CHEMISTRY OF HETEROCYCLIC N-OXIDES AND RELATED COMPOUNDS. V.* DEHYDROGENATION OF THE HANTZSCH ESTER BY MEANS OF PYRIDINIOACYLAMIDATES

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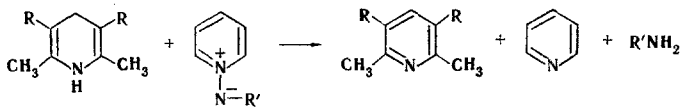
The dehydrogenating activity of pyridinioacetamidate, pyridiniobenzamidate, and pyridiniobenzenesulfonamidate was investigated in the case of reactions with the Hantzsch ester.

We have previously shown the possibility of the application of the hydrochlorides and N-tosyl derivatives of N-imines of pyridine bases as homogeneous dehydrogenating agents for the dehydrogenation of completely or partially hydrogenated compounds of the pyridine series [1, 2]. The reactivities of other N-acyliminopyridines have not been investigated. In the present research in the case of reactions with the Hantzsch ester (I), we have studied the dehydrogenating capacity of pyridinioacetamidate (II), pyridiniobenzamidate (III), and pyridiniobenzenesulfonamidate (IV).



I II–IV V VI–VIII

I, V $R=COOC_2H_5$; II, VI $R'=COCH_3$; III, VII $R'=COC_6H_5$; IV, VIII $R'=SO_2C_6H_5$

Dehydrogenation of Hantzsch ester I by means of II and III gives diethyl 2,6-lutidine-3,5-dicarboxylate (V) in high yields (Table 1). The yields of amides VI and VII in these cases are low, probably due to side processes involving the participation of the carbonyl groups. In particular, the results of a control experiment with benzamide, in which, in addition to the dehydrogenation products, the formation of a complex mixture of side products is noted, constitute evidence for this.

The dehydrogenation of ester I by means of sulfimido derivatives — IV, pyridinio-p-toluenesulfonamidate (IX) [2], and dipyridinio-p-toluenesulfonamidates [1] — is realized more smoothly and at a higher rate. This is explained by the higher polarizing capacity of the sulfonyl group as compared with the carbonyl group [3].

Thus the results make it possible to conclude that, of the derivatives of N-imines of pyridine bases, it is preferable to use N-sulfimido derivatives as hydrogen acceptors.

It is interesting to note that, in contrast to pyridinioacylamidates, the dehydrogenation of ester I by means of benzamide gives a lower yield and that the reaction does not proceed at all with benzenesulfonamide.

EXPERIMENTAL

The purity of the substances was monitored by means of paper chromatography ("fast" grade paper) in an n-butanol—hydrochloric acid—water system (50:7:14, system A) with develop-

*See [1] for communication IV.

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TABLE 1. Results of Dehydrogenation of the Hantzsch Ester

Dehydrogenating agent	Yield, %		
	V	amide	XI
IX[2]	92	87	88
IV	78	77	79
III	99	33	21
II	94	—	25
VII	33	—	—
VIII	—	—	—

ment by Dragendorf's reagent and by means of thin-layer chromatography (GLC) on activity-II aluminum oxide in chloroform–benzene–alcohol (22:8:2, system B) and hexane–acetone (1:1, system C) systems with development by iodine vapors.

Pyridinioacetamidate (II) was obtained by the method in [4] in 66% yield and had R_f 0.6 (system B). The picrate had mp 164°.

Pyridiniobenzamidate (III). A mixture of 1.3 g (10 mmole) of pyridine-N-imine hydrochloride (X) and 6 ml of benzoyl chloride was heated on a water bath until HCl evolution ceased, after which the excess benzoyl chloride was removed by distillation at reduced pressure, and the residue was dissolved in a small amount of water. The aqueous solution was made alkaline to pH 7 with sodium carbonate and extracted with chloroform. The solvent was then removed by distillation to give 1.9 g (96%) of III with mp 177-178° (mp 177.5° [4]) and R_f 0.2 (system B).

Pyridiniobenzenesulfonamidate (IV). This compound, with mp 148-149° (152° [4]) and R_f 0.6 (system B), was similarly obtained in 55% yield from X and benzenesulfonyl chloride.

Dehydrogenation of Hantzsch Ester I. A) With pyridinioacetamidate (II). A mixture of 0.63 g (2.5 mmole) of ester I and 0.34 g (2.5 mmole) of II was heated at 160-170° for 30 min (until the mixture gave a negative test for the presence of ester I with picric acid). The melt was cooled, treated with water, and extracted with ether. The solvent was removed by distillation to give diethyl 2,6-lutidine-3,5-dicarboxylate (V) with mp 72° (73° [5]) and R_f 0.9 (system B). Dry HCl was bubbled through the ether distillate, and the solvent was removed by distillation to give pyridine hydrochloride (XI) with R_f 0.28 (system A); the picrate had mp 160°.

