Ph.D. Open Seminar

Title of Thesis: **"Total Syntheses of Naturally Occurring Clavine Alkaloids"**

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Abstract

Clavine (**1a-e** and **2a-e**) subclass of ergot alkaloids are pharmacologically important indole alkaloids and are produced mainly by fungi of the families *Clavicipitaceae*.[1] Most ergot alkaloid structures contain a tetracyclic ergoline ring system (**1b-e** and **2a-e**), except cycloclavine (**1a**), which is sharing a pentacyclic framework with a vicinal all-carbon stereogenic centers.[1c] Reportedly, members of this family possess a broad spectrum of pharmacological activities, which include modulation of blood pressure, control of the secretion of pituitary hormones, migraine prevention, and dopaminergic and neuroleptic activities.[1b-c] Because of the varied and powerful biological activities of several congeners of this family, these alkaloids have long attracted the interests of synthetic chemists.

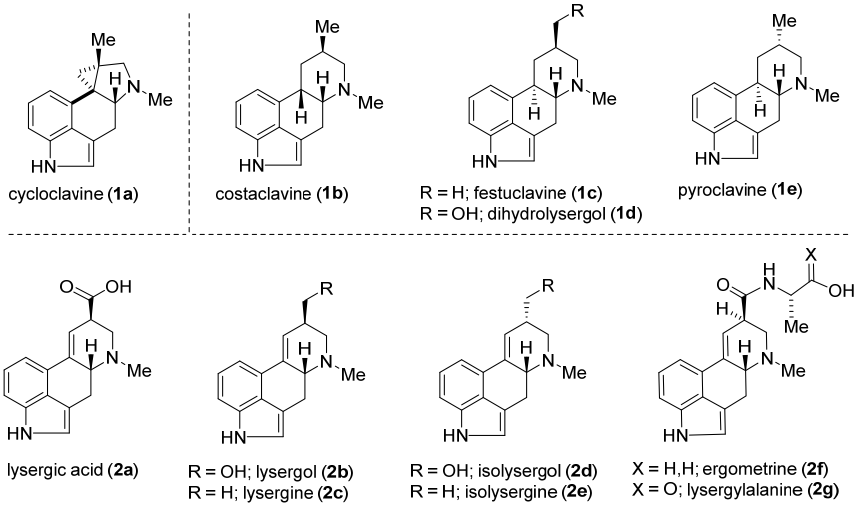

Figure. Selected clavine alkaloids (**1a-e**) and lysergine alkaloids (**2a-g**) of biological relevance.

Although few approaches to the total syntheses of this class of alkaloids have been reported,[2] however, majority of them are in racemic form. In this context, development of a unified asymmetric approach to synthesize majority the congeners remains still challenging.[3]As a part of my Ph.D. thesis, I undertook in developing unified strategy for the asymmetric total syntheses of clavine (**1a-e**) and lysergine (**2a-e**) subclasses of ergot alkaloids (Figure). Towards this, I will be discussing thio-urea catalyzed nitro-Michael reaction[4a] and an unprecedented Heck cyclization to set vicinal stereocenters required for these ergot alkaloids.[4b] I will also talk about synthesis of asymmetric synthesis of key intermediate for Heck cyclization via catalytic enantioselective α-aminoxylation strategy.[5]

References and Notes:

1. (a) Isolation of lysergic acid: Jacobs, W.; Craig, L. *J. Biol. Chem.* **1934**, *104*, 547. (b) Review: Wallwey, C.; Li, S.-M. *Nat. Prod. Rep.* **2011**, *28*, 496.
2. For excellent reviews, see: (a) McCabe, S. R.; Wipf, P. *Org. Biomol. Chem.* **2016**, *14*, 5894. (b) Liu, H.; Jia, Y. *Nat. Prod. Rep.* **2017**, *34*, 411.
3. For our approach via 2-oxindole pathway, see: (a) Bhunia, S.; Ghosh, S.; Dey, D.; Bisai, A. *Org. Lett.* **2013**, *15*, 2426. 2-Oxindoles in total syntheses, see; (b) Ghosh, S.; Chaudhuri, S.; Bisai, A. *Org. Lett.* **2015**, *17*, 1373. (b) Ghosh, S.; Chaudhuri, S.; Bisai, A. *Chem. –Eur. J.* **2015**, *21*, 17479.
4. (a) Bhunia, S.; Chaudhuri, S.; Bisai, A. *Chem. –Eur. J.* **2017**, *23*, DOI: 10.1002/chem.201702459. (b) Chaudhuri, S.; Ghosh, S.; Bhunia, S.; Bisai, A. *Manuscript Communicated*.
5. Total syntheses of clavine alkaloids: Chaudhuri, S.; Bhunia, S.; Roy, A.; Bisai, A. *Manuscript under preparation*.