STUDIES IN THE PYRIDINECARBOXYLIC ACID SERIES.

IV. SYNTHESIS OF NICOTINIC ACID AND NICOTINAMIDE BY VAPOR-PHASE OXIDATIVE AMMONOLYSIS OF QUINOLINE

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One of the methods for preparing nicotinic acid is the vapor-phase oxidative ammonlysis of β-substituted alkylpyridines or quinoline. The 3-cyanopyridine obtained thereupon can be hydrolyzed to nicotinic acid or its amide in high yield [1]. The Institute of Chemical Sciences of the Academy of Sciences of the Kazakh SSR has worked out such a method of synthesizing 3-cyanopyridine in 70% yield from β-picoline and has suggested it for practical use [2]. With the objective of broadening the raw material base for nicotinic acid synthesis, we have carried out studies on the oxidative ammonlysis of technical quinoline.

Chekmareva [1] has investigated the possibility of preparing 3-cyanopyridine (I) by vapor-phase oxidative ammonolysis of technical 67% quinoline over a vanadium – tin catalyst of the composition $V_2O_5:SnO_2 = 1:1.5$. The yield of I was 21%, and benzonitrile (II) and 4-cyanopyridine (III) were present in the product obtained: the catalyst caked rapidly, which limited its service life to a few hours. At present 92-95% quinoline containing 4-5% isoquinoline has become an available raw material. We have used this product as a starting material. The purpose of this study was selecting a catalyst and process conditions which would enable us to increase the yield of I. Two groups of fused catalysts were investigated: vanadium – tin catalysts (V_2O_5, SnO_2) and vanadium – molybdenum catalysts (V_2O_5, MoO_3) with component ratios of 2:1, 1.5:1, 1:1, 1:1.5, and 1:2. The V_2O_5, SnO_2 catalyst with a component ratio of 1:1.5 (yield of I, 28-32%) and the V_2O_5, MoO_3 catalysts with component ratios of 1.5:1 and 1:1 (yield of I, 31-35%) proved best. Preference was given to the vanadium – molybdenum catalysts, since they selectively cleave the aromatic nucleus of quinoline. When they were used, the impurity of II did not exceed 2%, and no appreciable impurity of III was detected. Considering possible resin formation, the catalyst was diluted with granulated quartz in a proportion of 1:1 or 2:1 to avoid caking. The reaction products were analyzed by the methods previously worked out [3-5]. Liquid reaction products were preliminarily extracted from the catalyzate with ether or chloroform at pH 8.0 or 5.0-6.0; the extract was dried over sodium sulfate and the solution was evaporated. Before analysis by gas chromatography, the amides were converted into the corresponding nitriles by treatment with phosgene and dimethylformamide [6] or with phosphorus oxychloride in pyridine; the carboxylic acids were converted into the corresponding ethyl esters [6]. Amides and carboxylic acids were detected in the residue after evaporating the aqueous layers of the catalyzates.

The gaseous reaction products were represented by carbon oxides and hydrogen cyanide. In the reaction mixtures we detected benzene, pyridine, benzaldehyde, benzonitrile, 3-cyanopyridine, quinoline, isoquinoline, benzoic acid, and also small amounts of benzamide and nicotinamide. Other substances were also represented on the chromatogram; these were not identified. We identified fumaric, benzoic, nicotinic, and quinolinic acids as their ethyl ester.

The influence of temperature on the quantitative composition of the aromatic by-products is shown in Fig. 1. The optimum temperature for forming most of them is 370-410°. The content of each of these by-products did not exceed 2%.

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* Deceased.

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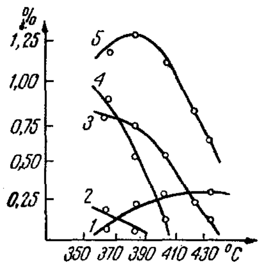

Fig. 1. Dependence of yield of impurities on reaction temperature in the process of oxidative ammonolysis of quinoline. 1) Pyridine; 2) benzene; 3) benzaldehyde; 4) benzoic acid; 5) benzonitrile.

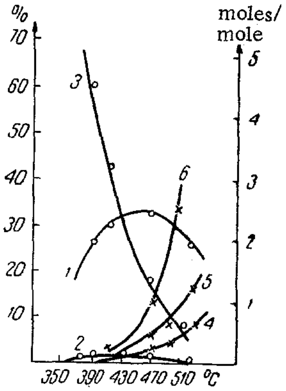

Fig. 2. Dependence of yield of 3-cyanopyridine (1), carbon monoxide (5), carbon dioxide (6), and hydrogen cyanide (4) on reaction temperature in oxidative ammonolysis of quinoline. 2) Benzonitrile; 3) recovered quinoline.

We have investigated and selected optimum conditions for carrying out this process. The maximum yield of I (34% based on quinoline taken, or 41% after allowing for quinoline recovered) was attained under the following reaction conditions (calculated per 1 liter of catalyst per hour): 30 g of quinoline; air velocity, 1400 liters/h; 600 ml of 25% ammonia solution; reaction temperature, 460-480°. When the reaction temperature is further increased, the yield of nicotinonitrile is appreciably reduced and the formation of gaseous reaction products is increased (Fig. 2).

