CHEMISTRY OF HETEROCYCLIC N-OXIDES AND RELATED COMPOUNDS

III.* HOMOGENEOUS DEHYDROGENATION OF ANABASINE AND THE HANTZSCH ESTER WITH HETEROAROMATIC N-IMINES

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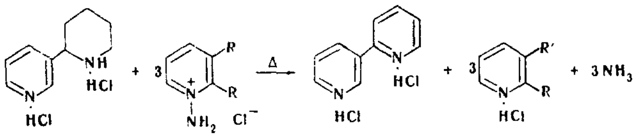
The possibility of homogeneous dehydrogenation of anabasine with N-imines of pyridine, 2-picoline, and quinoline and of the Hantzsch ester with N-tosylimidopyridine and N-tosylimidoquinoline is shown.

Heteroaromatic N-oxides can be used as effective hydrogen acceptors for the dehydrogenation of fully or partially hydrogenated nitrogen-containing heterocycles (see [2] and the literature cited there). On the basis of a comparison of the properties of N-oxides [3] and their nitrogen analogs – N-imines [4] – it might have been assumed that the latter also would prove to be sufficiently active dehydrogenating agents. The validity of this assumption is completely confirmed by the results of the present investigation, the aim of which was a study of the dehydrogenation of anabasine and the Hantzsch ester by means of a number of N-imines of pyridine bases – pyridine, 2-picoline, and quinoline. Since heteroaromatic N-imines are unstable [5], the components of the reaction mixture for the dehydrogenation of anabasine were used in the form of the hydrochlorides, while those for the dehydrogenation of the Hantzsch ester were used in the form of the N-tosyl derivatives.

The hydrochlorides of the N-imines were obtained by N-amination of the corresponding bases by means of O-hydroxylaminesulfonic acid, while the N-tosyl derivatives of the N-imines of pyridine and quinoline were obtained by the action of p-toluenesulfonyl chloride on the N-imines in alkaline media in aqueous acetone solutions.

The dehydrogenation of anabasine is accomplished at 175-220°C to give moderate yields (22-38%) of the dehydrogenation product – 2,3'-dipyridyl, the corresponding deamination products, and ammonia.



a $R=R'=H$; b $R=CH_3$, $R'=H$; c $R-R'=\rangle C_4H_4$

The N-tosyl derivatives of N-imines also have dehydrogenating ability. The results of a study of the homogeneous dehydrogenation of one of the standard compounds – diethyl 1,4-dihydro-2, 6-lutidine-3,5-dicarboxylate (the Hantzsch ester) [6] – show that the indicated compounds are effective hydrogen acceptors that convert the dihydro derivative of pyridine to the corresponding aromatic compound (diethyl 2,6-lutidine-3,5-dicarboxylate) in high yields (92-95%). The corresponding products of the reductive deamination – pyridine and p-toluenesulfonamide – are also formed in the reaction with N-tosylimidopyridine.

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*See [1] for communication II.

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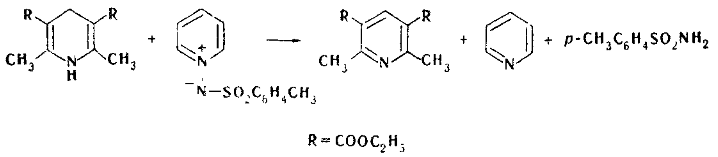

Deamination products are not formed in the reaction with quinoline derivatives. The reaction mixture contains at least nine substances, the presence of which was shown by chromatographic analysis.

Thus the results attest to the fundamental possibility of using N-imines of pyridine bases as homogeneous dehydrogenating agents.

EXPERIMENTAL

The course of the reaction and the operations involved in the isolation of the reaction products were monitored by paper chromatography in the systems: n-butanol—hydrochloric acid—water (50 : 7 : 14, system 1) and n-butanol—acetic acid—water (50 : 7 : 14, system 2) with the Dragendorff reagent as the developer and by thin-layer chromatography (TLC) on activity-II Al_2O_3 in chloroform—benzene—alcohol (22 : 8 : 2, system 3), petroleum ether—ether (system 4), and benzene—alcohol—petroleum ether (16 : 2 : 5, system 5) with iodine vapors as the developer.

Pyridine N-Imine Hydrochloride (I). A solution of 151 g (1 mole) of potassium O-hydroxylaminesulfonate was added in the course of 10 min with vigorous stirring to a heated (to 70°) solution of 39.5 g (0.5 mole) of pyridine in 100 ml of water, after which a solution of 34.5 g of potassium carbonate in 200 ml of water was added, and the mixture was held at 70° for 1 h. It was then cooled and acidified with 20% hydrochloric acid until it was strongly acidic. An equivalent amount of barium chloride was then added to precipitate the sulfates. The precipitate was removed by filtration and washed with water, and the filtrate was vacuum-evaporated to dryness. The residue was extracted in a Soxhlet apparatus with dry acetone to give 28-30 g (43-46%) of hydrochloride I with mp 160-160.5° (mp 160° [5]) and R_f 0.41 (system 1). Found: Cl 27.8%. $C_5H_6N_2 \cdot HCl$. Calculated: Cl 27.2%. The picrate had mp 153-154° (from water) (mp 154-155° [7]).

2-Picoline-N-imine Hydrochloride (II). This compound was similarly obtained in 48% yield and had mp 144-145° (from alcohol) and R_f 0.41 (system 1). Found: Cl 23.7%. $C_6H_8N_2 \cdot HCl$. Calculated: Cl 24.5%. The picrate had mp 129-131° (from water).

