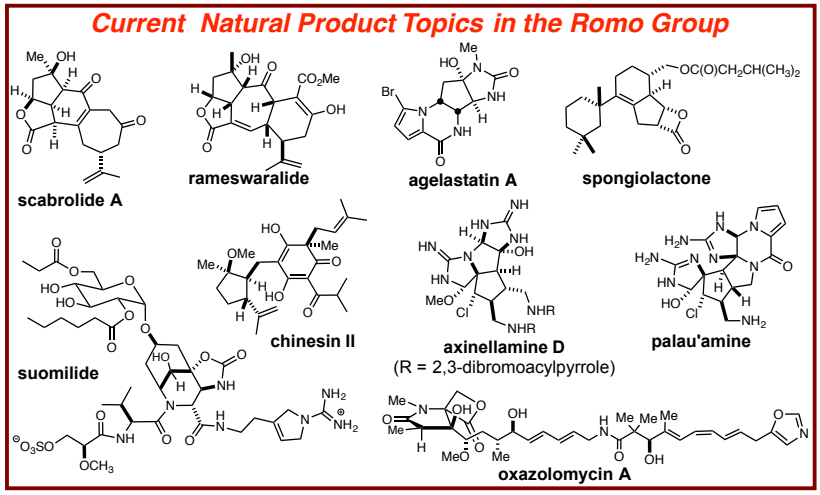
Romo Group Research Synopsis

At the heart of our research interests are the chemistry and biology of natural products, enduring leads for basic cell biology studies and drug development. These are unique and often structurally complex molecules that are designed to interact in highly specific ways with various cellular receptors and by homology those found in humans. Our interest in a particular natural product target typically stems from a combination of biological activity and unique and sometimes complex structure. The presence of β-lactones, often directly coupled to biological activity, or the potential of accessing functionality found in these bioactive compounds from β-lactones also drives our interest. Directly coupled to this latter goal has been explorations in the area of asymmetric organocatalysis wherein unique activation modes for commodity chemicals are being sought. Thus, overall our group is engaged in developing novel synthetic strategies and methods towards the total synthesis of natural products and more recently, isotopically-labelled biosynthetic precursors, to enable further inquiries into their biological mechanism of action at the molecular level, opening possibilities for drug development, and fundamental questions regarding the biosynthesis of these genetically encoded small molecules.



•Structural, Synthetic, and Biomechanistic Investigations of Bioactive Marine Natural Products
One focus of our research efforts is the structure elucidation, total synthesis, and determination of the mode of action of natural products that display significant physiological activity. Our total synthesis strategies are designed to allow highly efficient access to the natural product in addition to structural derivatives and conjugates for studies aimed at elucidating their mechanism of action at the molecular level.

•Enantioselective Organocatalysis and Organocascade Processes: Novel Routes to Important Chiral Intermediates, Including 2-Oxetanones (β-Lactones), Biological Probes and Natural Products. We are developing novel enantioselective organocatalytic reactions and organocascade processes to rapidly assemble complex, polycyclic heterocyclic and carbocyclic systems including those bearing β-lactones. Guided by a search for novel activation modes for organocatalysis and practicality, we are seeking economical and highly enantioselective, synthetic methods with a focus on commodity chemicals as substrates. The designed incorporation of β-lactones (and functional groups for conjugation) in our synthetic targets renders these compounds useful as activity-based probes to screen various cellular proteomes for novel therapeutic targets for infectious and oncogene-mediated disease.

•Novel Strategies for Structure-Activity Studies and Arming of Natural Products. We are developing strategies to more rapidly perform SAR studies with natural products, access novel derivatives, and ultimately identify their putative cellular targets. The strategy bypasses the usual bottleneck of structure elucidation of a bioactive natural product requiring only knowledge of functional groups present. Developed strategies involve mild chemo- and variably site-selective derivatizations that enable simultaneous arming and SAR studies of bioactive natural products to determine a suitable site for probe attachment while simultaneously appending suitable groups (*e.g.* alkynes) for conjugation to probe molecules (*e.g.* biotin, fluorophore, photoaffinity tags). To date, we can simultaneously perform SAR and 'arm' natural products possessing alcohols, alkenes, arenes, benzylic/allylic CH bonds, α-N CH bonds, and tertiary amines. The *Natural Products LINCHPIN Laboratory* (located on the floor below the Romo Group, visit: linchpin.tamu.edu) utilizes these methods in worldwide collaborations with isolation, synthetic chemists and biologists to advance a molecular level understanding of a natural product's mechanism of action. In addition, LINCHPIN scientists assist in translating bioactive small molecules to therapeutic leads by assistance with detailed SAR studies and scale-u of lead compounds for preclinical studies.