Diversity oriented synthesis of tricyclic compounds

In the era of chemical genetics, small molecules are receiving unprecedented attention in order to understand and eventually modulate various biosynthetic pathways. Increased laboratory automation has improved the efficiency of screening for bioactives thereby demanding diverse chemical libraries for high-throughput screening. Diversity oriented synthesis is a newly proposed algorithm which enables synthesis of diverse molecular scaffolds within the ambit of combinatorial chemistry.

Diversity Oriented Synthesis

Dr. Hotha’s group at National Chemical Laboratory (NCL), Pune (http://www.ncl-india.org/) hypothesized that carbohydrate templates enable syntheses of oxygen-rich, chirally homogenous, complex, multi-cyclic and natural product-like chemical scaffolds exploiting various complexity generating reactions such as Pauson-Khand, Hashmi’s, Metathesis and Diels-Alder reactions. A Lewis acid mediated S$_2$2’ addition of alcohols to per O-acetylated glycals is known as the Ferrier reaction and a Co$_2$(CO)$_8$ promoted 2+2+1 cyclization of an alkyne and an alkene is the Pauson-Khand reaction. Hotha and his graduate student Tripathi achieved a natural product-like tricyclic enone library by performing the stereoselective Ferrier reaction to obtain α-glycosides, introduced a propargylic moiety for the stereoselective Pauson-Khand reaction to obtain tricyclic enones which was further diversified using several mercaptans by Michael’s thiolate addition on to the enone.

It is pertinent to mention that the complexity generating reactions viz. the Ferrier, Pauson-Khand and the Michael addition reactions were highly diastereoselective thereby enabling chirally pure, oxygen-rich, tricyclic derivatives from easily accessible glycals. Hotha’s team is currently engaged in developing diversity oriented pathways for chirally pure, oxygen-rich, multi-cyclic and natural product-like libraries from carbohydrate templates.

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For further information on this work, contact Dr. Srinivas Hotha