Oxidative Ammonolysis of 3(4)-Methyland 3,4-Dimethylpyridines Using Vanadium Oxide Catalysts

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Abstract—Oxidative ammonolysis of 3(4)-methyl- and 3,4-dimethylpyridines using vanadium oxide catalyst doped with Cr_2O_3 , SnO_2 , and ZrO_2 was studied. The yields of nitriles and conversion of the starting compounds were found to depend on the CH-acidity of the latter in the gas phase. The possible mechanisms of the formation of pyridine-3,4-dicarboxylic acid imide at the oxidative ammonolysis of 3,4-dimethylpyridine was discussed. The relation between the activity of the modified catalysts and the proton affinity of the vanadyl oxygen calculated by the extended Hückel method was established.

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Oxidative ammonolysis of mono- and dimethylpyridine is the most rational method of obtaining the practically important mono- and dicyanopyridines [1, 2]. The relationship between the structure and the reactivity of monomethylpyridines in oxidative ammonolysis was studied in [3]. Oxidative ammonolysis of isomeric dimethylpyridines using the Cr₂O₃· Al₂O₃ catalyst was studied at 360°C with the conversion of ~20%. Under these conditions 3,4-dimethylpyridine was converted to 4-cyano-3-methylpyridine with the selectivity of 92% [4]. The different order of entering the reaction of the substituents of asymmetric dialkylpyridines was ascribed in [5] to the difference in the deprotonation enthalpy values of methyl substituents in the gas phase and to the surface state associated with the acid center.

The purpose of this work is the experimental and quantum-chemical study of the relationship between the reactivity of 3-methyl- (I), 4-methyl- (II) and 3,4-dimethylpyridines (III) under the oxidative ammonolysis conditions and some features of their structure, of the possible formation mechanism of pyridine-3,4-dicarboxylic acid imide IX from compound III, and also of the effect of different oxide promoters on the activity of vanadium oxide binary catalysts.

The studied processes are characterized by a high selectivity of transforming the methyl groups into the nitrile groups and by the small contribution of the destructive oxidation reactions. Therefore the total reactivity of the starting compounds was evaluated from their conversion, and the reactivity of the methyl groups, from the yields of 3-cyano- (IV), 4-cyano- (V), and 3-methyl-4-cyanopyridines (VI).

experimental data on The the oxidative ammonolysis of pyridines I-III using the V-Sn-oxide catalyst under the standard conditions are shown in Fig. 1. As can be seen, in the temperature range of 270-330°C the conversion of the starting material increases in the sequence of I < III < II (Fig. 1a). The reactivity of the methyl groups evaluated by the monocyanides yields increases similarly: IV < VI < V(Fig. 1b). The observed decrease in the yield of compound VI as the temperature increases is due to its conversion into pyridine-3,4-dicarboxylic acid imide IX. The latter accumulates in the reaction products in a significant amount.

Similar pattern of the temperature effect on the oxidative ammonolysis of compounds **I–III** was observed when chromium(III) oxide and zirconium dioxide were used as modifiers of vanadium oxide catalyst.

Methylpyridines are weak CH-acids and can eliminate a proton from a methyl group at the action of a strong base to form a carbanion, for example, in the liquid-phase deuterium exchange reaction [6]. This fact should be taken into account when interpreting the experimental data on the relative reactivity of the



Fig. 1. The dependence on the temperature of the conversion of the starting materials (a) and the yields of the reaction products of oxidative ammonolysis (b) on the catalyst with a molar ratio of V_2O_5 : $SnO_2 = 1:2$. (1) 3-methylpyridine and 3-cyanopyridine, (2) 4-methylpyridine and 4-cyanopyridine, (3) 3,4-dimethylpyridine and 3-methyl-4-cyanopyridine, (4) pyridine-3,4-dicarboxylic acid imide. The starting compound:oxygen:ammonia:water = 1:15:3:32. Here and hereinafter the feed rate of the reactants is 40 g l⁻¹ of the catalyst per hour.

starting materials. In the catalytic reaction a nucleophilic oxygen of the surface can be used as a proton acceptor. Obviously, the conversion of compounds I–III depends on the value of deprotonation enthalpy of methyl substituents transformed into the cyano groups.

