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CYCLIZATION REACTIONS
31.* SYNTHESIS OF 2-METHYL-2-HALOMETHYLBENZIMIDAZO[2,1-b]THIAZOLIDINIUM SALTS AND THEIR CONVERSIONS TO N-(2-METHYL-2,3-EPITHIOPROPYL)BENZOTHIAZOL-2-ONES

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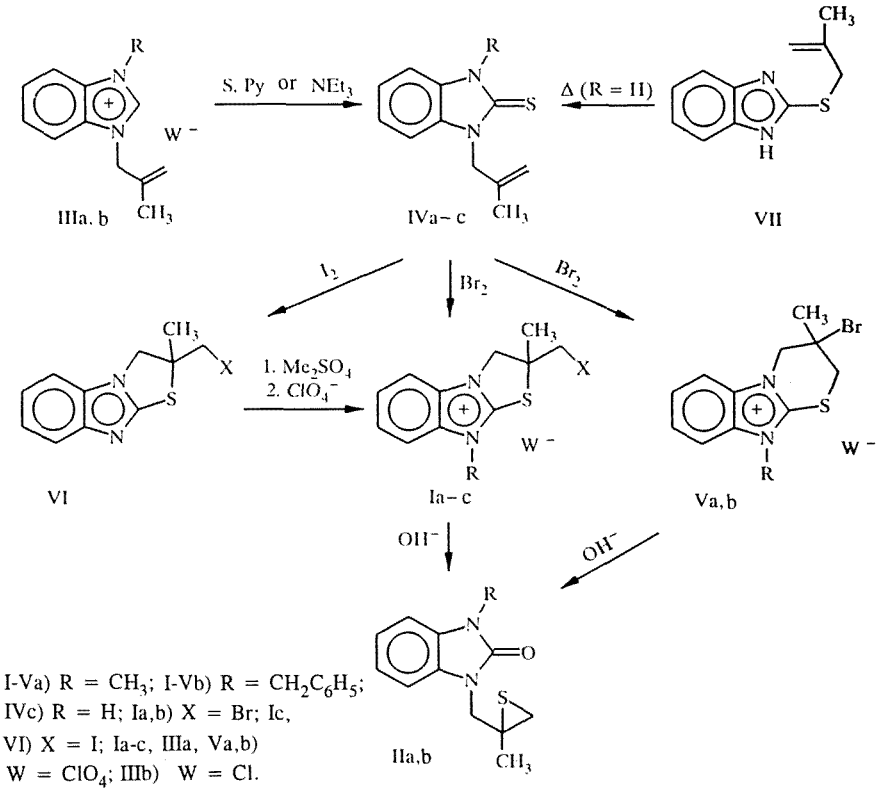
In a novel synthesis, from 2-methyl-2-halomethylbenzimidazo[2,1-b]thiazolidinium salts, by means of their recyclization under the influence of alkali, N-(2-methyl-2,3-epithiopropyl)benzimidazol-2-ones have been obtained. Syntheses of the indicated salts from N-methallylbenzimidazole-2-thiones are described.

It is known that, through recyclization of 3-hydroxy- and 3-haloazolothiazanium salts under the influence of alkali, azacyclic derivatives of thiiranes are obtained [2, 3], and from 3-halomethylchalcoazolidinium salts — derivatives of thietanes and celenetanes [4].

We have shown for the first time that by the action of alkali on 2-halomethylbenzimidazo[2,1-b]thiazolidinium salts (Ia-c), which are isomeric to the above-indicated ionic structures, azolone derivatives of thiiranes (IIa, b) are obtained in high yields (see the reaction scheme and Table 1).



*For communication 30, see [1].