Quinoline N-Imine Hydrochloride (III). This compound was obtained in 39-40% yield and had mp 166° (from water) and R_f 0.50 (system 1). Found: Cl 19.1%. $C_9H_8N_2 \cdot HCl$. Calculated: Cl 19.6%. The picrate had mp 189° (from water) (mp 169° [8]). Found: N 18.6%. $C_6H_8N_2 \cdot C_6H_3N_3O_7$. Calculated: N 18.7%.

Dehydrogenation of Anabasine (IV) with Pyridine N-Imine. A mixture of 1.17 g (5 mmole) of hydrochloride IV and 2 g (15 mmole) of I was heated at 210-220° for 3 h, after which the mixture was dissolved in water. The solution was made alkaline to pH 4-5 and extracted with ether. The extract was dried with anhydrous sodium sulfate, and the solvent was removed by distillation. The residue contained 0.2 g (26%) of 2,3'-dipyridyl (V). The picrate had mp 154-155° (from water; no melting-point depression was observed for a mixture with an authentic sample), R_f 0.90 (system 2); this is in agreement with the data for V. Dry hydrogen chloride was bubbled through the ether distillate, after which the solvent was removed. The residue contained 0.25 g (20%) of pyridine hydrochloride (VI). The picrate had mp 160° (from water). A mixture with a sample of the picrate of VI had mp 160°. The R_f value was 0.28 (system 1), which is in agreement with the value for VI. The aqueous mother liquor was made alkaline to pH 8 and extracted with ether. The usual workup gave 0.58 g (50%) of IV. The picrate had mp 200-202° (from water). The melting point of a mixture with a sample of the picrate of IV was 200-202°; R_f 0.56 (system 2). The presence of ammonia in the residual aqueous solution was proved with Nessler's reagent.

Dehydrogenation of Anabasine with 2-Picoline N-Imine. The reaction was carried out at 180-190° for 5 h, after which the mixture was worked up to give V [in 22% yield; R_f 0.90 (system 2); picrate, mp 150°; no melting-point depression was observed for a mixture with the picrate of a genuine sample], 2-picoline hydrochloride [in 13% yield; R_f 0.45 (system 1)], unchanged IV [0.23% yield; R_f 0.54 (system 2); the picrate had mp 203-205°], and unchanged 2-picoline-N-imine hydrochloride (18%).

Dehydrogenation of Anabasine with Quinoline N-Imine. A mixture of 0.87 g (0.003 mole) of hydrochloride IV and 2 g (0.11 mole) of III was heated at 175-200° for 5 h, after which the mixture was treated with water and extracted (at pH 5) with ether. The solvent was removed by distillation to give a mixture of V and quinoline (VII), which was then separated by fractional steam distillation to give 0.22 g (38%) of V with R_f 0.90 (system 2). The picrate had mp 150-151°. The melting point of a mixture with the picrate of a sample of V was 150-151°. The yield of VII was 0.4 g (28%); R_f 0.93 (system 2). The picrate had mp 202-203°. The melting point of a mixture with the picrate of a sample of VII was 200-203°. The mother liquor was extracted with ether (at pH 8) to give 0.35 g (40%) of unchanged IV with R_f 0.54 (system 2); the picrate had mp 203-205°. The mother liquor remaining after the isolation of IV was acidified with hydrochloric acid and evaporated, and the residue was extracted with acetone to give unchanged III; the picrate had mp 188-189°.

N-Tosylimidopyridine (VIII). Potassium carbonate was added to 1.3 g (0.01 mole) of I in 4 ml of water until the mixture was strongly alkaline, after which a solution of 2.5 g (0.013 mole) of p-toluenesulfonyl chloride in 10 ml of acetone was added. The mixture was shaken for a few minutes and allowed to stand overnight. The precipitated crystals were removed by filtration, washed with water, and recrystallized from alcohol to give 1.6 g (64%) of a product with mp 209° (mp 210° [9]); R_f 0.31 (system 3).

N-Tosylimidoquinoline (IX). This compound was similarly obtained in 70% yield and had mp 227° (mp 227-228° [10]); R_f 0.35 (system 3).

Dehydrogenation of the Hantzsch Ester with N-Tosylimidopyridine. A mixture of 0.63 g (2.5 mmole) of the Hantzsch ester (X) and 0.62 g (2.5 mmole) of VIII was heated at 175-200° for 5 min. The mixture was cooled and treated with 2 N potassium hydroxide solution, and extracted with ether. The extract was dried with anhydrous sodium sulfate, and the solvent was removed by distillation to give 0.58 g (92%) of diethyl 2,6-lutidine-3,5-dicarboxylate (XI) with mp 71-72° (mp 73° [11]); R_f 0.9 (system 4). Passage of dry hydrogen chloride through the ether distillate and removal of the solvent yielded 0.25 g (88%) of hydrochloride VI. The mother liquor was acidified to pH 3 and extracted with ether. Removal of the solvent by distillation gave 0.37 g (87%) of p-toluenesulfonamide with mp 136-137° and R_f 0.25 (system 3); this corresponds to the data for a genuine sample.

Dehydrogenation of the Hantzsch Ester with N-Tosylimidoquinoline. A mixture of 0.63 g (2.5 mmole) of X and 0.74 g (2.5 mmole) of VIII was heated at 140-150° for 7-8 min. The reaction was accompanied by pronounced resinification. Chromatography in system 4 yielded 0.6 g (95%) of XI with mp 71-72° and R_f 0.9. The residue was a complex mixture of substances, which gave the following R_f values on chromatography in system 5: 0.30, 0.46, 0.54, 0.56, 0.60, 0.64, 0.68, 0.74, and 0.79.

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