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REACTIONS OF 2-AMINOBENZOTHIAZOLES WITH ETHYLENE CHLOROHYDRIN. MOLECULAR AND CRYSTAL STRUCTURE OF BIS[(3-β-HYDROXYETHYL)BENZOTHIAZOLYL-2-INDENE]AMMONIUM CHLORIDE

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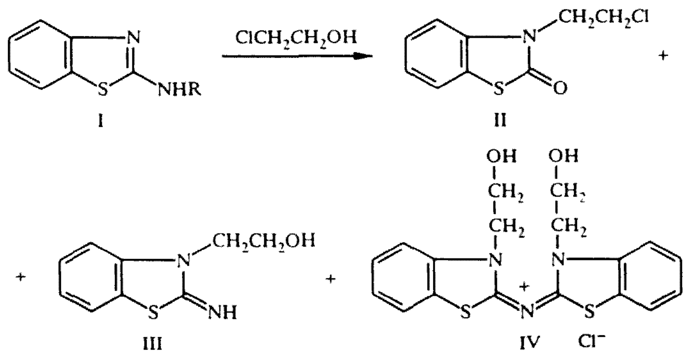
Hydroxyethylation of 2-aminobenzothiazoles by ethylene chlorohydrin unexpectedly led to preferential formation of 3-β-chloroethylbenzothiazolin-2-one. In the case of unsubstituted 2-aminobenzothiazole, we also isolated the target 2-imino-3-β-hydroxyethylbenzothiazoline and bis[(3-β-hydroxyethyl)benzothiazolyl-2-indene]ammonium chloride. As a result of reaction of 2-aminobenzothiazole with 3-β-chloroethylbenzothiazolin-2-one, we obtained 2-(benzothiazolyl-2-imino)-3-[β-(2-oxobenzothiazolin-3-yl)ethyl]benzothiazoline. The structure of the synthesized compounds was established based on x-ray diffraction, PMR, IR, UV, and mass spectra.

Ethylene chlorohydrin, used for introducing hydroxyethyl groups into molecules of amines, including heterocyclic amines, has been used for obtaining aminoalcohols based on aminopyrimidine [1], aminotriazole [2], aminopyridines [3,4], and aminobenzimidazoles [5-7].

This investigation was undertaken with the goal of studying the orientation of hydroxyalkylation of 2-aminobenzothiazole (Ia, R = H) and its 2-substituted derivatives (Ib-e, R = Me, Et, CH_2CH_2OH, Ph respectively) by ethylene chlorohydrin and development of methods for synthesis of ambifunctional heterocyclic aminoalcohols containing a benzothiazole ring. However, when amine Ia is boiled in a solution of ethylene chlorohydrin, as the major reaction product we isolated 3-β-chloroethylbenzothiazolin-2-one (II), the yield of which increased from 27% to 76% when we increased the reaction time from 1 h to 5 h. The target 2-imino-3-β-hydroxyethylbenzothiazoline (III) was obtained in 10-15% yield. From the reaction mixture we also isolated the high-melting product IV, difficultly soluble in organic solvents and water.



In order to determine the structure of the latter, we studied the possibility of reaction of the products of reaction of II and III with each other or with the starting amine Ia. We could only accomplish reaction of amine Ia with 3-β-chloroethylbenzothiazolin-2-one (II), and in this case we isolated and identified 2-(benzothiazolyl-2-imino)-3-[β-(2-oxobenzothiazolin-3-yl)ethyl]benzothiazoline V.

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TABLE 1. Bond Lengths (*d*) in Structure IV

Bond	*d*, Å	Bond	*d*, Å
$S_{(1)}—C_{(2)}$	1,759(6)	$S_{(1)}—C_{(8)}$	1,749(6)
$C_{(2)}—N_{(3)}$	1,352(7)	$C_{(2)}—N_{(13)}$	1,310(7)
$N_{(3)}—C_{(9)}$	1,406(7)	$N_{(3)}—C_{(10)}$	1,485(9)
$C_{(4)}—C_{(5)}$	1,366(9)	$C_{(4)}—C_{(9)}$	1,389(8)
$C_{(5)}—C_{(6)}$	1,400(9)	$C_{(6)}—C_{(7)}$	1,380(9)
$C_{(7)}—C_{(8)}$	1,382(9)	$C_{(8)}—C_{(9)}$	1,400(9)
$C_{(10)}—C_{(11)}$	1,500(9)	$C_{(11)}—O_{(12)}$	1,429(9)
$N_{(13)}—C_{(2')}$	1,312(7)	$S_{(1')}—C_{(2')}$	1,760(6)
$S_{(1')}—C_{(8')}$	1,725(6)	$C_{(2')}—N_{(3')}$	1,342(7)
$N_{(3')}—C_{(9')}$	1,399(7)	$N_{(3')}—C_{(10')}$	1,495(8)
$C_{(4')}—C_{(5')}$	1,386(9)	$C_{(4')}—C_{(9')}$	1,395(8)
$C_{(5')}—C_{(6')}$	1,400(9)	$C_{(6')}—C_{(7')}$	1,371(9)
$C_{(7')}—C_{(8')}$	1,400(9)	$C_{(8')}—C_{(9')}$	1,387(9)
$C_{(10')}—C_{(11')}$	1,494(8)	$C_{(11')}—O_{(12')}$	1,426(9)

