SYNTHESES IN THE PYRIDINE SERIES

IX. A Study of the Properties of Some Pyrid-2-yl Sulfides*

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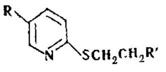
It has been shown that when they are heated in 2 N caustic soda solution alkyl pyrid-2-yl sulfides are hydrolyzed at the Py—S bond with the formation of pyridones and the corresponding thiols. The latter were determined quantitatively by iodometric titration.

It is known that halogens and also nitro, sulfo, and alkoxyl groups in the α and γ-positions of heterocycles, since they bear a positive charge, can be replaced by nucleophilic agents. There is no similar information on the pyridyl sulfides. However, quaternary salts of the alkyl pyrid-2-yl sulfides are hydrolyzed in alkaline solutions to form N-alkylpyrid-2-ones [2]. In the present work we have studied the behavior of a number of pyrid-2-yl sulfides and their quaternary salts in 2 N caustic soda solution on heating. For this purpose, using literature sources, we synthesized ethyl pyrid-2-yl sulfide (I) [3] and ethyl 5-nitropyrid-2-yl sulfide (IV) [4]. Both substances were insoluble in water but soluble in ether. Unlike **I**, **IV** does not add alkyl iodides. On being boiled in 2 N NaOH solutions for 4–5 hr, they were completely hydrolyzed, liberating ethyl mercaptan, which was determined quantitatively by iodometric titration [5].



Compound	R	R′	Time of hydrolysis, hr
I	H	H	4—5
II	H	$N(CH_3)_2$	5
III	H	$N(C_2H_5)_2$	5—6
IV	NO_2	H	4
V	NO_2	$N(CH_3)_2$	4—5
VI	NO_2	$N(C_2H_5)_2$	4—5

In a consideration of the properties of other 5-nitropyrid-2-yl sulfides synthesized by Renault [3] and a comparison of their properties with I and IV we directed our attention to the marked rise in the melting point on passing from n-propyl and n-butyl 5-nitropyrid-2-yl sulfides to their isopropyl and isobutyl analogs. This lack of correspondence with general ideas on the higher boiling and melting points of compounds with a normal hydrocarbon chain as compared with their isomers forced us to repeat the synthesis of the assumed isopropyl 5-nitropyrid-2-yl sulfide from 2-mercapto-5-nitropyridine and isopropyl bromide under the conditions reported. We obtained a substance with the mp of 270° C given by the author. However, the compound obtained contained neither sulfur nor bromine and, in contrast to I and IV was soluble in water but insoluble in ether. Its nitrogen content was correct for the corresponding alkyl derivative of 5-nitropyrid-2-one. The identical substance was obtained by heating 5-nitropyrid-2-one with isopropyl bromide in aqueous ethanolic solution in the presence of an equivalent amount of caustic potash. Consequently, the author was wrong in ascribing the structure of a sulfide to the substance concerned and it is actually N-isopropyl-4-nitropyrid-2-one (VII). As is well known, alkoxy derivatives of pyrid-2-one are not formed in aqueous solutions. The formation of VII can be explained by the fact that under the reaction conditions (excess of bromide and caustic potash), the first reaction product, the sulfide, undergoes hydrolysis and the resulting 5-nitropyrid-2-one then reacts with a second molecule of the bromide, forming **VII**. If potassium carbonate is used in place of caustic potash, a liquid product is formed which is soluble in ether and insoluble in water to which, consequently, the structure of the sulfide must be ascribed.

The property of the alkyl pyrid-2-yl sulfides of hydrolyzing in alkaline solutions at the Py—S bond was used for an additional proof of the structure of the aminoalkyl pyrid-2-yl sulfides that we had synthesized previously [6] (table) and also that of the monoethiodide of **VI**.

The formation of a thiol on the hydrolysis of a monoquaternary salt of the base **VI** shows that it is the ammonium salt formed by the nitrogen of the side chain, since in the alkyl 5-nitropyrid-2-yl sulfides the nitrogen of the ring does not form quaternary salts. If it is assumed that the ethiodide of the base **VI** has the thione structure, its hydrolysis at the Py—S bond should form a sulfide. The latter cannot be titrated with KIO_3.

EXPERIMENTAL

Hydrolysis of the alkyl pyrid-2-yl sulfides. A weighed sample of a sulfide of about 10 mg was boiled with 2 ml of 2 N caustic soda solution for 4–6 hr. Then the mixture was diluted with 15 ml of water and acidified with 3 ml of N HCl, after which 1 ml of 10% KI solution and 1 ml of starch solution were added and titration was performed with a 0.01 N solution of KIO_3. The percentage content of thiol in the reaction mixture was calculated from the formula:

$$\% = \frac{6v \cdot KIO_3 \cdot M \cdot 100}{\text{wt. of sample}}.$$

After the hydrolysis of 1.68 g of **IV** and neutralization of the reaction mixture, an almost quantitative yield (1.3 g) of 5-nitropyrid-2-one was obtained in the form of a precipitate.

N-Isobutyl-5-nitropyrid-2-one. A flask was charged with 1.4 g (0.01 mole) of 5-nitropyrid-2-one and 20 ml of ethanol. Then 0.6 g (0.01 mole) of KOH and 1.45 ml of isobutyl bromide were added to the

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*For part VIII, see [1].

solution. The mixture was heated in the boiling water bath for 3 hr, after which activated carbon was added and it was filtered. The filtrate was cooled and treated with 50 ml of ether. The light yellow crystals that separated out were filtered off and dried at 75–80° C. Yield 1.75 g; mp 270–271° C, without depression on being mixed with the substance obtained by Renault's method. Found, %: N 14.31, 14.15. Calculated for $C_9H_{12}N_2O_3$, %: N 14.25.

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