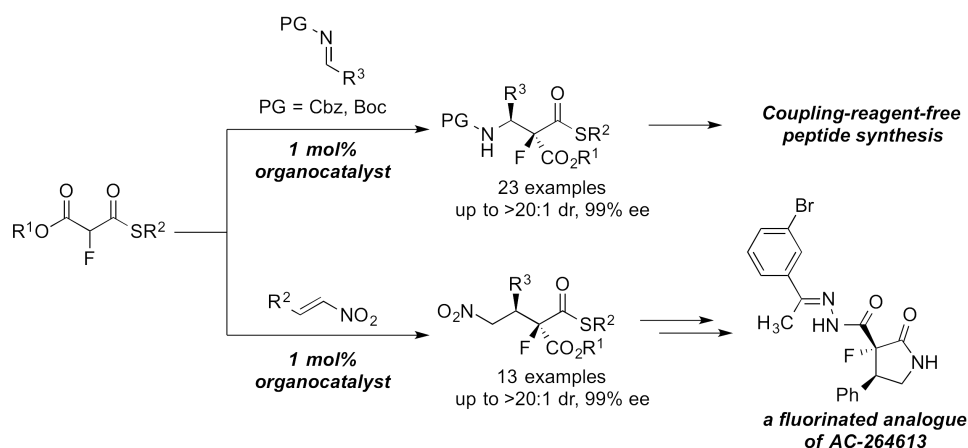


## Stereoselective Organocatalyzed Synthesis of $\alpha$ -Fluoro $\beta$ -Amino and $\alpha$ -Fluoro $\gamma$ -Nitro Thioesters

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Fluorination and the incorporation of  $\beta$ -amino acids into peptides represent powerful strategies to enhance their proteolytic stability and to control their conformation.<sup>[1]</sup> These features are combined in  $\alpha$ -fluoro- $\beta$ -amino acids, which influence the conformation of  $\beta$ -peptides.<sup>[2]</sup> Recently, our group developed a stereoselective method to access fluorinated aldol products using fluorinated malonic acid half thioesters (F-MAHTs) as building blocks.<sup>[3]</sup> 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.<sup>[4]</sup> These reactions require only 1 mol% of organocatalyst and provide access to the corresponding  $\alpha$ -fluoro  $\beta$ -amino thioesters and  $\alpha$ -fluoro  $\gamma$ -nitro thioesters, respectively.  $\alpha$ -fluoro  $\beta$ -amino thioesters can be directly used for peptide synthesis in solution and on solid phase, whereas  $\alpha$ -fluoro  $\gamma$ -nitro thioesters can be transformed into the corresponding fluorinated lactams, as showcased in the synthesis of a fluorinated analogue of AC-264613.<sup>[5]</sup>



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