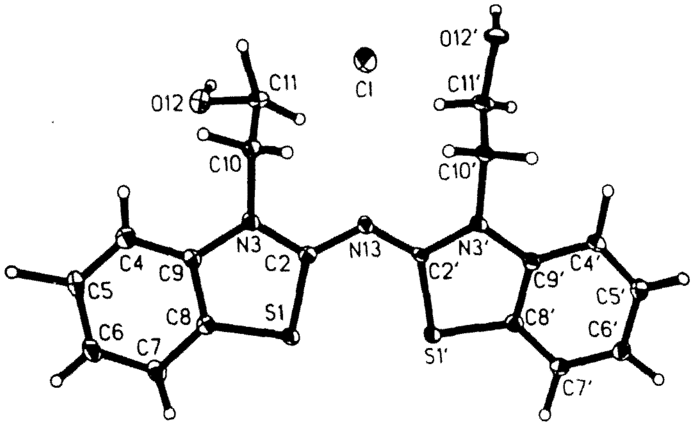
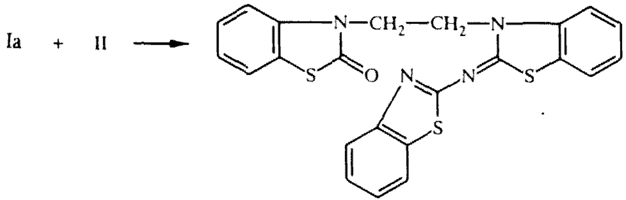


Fig. 1. Molecular structure of compound IV.



V

Product IV was different from compound V with respect to physical constants and spectral characteristics. In the liquid-matrix secondary-ion mass spectra (LSIMS) of this product, we detected a peak for the protonated ion with *m/z* 371 and fragments corresponding to sequential ejection of two oxirane molecules from it. These data are consistent with structure IV shown in the scheme, but for such a molecule it is difficult to represent the main direction of fragmentation with formation of a fragmentary ion with *m/z* 221 of maximum intensity.

The reaction of 2-alkyl- and 2-hydroxyethylaminobenzothiazoles Ib-d with ethylene chlorohydrin occurs even more specifically. In this case, as a result of 5 h boiling, only compound II is formed in 83-87% yield. On alkaline neutralization of the reaction mixture, we smell the odor of aliphatic amines, which are cleaved from compounds Ib-d. The 2-phenylaminobenzothiazole Ie under these conditions does not react with ethylene chlorohydrin.

The spatial structure of compound IV is shown in Fig. 1, from which we see that it is bis(3-β-hydroxyethylbenzothiazolylidene)ammonium chloride. The magnitudes of the symmetric torsional angles $N_{(13)}—C_{(2)}—N_{(3)}—C_{(10)}$ (−1.1°), $N_{(13)}—C_{(2')}—N_{(3')}—C_{(10')}$ (1.6°), and $C_{(2')}—N_{(13)}—C_{(2)}—S_{(1)}$ (1.3°), $C_{(2)}—N_{(13)}—C_{(2')}—S_{(1')}$ (2.7°) (Fig. 1) suggest that like heteroatoms (S, N) are located *syn* relative to the $N_{(13)}$ atom. The benzothiazoline rings in salt IV, bonded through $N_{(13)}$, are practically coplanar (rotated by only 6° relative to each other), which favors formation of a planar conjugated system.

