Building a Library of Difluoro- and Trifluoro-Artemisinins, Year Two

Ramayya, Shreya (School: Indus International School)

In recent years fluorine has become increasingly important to the pharmaceutical industry. Coupled with already-potent drugs, fluorine has allowed common therapies to become even more effective. For centuries malaria has been treated with artemisinin combination therapies, but drug resistance has drastically reduced their effectiveness. This study was begun to develop approaches to solve the malaria problem in a novel way. Recognizing the benefits of adding fluorine to create compounds of biologic value, this project focused on developing the process using both nucleophillic and electrophilic fluorination to successfully incorporate fluorine into molecules of biological importance. Initial success with trifluoromethylation of artemisinin paved the way for experimentation with difluoromethylation, a process that had not yet been studied. Nucleophilic trifluoromethylation of artemisinin using the Ruppert- Prakash reagent (TMS-CF3) was successful, giving high yields. Given the unique and delicate structure of artemisinin initial difluoromethylation is underway on simple molecules to assist in the development of a procedure that could work for artemisinin. NMR analysis revealed that although the reaction may have worked successfully, side products were formed in the process, indicating that further optimization and purification is necessary. In conclusion, while I have deduced that the addition of fluorine to various compounds is beneficial and possible, the procedures involved in adding fluorine to biologically active molecules must be refined and perfected. NMR Spectra will confirm the purity of the desired product at which point biological testing can be performed to test the potency of the newly synthesized library of compounds to treat malaria.

Awards Won:
Fourth Award of $500