FACULTY DEVELOPMENT ENDOWMENT FUNDS

Faculty Research Fund

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Proposal Title: Straightforward Synthesis of New 2-aminopyrimidines

Principal Investigator: John Hershberger

College of Sciences & Mathematics

Department of Chemistry and Physics

ABSTRACT

2-aminopyrimidines are privileged structures in medicinal chemistry due to this structural feature appearing in a number of valuable drugs. For example, Gleevec and Crestor are two well-known drugs that contain this component. The synthesis of these compounds can be expensive and time consuming. We propose a 3-step sequence consisting of two multicomponent reactions (MCRs) and an oxidation to synthesize molecules containing this feature. MCRs are extremely valuable in organic synthesis due to their ability to take easily available cheap starting materials and combine them into a more complex value-added product in a single step. The MCRs work because the choice of reactants leads to a particular end product. Two well-known MCRs are the Biginelli reaction and the Ugi reaction. The Biginelli reaction combines an aldehyde, a β-keto ester and urea to give a dihydropyrimidinone upon reaction. The Ugi reaction combines an aldehyde, an amine, an isocyanide, and a carboxylic acid to give a diamide product. This project proposes a three step sequence consisting of a Biginelli reaction, an oxidation of that Biginelli product to a 2-hydroxypyrimidine, and then a modified Ugi reaction (Ugi-Smiles reaction) to give 2-aminopyrimidine products. These products will then be evaluated against a number of pathogens and for other bioactivities.