BENZAZOLIN-2-THIONES IN THE MICHAEL REACTION.

1. REACTION OF BENZOTHIAZOLIN- AND BENZOXAZOLIN-2-THIONES WITH ACRYLONITRILE, ACRYLAMIDE, AND METHYLACRYLATE IN THE PRESENCE OF ACID CATALYSTS

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The reaction of benzothiazolin- and benzooxazolin-2-thiones with acrylonitrile, acrylamide, and methylacrylate under conditions of acid catalysis takes place at the sulfur atom. The formation of minor amounts of N-derivatives is attributed to isomerization of the principal reaction products.

In continuation of our study of the behavior of benzoazolin-2-thiones in nucleophilic addition reactions [1] intended for the synthesis of potential pesticides, we have investigated the effect of acid catalysts on the reactions of benzothiazolin- and benzoxazolin-2-thiones (Ia, b) with acrylonitrile, acrylamide, and methylacrylate (IIa-c).

It is known that benzothiazolin- and benzoxazolin-2-thiones add acrylonitrile at the nitrogen atom in the presence of basic catalysts, i.e., under conditions of anion formation [2, 3]. Information about the reactions of benzazolin-2-thiones in acid medium is limited to a report of the addition of benzimidazolin-2-thione to acrylonitrile and unsaturated aldehydes and ketones at the sulfur atom in the presenceof HCl [4, 5].

We used $AlCl_3$ and H_2SO_4 as catalysts. To thione I and $AlCl_3$ dissolved in chloroform was added an equimolar amount of electrophile II and the mixture was stirred at 25-40° for 1-48 h. Product yields were determined by a procedure that combined thin layer chromatography and spectroscopy (Experimental part). We isolated the S-derivatives, compounds IIa-f (Table 1).

Ia,b IIIa-h

I a X=S, b X=O; II a R=CN, b P=CONH$_2$, c R=COOCH$_3$; III a,c,e,g X=S, b,d,f,h X=O; a,b R=CN, c,d R=CONH$_2$, e,f R=COOCH$_3$, g,h R=COOH

The product yields are substantially affected by the amount of catalyst used. In the absence of catalyst there is no reaction. The maximum yield is achieved in the presence of 1-2 moles of $AlCl_3$ at 40°.

When thione Ia is boiled with acrylonitrile in toluene in the presence of $AlCl_3$, along with IIIa, the product of addition at sulfur (49%), the corresponding N-derivative, 3-(3-benzothiazolinyl-2-thiono)propionitrile, IVa, is also formed in 25% yield. A test of the stability of nitrile IIIa showed that after 1 h in toluene at 110° it is 15% isomerized to IVa. Under the same conditions thione Ia reacts with amide IIb only at the sulfur atom.

Replacement of $AlCl_3$ by H_2SO_4 does not affect the course of the reaction. The reaction of thiones Ia,b with IIa-c in the presence of H_2SO_4 in toluene at 110° also forms the S-derivatives (Table 2).

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Minor amounts of 3-(3-benzothiazolinyl-2-thiono)propionic acid IVg (1%) detected in the products of the reaction of Ia and IIb are apparently formed by hydrolysis of 3-(3-benzothiazolinyl-2-thiono)propionamide IVc. As established by a special experiment, the latter forms by isomerization of amide IIIc. However, in the reaction of thione Ib with amide IIb no products of reaction at nitrogen were found. A test of the stability of amide IIId under reaction conditions showed that it is partially hydrolyzed to acid IIIh (15%), but isomerization to the N-analog was not observed.

EXPERIMENTAL

IR spectra were obtained in KBr tablets on a UR-20 spectrophotometer; UV spectra, on a Hitachi EPS-3T spectrophotometer; PMR spectra, on a Jeol C60-H instrument (TMS internal standard); mass spectra, on a MX-1303 instrument. Identity and purity of synthesized compounds was monitored by TLC on Silufol-254.

