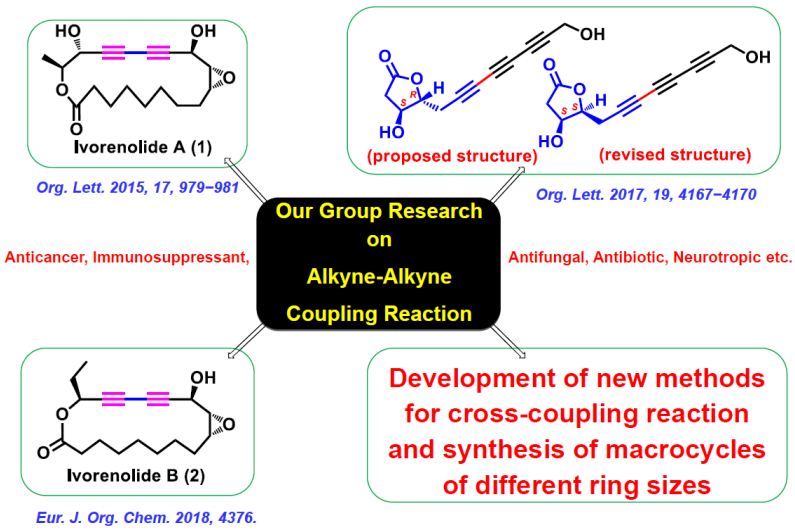
Alkyne-Alkyne Cross-Coupling: Total Synthesis of Di- and Triyne Containing Natural Products

Debendra Kumar Mohapatra
Department of Organic Synthesis and Process Chemistry
CSIR-Indian Institute of Chemical Technology, Hyderabad-500007, Telangana, INDIA
mohapatra@iict.res.in

Macrocycles are widespread structural motifs present in natural products,[1] pharmaceuticals,[2] material science compositions,[3] and have profound importance in supramolecular chemistry.[4] Among these, 1,3-butadiynes or di-acetylenic scaffolds occur widely and to date, over one thousand naturally occurring polynes were isolated and were found to display antibacterial, anti-cancer, anti-HIV, antifungal properties.[5] Metal mediated oxidative dimerization of terminal alkynes with stoichiometric amount of copper was developed by Glaser[6] about 160 years ago. Modified reactions such as Glaser-Hay and Cadiot-Chodkiewicz coupling reactions were developed later to prepare unsymmetrical conjugated diynes. Cadiot-Chodkiewicz coupling though powerful, often suffers from poor selectivity and formation of homo-coupled byproducts. To specifically address the problems related to optimizing chemoselectivity in homo-coupling of alkynes, either of the terminal alkynes should be immobilized on a solid support or should be converted to a haloalkyne under high dilution conditions. Less is known about the Glaser-Hay coupling for macrolactonization, although recent studies by Collins et al. disclosed a novel strategy employing copper catalysis and high concentrations for the synthesis of macrocycles using a "phase separation strategy". In this lecture, I will discuss the use of gold-copper synergistic catalyst system to effect direct macrocyclization. So far very few examples are reported to achieve intermolecular Glaser-Hay coupling reaction with gold complexes. Moreover, to date, gold-catalyzed intramolecular Glaser-Hay coupling was not utilized to synthesize diyne containing macrolactones.



In this talk, the first asymmetric total synthesis of proposed structures, correct structure and absolute configuration of cryptorigidifoliol K, Monocillin VII, and Diplopyrone will be discussed.[3-6]

References

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Dr. Debendra K. Mohapatra after completing his PhD at CSIR-IICT in 1999 and post-doctoral studies from USA, joined NCL, Pune, as a Scientist (2002-2008). During this period, he has also visited to UK and worked with Prof. Steven V. Ley (Cambridge Univ.) and Prof. Mark G. Moloney (Oxford Univ.) as a visiting scientist. He had collaboration with Prof. R. H. Grubbs and Prof. Ronald T. Raines of MIT, USA. In 2008, he moved to CSIR-IICT and currently working as a Chief Scientist. Very recently he has also joined as a Professor at IISER Berhampur. He has received INSA Young Scientist Award 2002, ICT Foundation Day Young Scientist Award 2004, D & O Pharmachem Inc., U. S. A. Young Scientist Award 2005, CDRI Award for Excellence in Drug Research 2007, AVRA Young Scientist Award 2008, CSIR-Technology Award 2014, NASI-Reliance Industries Platinum Jubilee Award 2017, CRSI Bronze Medal 2023.