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TABLE 1. Characteristics of Synthesized Compounds Ia-c, IIa,b, IIIa,b, IVa,b, and VI

Compound	Empirical formula	mp, °C (and solvent for crystallization)	R_f in 10:1 $CHCl_3$—MeOH system	Yield, %
Ia*	$C_{12}H_{14}BrClN_2O_4S$	154...156 (acetic acid)	0,39	80
Ib*	$C_{18}H_{18}BrClN_2O_4S$	210...212 (acetic acid)	0,47	88
Ic	$C_{12}H_{14}ClIN_2O_4S$	164...165 (isopropyl alcohol)	0,35	76
IIa	$C_{12}H_{14}N_2OS$	78...80 (hexane—isopropyl alcohol, 10:1)	0,82	82
IIb	$C_{18}H_{18}N_2OS$	Tarry product	0,92	70
IIIa	$C_{12}H_{15}ClN_2O_4$	151...151,5 (water—acetic acid, 2:1) 2 : 1)	—	56
IIIb	$C_{18}H_{19}ClN_2$	150...151 (dimethylformamide)	0,25	74
IVa	$C_{12}H_{14}N_2S$	80...82 (isopropyl alcohol)	0,90	94
IVb	$C_{18}H_{18}N_2S$	105...106 (isopropyl alcohol)	0,93	91
VI	$C_{11}H_{17}IN_2S$	121...122 (isopropyl alcohol)	0,75	83

*Yields and melting points of salts Ia, b are given for their mixtures with thiazanium salts Va, b (38% and 63% thiazane component), as the pair of salts separates and crystallizes together.

The starting compounds Ia, b were synthesized from the N-methallylbenzimidazolium salts (IIIa, b). Initially, by the action of bases (tertiary amines or alkalis) and sulfur, azolethiones (IVa, b) were obtained; these were converted by cyclization under the action of bromine in carbon tetrachloride. However, this latter reaction resulted in the formation of not only the thiazolidinium salts Ia, b, but also 3-bromothiazanium salts (Va, b), analogous to the products of heterocyclization of 2-allylthiobenzothiazole, which we had obtained previously [3].

The salt mixtures Ia, Va and Ib, Vb crystallize together. We were not able to separate these pairs of salts. According to the PMR spectra, the content of the salts Ia, b in these mixtures is 62% and 37%, respectively.

Compound Ic is obtained in two stages. Initially, by cyclization of the NH-containing thione IVc under the action of iodine in a two-phase system consisting of chloroform and an aqueous caustic solution, the iodomethylthiazolidine VI is obtained. In the same manner as in the heterocyclization of methallylthiazoles [4], in this case the reaction is clear-cut, proceeding only in the direction of derivatives of the five-membered rings, apparently because of steric hindrance to entry of the iodine into position 2 of the methallyl group. Quaternization of the thiazolidine VI by dimethyl sulfate, followed by replacement of the anion by perchlorate, leads to the salt Ic.

Preparation of the monosubstituted thione is performed by analogy with a method given in [5], by rearrangement of the 2-methallylthiobenzimidazole at 200°C to an N-methylpyrrolidone.

In contrast to the conversion of the salts Ia, b, the cyclization of compound Ic in an alkaline medium is not clear-cut: Along with the thiirane IIa, the reaction yields an approximately equal quantity of an unidentified product that we were not able to isolate in pure form.

Similar to the conversions of 3-bromothiazanium and 3-halomethylchalcoazolidinium salts [3, 4], the recyclization of the cations Ia-c probably includes successive formation of pseudobases (I, W = OH), meso-hydroxy derivatives (VII), and thiolate anions (VIII). (See scheme on following page.)

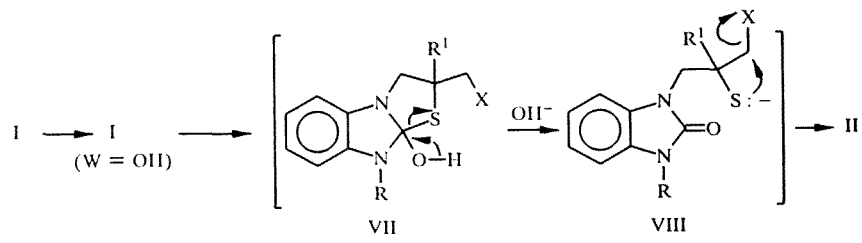
The compositions and structures of the synthesized compounds were confirmed by elemental analysis and by their IR and PMR spectra (Table 2); the individuality of the compounds was confirmed by thin-layer chromatography.

