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Functionally substituted pyrazines are widely used as starting compounds for obtaining a whole gamut of medicinal preparations for the most diverse purposes, of which tuberculostatic agents have won the greatest recognition [7, 16, 17]. One of the most well-known compounds in this series is pyrazine-2-carboxylic acid amide (I) – the preparation pyrazinamide. This compound, in turn, serves as the starting compound for the synthesis of effective low-toxicity tuberculostatic and bacteriostatic agents [3, 18].

Compound I is currently obtained either starting from the relatively accessible pyrazine-2,3-dicarboxylic acid through its monodecarboxylation, esterification, and aminolysis of the ester [5, 6], or by the action of sulfuric acid on ammonium pyrazine-2-carboxylate [4].

It is also possible to obtain I by homolytic carbamoylation of the pyrazine ring by the action of formamide in the presence of peroxides and iron sulfate [13]. The yield of I in this case does not exceed 49%.

A method for the synthesis of I via conversion of 2-methylpyrazine (II) initially to 2-cyanopyrazine (III) by oxidative ammonolysis with subsequent hydrolysis of it to amide I is promising.

Catalysts with the most diverse compositions for the oxidative ammonolysis of II that make it possible to obtain III in up to 80% yield are presently known; vanadium oxide catalysts with added metals and nonmetals with variable valences are used in most cases [1, 14, 15]. The next step – the hydrolysis of III – takes place under the influence of ammonium hydroxide at 60-90°C and gives I in 91% yield [2].

An alternative (relative to oxidative ammonolysis) method for obtaining III by replacement of a halo group by a cyano group in the pyrazine ring [12] can be regarded only as preparative.

To study the oxidative ammonolysis of II we initially selected KVTS-116-800 and KVOTS-1115-800 mixed oxide catalysts (vanadium-titanium and vanadium-tin-titanium catalysts sintered at 800°C with molar ratios of the oxides in them of 1:16 and 1:1:15, respectively), which displayed high activity and selectivity in the synthesis of isomeric cyanopyridines from the corresponding picolines [8, 9].

The II necessary for the oxidative ammonolysis was obtained as a result of the catalytic dehydrocyclization of propylene-1,2-glycol with ethylenediamine in the presence of modified zinc oxide catalysts [10, 11]. The yield of II reaches 81% under these conditions.

However, a study showed that the use of KVOTS-1115 and KVTS-116 catalysts gives a very low degree of conversion of starting II, and only trace amounts of III were present in the reaction products.

We subsequently investigated a number of vanadium-titanium catalysts modified by group VI metal oxides. Of greatest interest among them are catalysts with added MoO₃ (in molar ratios from 0.01 to 0.20), in the presence of which the principal product is not the expected III, but rather I. The results obtained in a study of the oxidative ammonolysis of II near the optimum temperature on such catalysts are presented in Table 1.

It is apparent from the data in Table 1 that the optimum temperature range of functioning of the catalysts is 390-410°C and that the II:ammonia:air molar ratio = 1:27:(65-80). Under these conditions in the presence of catalysts with the composition V₂O₅:TiO₂:MoO₃ = 1:0.5:(0.05-0.10), from 80% to 95% of the starting II is converted to I.

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TABLE 1. Dependence of the Yield of 2-Amidopyrazine on the Reaction Conditions

Composition of the $V_2O_5:TiO_3:MoO_3$ catalyst, mole fractions	II:ammonia:air ratio, moles	Reaction temp., °C	Yield, of I based on unchanged II, %
1,0:0,5:0,01	1:20:50	390	9,7
1,0:0,5:0,01	1:27:65	400	12,4
1,0:0,5:0,01	1:27:80	410	9,1
1,0:0,5:0,05	1:27:50	400	72,1
1,0:0,5:0,05	1:27:65	390	95,2
1,0:0,5:0,05	1:27:80	400	89,7
1,0:0,5:0,10	1:20:50	390	37,1
1,0:0,5:0,10	1:27:65	400	81,4
1,0:0,5:0,10	1:27:80	410	74,1
1,0:0,5:0,15	1:20:50	390	31,9
1,0:0,5:0,15	1:20:65	400	54,4
1,0:0,5:0,15	1:27:80	410	62,6
1,0:0,5:0,20	1:20:50	390	18,3
1,0:0,5:0,20	1:27:80	410	56,3

EXPERIMENTAL (CHEMICAL)

The oxidative ammonolysis of II was carried out in a flow apparatus with a stainless steel reaction tube with a length of 450 mm and an inner diameter of 20 mm, into which 30 ml of the catalysts was loaded. The catalyst was prepared by mixing vanadium, titanium, and molybdenum oxides in the proportions indicated in Table 1 by fusion in a muffle furnace at 800°C with subsequent granulation to grains 3-5 mm in diameter. The catalyst obtained in this way was loaded into the reactor and activated for 50 h. The starting reaction mixture of II, 25% ammonium hydroxide, and air was fed into the reactor containing the activated catalyst. The reaction products were trapped with a spent scrubber filled with methylene chloride. The methylene chloride was then removed by distillation, and the residue was treated with diethyl ether to remove the unchanged II and resinous substances. The ether-insoluble I was recrystallized from water. The melting point of the I obtained was 190°C, which was in agreement with the literature data.

The purity of the product obtained was 99.9% according to GLC (using a Biokhrom-1 chromatograph with a glass capillary column with a length of 30 m and a diameter of 0.3 mm packed with OV-101).

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