Bioinspired Total Syntheses of Indole Alkaloids: Spirocyclic Assembly of Pseudo-Dimeric Oligomers

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Monoterpene indole alkaloids (MIA) constitute a fascinating family of natural substances which displays high degrees of complexity and diversity¹ and tend to self-assemble in many cases spontaneously in Nature to yield bis-indolic natural products² of important biological relevance. Vobtusine³, voafoline and voafolidine⁴ are pseudo-dimeric natural products arising from pseudo-monomers displaying the polycyclic *aspidosperma* skeleton and bearing a challenging spirocyclic central motif, making them an attractive target for organic chemists. Although isolated fifty years ago by Poisson and co-workers at Châtenay-Malabry from two *voacanga* species, no total syntheses have yet been reported. Investigating the assembly of such compounds, will allow us to develop efficient and straightforward synthetic sequences inspired by nature to increment structural complexity starting from simple chemical building blocks. We have already obtained advanced dimeric intermediates towards these natural products.

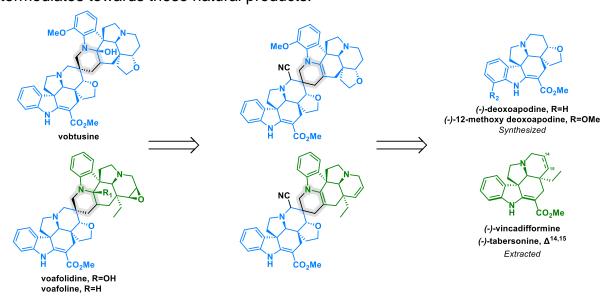


Figure 1. Structures of pseudo-dimeric oligomers and associated monomers.

² T.-S. Kam, Y.-M Chao, *The Alkaloids*, **2006**, *63*, chapter 4, 181.

¹ L. F. Szabó, *Molecules*, **2008**, *13*, 1875.

³A. Gorman, V. Agwada, M. Hesse, U. Renner, H. Schmid, *Helv. Chim. Acta*, **1966**, *49* (7), 2072.

⁴Y. Rolland, G. Croquelois, N. Kunesch, P. Boiteau, M. Debray, J. Pecher, J.Poisson, *Phytochemistry* **1973**, *12* (8), 2039.