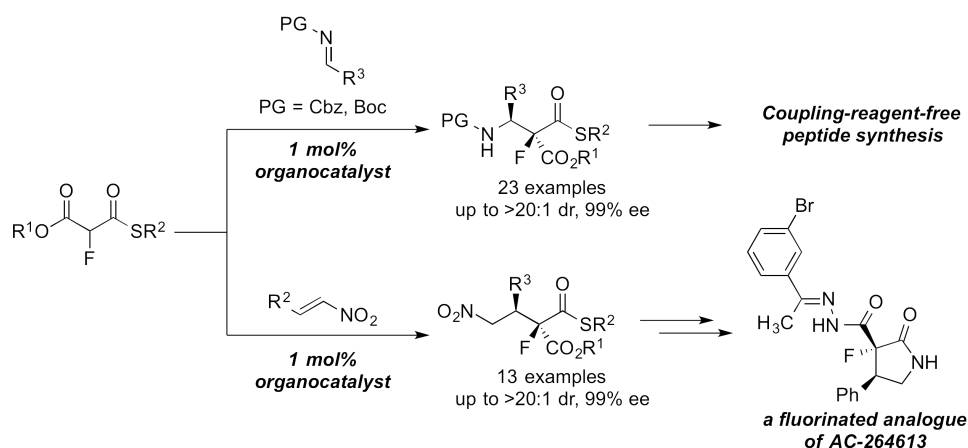


Stereoselective Organocatalyzed Synthesis of α -Fluoro β -Amino and α -Fluoro γ -Nitro Thioesters

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Fluorination and the incorporation of β -amino acids into peptides represent powerful strategies to enhance their proteolytic stability and to control their conformation.^[1] These features are combined in α -fluoro- β -amino acids, which influence the conformation of β -peptides.^[2] Recently, our group developed a stereoselective method to access fluorinated aldol products using fluorinated malonic acid half thioesters (F-MAHTs) as building blocks.^[3] Herein we present highly stereoselective organocatalyzed Mannich reactions between fluorinated monothiomalonates (F-MTMs) and N-Cbz and N-Boc protected imines as well as Michael reactions between F-MTMs and nitroolefins.^[4] These reactions require only 1 mol% of organocatalyst and provide access to the corresponding α -fluoro β -amino thioesters and α -fluoro γ -nitro thioesters, respectively. α -fluoro β -amino thioesters can be directly used for peptide synthesis in solution and on solid phase, whereas α -fluoro γ -nitro thioesters can be transformed into the corresponding fluorinated lactams, as showcased in the synthesis of a fluorinated analogue of AC-264613.^[5]



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