Dear Editor,

Thank you very much for considering our submission “Synthesis, crystal structure and biological activity of copper(II) complex with 4-nitro-3-pyrazolecarboxylic ligand” for publication in Journal of Serbian Chemical Society. We are very grateful to Reviewers for useful comments and suggestions that help us to improve the quality of our paper. The replays to reviewers comments are given below and the corresponding changes are highlighted within the manuscript.

Reviewer 1.

REPORT:

The manuscript presents rather small piece of work – synthesis and XRD

analysis of one Cu complex with biotest showing only modest activity.

However, authors were able to present the interesting aspect of the crystal

structure and thus I believe this ms could become suitable for publication

after addressing the following remarks.

Comments:

1.) Abstract should start with the synthesis of a compound and then with the

report on the crystal structure. Also, cell parameters should be removed

from the Abstract since they give no real info.

Abstract has been corrected as suggested

2.) In Abstract and throughout the text formula would be better replacing

the C4HN3O4 with an abbreviation.

Formula [Cu2 (C4HN3O4)2(H2O)6]·2H2O has been replaced with

[Cu2(4nitro-3pzc)2(H2O)6].2H2O, (4nitro-3pzc = 4-nitro-3-pyrazolecarboxylate)

3.) In the Introduction section authors could include the Scheme of

4-nitro-3-pyrazolecarboxylic acid.

Scheme of 4-nitro-3-pyrazolecarboxylic acid and the title complex has been included in the Introduction section

4.) Experimental section should start with Materials and Methods followed by

synthesis.

Experimental section has been modified accordingly

5.) Data on the producer should not be part of the Synthesis section. Also,

article number 414840-10G is totally unnecessary. Was it really used

anhydrous Cu(OAc)2 or actually a monohydrate? Please check. Reporting the

yield in % on four digits makes no sense, round it to 32%.

Experimental section has been modified accordingly

6.) Why no EA was performed? Analyzing new compound only with two techniques

is not desirable.

7.) ShelxL97 is outdated … in your next contribution newer versions should

be used.

Newer versions of ShelxL (2014) has been used in the refinement

8.) Description how H-atoms of water molecules were treated in the

refinement seems misleading. "… with a restrained O−H distance of

0.85(2) Å and fixed atomic displacement parameters Uiso(H) = 1.2 Ueq(O)"

would mean DFIX command was used, however, in cif file it's evident that

command AFIX 3 was implemented meaning those H-atoms were actually treated

as riding with fixed O−H distance of 0.85 Å (no standard deviations).

The treatment of the H-atoms of water molecules is now explained in the manuscript. Actually, the position of these H atoms was determined by program CALC–OHon the basis of hydrogen-bonding interactions (Nardelli M J. Appl. Cryst. 32 (1999) 563). We apologize for an oversight.

9.) Results and discussion section should start with short description on

synthesis followed by IR and then with XRD and bioassay.

Manuscript has been modified accordingly

10.) While discussion part regarding the existing complexes with pz is OK, I

do miss some comparison with known Cu complexes with 3-pyrazolecarboxylato

ligand (BEQGIQ, BIHHEI, BOYBOI, BOYBUO, DABRUW, LAGNIT, OJUKOU, RUNXOO).

This would surly be an added value.

We are grateful to reviewer on this suggestion. Revised manuscript now contains an extended comparison of the crystal structure features of novel complex to those of the previously reported Cu complexes with 3-pyrazolecarboxylato ligand. The comparison is given within the new added section *Results of CSD serach*

In my opinion, this manuscript should:

be published after minor revision without additional review

If manuscript is suitable for publishing, referees recommendation :

Original scientific paper

------------------------------------------------------

------------------------------------------------------

Reviewer B:

Does the manuscript contain enough significant original material?:

no

Is the manuscript clearly and concisely written?:

yes

Are the conclusions adequately supported by the data?:

yes

Does the manuscript give appropriate credit to related recent publications?:

no

Are the references appropriate and free of important omissions?:

no

Is the length of the manuscript appropriate?:

no

Does the manuscript need condensation or extension?:

yes

Is the quality of the figures (including legends and axes labelling)

satisfactory?:

yes

Are the nomenclature and units in accordance with SI?:

yes

Are the English grammar and syntax satisfactory?:

yes

ADDITIONAL COMMENTS

Please indicate the page numbers for suggested corrections.

Please, be as specific as possible if major correction by the author(s) is

recommended! :

My recommendation to the authors is to either resubmit the manuscript as short communication including only synthetic protocols and structural data

or to resubmit the manuscript as full paper adding further biological

screenings as indicated in the report.

REPORT:

I do not believe the manuscript is suitable for publishing in J. Serb.Chem. Soc and recommend the editor to decline the submission due to the

following considerations:

General consideration: The manuscript presents the synthesis of one novel

compound which is biologically inactive. The presentation and language level

are acceptable, while both the chemical and the biological parts require

major modifications.

The manuscript has been considerably modified and we hope that incorporated changes meet most of the suggestions given by the Reviewer. Modifications include chemical, biological and crystallographic parts of the manuscript.

