SYNTHESES IN THE PYRIDINE SERIES

X. A New Procedure for the Synthesis of Some Thipyridones and Thioquinolones

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A new procedure for preparing 2-methyl-6-methoxy-4-thioquinolone (I), 2-methyl-7-chloro-4-thioquinoline (II), 2-thiopyridone (III) and 5-nitro-2-thiopyridone (IV) has been proposed. This involves the reactions of the corresponding halogen derivatives of quinoline and pyridine with sodium thiosulfate. Compounds I and II were synthesized for the first time.

According to general methods, 2- and 4-thiopyridones and thioquinolones are prepared from the corresponding pyridones and quinolones by reactions with phosphorus pentasulfide [2], as well as from pyridyl and quinolyl halogen derivatives by the action of potassium hydrosulfide, thiourea, or thioacetamide [3–6].

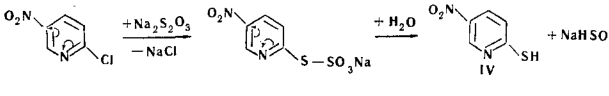
Characteristics of the Compounds Obtained

Initial halogen derivatives	Compound	Mp., °C.	Molecular formula	Found, %		Calculated, %		Yield, %
				N	S	N	S	
2-Methyl-6-methoxy-4-chloroquinoline	I	287—289	$C_{11}H_{11}NOS$	6.9 7.0	15.8 16.1	6.8	15.6	94
2-Methyl-4,7-dichloroquinoline	II	290—292	$C_{10}H_8ClNS$	6.5 6.6	15.4 15.6	6.7	15.2	94
2-Bromopyridine	III	125*	—	—	—	—	—	78—85
5-Nitro-2-chloropyridine	IV	169*	—	—	—	—	—	96

*The melting points of compounds III and IV corresponded to the liteature data [3,5].

It is known that aminoalkyl halogens react with sodium thiosulfate to form at first Bunte salts which by acid hydrolysis are then converted to aminothiols and disulfides. The latter are also formed in the absence of oxygen [7]. Halogenated quinolines and halogenated pyridines also react with sodium thiosulfate, but no disulfides are formed. The yields of thioquinolones and thiopyridones are almost quantitative (see the table).

Unlike the salts of alkylthiosulfuric acid, the hydroylsis of the salts of quinolyl- and pyridylthiosulfuric acids proceeds in the absence of mineral acids. Hence about two moles of sodium thiosulfate are required to prepare I, II, and III, while one mole is sufficient to prepare IV. Probably the velocity of the reaction to form intermediate compounds (salts of thiosulfuric acid) of the first three is close to the velocity of their hydrolysis. Both reactions proceed simultaneously. In this case the bisulfate formed reacts with sodium thiosulfate and removes it from the reaction sphere, as may be presumed from the separation of some sulfur. On the contrary, considering the significant positive charge on the second carbon atom of 5-nitro-2-chloropyridine, the velocity of the formation of the intermediate product probably exceeds by much the velocity of its hydroylsis. Therefore, both reactions do not proceed simultaneously, and one mole of thiosulfate is sufficient for the quantitative formation of IV.



Attempts to control the reaction velocity by titration of a sample of the reaction mass with alkali or with an iodine solution were not successful, since the reaction mass had a yellow or orange color. It was also difficult to determine the Cl⁻ concentration by Volhardt method. The presence of even small quantities of sodium thiosulfate provoked the formation of silver sulfide.

EXPERIMENTAL

Compounds I–III. Mixtures of 0.2 mole of the corresponding halogen derivative and 0.4 mole of sodium thiosulfate in 70 ml of 70% ethanol were heated in an autoclave for 4 hr at 120–130° C. The solution was then cooled to 5° C and neutralized with a 5% sodium bicarbonate solution. Compounds I and II separated out in the precipitate in an almost quantitative yield. To separate III, the reaction mass after neutralization was evaporated to dryness under vacuum and the residue extracted with boiling benzene. After distilling off the benzene, III was obtained with a 78–85% yield.

5-Nitro-2-thiopyridone (IV). A mixture of 0.2 mole of 5-nitro-2-chloropyridine and 0.2 mole of sodium thiosulfate in 50 ml of 70% ethanol was boiled for 3 hr. The further treatment of the reaction mass was similar to that described for I and II.

The compounds obtained were crystallized ex ethanol (see table).

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