REACTION OF SOME BENZOXAZOLINE-2-THIONE DERIVATIVES WITH AMINES

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Hydroxyphenylthioureas were obtained by the reaction of nitro, chloro, bromo, or amino derivatives of benzoxazoline-2-thiones with primary amines. If the substituent in the benzene ring is a nitro group, the reaction with certain secondary amines proceeds with the production of trisubstituted thioureas. It is shown that electron-acceptor substituents in the 5 and 6 positions of the benzene ring facilitate this reaction.

We have previously demonstrated that in the reaction of benzoxazoline-2-thione and its sulfonamido derivative (I, X = H, SO_2NH_2; Y = H) with primary aliphatic and aliphatic-aromatic amines the heterocyclic ring is opened with the addition of the amine and the formation of thiourea derivatives II [1-3], whereas 2-aminobenzoxazole derivatives are obtained in its reaction with certain secondary and aromatic amines [4]. With these peculiarities

TABLE 1. 2-Hydroxyphenylthioureas (II_{1-35})

Compound	R^1	R^2	X	Y	Reaction time, min	mp,[a] °C	N, %		Yield, %
							found	calc.	
1	H	C_2H_5	NO_2	H	30	138	17,6	17,4	89
2	H	$CH_2CH{=}CH_2$	NO_2	H	45	130	16,8	16,6	93
3	H	n-C_3H_7	NO_2	H	30	133	16,5	16,5	92
4	H	n-C_4H_9	NO_2	H	15	114—115	15,8	15,6	95
5	H	C_6H_{11}	NO_2	H	30	153	14,1	14,2	99
6	H	$CH_2C_6H_5$	NO_2	H	30	140	14,2	13,9	99
7	C_2H_5	C_2H_5	NO_2	H	180	114	15,6	15,6	88
8	n-C_4H_9	n-C_4H_9	NO_2	H	180	106	13,0	12,9	91
9	—$(CH_2)_5$—		NO_2	H	150	118	14,9	14,9	77
10	H	CH_3	H	NO_2	40	107	18,5	18,5	84
11	H	C_2H_5	H	NO_2	30	120—121	17,5	17,4	84
12	H	$CH_2CH{=}CH_2$	H	NO_2	60	98—99	16,8	16,6	85
13	H	n-C_3H_7	H	NO_2	60	103—104	16,5	16,5	85
14	H	n-C_4H_9	H	NO_2	25	92—93	15,5	15,6	90
15	H	C_6H_{11}	H	NO_2	40	128—129	14,0	14,2	91
16	H	$CH_2C_6H_5$	H	NO_2	45	153—154	13,9	13,9	98
17	C_2H_5	C_2H_5	H	NO_2	240	105	15,5	15,2	90
18	n-C_4H_9	n-C_4H_9	H	NO_2	240	123—124	13,1	12,9	95
19	—$(CH_2)_5$—		H	NO_2	180	171—172	14,8	14,9	98
20	H	CH_3	Cl	H	540	169—171	12,7	12,9	57
21	H	C_2H_5	Cl	H	60	130—132	11,9	12,1	68
22	H	n-C_3H_7	Cl	H	420	118—119	11,1	11,4	69
23	H	n-C_4H_9	Cl	H	300	118—120	11,1	10,8	65
24	H	C_6H_{11}	Cl	H	180	152—153	9,6	9,8	65
25	H	$CH_2C_6H_5$	Cl	H	150	134—135	9,5	9,6	76
26	H	C_2H_5	H	Br	120	165—167	10,2	9,9	67
27	H	n-C_3H_7	H	Br	120	120—122	9,7	9,6	69
28	H	n-C_4H_9	H	Br	120	118—120	9,2	9,4	69
29	H	C_6H_{11}	H	Br	150	139—140	8,5	8,4	52
30	H	$CH_2C_6H_5$	H	Br	90	134—136	8,3	8,2	82
31	H	C_2H_5	NH_2	H	180	173—174	15,2 (S)	15,4 (S)	64
32	H	n-C_3H_7	NH_2	H	240	154—155	18,7	18,4	75
33	H	n-C_4H_9	NH_2	H	600	80—82	13,4 (S)	13,3 (S)	70
34	H	C_6H_{11}	NH_2	H	960	176—178	12,0	11,8[b]	76
35	H	$CH_2C_6H_5$	NH_2	H	300	170—172	15,4	15,0	79

[a] Melts with decomposition. [b] The analysis pertains to the acetyl derivative.

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in mind and taking into account the valuable properties of the products, which have antivirus activity and accelerating action in the vulcanization of rubber mixtures [5], we continued our research in this direction.

To establish the effect of several substituents in the benzene ring on the properties of benzoxazoline-2-thione we investigated amino, halo, and nitro derivatives of benzoxazolinethiones I (X = Cl, NO_2, NH_2, Y = H; X = H, Y = Br, NO_2). The results show that the processes that occur in the reaction of these compounds with primary amines are similar to the previously investigated reactions with benzoxazoline-2-thiones (I, X = H, SO_2NH_2, Y = H). The reaction products are also 2-hydroxyphenylthioureas II$_{1-6}$, II$_{10-16}$, and II$_{20-35}$ (see Table 1). In the case of the reaction of nitro derivatives of benzoxazoline-2-thione (I, X = NO_2, Y = H; X = H, Y = NO_2) with secondary amines, viz., diethylamine, dibutylamine, and piperidine, the reaction takes place in the same way as with primary amines: Trisubstituted derivatives of thiourea (II$_{7-9}$, II$_{17-19}$) are obtained. In addition, it must be noted that the reaction proceeds at its highest rate when the substituent is a nitro group; other electron-acceptor substituents also accelerate this reaction. Of particular interest in the IR spectra of II is the region of the stretching vibrations of the N—H and O—H groups: The spectra of starting I (X = Cl, NH_2, Y = H; X = H, Y = Br) contain only one band of characteristic vibrations of the N—H group (3343-3345 cm^{-1}). Two peaks, the first of which (3395-3405 cm^{-1}) corresponds to the stretching vibrations of the N—H group, the second of which (3510-3530 cm^{-1}) is related to the characteristic vibrations of a hydroxy group in an aromatic ring, are observed in the spectra of the reaction products (in chloroform).

I

II$_{1-35}$

EXPERIMENTAL

N-(2-Hydroxyphenyl)thioureas (II$_{1-35}$). A mixture of 1 g (4-6 mmole) of benzoxazoline-2-thione I and 2 ml (12-30 mmole) of the amine was heated on a water bath, after which it was cooled and dissolved in 200 ml of ether. The ether solution was washed with 6% hydrochloric acid solution and extracted with a 5% solution of alkali. A precipitate formed when the alkaline extract was acidified. The yields and constants of the compounds are presented in Table 1.

The compounds are soluble in alcohol, acetone, ether, ethyl acetate, and alkali solution, slightly soluble in benzene, and insoluble in cold water and acid solutions. The thiourea derivatives that contain a nitro group in the hydroxyphenyl substituent decompose with hydrogen sulfide evolution when they are heated in a polar solvent, as a consequence of which they must be recrystallized from benzene or benzene—acetone.

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