REACTION OF 3H-OXAZOLO[4,5-b]PYRIDINE-2-THIONE WITH AMINES

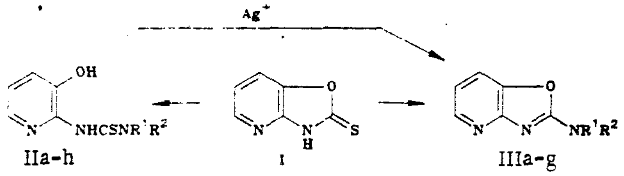
K. Davidkov, D. Simov, and V. Kalcheva

UDC 547.233'822.7'04'787.3.07

Primary amines and diethylamine react with oxazolo[4,5-b]pyridine thione to form N-(3-hydroxy-2-pyridyl)thioureas whereas cyclic secondary amines and aniline form 2-aminooxazolo[4,5-b]pyridines. Exchange of the benzene ring in benzoxazolinethione for pyridine causes the properties of the resultant oxazolopyridine-2-thione to resemble those of 5- and 6-nitrobenzoxazolinethiones.

We have previously shown [1, 2] that benzoxazolinethione reacts with amines to form 2-aminobenzoxazoles or N-arylthioureas depending upon the nature of the amine, the substituents in the thione ring, and the conditions for the reaction. These and related compounds often possess biological activity [3] and other useful properties [4]. With the aim of broadening the synthetic possibilities of this reaction and to synthesize new, practically useful investigational materials we have studied the interaction of amines with a pyridine analog of benzoxazolinethione (oxazolo[4,5-b]pyridine-2-thione [1]).

We have found that thione I reacts regioselectively with primary aliphatic amines and with diethylamine upon heating to form N-(3-hydroxy-2-pyridyl)thioureas (IIa-h) whereas secondary cyclic amine and aniline gave 2-aminooxazolo[4,5-b]pyridines (IIIa-e) under the same conditions. When treated with ammoniacal silver nitrate the thioureas IIf, g cyclized to the amines IIIf, g.



The thioureas obtained gave a coloration with ferric chloride, were soluble in base, and decomposed upon heating (with evolution of hydrogen sulfide). They showed IR spectral

TABLE 1. Physical Constants and Yields for II and III

Compound	R¹	R²	T_{mp}, °C	N, %		Yield, %
				found	calc.	
IIa	CH_3	H	199—200	23.2	23.0	82
IIb	C_2H_5	H	173—174	21.1	21.3	70
IIc	p-C_3H_7	H	186—187	19.6	19.9	85
IId	$CH_2{=}CHCH_2$	H	215—216	20.5	20.1	74
IIe	p-C_4H_9	H	137—138	18.4	18.7	90
IIf	$PhCH_2$	H	184—185	16.0	16.2	94
IIg	c-C_6H_{14}	H	187—189	16.4	16.7	86
IIh	C_2H_5	C_2H_5	138—140	18.9	18.7	95
IIIa	Ph	H	236	19.5	19.9	81
IIIb	$(CH_2)_5$		92—94	20.5	20.7	71
IIIc	$(CH_2)_2—O—(CH_2)_2$		156—158	20.4	20.5	70
IIId	$(CH_2)_4$		168—170	22.2	22.2	93
IIIe	$(CH_2)_2—NH—(CH_2)_2$		87—89	27.3	27.5	94
IIIf	$PhCH_2$	H	86—87	18.2	18.6	71
IIIg	c-C_6H_{11}	H	127—129	19.2	19.4	90

Kl. Okhridskii University, Sofia, Bulgaria, 1126. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1129-1130, August, 1987. Original article submitted April 14, 1986.

0009-3122/87/2308-0905$12.50

bands for the OH group (3100-3200 cm^{-1}). In contrast, the 2-aminooxazolopyridines III were soluble in acids and showed IR bands for C=N (1650) and NH (3400 cm^{-1}).

Thus the effect of the pyridine nucleus on the properties of the oxazolinethione ring was closely similar to the influence of a 5- or 6-nitrophenyl ring in benzoxazolinethiones and increased the tendency of the oxazolinethione ring toward cleavage.

EXPERIMENTAL

N-(3-Hydroxy-2-pyridyl)-N-alkylthioureas (II). A mixture of oxazolopyridine-2-thione (6.6 mmole) and amine (3 ml) [or for volatile amines an aqueous solution (35%, 6 ml in a sealed ampul)½ was heated on a water bath for 4 h. After cooling, the mixture was dissolved in ether, the ether solution washed with HCl (7%) to remove excess amine, extracted with aqueous alkali, and neutralized with dilute HCl. The precipitated solid was separated and recrystallized from aqueous ethanol. Physical constants and yields are given in Table 1.

2-Aminooxazolo[4,5-b]pyridines (III). A. A mixture of the thione I (3.3 mmole) and the amine (2 ml) was heated on a water bath for 4 h (for amines the reaction was carried out in acetonitrile which was distilled off before workup). After cooling, the mixture was dissolved in HCl (10%), filtered, and the filtrate neutralized with 25% base. The residue was separated and recrystallized from alcohol.

B. To a stirred solution of ureas IIf, g (4.6 mmole) in ethanol (50 ml) there was added silver nitrate (1.74 g, 10.2 mmole) dissolved in concentrated ammonia (during which a black precipitate was formed). The mixture was stirred for 1 h at 40-50°C and a further 5 ml of ammonia and 20 ml of ethanol added. After a further hour the mixture was filtered and the filtrate acidified with 10% HCl to pH 2-3. After 30 min the solution was filtered, the filtrate concentrated to one-third volume, and basified with 7% alkali to pH 8-9. The resultant solid was filtered off (yield of dry reaction product, 90%) and recrystallized from aqueous ethanol. Physical constants and yields are given in Table 1.

LITERATURE CITED

1. K. Davidkov and D. Simov, Khim. Geterotsikl. Soedin., No. 2, 180 (1981).
2. D. Simov and K. Davidkov, Khim. Geterotsikl. Soedin., No. 2, 173 (1976).
3. K. Davidkov, D. Simon, and B. Gylybov, Bulgarian Patent 21,488 (1973).
4. M. Nedev, Compt. Rend. Acad. Bulg. Sci., 21, 693 (1968).