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

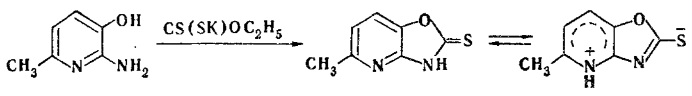
K. Davidkov and D. Simov

UDC 547.787.3'821

5-Methyl-3H-oxazolo[4,5-b]pyridine-2-thione, which exists in the dipolar form, was obtained by the reaction of 6-methyl-2-amino-3-hydroxypyridine with potassium ethylxanthate. The reaction of the product with amines leads to the corresponding thioureas.

In our previous papers we described the reaction of benzoxazoline-2-thione and its derivatives with various amines, as a result of which we obtained a number of derivatives of thioureas [1, 2]. We established certain principles that have to do with the rate of this process and the stability of the oxazolinethione ring as a function of the form of substituents in the benzene and heteroatomic rings [2-4].

We became interested in the synthesis and properties of other condensed systems that contain an oxazole-2-thione ring. For this, we obtained the methyl derivative of oxazolo-[4,5-b]pyridine-2-thione* by a method similar to that used to prepare benzoxazoline-2-thione from 6-methyl-2-amino-3-hydroxypyridine via the scheme:



Ia Ib

Absorption bands at 1616 and 1638 cm^{-1} are observed in the IR spectrum of I: The first can be assigned to the pyridine ring, while the second can be assigned to the azomethine group of a five-membered ring. Upon comparison of the spectra of this compound and benzoxazoline-2-thione (II) it is apparent that the absorption band that is characteristic for the NH group is absent here, whereas absorption at 3220-3330 cm^{-1} is observed at 3220-3330 cm^{-1}; however, there is a broad band at 2680-2720 cm^{-1}, which is characteristic for the NH bond of a quaternized nitrogen atom. Consequently, it may be assumed that the compound exists mainly in the Ib form. This is also indicated by the data from the PMR spectra recorded in dimethyl sulfoxide (DMSO), in which there is a shift of the signals of the protons of the methyl group to weaker field (2.69 ppm) as compared with 2-methylpyridine (2.37 ppm) of the same order of magnitude as the shift of the signal of the protons of the 2-CH_3 groups in

---

*For its preparation and investigation of its properties we obtained Inventor's Certificates Nos. 21488 and 26441 in Bulgaria with priority from September 5, 1973.

TABLE 1. UV Spectra of I-VIII in Alcohol

Compound	λ_{max}, nm	log ε	λ_{max}, nm	log ε	λ_{max}, nm	log ε	λ_{max}, nm	log ε
I	321	4,50	258	3,77				
II	302	4,23	264	3,78	215	3,89		
III	315	4,24	263	4,02	245	4,08	208	4,04
IV	315	4,20	265	4,01	247	4,09	208	4,02
V	315	4,17	265	3,95	247	4,05	208	4,96
VI	315	4,28	264	4,09	247	4,20	208	4,26
VII	315	4,13	264	3,97	247	4,13	208	4,32
VIII	315	4,26	263	4,28	248	4,38	210	4,89

K. Okhridskii Sofia University, Sofia, Bulgaria 1126. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 608-610, May, 1981. Original article submitted December 18, 1979; revision submitted July 7, 1980.

0009-3122/81/1705-0441$07.50

TABLE 2. N-(6-Methyl-3-hydroxy-2-pyridyl)thioureas (III-VIII)

Compound	Reaction time, h	mp, °C	S, %		Yield, %
			found	calc.	
III	6	190—191	16,1	16,2	34
IV	6	190—192	15,1	15,2	60
V	10	197—199	14,0	14,2	88
VI	7	188—190	13,3	13,4	92
VII	5	190—192	11,7	11,7	88
VIII	5,5	206—208	11,6	12,1	89

pyridinium salts [5] (2.72 ppm). The UV spectrum contains a maximum at 321 nm that is shifted bathochromically with respect to the maximum of benzoxazoline-2-thione (302 nm) (see Table 1). The structure of Ib is also confirmed by certain physical properties of the substance such as its high melting point and low [sic] solubility in water, alcohol, and acetone.

We then investigated the behavior of this compound with respect to nucleophilic reagents. In contrast to benzoxazoline-2-thione, which remains unchanged under the influence of alkalis and under very severe conditions [6], I undergoes a change when it is refluxed in a 30% solution of NaOH with H_2S evolution. The reaction of thione I with amines in the starting amine as the medium proceeds smoothly at a temperature below 100°C, leading, as in the reaction with benzoxazolinethiones, to the corresponding thioureas. The time required for the process depends on the type of amine (see Table 2).

EXPERIMENTAL

5-Methyl-3H-oxazolo[4,5-b]pyridine-2-thione (I). A solution of 10 g (0.080 mole) of 6-methyl-2-amino-3-hydroxypyridine and 20 g of potassium ethylxanthate in 100 ml of alcohol and 15 ml of water was heated on a water bath for 6 h, after which it was cooled and acidified with acetic acid, during which 10.6 g (91%) of thione I, with mp 290-292°C, precipitated. A pure substance, with mp 292-293°C, was obtained after recrystallization from alcohol. PMR spectrum (in DMSO), δ: 2.69 (5-CH_3), 7.33 (6-H), and 7.94 ppm (7-H). Found: S 19.1%. $C_7H_6N_2OS$. Calculated: S 19.3%. Compound I crystallized in the form of colorless acicular crystals that were soluble in alkali. The compound reprecipitated from the alkali solution upon acidification. The product was relatively insoluble in hot alcohol, acetone, and chloroform and was insoluble in cold benzene and water.

N-(6-Methyl-3-hydroxy-2-pyridyl)-N-benzylthiourea (VII). A 0.5-g (0.003 mole) sample of I and 1.96 g (0.019 mole) of benzylamine were heated with a reflux condenser at 100°C for 5 h, after which the mixture was cooled and dissolved in ether. The ether solution was washed with 5% hydrochloric acid. Extraction of the ether solution with 6% NaOH and acidification of the alkaline extract gave 0.72 g (87.8%) of precipitated urea VII with mp 180°C. Recrystallization from dilute alcohol gave a pure product with mp 190-192°C. Found: S 11.7%. $C_{14}H_{15}N_3OS$. Calculated: S 11.7%.

Similarly, III-VIII, respectively, were obtained by reaction of I with methylamine, ethylamine, n-propylamine, n-butylamine, and cyclohexylamine. The substances were colorless crystals that were soluble in alcohol, acetone and chloroform, slightly soluble in water, and insoluble in benzene. Their solubility in water increases in the direction of the first member of the table (see Table 2).

LITERATURE CITED

1. D. Simov and K. Atanasov, Dokl. Bulg. Akad. Nauk, 20, 433 (1967).
2. D. Simov and K. Davidkov, C. R. Acad. Bulg. Sci., 23, 1361 (1970).
3. D. Simov and K. Davidkov, C. R. Acad. Bulg. Sci., 22, 1119 (1969).
4. K. Davidkov and D. Simov, C. R. Acad. Bulg. Sci., 26, 777 (1973).
5. K. Undheim and L. Borka, Acta Chem. Scand., 23, 1715 (1969).
6. A. Kalskhoff, Chem. Ber., 16, 1825 (1885).