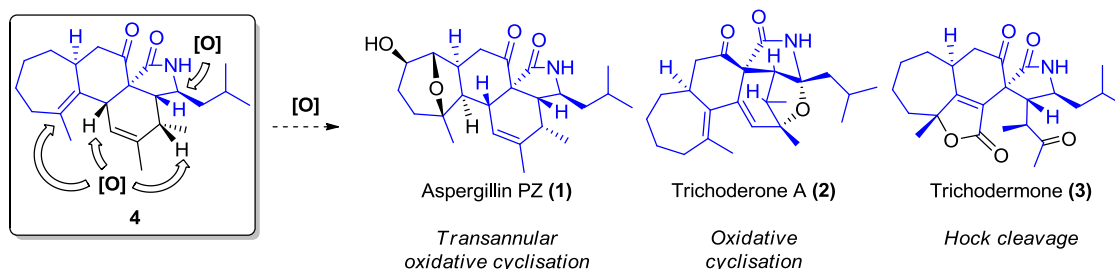


# TOTAL SYNTHESIS OF A KEY BIOMIMETIC PRECURSOR TOWARDS POLYCYCLIC CHALASANS AND BIOINSPIRED PHOTOXYGENATION OF NATURAL DITERPENES

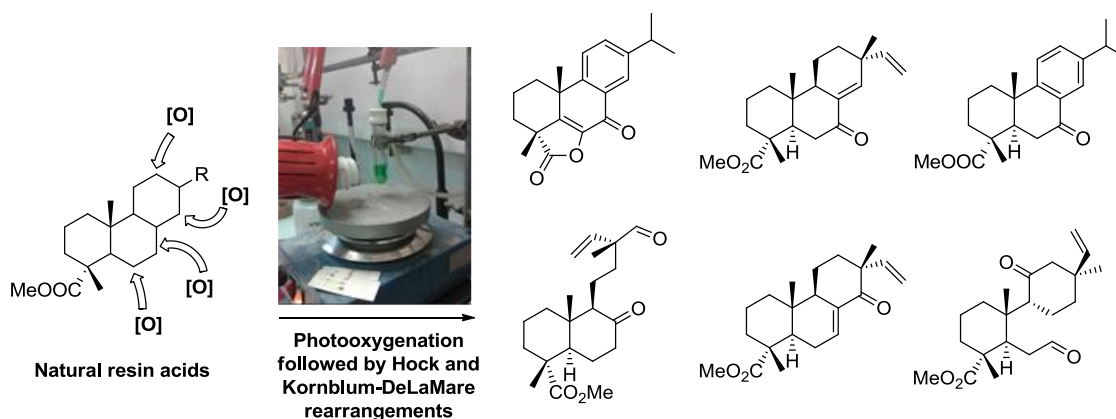
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Investigated for several decades, chalasans are fungal secondary metabolites showing a wide range of distinctive biological functions.<sup>1</sup> The total synthesis of such polycyclic polyketides is a tremendous challenge due to their complex structures. Overman and coworkers reported the first total synthesis of (+)-aspergillin PZ (**1**), a pentacyclic isoindolone alkaloid exhibiting antibiotic and anticancer activities.<sup>2</sup> Recently, the aspochalasans trichoderone A **2** and trichoderme **3** have been isolated from the plant endophytic fungus *Trichoderma gamsii*, showing biological activity against HeLa cell line. From a biosynthetic aspect, the leucine-based structure of these three hybrid polyketides suggests a common biosynthetic precursor **4** through oxidative transformations frequently occurring *in vivo*.<sup>3,4</sup>



More than a synthetic target, tetracyclic core **4** furnishes a platform to study the late stage biosynthetic functionalization happening in this series of compounds. This presentation will thereby emphasize the total synthesis of **4** including the development of a new methodology focused on ring-closing enyne metathesis of terminal alkynes with propargylic hindrance.<sup>5</sup> To support this reasoning, the development of a bioinspired photooxygenation methodology will also be depicted on natural diterpenes as model substrates using a “home-made” experimental tool.<sup>6</sup>



## References:

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- [1] See e.g. : W. B. Turner and S. B. Carter, *Proc. Biochem. Soc.*, **1971**, 127, 1P ; M. Binder and C. Tamm, *Angew. Chem. Int. Ed. Engl.*, **1973**, 12, 370–380 ; K. Scherlach, D. Boettger, N. Remme, C. Hertweck, *Nat. Prod. Rep.* **2010**, 27, 869-886.
- [2] S. M. Canham, L. E. Overman, P. S. Tanis, *Tetrahedron* **2011**, 67, 9837-9843.
- [3] G. Ding, H. Wang, L. Li, A. J. Chen, L. Chen, H. Chen, H. Zhang, X. Liu, Z. Zou, *Eur. J. Org.* **2012**, 2516-2519.
- [4] G. Ding, H. Wang, L. Li, B. Song, H. Chen, H. Zhang, X. Liu, Z. Zou, *J. Nat. Prod.* **2014**, 77, 164-167.
- [5] B. Laroche, M. Detraz, A. Blond, L. Dubost, P. Mailliet, B. Nay, *J. Org. Chem.* **2015**, 80 (10), 5359-5363.
- [6] B. Laroche, B. Nay, *Manuscript in preparation*.