OXIDATION OF ORGANIC COMPOUNDS

LI. Synthesis of 2,5-Dicyanopyridine*

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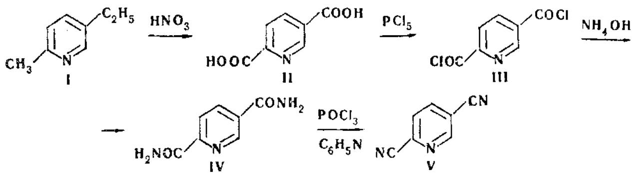
The synthesis of 2, 5-dicyanopyridine from the industrially available 5-ethyl-2-methylpyridine has been effected by oxidative ammonolysis in the presence of a vanadium-tin oxide catalyst and by oxidation with nitric acid to isocinchomeronic acid with the subsequent conversion of the latter into the dichloride, diamide, and dinitrile. The IR spectra of 2, 5-dicyanopyridine have been obtained and its polarographic behavior has been studied.

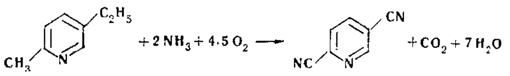
The object of the present work was to study the possible routes for the synthesis of 2,5-dicyanopyridine. Only one paper has appeared in the literature on this question [2], and in this it is shown that it can be obtained with a yield of 17% by the reaction of 3-cyano-1-methoxypyridine methosulfate with potassium cyanide.

One of the methods of synthesis that we have tried is represented by the scheme:



The starting material was 5-ethyl-2-methylpyridine (I), which was oxidized with nitric acid to isocinchomeronic acid (II). The reaction of II with phosphorus pentachloride at a temperature not exceeding 45–50° C yielded the dichloride of isocinchomeronic acid (III). Without the isolation of the III, the reaction solution was treated with 25% aqueous ammonia solution to give isocinchomeronic diamide IV. The dehydration of IV in the presence of phosphorus oxychloride and pyridine with strong cooling led to 2,5-dicyanopyridine (V) with an over-all yield of 28% calculated on the I taken.

A second method of synthesizing V is based on the oxidative ammonolysis of I:



The process is carried out in one stage under approximately the same conditions as those for the formation of terephthalodinitrile from p-xylene [3]. The yield of V amounts to 35%, calculated on the I taken.

EXPERIMENTAL

Isocinchomeronic acid (II). The nitric acid oxidation of 30 g of I with bp 172–174° C (700 mm), d_4^{20} 0.9198 and n_D^{20} 1.4985 by a published method [4] yielded 36.2 g (87.4%) of II with mp 237° C and the theoretical neutralization equivalent. Found, %: C 48.96, 49.48; H 2.97, 3.01; N 8.57, 8.87. Calculated for $C_7H_5NO_4$, %: C 50.30; H 3.00; N 8.38.

Isocinchomeronyl dichloride (III). When 33.4 g (0.20 mole) of II and 85 g (0.40 mole) of phosphorus pentachloride were carefully mixed, the reaction began instantaneously. To promote the elimination by distillation of the phosphorus oxychloride and hydrogen chloride formed, the reduced pressure created by a water pump was applied. After some minutes, to accelerate the process the reaction mixture was heated in the water bath to 45–50° C. The reaction was complete after 1 hr 30 min and the resulting reddish mixture was cooled, diluted with 100 ml of dioxane, and left overnight. On the following day the solution of III was decanted from the solid matter and was used as such for the synthesis of IV.

Half-Wave Potentials of Isocinchomerondinitrile as a Function of the pH of a Buffer Solution

pH	$E'_{1/2}$, V	$E''_{1/2}$, V	pH	$E'_{1/2}$, V	$E''_{1/2}$, V
2.4	−0.81	−1.15	6.4	−1.00	−1.20
2.6	−0.82	−1.13	7.0	−1.03	−1.20
3.0	−0.83	−1.16	7.3	−1.06	−1.21
3.4	−0.86	−1.19	7.6	−1.05	−1.20
3.6	−0.86	−1.18	8.0	−1.06	−1.20
3.9	−0.87	−1.20	8.5	−1.08 (Pre-wave)	−1.21
4.2	−0.88	−1.20	9.0	Pre-wave	−1.22
4.5	−0.91	−1.18	9.6	"	−1.23
4.8	−0.90	−1.19	10.0	"	−1.23
5.2	−0.93	−1.19	10.6	"	−1.22
5.5	−0.98	−1.21	11.2	"	−1.22
5.8	−0.98	−1.19	12.0	None	−1.22
6.0	−1.00	−1.20	12.6	"	−1.26
6.2	−1.00	−1.20	0.1 *N* HCl	−0.70	−1.05

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*For part L, see [1].