TABLE 2. Bond Angles (φ, degrees) in Molecule IV

Angle	φ	Angle	φ
$C_{(2)}S_{(1)}C_{(8)}$	91,6(3)	$C_{(2')}S_{(1')}C_{(8')}$	90,9(3)
$C_{(2)}N_{(3)}C_{(9)}$	115,3(5)	$N_{(13)}C_{(2')}N_{(3')}$	121,5(5)
$C_{(9)}N_{(3)}C_{(10)}$	123,3(5)	$C_{(2')}N_{(3')}C_{(9')}$	114,9(5)
$C_{(4)}C_{(5)}C_{(6)}$	120,9(6)	$C_{(4')}C_{(5')}C_{(6')}$	122,0(6)
$C_{(6)}C_{(7)}C_{(8)}$	116,8(6)	$C_{(6')}C_{(7')}C_{(8')}$	118,3(6)
$S_{(1)}C_{(8)}C_{(9)}$	110,3(4)	$S_{(1')}C_{(8')}C_{(9')}$	111,6(4)
$N_{(3)}C_{(9)}C_{(4)}$	128,1(6)	$N_{(3')}C_{(9')}C_{(4')}$	126,5(6)
$C_{(4)}C_{(9)}C_{(8)}$	119,5(5)	$C_{(4')}C_{(9')}C_{(8')}$	121,6(6)
$S_{(1)}C_{(2)}N_{(3)}$	110,4(4)	$C_{(2)}N_{(13)}C_{(2')}$	123,8(5)
$C_{(5)}C_{(4)}C_{(9)}$	118,8(6)	$S_{(1')}C_{(2')}N_{(3')}$	110,6(4)
$C_{(5)}C_{(6)}C_{(7)}$	121,6(6)	$C_{(5')}C_{(4')}C_{(9')}$	116,8(6)
$S_{(1)}C_{(8)}C_{(7)}$	127,3(5)	$C_{(5')}C_{(6')}C_{(7')}$	120,7(6)
$C_{(7)}C_{(8)}C_{(9)}$	122,4(5)	$S_{(1')}C_{(8')}C_{(7')}$	127,7(5)
$N_{(3)}C_{(9)}C_{(8)}$	112,3(5)	$C_{(7')}C_{(8')}C_{(9')}$	120,7(5)
$N_{(3)}C_{(2)}N_{(13)}$	120,3(6)	$N_{(3')}C_{(9')}C_{(8')}$	111,9(5)
$C_{(2)}N_{(3)}C_{(10)}$	121,4(5)	$C_{(9')}N_{(3')}C_{(10')}$	123,0(5)
$S_{(1)}C_{(2)}N_{(13)}$	129,4(5)	$C_{(2')}N_{(3')}C_{(10')}$	122,1(5)
$N_{(3)}C_{(10)}C_{(11)}$	112,4(6)	$N_{(3')}C_{(10')}C_{(11')}$	110,4(5)
$C_{(10)}C_{(11)}O_{(12)}$	109,0(5)	$C_{(10')}C_{(11')}O_{(12')}$	109,7(6)
$N_{(13)}C_{(2')}S_{(1')}$	127,9(4)		

TABLE 3. Coordinates of Atoms ($\times 10^4$) and Temperature Factors U_{eq} ($Å^2 \times 10^3$) for Structure IV

Atom	x	y	z	U_{eq}
Cl	5526(3)	3178(2)	7429(2)	54
$S_{(1)}$	2048(2)	-1620(2)	5642(1)	35
$C_{(2)}$	2236(8)	-61(6)	6050(5)	30
$N_{(3)}$	1984(6)	-144(5)	7186(4)	32
$C_{(4)}$	1346(9)	-1797(7)	8933(5)	43
$C_{(5)}$	1137(9)	-3115(7)	9345(6)	43
$C_{(6)}$	1245(9)	-4071(7)	8619(6)	49
$C_{(7)}$	1521(9)	-3714(6)	7462(5)	42
$C_{(8)}$	1697(8)	-2371(6)	7055(5)	32
$C_{(9)}$	1643(8)	-1412(6)	7773(5)	31
$C_{(10)}$	2141(9)	1016(6)	7762(5)	42
$C_{(11)}$	469(10)	2067(6)	7656(5)	46
$O_{(12)}$	-874(7)	1493(5)	8320(4)	56
$N_{(13)}$	2600(7)	1065(5)	5426(4)	32
$S_{(1')}$	2731(2)	47(2)	3416(1)	36
$C_{(2')}$	2869(8)	1221(5)	4321(5)	27
$N_{(3')}$	3348(6)	2365(5)	3732(4)	31
$C_{(4')}$	4002(8)	3464(6)	1753(5)	37
$C_{(5')}$	4171(8)	3260(7)	633(5)	42
$C_{(6')}$	3933(9)	2035(7)	322(5)	43
$C_{(7')}$	3463(9)	998(6)	1117(5)	40
$C_{(8')}$	3273(8)	1186(6)	2252(5)	33
$C_{(9')}$	3546(8)	2395(6)	2558(5)	33
$C_{(10')}$	3649(8)	3511(6)	4299(5)	34
$C_{(11')}$	1994(9)	4562(6)	4244(6)	46
$O_{(12')}$	2352(6)	5715(4)	4677(4)	51

