

Review of: "Synthesis of 1, 2-Disubstituted Benzimidazoles at Ambient Temperature Catalyzed by 1-Methylimidazolium Tetrafluoroborate ([Hmim] BF₄) and Investigating Their Anti-ovarian Cancer Properties Through Molecular Docking Studies and Calculations"

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Potential competing interests: No potential competing interests to declare.

The manuscript titled "Synthesis of 1,2-disubstituted benzimidazoles at ambient temperature catalyzed by 1-methylimidazolium tetrafluoroborate ([Hmim]BF₄) and investigating their anti-ovarian cancer properties through molecular docking studies and calculations," written by Dehghani and collaborators, is well written and organized. However, some details must be considered before final publication.

Is it necessary to put ([Hmim]BF₄) in the title? The number 4 should be subscripted. Check the use of capital/lowercase letters in the title according to the authors' guide. In the final part of the title, I would remove the word "studies" or "calculations"; for example, through molecular docking studies Direct and simple.

The use of benzimidazoles in the treatment of ovarian cancer is not justified in the introduction; some useful articles are:

- Benzimidazole derivatives as potential anticancer agents. El Rashedy, Ahmed A.; Aboul-Enein, Hassan Y. *Mini-Reviews in Medicinal Chemistry* (2013), 13(3), 399-407
- Benzimidazole Ring System as a Privileged Template for Anticancer Agents. Kanwal, Afshan; Saddique, Furqan Ahmad; Aslam, Sana; Ahmad, Matloob; Zahoor, Ameer Fawad; Mohsin, Noor-ul-Amin. *Pharmaceutical Chemistry Journal* (2018), 51(12), 1068-1077
- Recent Progress of Benzimidazole Hybrids for Anticancer Potential. Akhtar, Jawaid Md.; Yar, Mohammad Shahar; Sharma, Vinod Kumar; Khan, Ahsan Ahmed ; Ali, Zulphikar; Haider, Rafi Md. ; Pathak, Ankita, *Current Medicinal Chemistry* (2020), 27(35), 5970-6014
- Benzimidazole derivatives as potential chemotherapeutic agents, El Rashedy, Ahmed A.; Aboul-Enein, Hassan Y. *Current Drug Therapy* (2013), 8(1), 1-14
- Benzimidazole based derivatives as anticancer agents: Structure activity relationship analysis for various targets. Satija, Garvit; Sharma, Barkha; Madan, Anish; Iqbal, Ashif; Shaquiquzzaman, Mohammad; Akhter, Mymoona ; Parvez, Suhel ; Khan, Mohammad Ahmed; Alam, Mohammad Mumtaz. *Journal of Heterocyclic Chemistry* (2022), 59(1), 22-66
- Benzimidazole: A Multifaceted Nucleus for Anticancer Agents. Bansal, Yogita; Minhas, Richa; Singhal, Ankit; Arora,

Radhey Krishan; Bansal, Gulshan. *Current Organic Chemistry* (2021), 25(6), 669-694

- Recent developments of target-based benzimidazole derivatives as potential anticancer agents. Goud, Nerella Sridhar; Kumar, Pardeep; Bharath, Rose Dawn. Edited by Nandeshwarappa, Belakatte Parameshwarappa; S. O., Sadashiv, *Heterocycles* (2020), 1-18
- Second and third-row transition metal compounds containing benzimidazole ligands: An overview of their anticancer and antitumour activity. Suarez-Moreno, Galdina V.; Hernandez-Romero, Delia; Garcia-Barradas, Oscar; Vazquez-Vera, Oscar; Rosete-Luna, Sharon; Cruz-Cruz, Carlos A.; Lopez-Monteon, Aracely; Carrillo-Ahumada, Jesus; Morales-Morales, David; Colorado-Peralta, Raul, *Coordination Chemistry Reviews* (2022), 472, 214790
- First-row transition metal compounds containing benzimidazole ligands: An overview of their anticancer and antitumor activity, Hernandez-Romero, Delia; Rosete-Luna, Sharon; Lopez-Monteon, Aracely; Chavez-Pina, Aracely; Perez-Hernandez, Nury; Marroquin-Flores, Jazmin; Cruz-Navarro, Antonio; Pesado-Gomez, Gustavo; Morales-Morales, David; Colorado-Peralta, Raul, *Coordination Chemistry Reviews* (2021), 439, 213930

Scheme 1 is ambiguous since it suggests that compounds 3a-3l and 4a-4l are obtained separately when it is evident that they are obtained as a mixture. In the same Scheme 1, put "2-substituted" instead of "1-substituted."

In the experimental part, report the weight in grams of each of the benzaldehydes used, as well as the weight in grams of the 1-methylimidazolium tetrafluoroborate and *ortho*-phenylenediamine.

In the same experimental section, it is not reported how compounds 3a-3l were separated from compounds 4a-4l.

In entry 6 of Table 1, no solvent was reported. How was the reaction carried out?

It is not clear from the manuscript whether the authors managed to separate the mixtures of 3a-3l from 4a-4l.

The yields reported in Tables 1 and 2 are ambiguous. Are they stoichiometric yields? Are the yields obtained from NMR signals? What do you mean by isolated yield?

In the second paragraph after Table 2, check the sequence of words "In order for proper."

Check the headings of Tables 3, 4, and 5. They refer to compounds 3a-3l and not 4a-4l.

Further discussion of Table 6 would highlight the relevance of the results found by the authors. At first glance, silica gel/acetic acid, erbium(III) triflate, and phosphoric acid are better methods than the one reported in this document.

"Thus significantly contributes to the practice of green chemistry" and "It was found that these compounds have the potential to become an oral anti-cancer drug." I do not agree with these two sentences in the conclusion. I do not consider the synthesis technique to be green, and many analyses are needed to consider these molecules as anticancer drugs.