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BENZAZOLIN-2-THIONES IN THE MICHAEL REACTION.

2.* REACTION OF BENZOTHIAZOLIN- AND BENZOXAZOLIN-2-THIONES WITH ACRYLONITRILE, ACRYLAMIDE, AND METHYL ACRYLATE IN THE PRESENCE OF BASIC CATALYSTS

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787.3'789.6.04

Depending on the structure of the reagents and the kind of basic catalyst, the addition of benzazolin-2-thiones to an activated double bond takes place at either nitrogen or sulfur. Acrylonitrile, regardless of the catalyst, reacts at the nitrogen atom. In the presence of sodium methylate, addition to acrylamide takes place only, and to methyl acrylate predominantly at nitrogen. In the presence of triethylamine, a mixture of compounds with a high content of S-derivatives forms.

As is well known [2, 3], under conditions of basic catalysis azolin-2-thiones react as ambidentate anions, and depending on conditions and reagent structure can give either S- or N-derivatives. Thus benzothiazolin-2-thione reacts reacts with methacryloyl chloride in alkaline medium at the sulfur atom [4]. Addition of benzoxazolin-2-thione to methyl acrylate in the presence of Triton B takes place at the nitrogen atom [5]. The products of the reaction of benzothiazolin- and benzoxazolin-2-thiones with acrylonitrile in basic medium have been assigned the structures of both S-derivatives [6, 7] and N-derivatives [2, 5] by various authors.

In order to elucidate the dependence of the course of benzazolin-2-thione addition to an activated double bond on reagent structure and kind of basic catalyst, we have studied the reactions of benzothiazolin- and benzoxazolin-2-thiones (Ia, b) with acrylonitrile (IIa), acrylamide (IIb) and methyl acrylate (IIc) in the presence of triethylamine (TEA) and sodium methylate. The reaction was carried out at an equimolar ratio of reagents and catalyst in dry

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*For 1, see [1].

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TABLE 1. Synthesis Conditions and Product Yields of Reaction of Thiones Ia, b with Electrophiles IIa-c*

Electrophile	Time, h[a]	Yield, %	
		reaction products of Ia	reaction products of Ib
IIa^b	1	6,7 (IVa), 2,7 (IVg)	6,3 (IVb), 1,0 (IVd)
	5	7,0 (IVa)	4,4 (IVb)
IIa^c	1	22,7 (IVa), 0,3 (IIIc), 1,0 (IIIg)	27,8 (IVb), 1,3 (IIId), 2,6 (IVh)
	5	40,0 (IVa), 0,8 (IIIc), 0,7 (IIIg)	42,2 (IVb)
IIa^d	1	7,8 (IVa), 1,8 (IIIg)	
	5	15,3 (IVa), 1,0 (IIIc)	
IIb^b	1	1,8 (IVc)	1,7 (IVd) 0,7 (IVh)
IIb^c	1	35,5 (IIIb), 6,7 (IVg)	31,9 (IIId), 5,1 (IVh)
IIc^b	1	6,8 (IIIe), 13,8 (IVe), 5,7 (IVg)	17,3 (IVf), 2,3 (IVh)
	5	3,3 (IIIe), 16,2 (IVe), 5,9 (IVg)	
IIc^c	1	63,7 (IIIe), 3,5 (IVe), 0,4 (IIIg)	40,8 (IIIf), 17,5 (IVf), 0,6 (IIIh), 0,5 (IVh)
	5	79,0 (IIIe), 5,9 (IVe), 0,8 (IIIg)	
IV^c	5	19,0 (IIIg)	63,8 (IIIf), 27,3 (IVf), 1,0 (IIIh), 0,5 (IVh)

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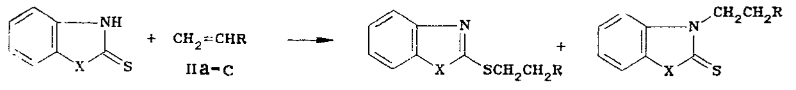
*a) In toluene at 110°. b) In presence of equimolar amount of sodium methylate. c) In presence of equimolar amount of triethylamine. d) In presence of catalytic amount of triethylamine.

toluene at 110° for 1-5 h. Depending on the catalyst and the structure of the reagents, products of reaction at both sulfur (IIIa-f) and nitrogen (IVa-f) are formed (Table 1). Furthermore in each reaction, products were found that could not be identified.