The bond lengths (Table 1) and bond angles (Table 2) in molecule IV are consistent with the observed values in other iminobenzothiazolines [8-10]. We should note that, although the $C_{(2)}—N_{(13)}$ and $C_{(2')}—N_{(13)}$ bonds are shortened the most, the multiplicity of the $C_{(2)}—N_{(3)}$ and $C_{(2')}—N_{(3')}$ bonds also is increased, i.e., we observe redistribution of the electron density owingto $p—\pi$ conjugation of the unshared electron pair of the $N_{(3)}$ and $N_{(3')}$ atoms with the π-electron system of these bonds. According to the Bayer scheme in [11], the formally single bonds $C_{(2)}—N_{(3)}$ and $C_{(2')}—N_{(3')}$ and the formally double bonds

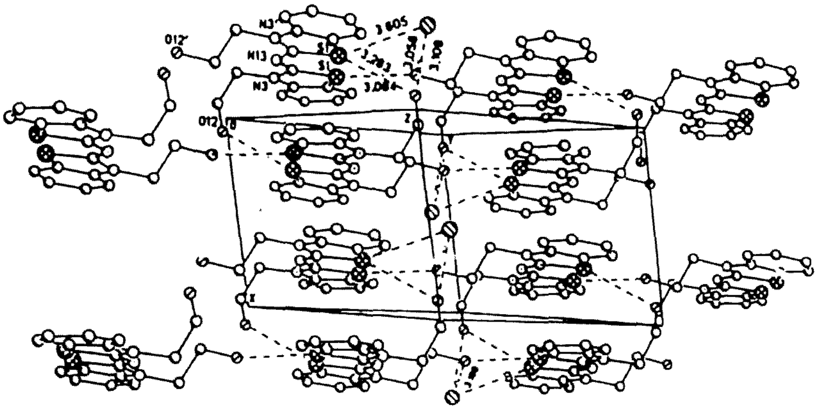


Fig. 2. Packing of molecules of compound IV in the crystal.

$C_{(2)}—N_{(13)}$ and $C_{(2')}—N_{(13)}$ have multiplicity on the average of 1.45 and 1.65 respectively. Delocalization of these bonds is confirmed by the absence in the IR spectrum of an absorption band for the exocyclic C—N bond in the 1610-1650 cm^{-1} region.

The fact that the $C_{(2)}—S_{(1)}$ and $C_{(2')}—S_{(1')}$ bonds are longer than the $C_{(8)}—S_{(1)}$ and $C_{(8')}—S_{(1')}$ bonds (Table 1) indicates stronger conjugation of the unshared electron pairs of the S atoms with the p-electron systems of the benzene rings than with the p-electrons of the C—N bonds.

On the whole, the molecule is symmetric, although the torsional angles formed by the hydroxyethyl groups are different from each other: in the case of $N_{(3)}C_{(10)}C_{(11)}O_{(12)}$, this angle is −69.0°, while for $N_{(3')}C_{(10')}C_{(11')}O_{(12')}$ it is −173.8°.

In Fig. 2, we show the packing of molecule IV in the crystal. The Cl^- anion participates in the intermolecular interactions and is bonded through a hydrogen bond with the hydroxyl groups of both moieties (the distances $Cl...O_{(12)}$ and $Cl...O_{(12')}$ (1+x, −y,z) are respectively 3.058 and 3.109 Å). The Cl^- ion also participates in a donor—acceptor interaction with the $S_{(1')}$ atom, evidence for which comes from the distance between them, equal to 3.605 Å (x, −y,z). Furthermore, we observe interaction of the hydroxyl groups also with the sulfur atoms of the benzothiazoline rings ($S_{(1)}...O_{(12')}$ (x, −y,z) and $S_{(1')}...O_{(12)}$ (1+x,y,z) equal to 3.084 and 3.283 Å respectively). All these interactions create an intricate unbroken chain, directed along the crystallographic *b* axis.