Reactions were carried out in absolute solvents (chloroform, toluene) in the presence of catalyst ($AlCl_3$ or H_2SO_4) at constant temperature, with hydroquinone as polymerization inhibitor. After cooling, the reaction mixture was transferred to a volumetric flask (if heterogeneous, with the aid of a solvent). A sample removed by microsyringe was placed on a Silufol-254 sheet and chromatographed in 14:2 benzene–acetone, 3:1 chroroform–benzene, 20:1 chloroform–ethanol, and 14:5:5 petroleum ether–chloroform–acetone. After development in the chromatoscope the bands with individual fractions were cut out, powdered, and extracted with ethyl alcohol. Extract volume was carefully dispensed into volumetric flasks. Optical densities of the solutions were measured on a SF-16 spectrophotometer. Product content (moles) was calculated by the formula:

$$x = (D \cdot V_r \cdot V_e \cdot 10^{-3}) / (E \cdot V_s),$$

here D is optical density; E is extinction coefficient; V_r is volume of reaction mixture transferred to volumetric flask; V_s is volume of sample placed on sheet; V_e is volume of extract.

3-(2-Benzothiazolylthio)propionitrile (IIIa). To a mixture of 0.84 g (5 mmoles) of thione Ia and 1.4 g (10 mmoles) of $AlCl_3$ in 30 ml of dry chloroform was added 0.3 g (5 mmoles) of acrylonitrile, and the mixture was heated under reflux at 40° for 1 h. After the solvent was removed, IIIa was extracted with cold hexane and finally purified by preparative separation on sheets with attached SiO_2 layer. R_f 0.8, (3:1 chloroform–benzene). There was separated 0.91 g (82%) of lemon-colored oil, n_D^{20} k,6539, IR spectrum (KBr): 2260 cm^{-1} (CN). UV spectrum (ethanol, c 0.012 mg/ml), λ_{max} (log ε): 276 nm (4.08). PMR spectrum ($CDCl_3$): 2.8 (2H, t, CH_2R), 3.4 (2H, t, CH_2S), 7.75-7.25 ppm (4H, m, Ar). Found: C 54.5; H 3.5; N 12.7%; M 220. $C_{10}H_8N_2S_2$. Calculated: C 54.4; H 3.6; N 12.7%; M 220.

3-(2-Benzoxazolylthio)propionitrile (IIIb) was obtained analogously in 85% yield as scaly light cream-colored crystals, mp 43° (from hexane). R_f 0.95 (20:1 chloroform–ethanol). IR spectrum (KBr): 2256 cm^{-1} (CN). UV spectrum (ethanol, c 0.015 mg/ml), λ_{max} (log ε): 287 (4.04), 280 nm (0.04). PMR spectrum ($CDCl_3$): 3.0 (2H, t, CH_2), 3.5 (2H, t, CH_2S), 7.4 ppm (4H, m, Ar). Found: C 58.6; H 3.9; N 13.5%; M 204. $C_{10}H_8N_2OS$. Calculated: C 58.8; H 3.9; N 13.7%; M 204.

3-(2-Benzothiazolylthio)propionamide (IIIc). A mixture of 0.84 g (5 mmoles) of thione Ia and 0.3 g (5 mmoles) of acrylonitrile in 20 ml of 80% H_2SO_4 was held at room temperature for 5 h, then poured on ice. The precipitate was separated and washed with 5% alkali solution and water. There was separated 1.12 g (95%) of white needle-shaped crystals, mp 136° (from aqueous alcohol). R_f 0.20 (20:1 chloroform–ethanol). IR spectrum (KBr): 3420-3210 (NH_2), 1670 cm^{-1} (CO). UV spectrum (ethanol, c 0.015 mg/ml), λ_{max} (log ε): 280 (4.14), 230 nm (4.35). PMR spectrum (CF_3COOH): 2.72 (2H, 6, CH_2), 3.45 (2H, t, CH_2S), 7.5 ppm (4H, m, Ar). Found: C 50.4; H 4.1; N 11.7%. $C_{10}H_{10}N_2OS_2$. Calculated: C 50.4; H 4.2; N 11.7%.

3-(2-Benzoxazolylthio)propionamide (IIId) was obtained analogously in 96% yield as white crystals, mp 132° (from aqueous alcohol). R_f 0.27 (20:1 chloroform–ethanol). IR spectrum (KBr): 3420-3210 (NH_2), 1670 cm^{-1} (CO). UV spectrum (ethanol, c 0.015 mg/ml), λ_{max} (log ε): 287 (4.09), 279 (4.12), 250 nm (4.10). PMR spectrum (CF_3COOH): 2.85 (2H, t, CH_2), 3.65 (2H, t, CH_2S), 7.5 ppm (4H, m, Ar). Found: C 54.3; H 4.0; N 12.6%. $C_{10}H_{10}N_2O_2S$. Calculated: C 54.0; H 4.0; N 12.6%.

