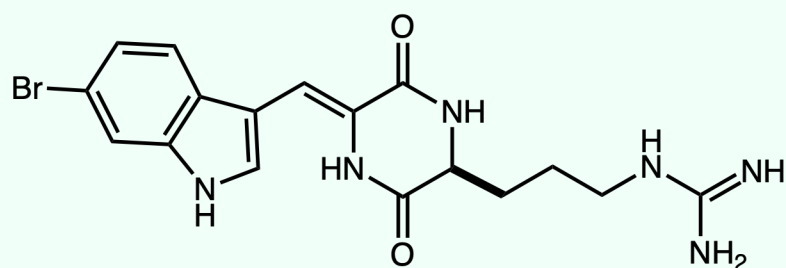
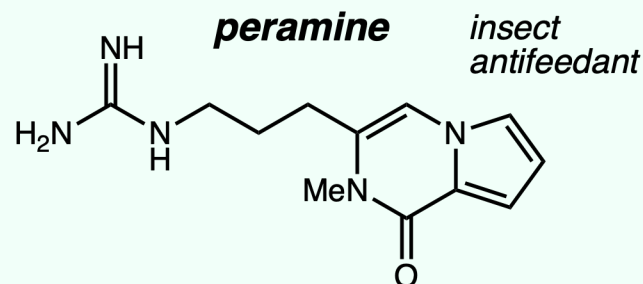
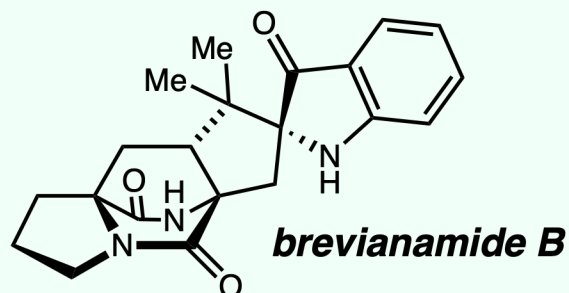
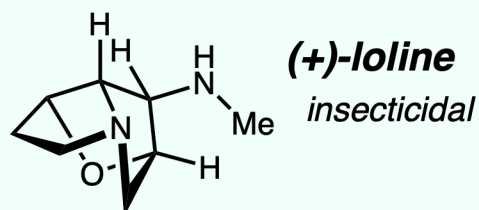
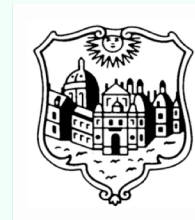
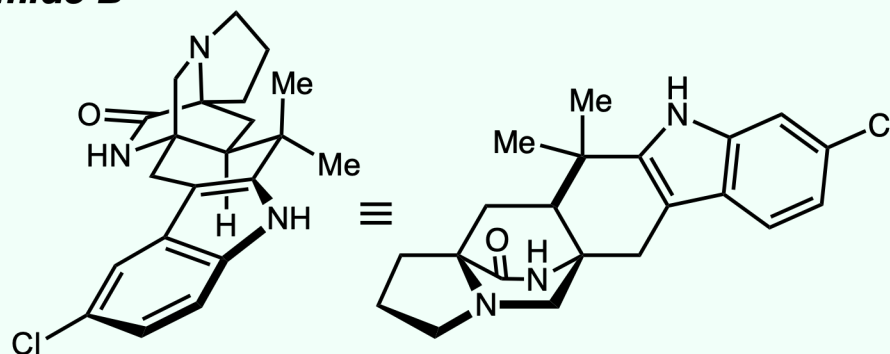


Synthesis of Polycyclic Alkaloid Natural Products



*Antibiofouling
selective 5HT ligand*



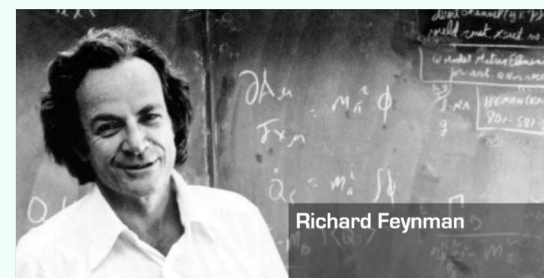
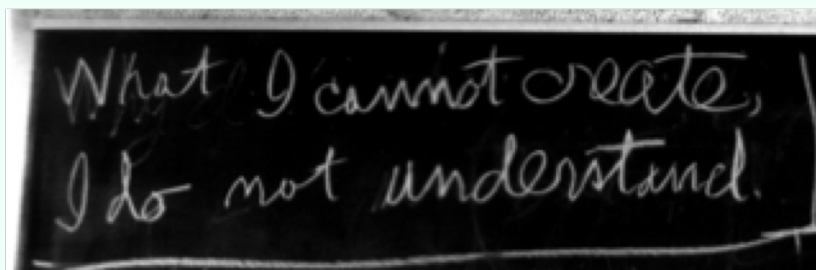
PDE1 inhibitor

The Scheerer lab is primarily engaged in research directed to the synthesis of nitrogen-containing polycyclic molecules. Our efforts are divided between two arenas: advancing new methods (or developing new chemical reactions that form heterocyclic ring systems) or synthesis of biologically-active molecules.