TABLE 2. IR and PMR Spectra of Synthesized Compounds

Compound	IR spectrum, cm^{-1}	PMR spectrum, δ, ppm*
Ia**	3040 w (C—H arom.); 1550 av ($C=N^+$); 1610 w, 1515 w (C=C arom.); 1100 s (ClO_4)	1,96 (3H, s, CH_3C); 3,92 (3H, m, CH_3N); 4,28 (2H,m, CH_2Br); 4,65 (1H, d, CH_2N); 4,87 (1H, d, CH_2N); 7,59, 7,85 (4H, m, Ar)
Ib**	3080 w (C—H arom.); 1520 av ($C=N^+$); 1605 w, 1500 sh (C=C arom.); 1100 s (ClO_4)	1,87 (3H, s, CH_3C); 4,20 (2H, m, CH_2Br); 4,58 (1H, d, CH_2N); 4,81 (1H, d, CH_2N); 5,59 (2H, d, CH_2N); 7,36, 7,55, 7,90 (9H,m, Ar)
Ic	—	1,97 (3H, s, CH_3C); 3,90 (2H, s, CH_3N); 4,10 (2H,m, CH_2I); 4,68 (1H, d, CH_2N); 4,75 (1H, d, CH_2N); 7,58, 7,84 (4H,m, Ar)
IIa	3060 w (C—H arom.); 1720 s, 1690 s (C=O); 1618 av (C=C arom.)	1,60 (3H, s, CH_3C); 2,42 (1H, s, CH_2S); 2,74 (1H, s, CH_2S); 3,44 (3H, s, CH_3N); 4,16 (2H, d, CH_2N); 7,00, 7,12 (4H,m, Ar)
IIb	—	1,62 (3H, s, CH_3C); 2,40 (1H, s, CH_2S); 2,75 (1H, s, CH_2S); 4,22 (1H, d, CH_2N); 5,08 (2H, s, CH_2N); 7,00, 7,28 (4H, m, Ar)
IIIa	3140 w (C—H imide); 3080 w (C—H arom.); 1655 w (C=C aliph.); 1575 av ($C=N^+$); 1606 av, 1485 sh (C=C arom.)	1,75 (3H, s, CH_3C); 4,12 (3H, s, CH_3N); 5,02 (2H, d, CH_2=C); 5,13 (2H, s, CH_2N); 7,72, 8,00 (4H,m, Ar); 9,69 (1H, s, CHN)
IIIb	3122 w (C—H imide); 3055 w (C—H arom.); 1655 w (C=C aliph.); 1560 av ($C=N^+$); 1610 cp, 1490 sh (C=C arom.)	1,74 (3H, s, CH_3C); 5,00 (2H, d, CH_2=C); 5,24 (2H, s, CH_2N); 5,90 (2H, s, CH_2N); 7,36, 7,70, 8,05 (9H,m, Ar); 10,51 (1H, s, CHN^+)
IVa	3080 w (C—H arom.); 1610 w, 1485 sh (C=C arom.); 1352 av (NC=S)	1,77 (3H, s, CH_3C); 3,02 (3H, s, CH_3N); 4,50 (1H, s, CH_2=C); 4,95 (1H, s, CH_2=C); 4,95 (2H, s, CH_2N); 7,20 (4H,m, Ar)
IVb	3060 w (C—H arom.); 1605 w, 1490 sh (C=C arom.); 1340 av (NC=S)	1,79 (3H, s, CH_3C); 4,80 (1H, s, CH_2=C); 4,97 (1H, s, CH_2=C); 5,00 (2H, s, CH_2N); 5,62 (2H, s, CH_2N); 7,17, 7,33 (9H,m, Ar)
Va	—	2,14 (3H, s, CH_3C); 3,92 (3H, s, CH_3N); 3,99 (2H, s, CH_2S); 4,66 (1H, d, CH_2N); 5,07 (1H, d, CH_2N); 7,59, 7,85 (4H,m, Ar)
Vb	—	2,09 (3H, s, CH_3C); 3,93 (2H, s, CH_2S); 4,63 (1H, d, CH_2N); 5,07 (1H, d, CH_2N); 5,67 (2H, d, CH_2N); 7,36, 7,55, 7,90 (9H,m, Ar)
VI	—	1,92 (3H, s, CH_3C); 3,78 (2H, m, CH_2I); 4,02 (1H,m, CH_2N); 4,52 (1H, m, CH_2N); 7,24, 7,65 (4H,m, Ar)

