# Ph.D. Open Seminar

Title of Thesis: "**Asymmetric Total Syntheses of *Amarylidaceae* Alkaloids Sharing *cis*-3a-Aryloctahydroindole Skeleton**"

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Date: **June 26**, **2018** (Tuesday) Time: **4:00 PM** Venue: **AB2-401**

## Abstract

The *Amaryllidaceae* alkaloids (**1a-j** and **2**, Figure 1) are a subset of compounds that have received substantial interest due to their medicinal properties and impressive structures (Figure 1).[1,2] Structurally, these alkaloids share *cis*-3a-aryloctahydroindole structure (along with more complex structure e.g. **2**)[2c] and display vicinal quaternary and tertiary carbon stereocenters with a fused pyrrolidine ring whose stereochemical incorporation is indeed a challenge.[2, 3] Importantly, both enantiomers of same structural scaffold were isolated from various *Amaryllidaceae* species [such as (+)-vittatine (**1g**) with an opposite configuration to that of (–)-crinine (**1c**)].[4a] Reportedly, the biological potential of several of these alkaloids is significantly manifested by anti-tumor, anti-viral, anti-cholinergic, and cytotoxic activities.[2]

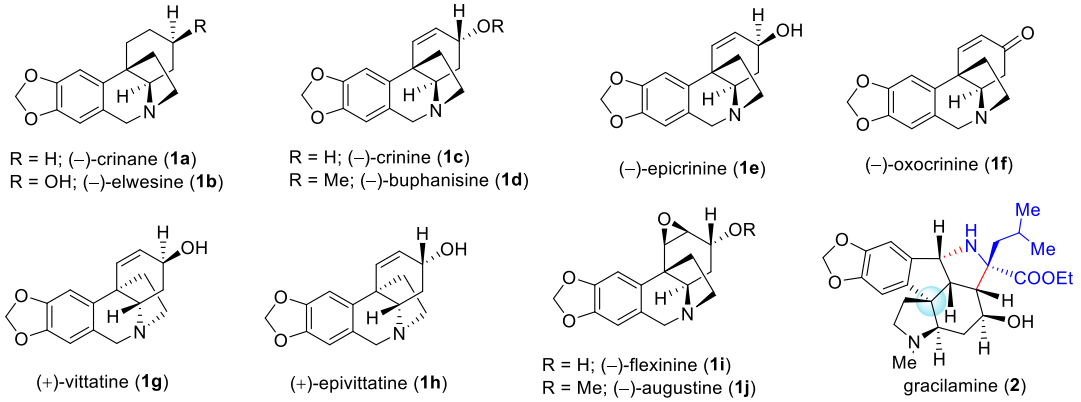


**Figure 1.** *Amaryllidaceae* alkaloids sharing *cis*-3a-aryloctahydroindole structure (**1a-j**) and **2**.

Although great efforts have been devoted to the development of synthetic methods to obtain crinine-type alkaloids, most of the reported approaches provided racemic products,[3] and only a few asymmetric syntheses of crinine or vittatine have been reported.[4] During my Ph.D. programme, I undertook unified asymmetric synthetic approaches to both enantiomers of the *Amaryllidaceae* alkaloids (**1a-j** and **2**) via the development of catalytic asymmetric methodologies to address all-carbon quaternary center (at the pseudobenzylic position) required for alkaloids **1a-j**.[5] Finally, we have applied these strategies for total syntheses of a number of naturlally occurring *Amaryllidaceae* alkaloids[6] with an intention of taking them further for biological evaluation.

## References and Notes:

1. (a) Douglas, C. J.; Overman, L. E. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5363. (d) De, S.; Das, M. K.; Bhunia, S.; Bisai, A. *Org. Lett.* **2015**, *17*, 5922. (c) Kumar, N.; Das, M. K.; Ghosh, S.; Bisai, A. *Chem. Commun.* **2017**, *53*, 2170. (d) Chaudhuri, S.; Bhunia, S.; Roy, A.; Das, M. K.; Bisai, A. *Org. Lett.* **2018**, *20*, 288.
2. Reviews, (a) Jin, Z.; Li, Z.; Huang, R. *Nat. Prod. Rep.* **2002**, *19*, 454. (b) Jin, Z. *Nat. Prod. Rep.* **2009**, *26*, 363. (c) N. Ünver, G. I. Kaya, *Turk. J. Chem.* **2005**, *29*, 547.
3. (a) Das, M. K.; De, S.; Shubhashish, S.; Bisai, A. *Org. Biomol. Chem.* **2015**, *13*, 3585. (b) Das, M. K.; De, S.; Shubhashish, S.; Bisai, A. *Synthesis*, **2016**, *48*, 2093 and references cited.
4. (a) Zuo, X.-D.; Guo, S.-M.; Yang, R.; Xie, J.-H.; Zhou, Q.-L. *Chem. Sci.* **2017**, *8*, 6202. (b) Du, K.; Yang, H.; Guo, P.; Feng, L.; Xu, G.; Zhou, Q.; Chung, L. W.; Tang, W. *Chem. Sci.* **2017**, *8*, 6247.
5. (a) Total Synthesis of (-)-buphanisine (**1d**): Das, M. K.; Kumar, N.; Bisai, A. *Manuscript Submitted*. (b) (+)- and (–)-Crinane (**1a**): Das, M. K.; Majumdar, S.; Khatua, A.; Bisai, A. *Manuscript under Preparation.*
6. Unified approach to total syntheses of both enantiomers of *Amaryllidaceae* alkaloids [e.g. (–)-crinine (**1c**) and (+)-vittatine (**1g**)]: Das, M. K.; Kumar, N.; Bisai, A. *Manuscript under Preparation*.