Synthesis of Polycyclic Alkaloid Natural Products in the Scheerer Lab

"In all things of nature there is something of the marvelous."

Aristotle
4th c. BC



on Richard Feynman's office blackboard at the time of his death (CalTech 1988)

We ground our research in Polycyclic Alkaloid Natural Products for a few reasons. First, some definitions:

Synthesis is the art and practice of making molecules. Mostly we are concerned with how to make complex structures from simple (ideally inexpensive commercially-available) precursors.

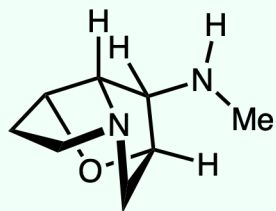
Alkaloids are molecules that contain basic nitrogen. (latin: alkaloid = "alkali like")

Natural products (NPs) are chemical compounds produced (originally) by a living organism. **Secondary metabolites** are NPs that are not essential for survival, but provide host organism with evolutionary advantage. These often have a pharmacological or biological activity which we can leverage.

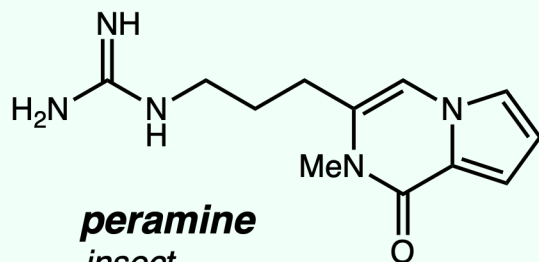
We work in this space because (1) the majority of New Therapeutic Chemicals (>63% since 1981) are derived or inspired by natural products, (2) >90% of new therapeutics contain nitrogen, (3) >95% top 200 prescribed medicines contain N. (4) >95% contain at least one ring.

In summary, **Polycyclic Alkaloid Natural Products have had and continue to have the largest impact on human health** and we want our chemistry to be connected to problems of significance in this area.

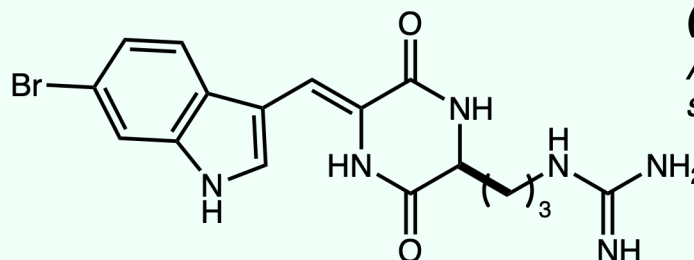
Area 1: Natural Products with Insecticidal, Herbicidal, Antifouling Activities



(+)-loline
insecticidal



peramine
insect
antifeedant



(±)-baretin
Antibiofouling
selective 5HT ligand

Examples of molecule in this project area that we have made include the above structures. Our most recent efforts in this area were directed to new methods to construct the core present in peramine.

JOC *The Journal of Organic Chemistry*
pubs.acs.org/joc Article

Synthesis of Pyrrolopyrazinones by Construction of the Pyrrole Ring onto an Intact Diketopiperazine

Susanna K. Maisto, Angela P. Leersnyder, Gwyneth L. Pudner, and Jonathan R. Scheerer*

Cite This: *J. Org. Chem.* 2020, 85, 9264–9271 [Read Online](#)

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ABSTRACT: This study reveals an alternative sequence for the synthesis of compounds that contain the pyrrolo-diketopiperazine structural motif. Starting with a diketopiperazine precursor, a mild aldol condensation precedes pyrrole annulation and bicyclic ring fusion. The derived intermediate aldol condensation products, which bear either a protected carbonyl or a functionalized alkyne, can be cyclized to the pyrrolo-diketopiperazine by protic or gold Lewis acid catalysis.