The experimental data on the CH-acidity in the gas phase [7–10] are known only for monomethylpyridines. For dimethylpyridines these features are not currently available. Therefore we calculated the deprotonation enthalpies for the methyl groups (ΔH_d) based on the total energy values of the initial molecules and the corresponding anions using *ab initio* quantum chemical method (RHF/6-31G*).

$$PyCH_{3} \rightleftharpoons PyCH_{2}^{-} + H^{+} - \Delta H_{d},$$
(1)
$$\Delta H_{d} = E_{tot}(PyCH_{2}^{-}) - E_{tot}(PyCH_{3}).$$

A comparison of the experimental data (Fig. 1) and the results of quantum chemical calculations (Table 1) show that there is an inverse relationship between the conversion of the starting compound, yield of the corresponding nitrile, and the deprotonation enthalpy of the methyl group of the starting compound (ΔH_d): the conversion of the reactants and yield of corresponding nitrile increase in the sequence of $\mathbf{I} < \mathbf{III} < \mathbf{II}$ as the deprotonation enthalpy decreases. It should be noted that the reactivity of 3,4-dimethylpyridine, in particular, in the low-temperature experiments, is determined solely by the conversion of a methyl group in the position 4, which has the lowest ΔH_d value. At higher temperature, the rate of the compound **VI** accumulation is reduced as a result of its consumption in the intramolecular cyclization stage to form the reaction product **IX** (Fig. 1b).

The lone electron pair of the carbanion is located on the highest occupied molecular orbital (HOMO). The carbanion stability is determined by a degree of the negative charge delocalization [11]. The more delocalized is the lone electron pair, the lower is the HOMO energy level and, therefore, the more stable is the carbanion. In turn, the more stable is the carbanion, the stronger the reaction (1) equilibrium is shifted to the right and the faster is further transformation of the carbanion into the nitrile. There is a direct relationship between the E_{HOMO} values of the carbanions resulting from deprotonation of the methyl substituents of the studied compounds, the values of conversion, and the yields of the corresponding nitriles in the oxidative ammonolysis.

Thus, the conversion of the studied methylpyridine derivatives into cyanopyridines (in the case of 3,4dimethylpyridine also the order of the substituents entering into the reaction) is determined by the deprotonation enthalpy values.

Table 1. The total energies of the molecules of pyridines I–III, the corresponding anions ($-E_{tot}$), the deprotonation enthalpy of the methyl groups in the gas phase (ΔH_d), the energy of the higher occupied molecular orbitals of the anions ($-E_{HOMO}$) calculated *ab initio* by the quantum-chemical method (RHF/6-31G)^a

Compound	$-E_t$	_{ot} , au	$\Delta H_{\rm d}$,	$-E_{\rm HOMO}$, (au) kJ mol ⁻¹		
	molecules	anoins	kJ mol ⁻¹			
I	285.6154165845	284.9670478655	1702.3	(0.0179) 47.0		
II	285.6168469440	284.9831732710	1663.7	(0.0371) 97.4		
III	324.6357600925	323.9848150532(3) 323.9982872763(4)	1709.0(3) 1673.7(4)	(0.0198) 52.0(3) (0.0360) 94.5(4)		

^a $\Delta H_d = [E_{tot}(anion) - E_{tot}(molecule)] \cdot 627.5 \cdot 4.184.$

3,4-Lutidine is similar to *o*-xylene in the ability to the intramolecular cyclization. As known, one of the primary products of the oxidative ammonolysis of *o*xylene is *o*-tolunitrile. Its nitrile group in the oxidation reaction is able to react with the adjacent methyl substituent to form phthalimide [12].

The mechanism of the imide ring formation in the oxidative ammonolysis of *o*-xylene and 3,4-dimethylpyridine is of great interest. Chukhno et al. [12] suggested that the conversion of *o*-xylene to phthalimide proceeded through the tolunitrile formation, the oxidation of the methyl substituent followed by the reaction of its oxidized form with the

triple bond of the nitrile group resulting in phthalic acid isoimide. The latter is easily converted into phthalimide at a high temperature. For example, the intermediate formation of the substituted benzoate ions on the surface of the V_2O_5/Al_2O_3 catalyst in the xylene oxidative ammonolysis was detected by the infrared spectroscopy [13].

Given the above and a similarity in the structure of *o*-xylene and 3,4-dimethylpyridine, we suggest a scheme for the imide **IX** formation in the pyridine **III** oxidative ammonolysis, which includes the formation of 4-cyanonicotinic acid **VII** and pyridine-3,4-di-carboxylic acid isoimide **VIII**.



