Dear Prof. Obsenica!!

We answered the questions of the reviewers and made appropriate changes to the manuscript. We sincerely thank you for your detailed analysis of our manuscript, valuable comments and suggestions. We look forward to productive cooperation.

Reviewer A:

1. HF with a small basis set is very crude theoretical approach. Why have
not you used the B3LYP functional (that you mention), through the manuscript?

We performed calculations using the B3LYP functional with a wider, three-exponential basis set (6-311 + G \*\*). It turned out that this method incorrectly reflects the energy levels of the highest occupied molecular orbitals EHOMO of carboanions (they take positive values, though should be less than zero). So we returned to the calculations according to Hartree-Fock, but with a wider basis set than at the beginning (HF / 6-311 + G \*\*). Results are given in Table 1 and they do not contradict the text.

1. On line 25 you state: “Mono- and dicyanopyridines have acquired a
tremendous importance in the recent years….” but you support this
statement with only one reference, in which there is no explicit mentioning
of any cyano derivative.  – Done:
* [Reference 1] - Scheme 4 shows an application of 3.4-Pyridinedicarboxamide (8) in synthesis of Isonicotinoylnicotinamide Framework (5), wich has antituberculosis properties.

+ we added 2 references.

3. On line 98 you write: “Born-Oppenheimer approximation, which does not
consider the moving of the nucleus” Born-Oppenheimer approximation
considers movement of the nucleus, it just assumes that they are not
strongly coupled with the changes in the electronic states.

At non-empirical calculations of energy and optimization of geometry of molecules, Born-Oppenheimer approximation considers movement of the nucleus, it just assumes that they are not strongly coupled with the changes in the electronic states, was used.

1. On line 113 you state: “The energy of heterocyclic cleavage of С−Н
bond” but I assume you wanted to say heterolytic.  – Done.
2. Could you comment why is the energy difference for the heretolytic
cleavage of C−H with proton transfer to vanadyl oxygen so dramatically
different then the simple C−H bond cleavage (238.2-157.1=81.1 kJ/mol vs.
1178.2-1070.6= 107.6 kJ/mol), i.e. why is the protonation of vanadyl oxygen
not a simple constant shift but it affects the energy difference. All the
data is from the Table II.

There should not be a constant shift, because protonation of vanadyl oxygen in the complexes of 3- and 4-anions releases different energy values: Etot = Etot initial - Etot end = (922.72206-922.36405) • 2625.5 = 940.0 kJ·mol-1 (for the 3-anion complex), Etot = (922.75297-922,40501) • 2625.5 = 913.6 kJ·mol-1 (for the 4-anion complex). Subtracting the obtained energy values ​​from the values ​​of EC-H, we obtain the values ​​of the deprotonation energy (DE) (Table II): 1178.2-940,0 = 238.2 kJ·mol-1 and 1070.6-913.6 = 157.0 kJ·mol-1.

1. and Regarding the statement, on line 319, that “The mechanism of formation of an imide cycle in oxidative ammonolysis of o-xylene and 3,4-dimethylpyridine is of the utmost interest.” Could you please elaborate a bit more what are the reasons for this importance? Also, cold you clarify what steps from the suggested mechanism, provided on the Scheme 1, are confirmed or analyzed in this manuscript.

The scheme includes 4-cyannicotinic acid and pyridine-3,4-dicarboxylic acid isoimide as hypothetical intermediates. We assume that the conversion of 3-methyl-4-cyanopyridine to imide includes surface oxidation of the methyl group at position 3 and an electrophilic proton attack on the nitrogen atom of the nitrile group. In the scheme, the proton belongs to the carboxyl group; however, the sources of the proton can be hydrogen donors present in the reaction mixture (ammonia, water vapor), capable of heterolytic breaking of N ‒ H or O ‒ H bonds under the effect of the catalyst. This hypothesis about the mechanism of imide formation is supported by the results of our non-empirical quantum-chemical calculations (HF/ 6-31G\*). An isolated 3-methyl-4-cyanopyridine molecule is characteristic a noticeable polarization of the triple bond in the nitrile group, as the result the carbon atom receives a positive charge (δC = +0,2739) and the nitrogen atom is negatively charged (δN = −0,4471). This favours the electrophilic attack of the proton on the nitrogen atom to form an isoimide. The total energy of isoimide (Etot. = –526.039 u) is higher than that of the imide (Etot. = –526.067 u) by 73.5 [(526,067-526,039)]·2625,46] kJ ∙ mol-1. This indicates the possibility of converting a thermodynamically less stable isoimide to the pyridine-3,4-dicarboxylic acid imide.