Alumni of this project include

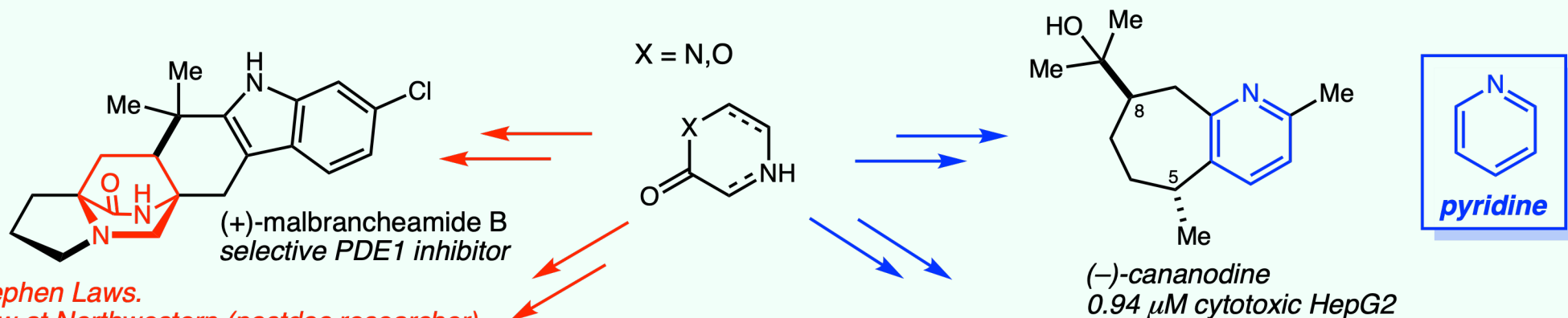
Gwyneth Pudner (BS2022)
on new honors project in Scheerer lab.

Susanna Maisto (BS2021)
at NIH, applying for PhD programs
in environmental engineering

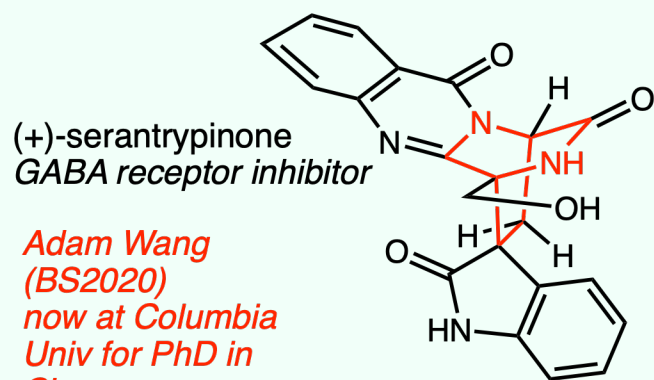
Angela Leersnyder (BS2021)
at EPA, applying to graduate programs in
art conservation

Scheerer Lab

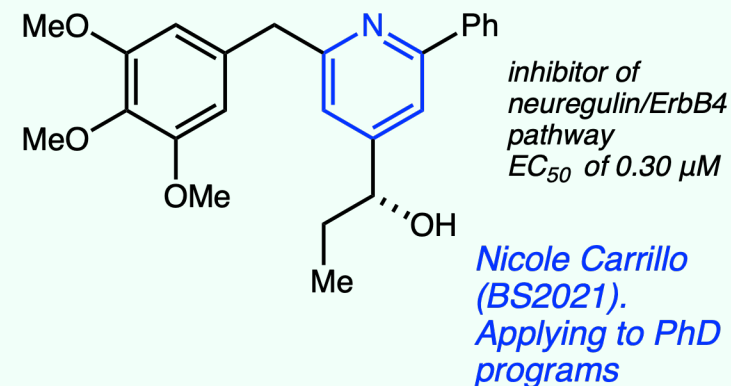
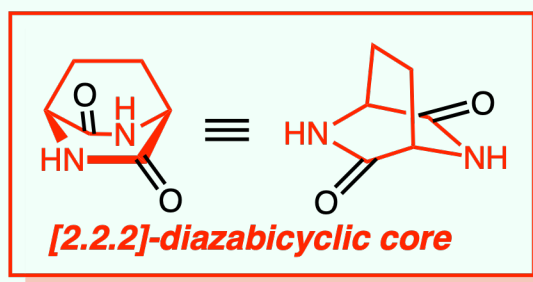
Area 2: Diverse Bioactive Structural Motifs from a Common Precursor



Stephen Laws.
Now at Northwestern (postdoc researcher)



Adam Wang
(BS2020)
now at Columbia
Univ for PhD in
Chem



Devin Mickles
(BS2020) now at
UNC for PhD in
Chem

The other main area of research in the Scheerer lab is directed toward developing new reactions that can be used for the construction of several nitrogen-containing structures. Students who have worked on recent projects in this area have gone on to advance their careers in many places and many different areas of science.