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EXPLORING THE ANTIMICROBIAL ACTIVITY OF BETA-LACTONES TO COMBAT ANTIBIOTIC RESISTANCE

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Antibiotic resistance is one of the world's most urgent health crises. By their very nature, antibiotics tend to select for resistance in bacteria, killing off non-resistant strains in the process of fighting infection and leaving only resistant strains to reproduce, making each successive generation harder to treat. In the past, antibiotic drug development has focused on a small number of classes of antibiotics, directly combating bacterial resistance mechanisms by modifying the functional groups surrounding the drug's active core. However, diminishing returns in the efficacy of these alterations have driven antibiotic drug development to branch out into new classes of antibiotics that hit different targets within the bacteria, circumventing evolved resistance mechanisms. I am studying one such under-explored class: beta-lactones. The beta-lactone ring is a relatively uncommon functional group that is very similar in structure to the beta-lactam active group in common antibiotics such as Penicillin. Although a few beta-lactone lipase inhibitors such as lipstatin, hymeglusin, and ebelactone have been approved for clinical use as anti-obesity drugs, the antibiotic activity of beta-lactones is not well characterized. In order to explore this property, we synthesized a library of simple beta-lactones to test their antimicrobial activity. I used the Mitsunobu cyclization on L-serine followed by an acylation to synthesize simple substituted beta-lactones. These compounds were then assayed with *E. coli* and showed dose dependent activity. This suggests that beta-lactones, even in their simplest form, possess bacteriostatic antimicrobial activity.