

OXIDATIVE AMMONOLYSIS OF 2,4,6-COLLIDINE AT VANADIUM-TITANIUM OXIDE CATALYST

A. D. Kagarlitsky and L. A. Krichevsky

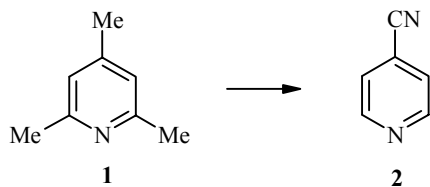
4-Cyanopyridine was synthesized from the readily obtainable 2,4,6-collidine by oxidative ammonolysis in the presence of vanadium-titanium oxide catalyst. Conditions under which the yield of the product amounted to 73% on the amount of the trimethylpyridine were found.

Keywords: 2,4,6-collidine, oxidative ammonolysis, vanadium-titanium oxide catalyst.

The nitriles produced during the oxidative ammonolysis of alkylpyridines [1] have been used as intermediates in the production of drugs – tuberculostatics [2, 3], vitamins [4], cardiogenic agents [5] – and also in the synthesis of heat-resistant polymeric materials [6].

2,4,6-Collidine (**1**) numbers among the readily obtainable compounds, but its oxidative ammonolysis has hardly been studied at all. In the single paper devoted to this question [7] it was shown that in the presence of vanadium oxide catalyst promoted with silver (V:Ag = 1:0.003 at.%) the main reaction products were 2-cyano-4,6-dimethylpyridine and 2,4-dicyano-6-methylpyridine with yields of 19.4 and 11.5% respectively, calculated on the reacted material.

We investigated the oxidative ammonolysis of compound **1** in the presence of vanadium-titanium oxide catalyst with $V_2O_5:TiO_2 = 1:16$ (molar ratio). The basis for the choice of such a catalyst was the fact that, as previously established by one of us with colleagues, methyl groups at position 2 of the pyridine ring underwent dealkylation in this reaction, where the reaction mixture was rich in water [8], while those at position 4 were converted under analogous conditions into a cyano group [9]. Thus, it was proposed to attempt the transformation of compound **1** into isonicotinonitrile **2**:



This conclusion was supported by experiment. The main product from oxidative ammonolysis of the collidine **1** under the selected conditions was cyanopyridine **2**. The minor products of the reaction were 2-amido-4-methylpyridine **3** and 2-amido-4-cyanopyridine **4** and also the pyridine **5** and picolinic acid **6** (Table 1), formed as a result of hydrolysis of the 2-cyanopyridine.

Institute of Phytochemistry, Ministry of Education and Science of the Kazakhstan Republic, Karaganda 470032; e-mail: arglabin@phyto.karaganda.su. Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 3, pp. 358-360, March, 2003. Original article submitted November 22, 2001.

TABLE 1. The Dependence of the Yield of the Products from Oxidative Ammonolysis of Collidine **1** on the Process Parameters (Delivery Rate of 2,4,6-Collidine 21.32 g/l_{cat}·h, Oxygen 17 mol/mol of 2,4,6-Collidine)

Experiment	T, °C	NH ₃ : 1 , mol/mol	H ₂ O: 1 , mol/mol	1 *, %	Yield, %				
					2	3	4	5	6
1	300	8	10	92	2	2	1	—	1
2	320	8	10	82	8	4	—	4	2
3	340	8	10	54	26	4	—	8	4
4	360	8	10	28	48	2	—	20	—
5	380	8	10	20	51	—	—	24	—
6	300	8	20	48	2	28	8	2	8
7	320	8	20	44	18	16	4	10	—
8	340	8	20	36	40	5	5	14	2
9	360	8	20	20	52	—	—	24	—
10	380	8	20	14	56	—	—	28	—
11	300	6	30	30	48	—	—	5	14
12	320	6	30	20	60	—	—	16	1
13	340	6	30	10	70	—	—	20	—
14	360	6	30	6	72	—	—	22	—
15	380	6	30	3	76	—	—	21	—
16	400	6	30	1	74	—	3	20	—

* Unreacted collidine **1**.

Under optimum conditions (380°C, molar ratio 1:oxygen:ammonia:water = 1:17:6:30) the yield of cyanopyridine **2** amounted to 76%. This makes it possible to use the oxidative ammonolysis of collidine **1** for the production of this compound, which is an intermediate in the synthesis of the antituberculosis product Isoniazid.

EXPERIMENTAL

The oxidative ammonolysis of collidine **1** was studied in the range of 300-400°C. The flow rate of the reaction mixture was 370-555 h⁻¹ by volume, and the molar ratio collidine 1:oxygen:ammonia:water was 1:17:(2-10):(10-50). A flow-type stainless steel reactor, in which 43 cm³ of the catalyst was placed, was used for the experiments. The reaction products were isolated by column chromatography (a column of silica gel L100/160) and identified by elemental analysis and IR and NMR spectroscopy.

The amounts of the unreacted compound **1** and the reaction products were determined by GLC on a Chrom-5 chromatograph with a flame-ionization detector. Silicone elastomer SE-30, deposited on Chromaton NAW-HMDS at the rate of 5% was used as stationary phase (column temperature 130°C, length 2.5 m, internal diameter 3 mm). Benzonitrile was used as internal standard for quantitative analysis.

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