Review of: "A Novel One-Pot Three-Component Approach to Orthoaminocarbonitrile Tetrahydronaphthalenes Using Triethylamine (Et_3N) as a Highly Efficient and Homogeneous Catalyst Under Mild Conditions and Investigating Its Anti-cancer Properties Through Molecular Docking Studies and Calculations"

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Potential competing interests: No potential competing interests to declare.

- In order to make the reading of the article more intuitive and fluid, I recommend sending the “representative spectral data” to the final part of the article or, at least, after Table 2 (where the compound markers are assigned).
- Due to the anticancer properties these compounds potentially have, it is necessary to ensure their purity. Please, provide the full NMR spectra to check the efficacy of the isolation.
- Please, provide more information about the docking parameters you used to elucidate the interaction with the 3A8P protein.
- On page 6, you say that 1, 3, and 5 mmol of catalyst were tested as catalyst loading. As it was added 1 mmol of limiting reactant, I assume that in fact 0.3 mmol of catalyst was added (30 mmol%), not 3 mmol. Please, check it.
- The proposed mechanism is quite interesting. However, the role of the catalyst is not described herein. Some of the steps, apparently, should be promoted by the effect of the base. Consequently, the catalyst should be recovered to close the catalytic cycle. Please, include the catalyst inside the reaction mechanism and in the steps you suppose it is involved.
- On page 12, there is a phrase that says “[…] all the synthesized compounds bind to an **agonist** at the active site of the 3A8P protein, which leads to the **inactivation** of this protein […]”. It does not seem to be very clear talking about an agonist that inactivates a protein. Are you talking about an inverse agonist? In that case, it might make more sense to me. Consider rephrasing that part to avoid the supposition of a conventional agonist.
- Maybe you can refer to a “less hazardous and contaminant procedure” instead of a “green one” because heating at 70 ºC can raise some doubts about its sustainability.
- There are some grammatical errors. It should be nice to check them.
- In terms of novelty, there doesn’t seem to be a substantial difference with the article of B. Maleki *et al.* (ref. 42: B. Maleki, R. Rooky, E. Rezaei-Seresht, R. Tayebee *Org Prep Proced Int. 49*, 557-567 (**2017**)). Please, consider expanding the scope of the reaction to other reactants with different structures. Maybe it is enough pointing out which are the key factors that make this work substantially different from the previous one; or, at least, improve the

methodology by far. At first sight, it seems that the major change is the use of triethylamine as a catalyst instead of ammonium acetate, but since the first step of the proposed mechanism involves the triethylamine in a protonation process, even the catalytic active species may be the same in both articles.

- As a conclusion, if the novelty of the synthetic methodology is demonstrated, despite some corrections, the article is easy to read and clear to most chemical readers. Docking studies, with some clarifications and details in the calculus, highlight a not-as-new synthetic procedure. Nevertheless, the work is quite complete, the application of the compounds is clear, and the way of presenting all the data and information is appropriate. I would also like to highlight the aesthetic of the manuscript, being concise, and minimalist, and letting each image illustrate and clarify the text.