1. On line 320 you state “By its ability to intramolecular cyclization
3,4-dimethylpyridine is similar to о-xylene.” Should not the
3,4-dimethylpyridine be more active substrate for initial deprotonation then
о-xylene? Could you explain this shortly?

3,4-Dimethylpyridine is more reactive than o-xylene due to the presence of a nitrogen heteroatom in the aromatic cycle. The “NH” fragment in the pyridine cycle acts as an electron-withdrawing substituent added into the benzene ring.

8. Answer is the same as on question 6.

9. Regarding the charges utilized on lines 345 nad 345, are they obtained
from Mulliken population analysis?

Yes, the charges utilized on lines 345 nad 345 are obtained from Mulliken population analysis.

10. “methylpyridines are related to weak СН-acids” could be rephrased
to  “methylpyridines represent weak СН-acids” – Done.

11..The "undivided electron pair" phrase is not common, Google gave 200
appearances but only from the authors whose native languish is not English.

We rephrased "undivided electron pair" to “nonbonding electron pair”

<https://goldbook.iupac.org/html/L/L03618.html>

12. “Stabilization of the intermediate carbanions proceeds as a result
of” could be rephrased to “Stabilization of the intermediate
carbanions is a consequence of” – Done.

13.“This is favored by the location of a substituent - СН2- on the
cycle plane” could be rephrased to “This is favored by the benzylic
nature of the analyzed position and the possibility of extensive anion
delocalization”

14.“more shifted to the right is the reaction equilibrium (5) and the
higher is the rate of the further transformation of the carbanion into
nitrile” these are two different aspects, kinetic and thermodynamic behavior. It is
not clear why would carbanion in position 4 be kinetically more reactive
than less favorable (but more nucleophilic) analog in position 3.

We have removed the arguments about the shift of equilibrium. The main factor determining the reactivity of the methyl substituent and its sequence of entry into the reaction is the enthalpy of its deprotonation. The substituent at position 4 of the pyridine cycle has a lower DE value and therefore reacts first.

15. cyanogroup should be cyano group – Done.

16. On Scheme 1 you have suggested the proton abstraction by the cyano
nitrogen, but the mechanistic arrow is directed in the opposite way. – Done.

Reviewer D:

1. The introduction part is too long, reduce it. – Done.

2. The reason for choosing a particular approach / methodology is not given
or is not clear

Quantum-chemical methods for studying the acid-base properties of the initial 3,4-dimethylpyridine and its adsorption interaction with the active centers of vanadium oxide catalysts were used in interpreting the experimental results.

3. The authors have not provided the background information to the objective
in this paper

The main goal of this work was an experimental and quantum chemical study of the reactivity of methyl groups of 3,4-dimethylpyridine in oxidative ammonolysis. The tasks of the work included studying the effect of oxides-promoters, SnO2 and ZrO2, on the activity of binary vanadium oxide catalysts.

4. What happens if its’ calcined above 650 оС (Page 2, line number 67)?
We have prepared and tested catalysts with different calcination temperatures. However, to prevent melting of vanadium pentoxide оptimal temperature of 650 °C was chosen.

5. Please provide the purity details of vanadium oxide and binary catalysts.

3,4-dimethylpyridine ( Sigma-Aldrich [583-58-4])

 V2O5,SnO2 and ZrO2 (analytical grade)

6. Authors have not followed the International System of Units (SI) – Done.

7. The authors have not concluded anything but just summarized what they
have done. Hence, conclusion part should be rewritten. -

* Done. Conclusion was rewritten.

8. Carefully check all grammatical mistakes – Done.

9. Carefully check all the references for correctness – Done.