An increase in the charge of raw material onto catalyst decreases the yield of nicotinonitrile, which can be explained by the small specific surface (S_{sp}) of most of the fused catalysts (according to our data, $S_{sp} = 1\text{-}3\ m^2/g$ for tin or molybdenum vanadates). The maximum yield of nicotinonitrile was observed at space velocities of 1600-2400 liters/h per liter of catalyst and a contact time of 0.19-0.2 sec. It was found that a 15-20-fold amount of 15% aqueous ammonia solution based on weight of quinoline is required to suppress formation of resinous by-products. A study of the rate of formation of gaseous products on fused vanadium – molybdenum catalyst showed that oxidation of quinoline sets in and then grows rapidly from a temperature of 430-450° and above (see Fig. 2).

Studying the effect of amount of ammonia on the yield of gaseous products, we established that addition of ammonia suppresses deep-seated oxidation processes.

A mixture composed of I (33-35%) and unreacted quinoline is usually obtained after vapor-phase oxidative ammonolysis of technical quinolines. To obtain nicotinic acid and nicotinamide, I was hydrolyzed in the presence of quinoline with potassium hydroxide or sodium hydroxide, or also using AV-17 ion-exchange resin [7].

EXPERIMENTAL

Preparation of Fused Catalyst. A mixture of 273 g (1.5 mole) of vanadium pentoxide (V_2O_5) and 144 g (1 mole) of molybdenum trioxide (MoO_3) was roasted in a muffle furnace for 3-4 h at 1000-1100°. The melt obtained was poured onto a tray, it was cooled and ground, and the particles 2-5 mm in size were selected. $S_{sp} = 2.4\ m^2/g$.

The ammonium salts, NH_4VO_3 and $(NH_4)_6Mo_7O_{24} \cdot 4H_2O$, can be used to prepare the catalyst instead of V_2O_5 and MoO_3. The fused catalysts with other ratios of ingredients are prepared similarly.

Ammonolysis of Quinoline. A mixture of 10 g of quinoline, 200 ml of 15% aqueous ammonia solution, and 550 liters of air was passed through a catalyst tube 1000 mm long and of 30 mm internal diameter, filled with 250 ml of catalyst ($V_2O_5:MoO_3=1:1$, the 2-5 mm fraction) mixed with granulated quartz (1:1), at 455-465° in the course of one hour. The reaction products from the catalyzate and wash waters, after extraction and drying, were concentrated, and there was obtained 4.98 g of a mixture composed of 2.79 g (33.3%) of 3-cyanopyridine (40.7% after allowing for quinoline recovered), 2.55 g (25.5%) of unreacted quinoline, and 0.21 g of other substances.

Nicotinamide. A. A mixture of 3 g of 3-cyanopyridine and 2.8 g of quinoline was heated with 75 ml of distilled water and 15 g of AV17 × 84 ion-exchange resin in the OH-form for 2 h at 55-60°. The resin was separated and washed with 25 ml of distilled water, the quinoline was removed from the combined filtrates, the aqueous solution was boiled with activated charcoal, it was filtered, and the filtrate was evaporated under a vacuum of 40-60 mm. The yield of nicotinamide was 3.02 g (85.8%), mp 128-129°.

B. A mixture of 10 g of 3-cyanopyridine and 9.34 g of quinoline with 40 ml of water was boiled for 15 min, 0.1 g of potassium hydroxide was added, the mixture was boiled for another 45 min, it was cooled, the quinoline was separated, and the aqueous solution was evaporated to dryness under mild conditions. The residue was crushed, dried at 60-70°, and dissolved in 150 ml of acetone; the solution was boiled in the presence of 0.2 g of activated charcoal, the hot solution was filtered, it was evaporated, and was cooled to 0-2° to cause nicotinamide to crystallize. There was obtained 6.35 g (54.3%) of material, mp 128.5-130° (87.4% after allowing for 3.8 g of 3-cyanopyridine recovered in the quinoline).

Nicotinic Acid. A mixture of 10 g of 3-cyanopyridine, 9.34 g of quinoline, and 5.7 g of potassium hydroxide in 50 ml of water was boiled for 3-4 h; it was cooled, the quinoline was removed, the mixture was boiled for another 30 min with 0.2 g of activated charcoal, it was filtered, an 18% hydrochloric acid solution was added to pH 3.4, and the solution was evaporated and cooled; the product obtained was recrystallized from water, with boiling with activated charcoal. The nicotinic acid which separated was filtered off, it was dried at 100-105°, and 9.94 g (84.0%) of product was obtained, mp 235-236°.

Ethyl Nicotinate. To the mixture of nicotinic acid and inorganic salts obtained after evaporation (preceding example) was added 75 ml of dry alcohol and 30 ml of sulfuric acid (sp. gr. 1.84), and the mixture was heated for 4 h. After neutralization with sodium carbonate and isolation of the product there was obtained 8.95 g (61.4% based on 3-cyanopyridine) of the ethyl ester, bp 85.8-86.5° (3 mm).

CONCLUSIONS

1. The vapor-phase oxidative ammonolysis of technical quinoline on a fused vanadium – molybdenum catalyst has been studied.

2. Nicotinic acid and nicotinamide have been synthesized from 3-cyanopyridine.

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