Ia,b IIa-c IIIa-f IVa-f

Ia X=S, b X=O; IIa R=CN, b R=CONH$_2$, c R=COOCH$_3$; III, IV 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

According to the distribution of electron density at the β-carbon of the C=C bond [8], acrylonitrile is the most electron-deficient; regardless of the kind of basic catalyst (TEA, CH_3ONa) or solvent (toluene, methanol), it reacts predominantly at the rigid basic center of the ambifunctional anion, viz., the nitrogen atom. The kind of catalyst exerts a decisive effect on the course of the reaction of benzazoline-2-thiones with the less rigid electrophiles. According to the UV spectrum for compound Ia•TEA, λ_{max} is 335 nm, i.e., access is open to the soft reaction center, viz., the sulfur atom (for S-derivatives, λ_{max} is 278 nm). For this reason, apparently, thiones Ia, b react with electrophiles IIb, c to form a mixture of products with a high content of S-derivatives. For the sodium salt of thione Ia, λ_{max} is 312 nm (for N-derivatives, 328 nm), and addition to amide IIb takes place only, and to ester IIc predominantly, at the nitrogen atom.

Because of the thermal instability of the reaction products under the test conditions it is not possible to relate the reactivity of the test electrophiles to the parameters that characterize the double bond.

In order to determine the path by which the N-derivatives form, the possibility of S-analog isomerization in the presence of sodium methylate and TEA was tested. When ester IIIe was heated with TEA at 110°, along with unchanged S-product, 9.7% of N-isomer IVe was isolated. This permitted us to consider that some ester IVe formed when compounds Ia and IIc react, as a result of isomerization of the main reaction product. In the other cases no isomerization was observed, and consequently it can be concluded that direct N-alkylation occurs along with S-alkylation.

In the reaction of thiones Ia, b with electrophiles IIa-c besides the principal products the corresponding acids IIIg, h and IVg, h were separated. Two routes to their formation can be presumed: hydrolysis of the reaction products, or initial hydrolysis of electrophiles IIa-c to acrylic acid followed by reaction with Ia, b. The ability of IIIa-f and IVa-f to hydrolyze under the reaction conditions, which we verified, permits us to consider the first route as more likely. Furthermore when Ia, b react with acid V under the same conditions

(CH_3ONa or TEA, 110°, 5 h) only the S-derivatives IIIg, h form. This also confirms that insignificant amounts of acids IVg, h form by hydrolysis of the products of the reaction of IIIa-f with IVa-f.

EXPERIMENTAL

IR spectra were obtained in KBr tablets with a UR-20 spectrophotometer; UV spectra, on a Hitachi EPS-3T spectrophotometer; mass spectra, on an MX-1303 instrument. The identity and purity of the synthesized compounds were monitored by TLC on Silufol-254.

Product yields were calculated from the optical density of the alcohol extract of fractions separated by TLC [1].

3-(3-Benzothiazolinyl-2-thiono)propionitrile (IVa). A mixture of 1.67 g (10 mmoles) of thione Ia, 0.5 g (10 mmoles) of acrylonitrile, and 1 g (10 mmoles) of triethylamine (or 2.2 ml of a solution of sodium methylate in methyl alcohol (10 mmoles Na)) was boiled in dry toluene. After 5 h the mixture was cooled and the solvent removed. The dry residue was treated with 5% alkali solution, then with water, to give nitrile IVa in 40% yield. mp 162-163° (from alcohol); according to [2], mp 162-163°. R_f 0.87 (14:5 benzene—acetone).

3-(3-Benzoxazolinyl-2-thiono)propionitrile (IVb) was obtained analogously to IVa in 42% yield. mp 172-173°; according to [5], mp 173-174°. R_f 0.93 (20:1 chloroform—ethanol).

3-(3-Benzothiazolinyl-2-thiono)propionamide (IVc). A mixture of 1.67 g (10 mmoles) of thione Ia, 0.7 g (10 mmoles) of acrylamide, and 1 g (10 mmoles) of triethylamine (or the same amount of sodium methylate in methyl alcohol) was boiled in dry toluene for 1 h. The mixture was treated just as for the separation of IVa. There was obtained 35% of amide IVc, with mp 224° (from aqueous alcohol); according to [9], mp 224-225°, erroneously assigned the structure of 3-(2-benzothiazolylthio)propionamide. R_f 0.14 (20:1 chloroform—ethanol). IR spectrum (KBr): 3420-3210 (NH_2), 1680 cm^{-1} (CO). UV spectrum (ethanol, c 0.014 mg/ml), λ_{max} 326 nm (log ε 4.40). Found: C 50.1; H 4.1; N 11.6%. $C_{10}H_{10}N_2OS_2$. Calculated: C 50.4; H 4.2; N 11.7%.

3-(3-Benzoxazolinyl-2-thiono)propionamide (IVd) was obtained analogously to IVc in 32% yield. mp 196° (from aqueous alcohol); according to [10], mp 196°. R_f 0.10 (20:1 chloroform—ethanol).