*PMR spectra of compounds Ia, b, IIIa, b, and Va, b were recorded in DMSO-d_6, compounds IIa, b and IVa, b in $CDCl_3$.

**IR spectra of compounds Ia, b were recorded for mixtures of isomers Ia, Va and Ib, Vb.



VII VIII

In the PMR spectra of the salts Ia-c, characteristic signals are observed from protons of CH_2Hal groups (4.1-4.3 ppm) and CH_2N (4.6-4.9 ppm); in the spectra of the salts Va, b, signals of CH_2S and CH_2N groups are observed in the respective regions 3.9-4.0 and 4.6-5.1 ppm, and the CH_3C group at approximately 2.1 ppm. The signals of CH_2I and CH_2N of the neutral thiazolidine VI are shifted upfield by 0.3-0.7 ppm relative to the signals of the salt Ic. In the spectra of the thiiranes IIa, b, characteristic signals are observed from cyclic protons CH_2S (2.4-2.8 ppm), CH_2N (4.2 ppm), and CH_3C (1.6 ppm); in the spectra of the methallylazolium salts IIIa, b, characteristic signals are observed from CH_2=C (5.0 ppm), CH_2N (5.1-5.9 ppm), and CH_3C (1.7-1.8 ppm); for the azolethiones IVa, b, characteristic signals are observed from CH_2=C (4.5-5.0 ppm), CH_2N (5.0-5.6 ppm), and CH_3C (1.8 ppm).

In the IR spectra of the salts Ia-c and Va, b, there are absorption bands from C—Br bonds (ν 760 cm^{-1}) and C=C aromatic bonds (1500-1610 cm^{-1}).

EXPERIMENTAL

The PMR spectra were taken in a Varian (USA) Gemini 200 spectrometer (200 MHz) in DMSO-d_6 or $CDCl_3$. Internal standards were tetramethylsilane and hexamethyldisiloxane. The IR spectra were recorded in a UR-20 instrument (Germany), in white mineral oil, with slit program 4, scanning rate 160 cm^{-1}/min. The thin-layer chromatography was performed on Silufol sorbent (Czech Republic), 10:1 mixture of chloroform and methanol as eluent, and iodine vapor as developer.

Elemental analyses of compounds Ia-c, IIa, b, IIIa, b, IVa, b, Va, b, and VI for C, H, Br, Cl, I, N, and S matched the calculated values.

2-Methyl-2-bromomethyl-9-alkyl(aralkyl)benzimidazo[2,1-b]thiazolidinium perchlorate (Ia, b). To a solution of 15 mmoles of 1-substituted-3-methallylbenzimidazole-2-thione IVa, b in 20 ml of CCl_4, at 60°C, 0.77 ml (15 mmoles) of bromine was added while stirring. The mixture was stirred for another 0.5 h at the same temperature and then cooled. The precipitate was filtered off and dissolved in 10 ml of acetone containing 2.45 g of sodium perchlorate. The sodium bromide precipitate that was formed was filtered off, and the filtrate was evaporated to dryness. The residue, consisting of a mixture of salts Ia, Va or Ib, Vb and sodium perchlorate, was washed with water and recrystallized.

2,9-Dimethyl-2-iodomethylbenzimidazo[2,1-b]thiazolidinium perchlorate (Ic). To a solution of 1g (3 mmoles) of the thiazolidine VI in 1 ml of dimethylformamide, 0.7 ml (7 mmoles) of dimethyl sulfate was added, and the mixture was held at 60°C for 5 h. The solution was diluted with ether; the oil that separated was removed by decantation, dissolved in 10 ml of water, and filtered. Then 1.2 g of sodium perchlorate was added to the filtrate. The precipitated salt Ic was filtered off, dried, and recrystallized.