Probably, the conversion of **VI** into the imide **IX** includes the surface oxidation of the methyl group at the position 3 and the electrophilic attack of the proton on the nitrogen atom of the nitrile group. In a scheme, the proton belongs to the carboxy group, but the proton source can be the hydrogen donors that are present in the reaction mixture (ammonia, water vapor), which are capable of the heterolytic rupture of the bonds (H₂N–H, HO–H) under the action of a catalyst. Such mechanism of the **VI** \rightarrow **IX** transformation is supported by the results of our *ab initio* quantum chemical calculations (RHF/6-31G*). A significant polarization of the triple bond in the nitrile group is characteristic of the isolated molecule of VI. As a result, the carbon atom is positively charged ($\delta_{\rm C}$ +0.081), and the nitrogen atom is negatively charged ($\delta_{\rm N}$ -0.2365). This favors the electrophilic attack of the proton on the nitrogen atom. The total energy level of compound VIII ($E_{\rm tot} = -525.7834274589$ au) is higher than that of imide IX ($E_{\rm tot} = -525.8232800546$ au), which indicates the possibility of transforming the thermodynamically less stable isoimide into the pyridine-3,4-dicarboxylic acid imide.

We have observed that under the comparable conditions of the oxidative ammonolysis of com-



Fig. 2. The temperature dependence of the conversion of 3-methylpyridine (a) and the yield of 3-cyanopyridine (b) under the conditions of oxidative ammonolysis using various catalysts. The starting compound: $O_2:NH_3:H_2O = 1:15.6:6:27.9$. Here and hereinafter: (1) V_2O_5 - Cr_2O_3 (1:1), (2) V_2O_5 - SnO_2 (1:4), (3) V_2O_5 - ZrO_2 (1:4).



Fig. 3. The temperature dependence of the conversion of 4-methylpyridine (a) and the yield of 4-cyanopyridine (b) under the conditions of oxidative ammonolysis using various catalysts. The starting compound: $O_2:NH_3:H_2O = 1:15.6:6:27.9$.

pounds I-III the conversion of the starting compound and the yields of mononitrile increases in the following catalyst series: V_2O_5 - $Cr_2O_3 < V_2O_5$ - SnO_2 , $< V_2O_5$ - ZrO_2 (Figs. 2–4). Generally, the activity and selectivity of the vanadium oxide catalysts for the hydrocarbons oxidation is caused by the presence of various forms of the active oxygen on the catalyst surface. The doublebonded oxygen atom (V=O) of the lattice plays an important role [14]. One reason for the different promoter activity of chromium(III), tin(IV), and zirconium(IV) oxides on the catalytic activity of the studied vanadium oxide contacts is the different degrees of the influence of oxide promoters on the reactivity of V=O bond involved into the proton eliminating from the methyl group transforming into the nitrile group. To test this hypothesis, we calculated

the proton affinity values of vanadyl oxygen for three clusters simulating the active sites of the studied catalysts containing the V_2O_5 fragments and various oxide-promoters using the extended Hückel method supplemented by the Anderson repulsive potential [15] (Table 2).

It is presumed that the minimal surface clusters can be used for such study because of the strong localized character of the V=O and V–O bonds [16]. The parameters for the V atoms are taken from [17]. The calculations by the extended Hückel method were performed by the optimization of the bond and dihedral angles. The V=O (1.58 Å) and V–O bonds lengths (1.83 Å), which were taken from the experimental data on the crystal structure of V₂O₅ [16],



Fig. 4. The temperature dependence of the conversion of 3,4-dimethylpyridine (a) and the yield of 3-methyl-4-cyanocyanopyridine (b) under the conditions of oxidative ammonolysis using various catalysts. The starting compound: $O_2:NH_3:H_2O = 1:15.6:6:32.1$.

Table 2.	The total	energies	of the	vanadium	-containing	clusters	and th	eir pi	rotonated	forms	$(E_{\rm tot}),$	the p	proton	affinity	of the
oxygen b	onded wit	h the vana	adium i	ons (PA)	calculated b	y the ext	tended	Hück	cel method	l ^a					



^a PA = $(E_{\text{initial}} - E_{\text{final}}) \cdot 23.07 \cdot 4.184$.

and the Cr–O (2.01 Å), Sn–O (2.06 Å) and Zr–O bond lengths (2.04 Å) remained constant [18].

