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SYNTHESES RELATING TO ANABASINE BASE

XX. Chlorination Of Anabasine*

V. K. Kiryukhin, V. S. Otroshchenko, and A. S. Sadykov

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Chlorination of anabasine and piperidine with chlorine at 220-230° leads to dehydrogenation and formation of respectively, 5-chloro-2,3'-dipyridyl and 3-chloropyridine.

Anabasine has previously been chlorinated in cooled alcoholic solution, using chlorine gas, and dichloroanabasine hydrochloride mp 203-207° [1]. A study has now been made of chlorination under more drastic conditions, approximating those used for chlorinating pyridine [2]. It proved possible to isolate a monochloro-base, a colorless liquid bp 147-150° (8 mm), which darkens on standing, and is insoluble in water. The base is characterized by its IR and UV spectra, as well as by its picrate, hydrochloride, and methiodide. The UV spectrum of the base (Fig. 1) is characterized by the presence of two absorption maxima, at 234 and 274 mμ, corresponding to the α,β-dipyridyl skeleton.

Comparison of the non-coplanar deformation vibrations of the C–H bond (650-880 cm^{-1}) of the compound obtained with those due to benzene substituents [3], shows that the 775 and 715 cm^{-1} bands indicate 1,3 substitution, while the 824 and 886 cm^{-1} bands indicate 1,2,4 substitution.

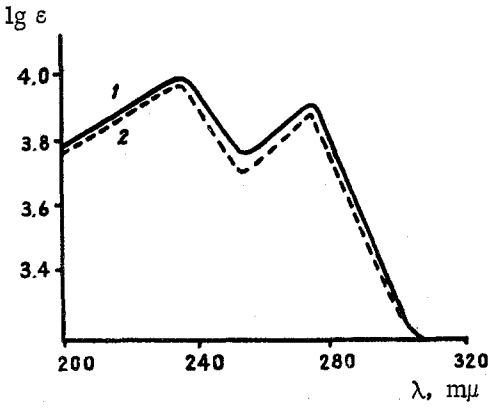
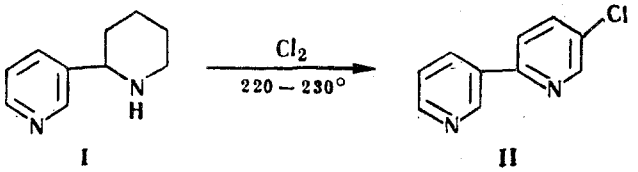


Fig. 1. UV spectrum of 5-chloro-2,3-dipyridyl (II). SF-4 spectrophotometer, in methanol: 1) obtained by chlorinating anabasine (I); 2) obtained from 5-hydroxy-2,3-dipyridyl (IV).

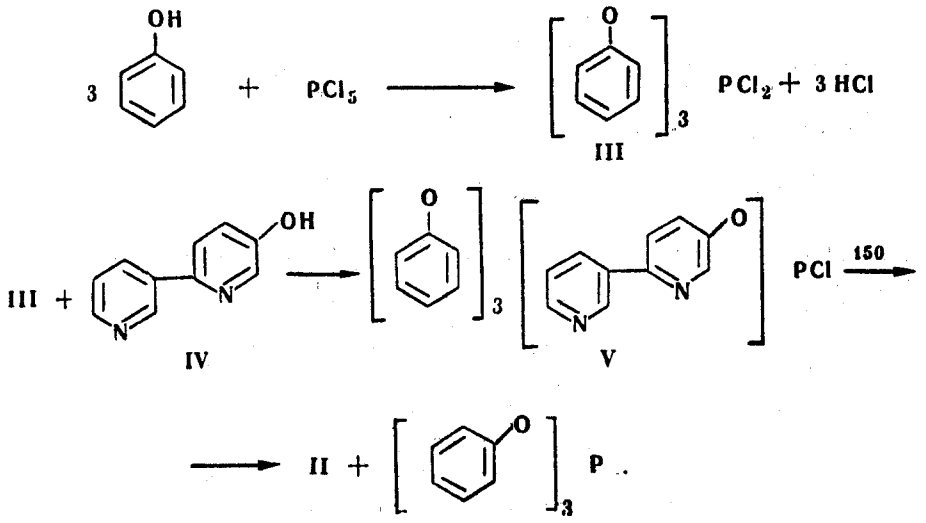
So it can be assumed that the anabasine chlorination product is 5-chloro-2,3-dipyridyl (II)



