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ROMP approaches for organic synthesis and efforts toward the synthesis of cyclipostins

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The work reported herein describes the applications of ring-opening metathesis polymerization (ROMP) using well-defined ruthenium-based catalysts for organic synthesis, and efforts toward the synthesis of cyclipostins.

A strategy to synthesize oligomeric sulfonamides employed both ring-closing metathesis (RCM) and ring-opening metathesis polymerization (ROMP). Amino acid-derived cyclic sulfonamides containing either exocyclic or  $\gamma$ -endocyclic stereogenic centers were generated via RCM. These cyclic sulfonamides underwent stereoselective Diels-Alder reactions to yield endo-norbornenyl sulfonamides as major diastereomers. Subsequent ROMP rapidly produced sulfonamide-based oligomers, and these oligomers exhibited different solubility in a variety of solvents. Based on the solubility difference of these oligomers, a capture-ROMP-release strategy for the chromatography-free purification of Mitsunobu reaction products is described. Oxo-norbornenyl-tagged reagents are utilized for standard solution phase Mitsunobu chemistry. Post-reaction, phase-switching was accomplished via in situ ROMP followed by precipitation of the polymer with methanol. Release of the product from the polymer afforded amines and alkyl hydrazine derivatives with good yields and purities.

The C-H activation strategy mediated by Rh<sub>2</sub>(OAc)<sub>4</sub> was utilized toward the synthesis of cyclipostins. This novel class of natural product possesses strong inhibitory action against hormone-sensitive lipase (HSL) and has potential in the development of therapeutic agents to regulate lipolysis for the treatment of noninsulin-dependent diabetes mellitus (NIDDM). The initial results of this project are reported.

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