Total Synthesis and Structural Revision of Solomonamides

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Two cyclic peptides called Solomonamide A and solomonamide B were isolated from marine sponge Theonella swinhoei, by Zampella’s group. Solomonamide A was reported to show very potent anti-inflammatory activity (∼60% paw edema reduction) in mouse model as low as 100 μg/kg IP dose. However, the closely related solomonamide B could not be tested due to the scarcity of the material. Owing to the tremendous potential of Solomonamides in developing anti-inflammatory agents and its interesting structural features, we became interested in the synthesis as well as their biological evaluation. Accordingly we have accomplished the total synthesis of the natural products, Solomonamide A and B with revision of the originally proposed structures. Besides we have achieved the total synthesis of proposed structure of Deoxy-solomonamide B starting from tryptophan by mimicking the proposed biogenetic route. In addition, during the total synthesis we have developed a simple and practical one-pot, two-directional approach to access olefinic esters through simultaneous breaking and making of olefins using ozonolysis of alkenyl aryl selenides. We have also synthesized more than 20 analogs around this scaffold and they are presently being evaluated biological assays. Details will be discussed at the conference.

References