The calculations show (Table 2) that the value of the proton affinity of the vanadyl oxygen increases in the catalyst series as follows: V_2O_5 - Cr_2O_3 , V_2O_5 - SnO_2 , V_2O_5 - ZrO_2 , i.e., it changes in the same manner as the activity of the studied catalysts under the conditions of oxidative ammonolysis of 3(4)-methyland 3,4-dimethylpyridines. This fact indicates that the mechanism of the promoting action of chromium(III), tin(IV), and zirconium(IV) oxides may be related to their effect on the nucleophilic properties of the vanadyl oxygen.

Thus, the study of the oxidative ammonolysis of 3(4)-methyl- and 3,4-dimethylpyridines using the vanadium oxide catalysts doped with Cr₂O₃, SnO₂, and ZrO₂ showed that there is a direct correlation between the CH-acidity of the starting compounds in the gas phase and the value of their conversion into the corresponding nitrile of pyridinecarboxylic acid. This favors the hypothesis of the mechanism that includes the heterolytic rupture of the C-H bond of the methyl group in the initial stages of the process. At the oxidative ammonolysis of 3,4-dimethylpyridine on the modified vanadium oxide catalysts the temperature increase favors the intramolecular cyclization to form pyridine-3,4-dicarboxylic acid imide. The activity of the studied vanadium oxide catalysts in oxidative ammonolysis of 3(4)-methyl- and 3,4-dimethylpyridines changes in the same order as the proton affinity values of the vanadyl oxygen calculated by the extended Hückel method. This regularity suggests that the promoters of different nature (Cr₂O₃, SnO₂, ZrO₂) affect differently the nucleophilicity of the doublebonded oxygen of the V₂O₅ lattice and catalytic activity of the modified vanadium oxide catalysts.

EXPERIMENTAL

The initial 3(4)-methyl- and 3,4-dimethylpyridines of chemically pure grade were dried from water and distilled. 3-Methylpyridine: bp 140°C (692 mm Hg), d_4^{20} 0.9566, n_D^{20} 1.5050; 4-methylpyridine: bp 141°C (695 mm Hg), d_4^{20} 0.9548, n_D^{20} 1.5058; 3,4-dimethylpyridine: bp 163.5–164.5 ° (760 mm Hg), d_4^{25} 0.9537, n_D^{25} 1.5099 [19].

The V₂O₅·Cr₂O₃ catalyst was prepared as in [20]. The catalyst based on V₂O₅ and SnO₂ was obtained by calcinating a mixture of oxides of analytical grade at 650° C for 2 h. The catalyst V₂O₅·4ZrO₂ was synthesized by calcinating a mixture of oxides at 620°C for 3 h.

The reaction products were trapped in a scrubber of airlift type irrigated with water. The conditions for the chromatographic analysis of 3(4)-methylpyridine and their transformation products are described in [21]. The conditions of the synthesis of 3-methyl-4-cyanopyridine and pyridine-3,4-dicarboxylic acid imide, analysis of the products of oxidative ammonolysis of 3,4-lutidine are described in [22]. The IR spectrum of 3-methyl-4-cyanopyridine contains the band at 2232 cm⁻¹ belonging to the nitrile group [23]. After recrystallization from ethanol, the imide melted at 224°C (sublimation). IR spectrum, v, cm⁻¹: 1777.7, 1727.7 [$v_{s,as}$ (C=O)], 3015.4 (NH). Found, %: C 56.76; H 2.20; N 18.40. C₇H₄N₂O₂. Calculated, %: C 56.76; H 2.70; N 18.90.

The oxidation products were analyzed on a LKhM-8MD chromatograph equipped with a thermal conductivity detector. The stainless steel column (l 3.5 m, d 3 mm) was used. An AG-5 charcoal (0.25×0.50 mm) and Polysorb-1 (0.16-0.20 mm) were used as an adsorbent for the determination of CO and CO₂, respectively. The columns were temperaturecontrolled at 40°C. In all experiments, the balance on the analytes was 95–100%.

The quantum chemical calculations were performed by GAMESS software [24]. The calculations of the clusters simulating the active sites of the modified surface of catalysts were performed using a PMX method by the program developed in the Laboratory of Quantum Chemistry of Boreskov Institute of Catalysis of Siberian Branch of the Russian Academy of Sciences (Novosibirsk). The calculation procedure is given in [25].

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