Ph.D. Open Seminar

Title of Thesis: **"Synthesis of 2-Oxindoles Sharing All-Carbon Quaternary Centers: Synthetic Approaches to Azonazine and Cyclotryptamine Alkaloids"**

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Abstract

The development of efficient methodologies to construct an all-carbon quaternary stereocenter remains a challenging task in organic chemistry. In this regard, naturally occurring indole alkaloids sharing quaternary stereocenter (**1-3**, **Figure**) always inspired to develop efficient strategy for their total syntheses. Towards this, architecturally interesting azonazine[1a] (**1a**) (Figure 1) isolated from a Hawaiian marine sediment-derived fungus *Aspergillus insulicola*, having a unique hexacyclic dipeptide structure, drew our interest. A variety of hexahydropyrrolo[2,3-*b*]indole alkaloids (**2a-c**) having an all-carbon quaternary stereocenter are also widespread in nature. Some members of this class of alkaloid (such as physostigmine **2c**) are known to function as an acetylcholinesterase inhibitor and, therefore, these are considered to be promising candidates for the treatment of Alzheimer's diseases.[1b] On the other hand, a range of biologically relevant dimeric pyrrolidinoindoline alkaloids were isolated from various sources (**3a-b**). Architecturally, these alkaloids possess four contiguous stereogenic carbons, among those two of them are situated at the vicinal C3a-C3a' position (**3a-b**) and thus are challenging target for synthetic community.[1c]

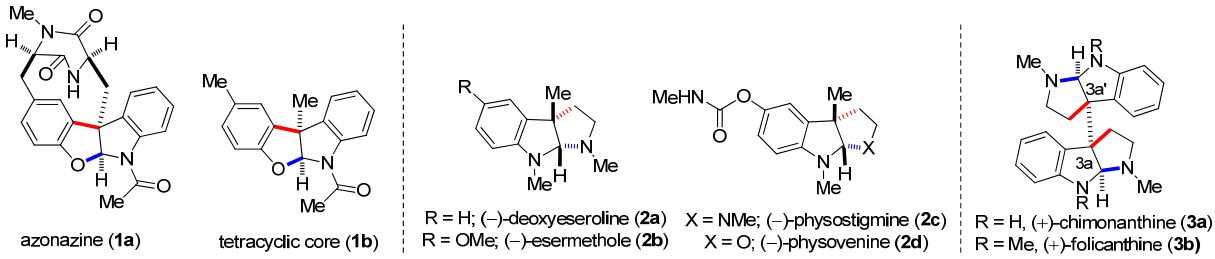

Figure 1. Selected indole alkaloids of biological relevance sharing all-carbon quaternary center.

As a part of my Ph.D. thesis, I undertook to develop efficient strategies for the synthesis of 2-oxindoles sharing an all-carbon quaternary center at the pseudobenzylic position. Towards this, in **Chapter I**, I will discuss about the development of efficient Lewis acid-catalyzed Fridel-Crafts alkylations of electron-rich aromatics with 3-hydroxy-2-oxindoles as electron-deficient partners for efficient synthesis of tetracyclic core (**1b**) of azonazine (**1a**).[2] The **Chapter II** of my thesis is focused on Lewis acid-catalyzed reaction of 3-hydroxy-2-oxindole with a variety of terminal alkynes and its applications towards the total syntheses of pyrrolidinoindoline alkaloids, (±)-deoxyeseroline (**2a**) and (±)-esermethole (**2b**).[3] Later, in **Chapter III**, I will discuss Lewis acid-catalyzed reaction of 3-hydroxy-2-oxindole with allyltrimethylsilane and its application to the formal syntheses of dimeric pyrrolidinoindoline alkaloids, (±)-folicanthine (**3b**).[4]

References and Notes:

1. (a) Crews et. al. *Org. Lett.* **2010**, *12*, 4458. (b) Luo et. al. *J. Med. Chem.* 2005, **48**, 986. (c) Douglas, C. J.; Overman, L. E. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5363.
2. (a) Ghosh, S.; **Kinthada**, **L. K.**; Bhunia, S.; Bisai, A. *Chem. Commun.* **2012**, *48*, 10132. (b) **Kinthada**, **L. K.**; Ghosh, S.; Babu, K. N.; Sharique, M.; Biswas, S.; Bisai, A. *Org. Biomol. Chem.* **2014**, *12*, 8152. (c) Babu, N. K.; **Kinthada, L. K.**; Ghosh, S.; Bisai, A. *Org. Biomol. Chem.* **2015**, *13*, 10641.
3. (a) **Kinthada**, **L. K.**; Ghosh, S.; De, S.; Bhunia, S.; Dey, D.; Bisai, A. *Org. Biomol. Chem.* **2013**, *11*, 6984. (b) **Kinthada**, **L. K.**; Babu, N. K.; Ghosh, S.; Parida, A. Bisai, A.* *Manuscript Under Preparation.*
4. **Kinthada**, **L. K.**; Ghosh, S.; Medisetty, M. S.; Bisai, A.* *Manuscript Under Preparation*.