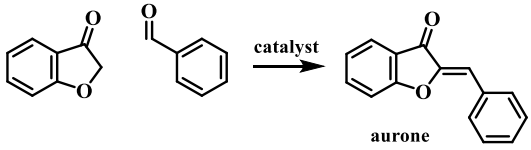
Independent Research Program Summary

Overview: Synthetic organic chemistry is an enabling science. It creates meaningful advances in medicine, materials, and humanity's fundamental understanding of the natural world through the preparation of intricate molecules originating in nature or our imaginations. It continues to offer abundant opportunities for exploration of methods that are increasingly selective, cost efficient, scalable, environmentally benign, and in control of structure to such a fine degree as to confer on the target extraordinarily specific sets of physical and biochemical properties.

New project launched 2022FA: **Design and synthesis of aurone analogs**

Aurones constitute an extensive class of molecules historically known for their function in plants as golden-colored pigments. We have developed a robust synthesis of the aurone molecular scaffold which by the nature of its high modularity and compatibility with a broad range of functionalized starting materials is amenable to the synthesis of analogs designed to serve the following applications.

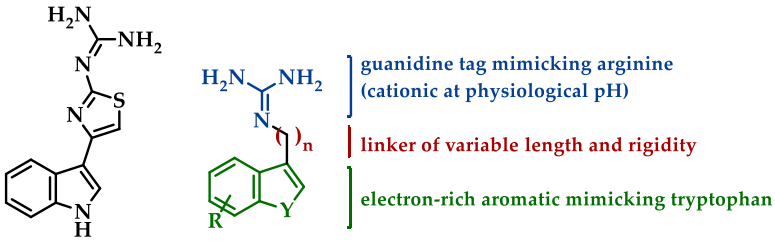
1. A blue pigment suitable for use in food and cosmetics.
2. A tunable fluorescent probe for use in cellular microscopy.
3. A folate-linked fluorophore for use in fluorescence-guided surgery, other imaging of cancers, and photodynamic or photothermal therapy.



Exploration of structure-function relationships is anticipated to allow optimization of properties such as solubility, toxicity, $T_{1/2}$ *in vivo*, cellular uptake, localization to cancerous cells or specific subcellular locations, Stokes shift, quantum yield, and stability to heat, oxygen, light, and extremes of pH.

Primary Project: **Design and synthesis of antifungal/antibacterial compounds with mimicry of natural antimicrobial peptides (AMPs).**

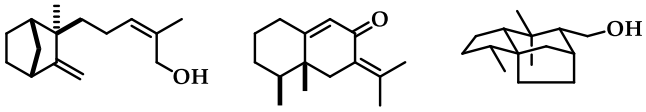
AMPs are antimicrobial compounds produced in nature whose tremendous potential to be developed into therapeutics is severely hindered by their proteolytic instability, poor tissue distribution, and high cost of synthesis. Through understanding how the molecules' structural features lead to key intermolecular affinities that disrupt cellular membranes, we aim to design out the undesirable properties while retaining selective pathogen killing activity so that these new synthetic mimics of AMPs may continue progression through the drug discovery pipeline. Biological evaluation of our synthesized compounds is conducted in collaboration with the Community for Open Antimicrobial Drug Discovery.



example target — general form (pharmacophore)

Secondary Project: **Synthesis of aroma molecules originating in trees of severely limited supply.**

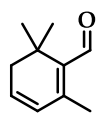
The oil rich woods of sandalwood (*Santalum* species) and agarwood (*Aquilaria* species) trees are of great importance commercially and culturally for their distinctive fragrance. We aim to achieve laboratory syntheses of the molecular components responsible for the desirable fragrance properties, ideally in a manner efficient enough to lead to a commercially viable process that would reduce demand on the natural source (endangered species).



β-santalol — dihydrokaranone — jinkohol II

Proposed Project: **Synthesis of safranal by a [4+2] cycloaddition strategy.**

Saffron, the dried stigma and style flower portions of *Crocus sativus*, widely regarded as the most expensive spice in the world, contains flavor and color components whose molecular structures are known. We aim to achieve a laboratory synthesis of the nature-identical organoleptic molecule safranal using a Diels-Alder cycloaddition strategy that circumvents temperature-induced decomposition of intermediates through the use of Lewis acid catalysis.



safranal