# Author's Reply to the Review Report (Reviewer 1)

In their manuscript Lee, Jeong and Awasthi describe preparation of 3 new compounds, comprising of pyridinol annulated with another heterocyclic ring, namely: aminopyrrole, aminooxazole, aminoimidazole. The Authors used reaction of pyridine derivatives with BrCN to accomplish the annulation of the second ring. The approach is not entirely new (see e.g. Org. Prep. Proc. Int., 2021, 528; J. Heterocyclic. Chem. 1976, 1103; J. Heterocyclic. Chem. 2003, 569; Chem. Eur. J. 2020, 13002). However, it is the first time, it was applied for 5-[protected]hydroxypyridines. Syntheses of 2-aminooxazolo[4,5-b]pyridine and 2-aminoimidazo[4,5-b]pyridine were successfully accomplished, while for pyrrolo[2,3-b]pyridine only 2-acetylamino-derivative was obtained. Target compound may be useful for subsequent modifications and elucidation of biological activity. In Reviewer's opinion the manuscript meets minimum requirements to be published. Major revision is required.

Obtained compounds were not characterized as is usually required. Elemental analysis or high-resolution mass spectra are not presented. Therefore brutto-formulas cannot be considered as adequately supported.

We have measured the HRMS of all new compounds as the reviewer requested. Sufficiently satisfactory data have been obtained for all the measured compounds, and they have been recorded in the experimental part.

Many Figures show reactions. Therefore, they should be called "Scheme".

As the reviewer pointed out, a "Figure" containing reactions has been re-named "Scheme".

Fig.2. "2 steps" and "1 step" repeated many times is confusing. Why not to write reagents and put a literature reference? Transformation **12**→**14** takes 3 steps (possibly, all are known in literature). What was the reason to show intermediate **13**? Why not to show **12**→ in 3 steps?

A revised scheme has been drawn to reflect the reviewer's opinion as much as possible.

Naming target compounds as **6A**, **6B** and **6C** is somewhat confusing. Please, use usual numeration, i.e., **6**, **7** and **8**.

A new compound numbering system has been applied to reflect the reviewer's comment.

Scheme 2. Upper side shows numerous reactions without reagents, conditions and so on. The Authors should either provide conditions (like it's done for cases a-f) or put a literature reference above the reaction arrow to indicate, that literature conditions were used.

A revised scheme containing reagents and conditions for all steps has been provided as per the reviewer's comment.

Numeration should be thoroughly checked and corrected. For instance, compounds **20** in Schemes 1 and 2 differs.

Thanks for the comment. The compound numbers for all compounds have been carefully checked again and properly corrected.

Why debenzylation to **6A** was accomplished with $H_2$, Pd/C, while for **6B** $BCl_3$ was employed?
Because we already knew that the substrate for **6B** (the benzyl-protected compound) had very poor solubility in methanol (solvent for the hydrogenolysis), we decided to use a $BCl_3$ system instead. Since we obtained a good result from the reaction, we did not try the debenzylation under hydrogenolysis conditions.

The authors could cite 'Tetrahedron Lett. 2014, 55, 1296', where synthesis of 2-aminooxazolo[4,5-b]pyridine is described. There authors used isothiocyanates, to produce N-substituted derivatives. In the presented manuscript BrCN is used to give $NH_2$-derivatives.
Thanks for the information. This paper has been newly added to the reference list.

line 139. The reviewer is curious why the authors compared their approach toward 2-amino-pyrrolo[3,2-b]pyridines with the preparation of aminoindoles. There is literature precedent for this particular type of heterocycles, 'Chem. Eur. J. 2020, 13002'.
Thanks for the information. An additional explanation for this part has been newly included in the text. As described, there have been no examples of synthesis of 2-amino-7-azaindole with unsubstitution at 3-position from the corresponding nitrile compound. So, we searched and referenced a 2-aminindole synthesis example, a benzene version. The paper mentioned by the reviewer is an example of a high-yielding reaction where the existence of a carbonyl group at 3-position is thought critical for the success of this type of cyclization. A new paragraph has been added, along with two schemes for explaining the differences between their works and ours.

Check the NMR description. For instance, compound **31**: “7.94 (td, J = 5.2, 2.0 Hz, 3H), 7.80 (dd, J = 5.5, 3.1 Hz, 3H).” – there are no three identical protons in the structure. There should be 9 aromatic protons, while (line 264) there are 3+3+9=15 protons is assigned. Is it a misprint or is compound impure? Compound **32** “7.41 (tdd, J = 10.6, 7.5, 5.9 Hz, 5H),” – 5 protons of phenyl group cannot be a tdd.
Thanks for the comments. We have closely looked at the NMR data of all compounds again and made corrections in several parts, including those pointed out by the reviewer.

line 52. C(5') position is better to be marked in the Scheme.
Thanks for the comments. Corrections have been made as the reviewer requested.

Fig.1, Now compound **2** is placed above the arrow. It is unclear, whether reactions 1→2→3,4,5,6 were really accomplished or compound **2** is just a general imaginary building block. Please, revise.
As the reviewer pointed out, a revised scheme has been prepared to remove the ambiguity.

Compounds **5** and **6**. A=C,N,O without valency is incorrect. $CH_2$, NH, O would be better.

Thanks for the comments. Corrections have been made as per the reviewer's suggestion.

Fig.3. What is c-HCl? Is it conc. aq. HCl?

Thanks for the comments. For clarity, c-HCl has been corrected to 12 M HCl.

Nomenclature “N-α-amino-” is somewhat confusing. Why not simply call “α-amino-“?

As per the reviewer's comment, "N-α-amino-" was changed to "α-amino-".

line 301. cyanomethyl, not acetonitrile.

Thanks for the comment. "acetonitrile" was changed to "cyanomethyl".

Please, provide references for the preparation of starting compounds.

We have looked carefully at the manuscript again and tried to put proper references for the synthesis of known compounds in the right places.

line 241, indicate solvent for 1M $BCl_3$.

Thanks for the comment. We have added the detailed information of 1 M $BCl_3$.