

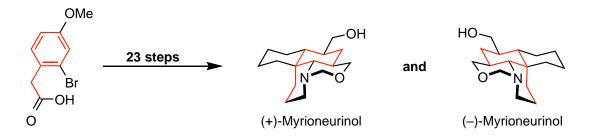
TOTAL SYNTHESES OF (+)- AND (-)-MYRIONEURINOL

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In 2007, Prof. Bernard Bodo's team at the Muséum National d'Histoire Naturelle (Paris - France) isolated a complex alkaloid from the North-Vietnamese shrub *Myrioneuron nutans*, and coined it (+) *Myrioneurinol*. These researchers not only elucidated its novel tetracyclic structure, but also demonstrated its moderate antimalarial activity against artemisinin-resistant *Plasmodium falciparum* strains (IC $_{50} = 11 \, \mu g/mL$). This discovery spurred the scientific community to engage several chemical campaigns towards a production of this molecule, resulting in three total syntheses: two racemic syntheses by the Weinreb¹ and Ma² groups in 2014 and 2022, respectively, and one formal asymmetric synthesis by the Smith³ group in 2022.

Since 2020, our group has also been working around the total synthesis of (+)-Myrioneurinol, and these efforts recently culminated in the isolation of both the enantiomers of this natural substance (*Scheme 1*).⁴ These results will be here presented, notably focusing on the key steps of our synthesis route, which include: 1- an hypervalent iodine-mediated phenol dearomatization, and 2- a novel approach allowing late-stage enantiomers resolutions, through a Barton-McCombie deoxygenation.



<u>Scheme 1</u>: Syntheses of both enantiomers of *Myrioneurinol* from 2-bromo-4-methoxyphenylacetic acid

Reference(s)

- ¹ a) Nocket, J. A.; Weinreb, S. M. Angew. Chem. Int. Ed. 2014, 53, 14162-14165.
- b) Nocket, J. A.; Feng, Y.; Weinreb, S. M. J. Org. Chem. 2015, 80, 1116-1129.
- ² Zhang, N.; Jiang, H.; Ma, Z. Angew. Chem. Int. Ed. **2022**, 61, e202200085.
- 3 Aquilina, J. M.; Smith, M. W. J. Am. Chem. Soc. 2022, 144, 11088-11093.
- ⁴ Denizet, A.; Nomula, R.; Edwards, R.; Toullec, P. Y.; Peixoto, P. A. *Chem.-Eur. J.* **2025**, e202500267.