I II

An attempt to prove the structure of this compound as the corresponding hydroxy derivative failed. Then the hydroxy product prepared from 2,3'-dipyridyl 5-sulfonic acid (IV) [4] was converted to the corresponding halogen derivative. Knowing [6] that the β-hydroxy group in pyridine cannot be replaced by the usual methods, i.e., by the action of phosphorus and sulfur halides, use was made of the decomposition reaction of tetraarylhydroxyphosphoric monohalogen compounds [5]. In this case the latter was prepared by reacting phenol with PCl_5, followed by heating with 5-hydroxy-2,3'-dipyridyl:

*For Part XIX see [8].



When heated for a short time at 150°, V decomposed to give the dipyridyl II. UV and IR spectra of 5-chloro-1, 2-dipyridyl obtained from IV, were identical with the spectra of the anabasine chlorination product (Figs. 1 and 2).

The melting point of the picrate of 5-chloro-2, 3'dipyridyl prepared by chlorinating anabasine, was undepressed when mixed with the picrate of the same compound prepared from 2, 3'dipyridyl-5-sulfonic acid.

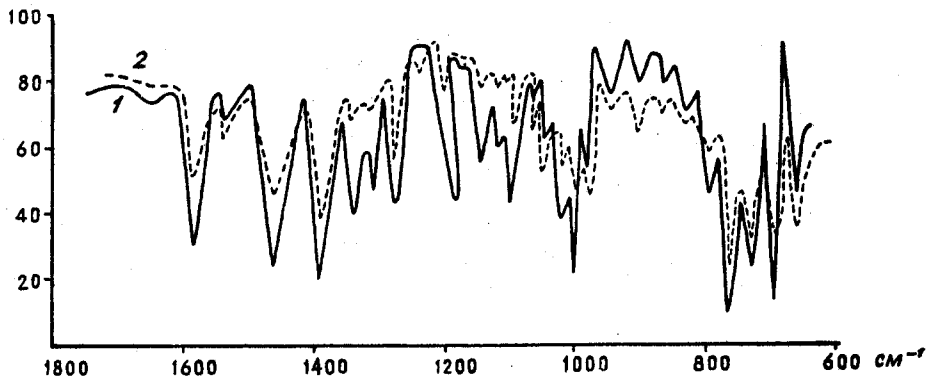


Fig. 2. IR spectrum of 5-chloro-2, 3-dipyridyl (II). IKS-14 spectrophotometer, NaCl prism: 1) obtained by chlorinating anabasine (I); 2) obtained from 5-hydroxy-2, 3-dipyridyl (IV).

Piperidine was chlorinated under similar conditions, and 3-chloropyridine isolated. For comparison, 3-chloropyridine was prepared by the Gatterman reaction from 3-aminopyridine and was diazotized in hydrochloric acid [7]. The mixed melting point of the picrates was undepressed.

Experimental

Anabasine chlorination. A dry acetone solution of HCl was added in small portions with cooling, to an acetone solution of 36 g anabasine, until a slightly acid reaction was obtained. The hydrochloride was separated from the solvent, carefully dried in a vacuum desiccator, and then heated for 1 hr 30 min to 2 hr at 220-230° in a stream of chlorine. Evolution of hydrogen chloride and marked tar formation were observed. At the end of the reaction, the mixture was dissolved in 50 ml methanol, and 15 ml acetone added to the cold solution. After removing the tarry matter the filtrate was distilled to dryness on a water bath, the dry residue taken up in 100 ml water, brought to alkaline pH 9-10 with potash, and extracted with ether. The ethereal extract was dried over potash. The solvent was distilled off, leaving an oil which distilled at 147-150° (8 mm). The yield of 5-chloro-2-3'-dipyridyl (V) was 13.2 g (31%); R_f 0.85 (butanol-water-hydrochloric acid 5:1:1), R_f of anabasine in this system was 0.47. Found: N 15.06, 15.04%. Calculated for $C_{10}H_7ClN_2$: N 14.70%.

