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Pyridine-Core Synthesis and Functionalization of HIV Integrase Inhibitors

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HIV integrase inhibitors are a class of anti-viral drugs that prevent the incorporation of the viral genome into the host cell genome. The three prominent targets in HIV therapy, integrase, reverse transcriptase and protease are all unique to the virus and thus are attractive foci in research. HIV Integrase inhibitors are mostly based on aromatic heterocycles such as pyridine and quinoline. In this project, we are constructing the pyridine core by reaction of substituted malonic esters with aminocrotonate ester. Variations in 2 positions on the heteroaromatic core allows for improving the drug-target interactions. The formation of the pyridine skeleton has been optimized and now requires only one step. Functionalization of the 4 and 6 position is performed by chlorination in preparation for palladium-catalyzed coupling reactions.

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