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SYNTHESIS OF AN ANTIBIOTIC SCAFFOLD INSPIRED BY THE TAN 1057-D BIOLOGICALLY ACTIVE NATURAL PRODUCT

Rachel Lou-LaVonne Cantrell (Prof. Ryan Looper)
Department of Chemistry

As bacterial resistance to drugs continues to rise, the search for new antibiotics is of paramount importance. One key element to finding successful antibiotics is to uncover small molecules that act through novel mechanisms of action in order to promote the efficacy of the antibiotic for a longer period of time. Based on previous work conducted in our research group, the TAN-1057 antibiotic family shows promise as new candidates in part due to their inhibition of protein synthesis at the point of tRNA acyl-transfer in the ribosome. This project involves the synthesis of the TAN-1057 D heterocyclic core, as well as the elucidation of TAN-1057 D interactions in the ribosome. A modular synthetic strategy has been implemented to construct the heterocyclic core of TAN-1057 D. This strategy was chosen in order to streamline analog development via facile functional group additions and control of the heterocyclic ring oxidation state. The core has been synthesized through the utilization of Ullman copper(I) chemistry, and manipulation of the core is currently in progress to allow for analog development. The installment of functional group handles will allow for a wide variety of analogs to be synthesized, and then undergo biological testing. Upon completion of TAN-1057 D derivatives, we will be able to explore the mechanism of action of the parent compound and gather insight into the structural characteristics of a future drug candidate.

Figure 1: Synthetic route taken in developing the scaffold core