5-Chloro-2,3'-dipyridyl hydrochloride was prepared by adding an acetone solution of HCl to an acetone solution of the base until an acid reaction to congo red was obtained; mp 217-220° (from methanol). Found: N 12.49; 12.19; Cl' 16.01; 15.90; ΣCl 31.70; 32.00%. Calculated for $C_{10}H_7ClN_2 \cdot HCl$: N 12.39; Cl' 15.63; ΣCl 31.26%.

The picrate was prepared by mixing alcoholic solutions of base and picric acid. After repeated crystallizing from methanol, the mp was 173°. Found: N 16.94%, 16.93%. Calculated for $C_{10}H_7ClN_2 \cdot C_6H_3N_3O_7$: N 16.70%.

The methiodide was obtained by heating together on a water bath 2 g CH_3I and 1 g base II in 10 ml methanol for eight hr. In 24 hr pale yellow crystals separated. After crystallizing from methanol, the mp was 162-163°. Found: I 39.64, 39.38%. Calculated for $C_{10}H_7ClN_2 \cdot CH_3I$: 39.16%.

Alkali melt treatment of 5-chloro-2,3'-dipyridyl (II). 1.2 g II was heated for 6 hr at 250-280° in an autoclave with 3.5 g potassium hydroxide and 3 ml water. Chromatography showed that the only substance present had R_f 0.85. As the reaction mixture became alkaline oil was precipitated and was extracted with ether. After distilling off the ether there remained a pale yellow oil, which was the original base.

Picrate: mp 170-171°, mixed mp with the picrate of 5-chloro-2,3' dipyridyl, 170°.

5-Chloro-2,3'-dipyridyl from 2,3' dipyridyl 5-sulfonic acid.

a) A mixture of 3 g of potassium-1,2'-dipyridyl-5-sulfonate and 9 g potassium hydroxide was heated at 280-300° for 30 min in a nickel crucible. The melt was dissolved in water, acidified to pH 3 with hydrochloric acid, then ammonia added to bring it to pH 7, which resulted in the formation of a white flocculent precipitate; this was filtered off, washed with water, and dried for 16 hr at 100° (20 mm). Yield 1.5 g (74%) 5-hydroxy-2,3'-dipyridyl, mp 179-180° (the literature [4] gives 179°).

b) 1.64 g phenol and 1.21 g PCl_5 were heated together on a steam bath for 6 hr, 1.0 g 5-hydroxy-2,3'-dipyridyl was added to the reaction products, after which the mixture was heated for 6 hr at 100° and 15 min at 150-155°. After cooling, the melt was dissolved in 50 ml 5% potash solution, and extracted with ether. The ether extract was dried over potash, the solvent distilled off, and the residue vacuum-distilled, a cut 150-153° (12 mm) being taken. Yield 0.7 g II, R_f 0.85. Found: N 15.30, 15.34%. Calculated for $C_{10}H_7ClN_2$: N 14.70%.

Picrate: mp 173° (from methanol). Found: 17.05, 16.15%. Calculated for $C_{10}H_7ClN_2 \cdot C_6H_3N_3O_7$: N 15.70%.

A mixed mp (172-173°) was obtained with the picrate of 5-chloro-2,3'-dipyridyl prepared either by chlorinating anabasine, or from 2,3'-dipyridyl-5-sulfonic acid.

Piperidine chlorination. Chlorine was passed for 1 hr 30 min to 2 hr through 30 g piperidine hydrochloride at 220°. At the end of the reaction the products were dissolved in 50-75 ml water, the solution made strongly alkaline, and steam distilled. The distillate was extracted with ether. The ethereal extract was dried over potash, the solvent distilled off, and the residue distilled. Yield of cut 149-151° 2.2 g (8%) 3-chloropyridine. Found: N 11.60; 11.51%. Calculated for C_5H_4ClN: N 11.45%.

Picrate mp 140-142° (from methanol). Found: N 16.70, 16.41, 16.52%. Calculated for $C_5H_4ClN \cdot C_6H_3N_3O_7$: 16.35%.

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Lenin Tashkent State University