Isocinchomerondiamide (IV). With careful stirring, the solution of **III** obtained as described above was slowly added dropwise to 150 ml of well-cooled 25% aqueous ammonia. It was necessary to keep the temperature of the reaction mixture below 15° C. The precipitate of **IV** that formed was filtered off and was washed with several portions of cold water, and then with two portions of ethanol and with three portions of ether. After drying at 120° C, 23.6 g (71.5%, calculated on the **II** taken) of **IV** was obtained with mp 300° C. Found, %: C 50.62, 50.85; H 4.23, 4.37; N 24.09, 24.29. Calculated for $C_7H_7N_3O_2$, %: C 50.90; H 4.24; N 25.45.

Isocinchomerondinitrile (V). A mixture of 23 g (~0.12 mole) of phosphorus oxychloride and 20 g (~0.25 mole) of dry pyridine were added over 5 min with stirring to a dispersion of 16.5 g (0.10 mole) of **IV** in 100 ml of dried and redistilled pyridine. In making up the mixture added, the two components were previously cooled to 0° C. After brief heating in the water bath, the reaction mixture rapidly boiled and assumed a brown color. After 3–5 min stirring was stopped and the thickening mass was left to cool, and then several pieces of ice were added to it and these were followed by 50 ml of 10% hydrochloric acid to bind the pyridine. After this, the reaction mixture was extracted with twelve 50-ml portions of ether, the ethereal extract was dried with sodium sulfate, and the ether was distilled off. The residue was recrystallized from boiling water. The yield of V was 5.7 g, which corresponds to 44.2% calculated on the **IV** and 27.8% calculated on the **I** taken. After sublimation and additional recrystallization from ethanol, the mp of the V was 112–113° C (according to the literature [2], 111–112° C). Found, %: C 65.23, 65.39; H 2.89, 2.98, N 32.56, 32.74. Calculated for $C_7H_3N_3$, %: C 65.11; H 2.32 N 32.55. IR spectrum*, cm^{-1}: 3070, 3030 (C–H), 1592, 1585, 1570, 1490 (pyridine ring), 2245 ($C{\equiv}N$).

The polarographic behavior of V was also studied. The polarograms were taken on a PE-312TsLA electronic polarograph in aqueous solutions on a support of veronal buffers in the range pH 2.4–12.0 (table). It was found that under these conditions V gives two reduction waves. The first of them is convenient for measurement at pH 2.4–6.8. As can be seen from the table, with an increase in the pH its $E_{1/2}$ (relative to the SCE) shifts in the negative direction. $E_{1/2}$ of the second wave is stable in the pH range from 3.6 to 12.0. The limiting current of both waves of V in the solutions studied depends linearly on the pH. The results obtained permit the conclusion that to determine V quantitatively it is best to use as support a buffer solution with pH 12.0, since in this case one clear reduction wave is found.

Oxidative ammonolysis of 5-ethyl-2-methylpyridine (I). The reaction was carried out in an apparatus of the continuous type with a stainless steel reaction tube 21 mm in diameter and 1100 mm long. The catalyst used was fused tin vanadate. The reaction products were trapped in zigzag glass tubes [5]. The experiment was carried out for 10 hr at a rate of feed of I of 50 g, of ammonia of 220 g, and of air of 4800 *l* per liter of catalyst per hour and contact time 0.3 sec. In all, 25 g of **I** was fed. The V was extracted from the system for trapping the reaction products and was purified by recrystallization from water, mp 109–110° C. In admixture with the **V** obtained from **I** via **II**, **III**, and **IV**, it gave no depression of the melting point. In all, 9.3 g (35%) of V was obtained.

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*The IR spectra were taken by Yu. A. Kushnikov and F. Ivanovskaya. Detailed information about these spectra and also the Raman and electronic spectra will be given in subsequent papers.