“Chemical Synthesis and Biological Studies of Antitumor Natural Products”

Abstract. We will describe development of a unified, biomimetic approach to the aglain-forbaglin-rocaglamide classes of natural products. This approach involves photogeneration of oxidopyryliums via excited-state intramolecular proton transfer (ESIPT) of 3-hydroxyflavones followed by [3+2] dipolar cycloaddition to assemble the aglain core. An alpha-ketol rearrangement was employed to transform the aglain core to the cyclopenta[b,c]benzofuran (rocaglate) framework. Using ESIPT photocycloaddition, approaches will be outlined to synthesize the natural product methyl rocaglate and derivatives as well as the promising anticancer agent silvestrol, a natural product derived from a plant found in Malaysia which is being developed as a treatment for acute lymphoblastic leukemia. The mode of action of the roca glates as inhibitors of translation initiation by acting as chemical inducers of dimerization (CID) of the RNA helicase eIF4A and RNA will also be discussed. Finally, the synthesis of the cyclopenta-[b,c]benzopyran natural products ponapensin and elliptifoline will be outlined. These studies determined that (-)-ponapensin and (-)-elliptifoline are enantiomeric to (-)-methyl rocaglate, suggesting a hypothesis for their biosyntheses.

Thursday, October 16, 2014
5:00 PM
Cram Conference Room - 3440 Molecular Sciences Bldg

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