

# ORGANIC SEMINAR

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“ $\alpha$ -(aminomethyl)- $\gamma$ -butyrolactones as a New Class of Antibiotics”

Antimicrobial resistance (AMR) is a growing threat to global human health. As first-line drug therapies become less efficient and fatalities tied to AMR associated infections rise, new antibiotics are desperately needed.  $\alpha$ -(methylene)- $\gamma$ -butyrolactones, a moiety common to 10% of all discovered natural products, have long been known for their anti-cancer properties. The  $\alpha$ -(aminomethyl) derivatives of these lactones have recently demonstrated potential to help fill the need for new antibacterial medications. Our lab has extensively developed new methodologies which make synthetic  $\alpha$ -(aminomethyl)- $\gamma$ -butyrolactones, particularly those containing aryl groups at the  $\beta$ - and  $\gamma$  - positions, readily available.

The CDC has identified methicillin-resistant *Staphylococcus aureus* and *Clostridioides difficile* as serious and urgent AMR related threats, respectively. Our structure activity relationship (SAR) studies utilizing  $\alpha$ -(aminomethyl)- $\gamma$ -butyrolactones against these two bacteria have highlighted potent and specific lead compounds which show no toxicity in in vivo models. Lastly, the development of new synthetic routes to the  $\alpha$ -(aminomethyl)- $\gamma$ -butyrolactam analogs will enable an expansion of the SAR studies.