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Prof. Vladimir Šindelář
Masaryk University
Faculty of Science
Department of Chemistry and RECETOX
Kamenice 5/A8
Brno 62500
Czech Republic

Re: Evaluation of Dr. Jakub Švenda's Habilitation

Dear Prof. Šindelář and Colleagues,

It is my pleasure to evaluate **Dr. Jakub Švenda's** habilitation at Masaryk University, Brno. I will keep this letter brief due to an onslaught of letter-writing duties and because this is a clear-cut case. Coming from a European tradition that values succinctness, I believe that the strength of a letter is not measured by its length. I consider Dr. Švenda as one of the most creative young colleagues in organic synthesis in Europe. His achievements would be sufficient to grant tenure, or at least a mid-career promotion, at a major U.S. university. Therefore, I fully support acceptance of his habilitation by your institution

I do not know Dr. Švenda personally but hope to meet him soon at a seminar in Brno, which has been rescheduled for October 31, 2024. However, I have read most, if not all, of his papers, which I have very much enjoyed. His debut paper on cephalomcins B and C first caught my eye as being highly creative (*Org. Lett.* **2017**, *19*, 750). His subsequent work on forskolin (*Angew. Chem. Int. Ed.* **2017**, *56*, 12586; *Angew. Chem. Int. Ed.* **2023**, *62*, e202213183) was of special interest to us since we are working on photoswitchable versions of this biologically intriguing natural product. Again he is approach was highly creative, paving the way for detailed SAR studies of tricyclic labdanes

terpenoids. I. know from our own studies that forskolin is not an easy molecule to work with. His syntheses surpassed Corey's pioneering work ad others' as it can deliver useful quantities of the natural product and analogs thereof for biological studies. The syntheses of (–)-bactobolin A (*J. Am. Chem. Soc.* **2020**, *142*, 7306), pseurotin A (*J. Org. Chem.* **2021**, *86*, 11845), and especially (+)-actinobolin (*Angew. Chem. Int. Ed.* **2022**, *61*, e202116520) are all marked by clever strategies and the elegant applications of modern methodology, especially convergent radical additions. Dr. Švenda even made original contributions to synthetic methodology with respect to enantioselective conjugate addtions (*Org. Lett.* **2018**, *20*, 7085–7089).

As for **Reviewer's questions for the habilitation thesis defence**, I would like to submit the following:

1) What determines your choice of target molecules? How can you build a lasting, sustainable program on the judicious choice of target molecules?
2) Where do you see the advantages and disadvantages of odd-electron chemistry (*i.e.* radical chemistry) over even-electron chemistry (e.g. ionic and concerted).
3) Where do you see the future of "total synthesis". Should we continue to fund it? How will computational methods, such as machine learning and AI, impact and potentially transform this venerable field?
4)

In summary, I believe that Dr. Švenda is a young colleague on a steep trajectory who will make many valuable contributions to the art and science of total synthesis and methods development in the years to come. The habilitation thesis entitled "Synthetically modified complex natural products" by Jakub Švenda **fulfils** requirements expected of a habilitation thesis in the field of Organic Chemistry.

Best wishes,

Dirk Trauner