Analogously, from 1-methallylbenzimidazole and alkylating agents (methyl iodide or benzyl chloride), the salts IIIa, b were obtained; in the case of compound IIIa, the anion was subsequently replaced by perchlorate.

Compounds Ic, IIIa, b, IVa, b, and the mixtures Ia, Va and Ib, Vb are colorless crystalline substances, soluble in aprotic polar solvents and in alcohols.

1-Alkyl-3-(2,3-epithiopropyl)benzimidazol-2-ones (IIa,b). ***A***. A 10-mmole mixture of the salt I with Va or Vb was suspended in 50 ml of ether and 50 ml of methanol, after which 4.0 g of a 20% aqueous sodium hydroxide solution was added dropwise over the course of 0.5 h. Stirring was continued for 0.5-1 h. The ether layer was separated and washed with water (3 × 20 ml), dried with anhydrous sodium sulfate, and evaporated; compound IIa was recrystallized.

B. To a solution of 10 mmoles of I with Va or Vb in 30 ml of dimethylformamide, 1.15 g of powdered potassium hydroxide was added over the course of 0.5 h. The mixture was stirred for another 3 h. To the suspension that was obtained, 200 ml of ether and 100 ml of water were added. The ether layer was washed with water (2 × 100 ml), dried with anhydrous sodium sulfate, and evaporated. Colorless oily products were obtained, from which compound IIa crystallized upon storage for several hours, after which it was purified by recrystallization.

The products IIa, b are soluble in most solvents other than hydrocarbons and water.

1-Alkyl(aralkyl)-3-methallylbenzimidazole-2-thiones (IVa, b). To a solution or dispersion of 47 mmoles of the benzimidazolium salt IIIa, b in 20 ml of acetonitrile, 1.76 g of sulfur and 7.6 ml of triethylamine were added, and the mixture was refluxed for 2 h. The resulting solution was poured into 100 ml of water. The precipitate was filtered off and purified by crystallization. We also used dimethylformamide solutions of the salt III, replacing the triethylamine by 20 ml of pyridine or by the gradual addition of 2 g (50 mmoles) of sodium hydroxide, at 20°C.

The colorless crystalline products IVa, b are soluble in alcohols, benzene, chloroform, ether, and aprotic polar solvents.

2-Methyl-2-iodomethylbenzimidazo[2,1-b]thiazolidine (VI). To a solution of 1.72 g (8.5 mmoles) of 1-methylbenzimidazole-2-thione IVc in 17 ml of chloroform, 4.3 g (17 mmoles) of iodine and 3 ml of water were added. The resulting two-phase system was stirred while gradually adding 2.22 g (39.3 mmoles) of pulverized solid potassium hydroxide until the solution was completely decolorized. The chloroform layer was separated, washed with water (3 × 10 ml), dried with anhydrous sodium sulfate, and evaporated under vacuum. The thiazolidine VI was obtained in the form of a yellowish powder, which was purified by recrystallization.

REFERENCES

1. N. I. Korotkikh and O. P. Shvaika, Khim. Geterotsikl. Soedin., No. 3, 412 (1993).
2. N. I. Korotkikh, A. F. Aslanov, and O. P. Shvaika, Zh. Org. Khim., **26**, 1761 (1990).
3. N. I. Korotkikh, A. F. Aslanov, and O. P. Shvaika, Khim. Geterotsikl. Soedin., No. 6, 855 (1990).
4. O. P. Shvaika, N. I. Korotkikh, and A. F. Aslanov, Dokl. Akad. Nauk Ukr. SSR, Ser. B, No. 4, 112 (1991).
5. K. M. Krivosheiko and A. V. El'tsov, Zh. Org. Khim., **4**, 1114 (1968).
6. O. P. Shvaika, N. I. Korotkikh, A. F. Aslanov, et al., Dokl. Akad. Nauk Ukr. SSR, Ser. B, No. 5, 46 (1990).