Methyl 3-(2-Benzothiazolylthio)propionate (IIIe). A mixture of 0.84 g (5 mmoles) of thione Ia and 0.43 g (5 mmoles) of methyl acrylate in 20 ml of 80% H_2SO_4 was held at room temperature for 5 h. Then the mixture was treated analogously to the procedure for the separation

TABLE 1. Synthesis Conditions in Presence of $AlCl_3$ and Yields of Compounds IIIa-h

Compound*	T, °C	Time, h	$AlCl_3$, moles	Yield, %
IIIb (IIIc)	25	1	2	65.6 (1.2)
	25	24	2	82.7 (2.9)
	25	48	2	89.9 (traces)
	40	1	0.001	23.9 (1.4)
	40	1	0.5	68.5 (0.8)
	40	1	1	71.9 (0.6), (1.1)†
	40	1	2	82.5 (0.9)
	40	1	3	27.6 (0.5)
	40	5	2	92.6 (1.6)
IIIc	110	1	1	48.0 (traces), (25.6)†
	110	1	1	57.6
IIIb (IIId)	40	1	1	85.8 (traces)
	40	1	2	80.2 (traces)
IIId	110	1	1	34.8
IIIe (IIIg)	40	1	1	50.6 (4.1)
IIIf (IIIh)	40	1	1	52.6 (10.4)

*IIIa (IIIc) and IIIb (IIId) were obtained by reaction with acrylonitrile; IIIc and IIId by reaction with acrylamide; IIIe (IIIg) and IIIf (IIIh) by reaction with methyl acrylate.
†Yield of 3-(3-benzothiazolinyl-2-thiono)propionitrile IVa.

TABLE 2. Synthesis Conditions in Presence of H_2SO_4 and Yields of Compounds IIIa-h

Benzazolin-2-thione	Electrophile	Time, h	Yield, %
Ia	IIa	1	4.3 (IIIa), 5.9 (IIIc), 7.1 (IIIg)
	IIa	5	6.5 (IIIa), 7.2 (IIIc), 18.5 (IIIg)
	IIb	1	14.4 (IIIc), 2.2 (IIIg), 1.4†
	IIc	1	36.9 (IIIe), 16.0 (IIIg)
	IIc	5	41.8 (IIIe), 26.9 (IIIg)
Ib	IIa	1	2.2 (IIIb), 5.7 (IIId), 15.7 (IIIh), 0.2‡
	IIa	5	7.6 (IIId), 21.0 (IIIh), 0.3**
	IIb	1	4.3 (IIId), 3.6 (IIIh)
	IIc	1	20.7 (IIIf), 4.9 (IIIh)
	IIc	5	28.2 (IIIf), 9.4 (IIIh)

*In toluene at 110°.
†Yield of 3-(3-benzothiazolinyl-2-thiono)propionic acid.
‡Yield of 3-(3-benzoxazolinyl-2-thiono)propionic acid.
**Probably should be labeled as † or ‡. The Russian has a B — Editor.

of IIIc. There was obtained 1.14 g (91%) of white crystals, mp 41° (from hexane). R_f 0.50 (14:5:5 petroleum ether—chloroform—acetone). UV spectrum (ethanol, c 0.01 mg/ml), λ_{max} (log ε): 276 nm (4.06). Found: C 52.3; H 4.3; N 5.8%. $C_{11}H_{11}NO_2S_2$. Calculated: C 52.1; H 4.3; N 5.5%.

Methyl 3-(2-benzoxazolylthio)propionate (IIIf) was obtained analogously to ester IIIe in 85% yield. Mp 40° (from hexane). R_f 0.57 (14:5:5 petroleum ether—chloroform—acetone). IR spectrum (KBr): 1760 cm^{-1} (CO). UV spectrum (ethanol, c 0.014 mg/ml), λ_{max} (log ε): 284 (4.08), 280 (4.08), 250 nm (4.06). PMR spectrum (CCl_4): 2.7 (2H, t, CH_2), 3.3 (2H, t, CH_2S), 7.11 ppm (4H, m, Ar). Found: C 55.4; H 4.5; N 5.8%; M 237. $C_{11}H_{11}NO_3S$. C 55.7; H 4.6; N 5.9%; M 237.