B) By pyridiniobenzamidate (III). A mixture of 0.63 g (2.5 mmole) of ester I and 0.49 g (2.5 mmole) of III was heated at 170-180° for 1 h, after which the mixture was cooled and treated with water. The insoluble portion was removed by filtration, washed with water, and extracted with ether. Workup of the ether solution yielded V with mp 72°. The aqueous solution was extracted with ether to give 0.1 g of benzamide (VII) with mp 129°. No melting-point depression was observed for a mixture of the product with an authentic sample. After isolation of ester V, dry HCl was bubbled into the ether distillate to give hydrochloride XI. Extraction of the aqueous mother liquor with chloroform yielded 0.11 g (22%) of unchanged III.

C) By benzamide (VII). The reaction was carried out in analogy with the dehydrogenation of ester I by means of III. Chromatography of the reaction mixture in system B yielded ester V, unchanged amide VII (77%), and ester I (22%).

D) By pyridiniobenzenesulfonamidate (IV). A mixture of 0.63 g (2.5 mmole) of ester I and 0.58 g (2.5 mmole) of IV was heated at 170-180° for 10 min, after which the melt was cooled and treated with water. The aqueous mixture was made alkaline to pH 8 and extracted with ether. The solvent was removed by distillation to give a mixture of ester V and unchanged IV, which was separated chromatographically in system B. Treatment of the ether distillate with dry HCl gave 0.15 g of hydrochloride XI with R_f 0.28 (system A). The mother liquor was acidified to pH 3 and extracted with ether to give benzenesulfonamide (VIII) with mp 155-156°, which was identical to an authentic sample.

LITERATURE CITED

1. Yu. V. Kurbatov, S. V. Zalyalieva, O. S. Otroshchenko, and A. S. Sadykov, Khim. Geterotsikl. Soedin., 225 (1975).

2. S. V. Zalyalieva, Yu. V. Kurbatov, O. S. Otroshchenko, A. S. Sadykov, and R. Azzamova, Khim. Geterotsikl. Soedin., 816 (1973).
3. V. A. Pal'm, Usp. Khim., 30, 1075 (1961).
4. T. Okamoto, M. Hirobe, C. Mizushima, and A. Ohsawa, J. Pharm. Soc. Japan, 83, 308 (1963).
5. E. Knoevenagel and J. Fuchs, Ber., 35, 1788 (1902).

CHEMISTRY OF HETEROCYCLIC N-OXIDES AND RELATED COMPOUNDS. VI.* REACTION OF PYRIDINE, DIPYRIDYL, AND QUINOLINE N-OXIDES WITH AMMONIA AND AMMONIUM SALTS

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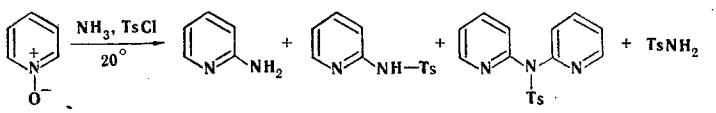
The amination of pyridine, quinoline, and 2,3'- and 4,4'-dipyridyl N-oxides with ammonia and ammonium salts in the presence of p-toluenesulfonyl chloride was studied. 2-Aminopyridine, N-(p-tosyl)-2-aminopyridine, and N-(p-tosyl)-2,2'-dipyridyls were obtained in reactions with pyridine N-oxide. 2-Aminoquinoline was obtained in the amination of quinoline N-oxide. Dipyridyl N-oxides do not undergo amination.

The nucleophilic amination of heteroaromatic N-oxides, which is realizable by the action of ammonia or amines in the presence of acyl halides [2], opens up extensive possibilities for the synthesis of hard-to-obtain α- and γ-amino derivatives of N-heterocycles.

Up until now, amination with ammonia has been investigated only in the case of the reaction with quinoline N-oxide [2]. In the present research we have studied the amination of pyridine, quinoline, and dipyridyl N-oxides with ammonia and ammonium salts in the presence of p-toluenesulfonyl chloride.

According to the data in [2] and our results, the amination of quinoline N-oxide (I) can be achieved by the action of various aminating agents (see Table 1). The utilization of ammonia and ammonium phosphate, which makes it possible to carry out the amination rapidly to give 2-aminoquinoline in high yield (82%), is the most effective procedure. The reaction can be used as a preparative method for the synthesis of aminoquinoline.

In the case of pyridine N-oxide (II), the amination proceeds in a more complex manner: In addition to the expected 2-aminopyridine (III), N-tosyl-2-aminopyridine (IV), N-tosyl-2,2'-dipyridylamine (V) (the chief reaction product), and p-toluenesulfonamide (VI) are formed.



II III IV V VI

In analogy with the scheme for the formation of III, it might have been assumed that the chief reaction product (V) is obtained as a result of amination of N-oxide II by amine III, formed as a result of the reaction, and subsequent tosylation of 2,2'-dipyridylamine (VII).

*See [1] for communication V.

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