Primary Presenter: Danielle R. Berry

Email: drberry@syr.edu

Phone: (315)278-2891

University: State University of New York College of Environmental Science and Forestry

Academic Field: Chemistry

Faculty Mentor: José -Luis Giner

Faculty Email: jlginer@esf.edu

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Synthesis of Cyclopropyl Inhibitors of Invertebrate Sterol Metabolism

Danielle R. Berry, SUNY-College of Environmental Science and Forestry
Co-Author(s): José-Luis Giner

Marine sterols are of great research interest due to their diverse structural properties. Although these sterols have been isolated and characterized, little is know about their biological importance. Cholesterol is an important lipid in animals. Many invertebrates such as insects cannot synthesize cholesterol, however, they can transform plant sterols from their diet into cholesterol through a series of biochemical reactions that result in dealkylation at C-24. Petrosterol is a cyclopropyl sterol found in *Petrosia ficiformis,* a marine sponge. Recent studies have shown that petrosterol inhibits the dealkylation. Inhibiting the formation of cholesterol would have a negative impact on the health, growth and reproduction of the copepods. The cyclopropyl group is known to lead to mechanism based irreversible enzyme inhibition through the formation of cyclopropylcarbinyl cations and radical intermediates. This study focused on the synthesis of simplified analogs of petrosterol and its possible enzymatic products. Synthesis of simplified petrosterol analogs was completed following literature procedures and the structures of the compounds synthesized were determined by ^{1}H, ^{13}C, COSY, HMBC and HSQC NMR spectroscopy. Successful synthesis of 3 out of 4 simplified analogs was achieved and verified through NMR spectroscopy. Future work includes successful synthesis of the fourth analog and synthesis of these compounds with ^{13}C labeling at the C-22 position. The ^{13}C labeled sterols will be fed to invertebrates and tracked to better understand their mechanisms of action.

Key Words: Cholesterol, insect dealkylation, marine sterols, petrosterol, *Petrosia ficiformis*.