Total Synthesis of Miyabeacin B Is Ansarane a potential 3D Bioisostere of Naphthyl group?

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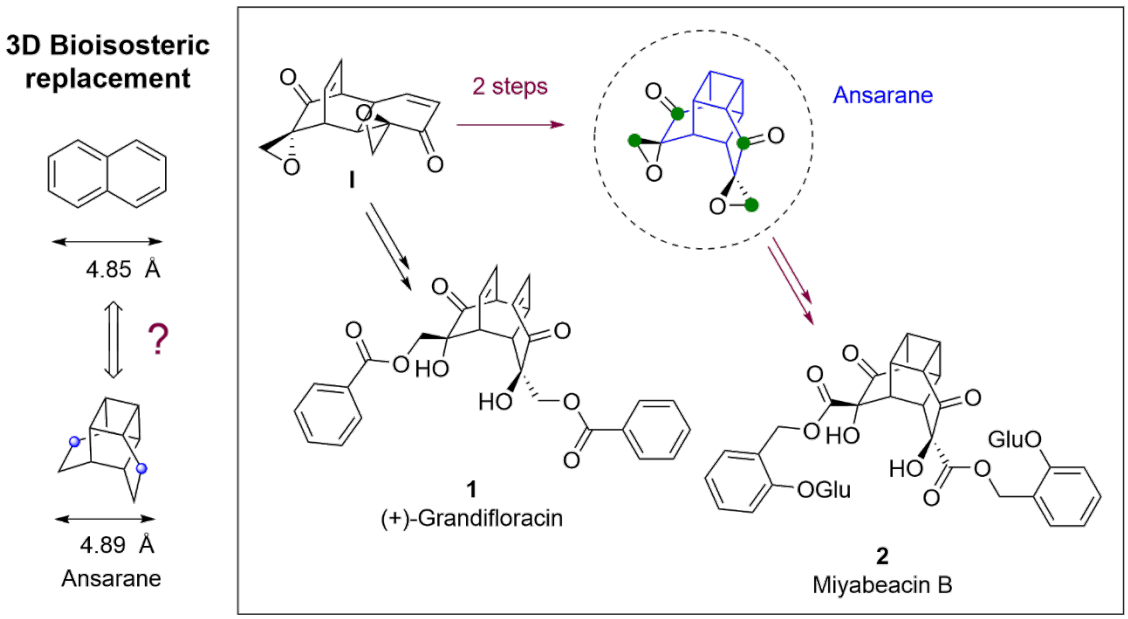
Willows consist of more than 1,500 distinct species and are a significant source of bioactive compounds, including salicylic acid and its derivatives. More complex structures have also been reported as (+)-Grandifloracin **1**, isolated in 2012 from the species *Uvaria dac*[1] and Miyabeacin B **2**, isolated in 2007 from *Salix Miyabeana*.[2] They both exhibit biological properties; in particular (+)-Grandifloracin which targets pancreatic cancer cell lines. Despite a modest activity (PC_{50} = 14.5 µM),[3] it nevertheless warrants particular attention, notably due to the marked resistance of pancreatic tumors to most currently available chemotherapeutic agents.

Thus, we set out to explore the potential of one of the precursors of (+)-Grandifloracin, possessing a spiroepoxycyclohexadienone **I** moiety which lends itself to numerous transformations and above all, offers a rapid access to ansarane structure using photochemistry. This caged compound exhibits a highly symmetric skeleton with intriguing chirality. Its properties are comparable to those of a naphthyl group and may be considered as a potential bioisostere.

Accordingly, we accomplished the total synthesis of Miyabeacin B and investigated a new 3D chemical space toward the preparation of novel constrained scaffolds inspired by this natural product.



Références

[1] Ueda, J. Y., et al. *Drug Des. Devel. Ther.* **2013**, *8*, 39–47.
[2] Ward, J.L., *et al. Sci Rep.* **2020**, *10*, 6477.
[3] Alexander, B.E., et al. *ChemMedChem*. **2020**, *15*, 125-135.