Synthesizing and Utilizing Difluoromethyl- & Trifluoromethyl- Artemisinins to Interrupt the Life Cycle of Malaria Parasites, Year III

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Fluorine has allowed common therapies to become even more effective in treating many diseases because of the small size, low polarizability, and high electronegativity of the fluorine atom. Malaria could benefit from such an approach as drug resistance has drastically reduced the effectiveness of artemisinin, a common malaria drug. This study focused on developing the methodology to utilize both nucleophilic and electrophilic fluorination methods to incorporate fluorine into antimalarials. The first step involved mastering the fluoroalkylation of simple aldehydes, esters, and ketones. The next step in the study involved nucleophilic trifluoromethylation of artemisinin using the Ruppert- Prakash Reagent (TMS-CF3). Successful trifluoromethylation led to difluoromethylation of artemisinin, a process that has not been studied in great detail before. The difluoromethyl (-CF2H) group is isosteric and isopolar to the hydroxyl (-OH) group, so the difluoromethyl- artemisinins may yield extremely desirable results. The methodology developed under the study produced high yields of a pure product The final step in evaluating the effectiveness of difluoromethyl- and trifluoromethyl- artemisinins to interrupt the production and transmission of gametocytes is underway. In vitro drug assays were used to monitor the effectiveness of trifluoromethyl artemisinins in halting the growth of malaria parasites in their highly virulent gametocyte phase. In conclusion, high yields of very pure fluorinated artemisinin were synthesized, as confirmed by nuclear magnetic resonance (NMR) spectrometry. Highly positive results have come from in vitro studies of parasitemia over time, indicating that the effects of fluorinated artemisinin last longer than those of traditional artemisinin.

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