Methyl 3-(3-benzothiazolinyl-2-thiono)propionate (IVe). A mixture of 1.67 g (10 mmoles) of thione Ia, 0.86 g (10 mmoles) of methyl acrylate, and 2.2 ml of a solution of sodium methylate in methyl alcohol (10 mmoles Na) was boiled in dry toluene for 1 h. After removal of the solvent the dry residue was treated with 5% alkali solution, then with water. The resulting mixture of esters IIIe and IVe was treated with concentrated HCl. The insoluble residue was filtered off and washed with water to give ester IVe in 14% yield. mp 86° (from benzene). R_f 0.43 (14:5 benzene—acetone). IR spectrum (KBr): 1730 cm^{-1} (CO). UV spectrum (ethanol, c 0.007 mg/ml), λ_{max} 328 nm (log ε 4.33). Found: C 52.5; H 4.0; N 5.4%; M 253. $C_{11}H_{11}NO_2S_2$. Calculated: C 52.1; H 4.3; N 5.5%; M 253.

After the removal of esters IIIe and IVe, when the alkaline solution was acidified, 3-(3-benzothiazolinyl-2-thiono)propionic acid separated in 6% yield; it was purified on sheets with attached SiO_2 layer. mp 161-162° (from alcohol); according to [11], mp 161-162°. R_f 0.45 (14:5 benzene—acetone).

Methyl 3-(3-benzoxazolinyl-2-thiono)propionate (IVf) was obtained similarly to ester IVe in 17% yield, mp 65°; according to [5], mp 64-65°. R_f 0.54 (10:5 hexane—acetone).

3-(3-Benzoxazolinyl-2-thiono)propionic acid (IVh) was obtained similarly to acid IVg in 2% yield, mp 141° (from alcohol); according to [10], mp 140-142°; in [5], mp 189-192°, the constants for 3-(3-benzoxazolinyl-2-thiono)propionamide given incorrectly. R_f 0.49 (20:1 chloroform—ethanol).

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HETEROCYCLIZATION OF COMPOUNDS CONTAINING DIAZO AND CYANO GROUPS.

2.* SYNTHESIS AND RECYCLIZATION OF 4-SUBSTITUTED 5-AMINO-1,2,3-THIADIAZOLES

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794.3'07

The reaction of carbonyl derivatives of diazoacetonitrile with hydrogen sulfide in the presence of triethylamine yields 4-substituted 5-amino-1,2,3-triadiazoles. Under analogous conditions, hydrogen selenide and ethyl mercaptan reduce the starting diazo compounds to hydrazones. Thiadiazoles are recyclized to 4-substituted 5-mercapto-1,2,3-triazoles by the action of bases.

In our previous work [1], we showed that the reaction of carbonyl derivatives of diazoacetonitrile with hydrogen halides leads to the formation of 4-substituted 5-halo-1H-1,2,3-triazoles. In the present communication, we studied the reactions of diazoacetonitriles with hydrogen sulfide and hydrogen selenide in order to obtain 4-substituted 5-amino-1,2,3-thiadiazoles, which are starting reagents for the preparation of various pesticides [2, 3] and their selenium analogs.

Diazoacetonitrile and its alkyl and aryl derivatives react with hydrogen sulfide in the presence of bases to form 5-amino-1,2,3-triadiazoles [4, 5]. In addition, the reaction of carbonyl derivatives of diazomethane with hydrogen sulfide, depending on the substituents, gives either thionylation of the carbonyl group with subsequent cyclization to 1,2,3-thiadiazole or reduction of the diazo compounds to hydrazones [6]. Thus, the formation of three different products may be expected in the reaction of carbonyl derivatives of diazoacetonitrile with hydrogen sulfide.

However, the only products of the reaction of 2-diazo-2-cyanoethyl acetate (Ia), 2-diazo-2-cyanoethylacetamide (Ib), 2-diazo-2-cyanoethyl-N-methylacetamide (Ic) and 2-diazo-2-cyanoethylacetophenone (Id) with hydrogen sulfide in the presence of triethylamine were 4-substituted 5-amino-1,2,3-thiadiazoles (IIa-d). The sturcture of thiadiazoles IIa-d was confirmed by IR, UV, and PMR spectroscopy and by the convergent synthesis of IIa and IId according to Goerdeler [7]. Thus, only the first of the three possible reaction pathways obtains.

We should note that formation of 5-amino-1,2,3-thidiazoles in this reaction may proceed by two different mechanisms, either through the α-diazothioamide or through the α-cyanothiadiazene with subsequent cyclization of these kinetically unstable intermediates. In order to distinguish between these two mechanisms, we carried out a comparative kinetic study of the reactions of 2-diazo-2-cyanoacetamide Ib and a compound with similar electronic structure but incapable of reacting through the first mechanism with hydrogen sulfide. 2-Diazomalondiamide III was taken as this model.

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*For 1, see [1].

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