,4-dihydro-2H-[1,3]thiazino[2,3-*b*][1,3]benzothiazolium (3b) Bromides. Yield 0.30 g (65%).

3-Iodomethyl-3-methyl-2,3-dihydro[1,3]thiazolo[2,3-*b*][1,3]benzothiazolium Iodide (2d). Yield 0.28 g (59%); mp 74–76°C. Found,%: I 53.68; S 13.44. $C_{11}H_{11}I_2NS_2$. Calculated, %: I 53.42; S 13.50.

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