3-(2-Benzothiazolylthio)propionic acid (IIIg) was obtained by hydrolysis of IIIa, IIIc, or IIIe with hydrochloric acid in ~95% yield. Mp 148-149°; according to [6], mp 148-149°. R_f 0.48 (14:2 benzene—acetone).

3-(2-Benzoxazolylthio)propionic acid (IIIh) was obtained analogously to IIIg in ~90% yield. Mp 87-88° (from water). R_f 0.44 (14:2 benzene—acetone). IR spectrum (KBr): 3000-2500 (COOH), 1710 cm^{-1} (CO). UV spectrum (ethanol, c 0.006 mg/ml), λ_{max} (log ε): 287 (4.20), 280 (4.0), 250 nm (3.90). PMR spectrum CR_3COOH): 2.20 (2H, t, CH_3), 3.50 (2H, t, CH_2S), 7.19-7.0 ppm (4H, m, Ar). Found: C 53.5; H 4.0; N 6.7%. $C_{10}H_9NO_3S$. Calculated: C 53.8; H 4.0; N 6.3%.

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PMR STUDY OF THE CONFORMATIONAL BEHAVIOR OF 2,5,5-TRISUBSTITUTED 1,3,2-DIOXABORINANES

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The conformational behavior of 2,5,5-trisubstituted 1,3,2-dioxaborinanes was studied by PMR spectroscopy. Molecules with similar substituents at $C_{(5)}$ are in a state of rapid ring inversion between two energetically equivalent forms. In the case of different substituents, the inversion proceeds between energetically inequivalent states with a shift in the equilibrium toward one of them.

The conformational freatures of 1,3,2-dioxaborinanes are a function of their substitution, the nature of the substituents in the carbon part of the ring and p,p-conjugation at the boron—oxygen bond [1-5]. In the present work, we studied the effect of the nature of the substituents at $C_{(5)}$ on the conformational behavior of 2,5,5-trisubstituted derivatives by PMR spectroscopy.

All the compounds studied (I-XXIV) fall into three groups relative to their conformational properties. The first group comprises compounds with substituents similar in nature and bulk at $C_{(5)}$, which leads to ring inversion between two energetically equivalent forms which is rapid on the NMR time scale (I-XIV, Table 1). This is indicated by the singlet nature of the signal for the ring methylene protons and the low-temperature PMR data. The magnitude of the inversion barrier for 5,5-dialkyl- and 5,5-diallyl-1,3,2-dioxaborinanes could not be determined due to the exceedingly low coalescence temperature (from —115 to —133°C for dimethyl analogs according to Carton et al. [3]). The coalescence temperature is —83°C for 2-isopropyl-5,5-dibenzyl-1,3,2-dioxaborinane corresponding to $\Delta G^{\neq} = 9.7$ kcal/mole, which hardly differs from the analogous value for 5,5-disubstituted 1,3-dioxanes [6]. The nature of the signal for the ring methylene protons at —100°C (Fig. 1a) indicates that cessation of ring inversion leads to an undistorted form. The x-ray structural [7-10] and dipole measurement dat. [11-13] indicate the predominance of a semiplanar or sofa form.

Analysis of the PMR spectra of analogs containing groups at $C_{(5)}$ differing in their bulk and electronic properties shows rapid ring inversion between two energetically inequivalent states. Compounds, for which the $\Delta\nu$ value for the ring methylene protons at room temperature for solutions in CCl_4 is not less than 0.09 ppm, belong to the second and third groups (the $\Delta\nu$ values for compounds in the first group do not exceed 0.02 ppm). In this case, the spectrum of these protons for compounds in the second group (XV-XIX) is a multiplet consisting of five lines with $\Delta\nu$ value from 0.09 to 0.17 ppm (Fig. 1b). With decreasing temperature, this multiplet degenerates into an AB system which, however, may also be a consequence not only of hindrance to inversion but also to a change in the chemical shifts of the protons at $C_{(4)}$ and $C_{(6)}$ with change in the temperature.

The signals for the ring methylene protons in the third group of compounds (XX-XXIV) at room temperature correspond to a usual AB system (Fig. 1c) with $\Delta\nu$ value in the range from 0.20 to 0.49 ppm (solutions in CCl_4).

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