Synthesis: The synthesis is poorly described. Use mL. What are the

concentrations of the solutions? Is the 2:1 ratio a volume ratio or a molar

ratio of the reagents? As it is the description of the synthesis is

inadequate and does not offer the reader enough information to reproduce the

experimental results.

Synthesis of the complex is now described in detail with enough information to reproduce the experimental results

Structural characterization: The comparison with structural data of similar

compounds is very limited. Authors should include comparison with data of

differently substituted pyrazole-3-carboxylates. There are very recent

papers with analogous dinuclear zinc, copper and nickel compounds with

parent unsubstituted pyrazole-3-carboxylate (examples include structures

with CCDC codes BEQGIQ, LAGNIT, RUNXOO published in Dalton Trans, 2016, 12,

5081; ICA, 2009, 362, 2247; Chin. J. Struct. Chem. 2018, 37, 329) as well as

analog ternary dinuclear compounds including additional N-ligands such as

pyridine, imidazole and phenanthroline.

Revised manuscript now contains an extended comparison of the crystal structure features of novel complex to those of the previously reported binuclear complexes involving 3-pyrazolecarboxylato ligand. The comparison is given within the new added section *Results of CSD serach*

Antimicrobial activity: Using a mass percentage as concentration unit is

highly uncommon. Generally, in more chemistry-oriented journals molar

concentrations are used, while more biologically oriented journals often use

mass concentrations. Moreover, the new compound is practically inactive. A

comparison at least with parent compounds copper acetate and free ligand

should be done and conclusions drawn whether complexation is beneficial or

detrimental to the biological activity. If biological studies should be

included authors might consider testing structurally similar compounds (even

if already published) from their own compound library to expand the scope of

the article. LSD001 should be defined below Table V.

Section regarding the antimicrobial activity of the complex now also includes the comparison with parent compounds copper acetate and free ligand

In my opinion, this manuscript should:

not be published for the reasons indicated above

If manuscript is suitable for publishing, referees recommendation :

Short communication

------------------------------------------------------

------------------------------------------------------

Reviewer C:

Does the manuscript contain enough significant original material?:

yes

Is the manuscript clearly and concisely written?:

yes

Are the conclusions adequately supported by the data?:

yes

Does the manuscript give appropriate credit to related recent publications?:

yes

Are the references appropriate and free of important omissions?:

yes

Is the length of the manuscript appropriate?:

no

Does the manuscript need condensation or extension?:

yes

Is the quality of the figures (including legends and axes labelling)

satisfactory?:

yes

Are the nomenclature and units in accordance with SI?:

yes

Are the English grammar and syntax satisfactory?:

no

ADDITIONAL COMMENTS

Please indicate the page numbers for suggested corrections.

Please, be as specific as possible if major correction by the author(s) is

recommended! :

This manuscript with Cu complex can be published, after some revision.

In the Introduction it should be mentioned what kind of materials can be pz

complexes.

Additional references describing the properties of pyrazole based materials (magnetic5, energetic6, luminescent7, catalytic7) have been cited in reference list.

In lines 158-159, the authors say „ the two strongest hydrogen bonds

O5-H52-O2 and O6-H61-O1“, while in the Table III O5-H5b-O8 is shorter than

O6-H61-O1. The authors probably consider also angle as the indication of the

hydrogen bond strength, however, it should be explained in the text.

In the Table III the H are labeled as „a“ and „b“, while in the text

they use „1“ and „2“.

The statement regarding the strongest hydrogen bonds has been clarified. Actually, the two mentioned interactions are not the strongest in the crystal structure but the strongest hydrogen bonds which directly connect the complex units (not involving the solvent water molecules *i.e*. O5-H5b-O8). The labels of H atoms have been corrected. We apologize for an oversight.

More comparison of the structures of the previously published Co and Cu

crystal structures should be given. Maybe data from previous structure

should be given in Table III. One can notice the coordinated water forms

stronger hydrogen bonds when it is H atom donor. It should be commented in

the text.

The authors should comment on the reason for using IR spectroscopy, since

structures is known from X-ray data. It seems that they can be able to make

some connection with the data from crystal structures.

The authors should give some explanation for the microorganism use for

testing. The reason is probably that Cu compound are fungicides.

In the Figure 2 the Cu that coordinated by water molecule should be labeled.

Revised manuscript now contains an extended comparison of the crystal structure features of novel complex to those of the previously reported binuclear complexes involving 3-pyrazolecarboxylato ligand. The comparison is given within the new added section *Results of CSD serach*. Biological section has been also modified.

Figure 2 has been corrected.

Corrections in writing

Line 37 a variety

Line 41 on the ability

Line 53 delete „,“

Line 54 the tetragonally

Line 67 a yield

Line 150 In the recently

Line 156 The „[„ and „]“ should be just normal „(„ and „)“.

Line 158 In each crystal structure, (add comma)

Line 162 Delete „.“ After „ligands“.

Line 180 in from „-d“ is just the box, symbol is missing.

Line 218 an incubator

Line 226 applied

Line 229 Studied complex has not expressed

Corrections in writing have been taken into account.