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer and the UV spectra were taken on a Hitachi EPS-3T instrument in ethanol. The PMR spectra in deuterochloroform were measured on a Tesla BS-567 spectrometer with operating frequency 100 MHz, internal standard TMS. The full-range mass spectra were recorded on a double-focusing MKh-1310 instrument, direct injection of the sample (SVP-5), temperature of the ionization chamber equal to 150-180°C, ionizing potential 70 eV. For recording the LSIMS spectrum, we used a beam of accelerated C_s ions with energy 7 keV, accelerating potential 5 kV. The sample of compound IV was dispersed in glycerin and deposited on a steel target with direct injection of the sample.

X-Ray Diffraction Study. Yellowish, needle-shaped crystals of salt IV were obtained from water. The space group and the unit cell parameters were established on a Syntex-$P2_1$ diffractometer using CuKα radiation, graphite monochromator, $\theta/2\theta$ scanning, $\theta < 58°$: $a = 7.664(2)$, $b = 10.090(2)$, $c = 11.899(2)$ Å, $\alpha = 79.30(3)$, $\beta = 89.19(3)$, $\gamma = 79.63(3)°$, $d_{calc} = 1.524$ g/cm^3, triclinic crystals, space group P1, Z = 2.

The full set of experimental reflections (2358) was obtained on the above-indicated diffractometer. In the primary treatment of the data file, we excluded the weak reflections with $I < 2\sigma(I)$. In the calculations, we used 1717 reflections with $|F| > 4\sigma(|F|)$. The structure was determined by the direct method using the program SHELXS-86 [12] and refined in the full-matrix isotropic—anisotropic approximation using the program SHELX-76 [13] (both programs in the PC version for MS DOS). The H atoms, whose original positions were calculated, were refined isotropically. The final value of the reliability index was $R = 0.053$ ($R_w = 0.053$). The coordinates of the nonhydrogen atoms are presented in Table 3.

Bis[3-β-hydroxyethyl)benzothiazolyl-2-idene)]ammonium Chloride (IV). A solution of 1.5 g (0.01 moles) amine Ia in 2.5 ml ethylene chlorohydrin was boiled for 1 h. The reaction mixture was evaporated in air to dryness and 0.57 g (27%)

3-β-chloroethylbenzothiazolin-2-one (II) was extracted with hot hexane (2×2 ml), mp 66-67° [11]. The residue after extraction was washed with acetone (2×2 ml), then with water (2×10 ml). Obtained: 0.41 g (20%) compound IV. mp 259-261°C. IR spectrum: 3260, 3210 (OH), 1535 cm^{-1} (C=N). UV spectrum, λ_{max}: 210, 269, 306, 369, 380 nm. Mass spectrum, *m/z* (I_{rel}, %): 371 (11), 327 (9), 283 (13), 256 (16), 221 (100), 202 (29), 177 (33), 164 (38), 151 (91), 150 (72), 149 (61), 136 (91). Found, %: C 53.0, H 4.4, N 10.3. $C_{18}H_{18}ClN_3O_2S_2$. Calculated, %: C 52.0, H 4.2, N 10.0. The wash waters were neutralized with base, and 0.23 g (12%) aminoalcohol III was obtained, mp 123-124°C (from ethanol) [15].

Reaction of amines Ib-d with ethylene chlorohydrin was carried out similarly.

2-(Benzothiazolyl-2′-imino)-3[β-(2′-oxobenzothiazolin-3′-yl)ethyl]benzothiazoline (V). 1.07 g (0.005 moles) oxazolidone II and 0.75 g (0.005 moles) amine Ia in 10 ml *m*-xylene were boiled for 30 h; the precipitate was filtered off and washed with ethanol. Obtained: 0.2 g (9%) compound V, mp 217-218°C (from ethanol). IR spectrum: 1685 (C=O), 1530 cm^{-1} (C=N). UV spectrum, λ_{max}: 214, 228 (shoulder), 255 (shoulder), 266 (shoulder), 290, 350 nm. PMR spectrum: 4.35 (2H, t), 4.60 (2H, t), 7.00-7.90 (12H, m). Mass spectrum, *m/z* (I_{rel}, %): 460 (36, M$^+$), 310 (11), 296 (3), 283 (100), 178 (6), 150 (8), 149 (9), 136 (15), 109 (24). Found, %: C 59.9, H 3.5, N 12.2. $C_{23}H_{16}N_4OS_3$. Calculated, %: C 60.0, H 3.8, N 12.2.

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