FLUORINATED ACYL ANHYDRIDES IN SWITCHABLE DIVERGENT PHOTOREDOX CATALYSIS

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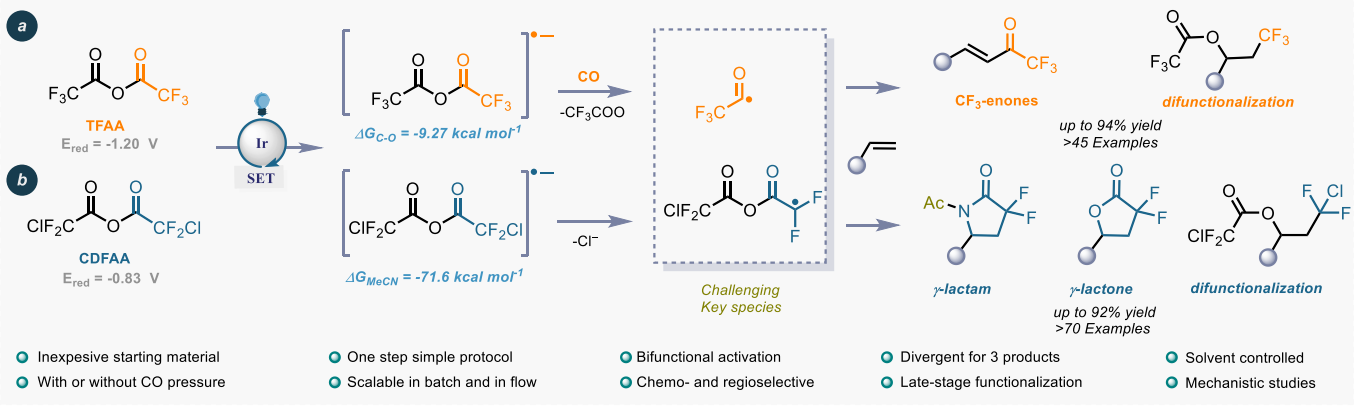
The outstanding impact of fluorine atom in drug discovery cannot be overestimated. Substantially, the incorporation of trifluoromethyl acyl (CF_3CO) and gem-difluoro (CF_2) moiety into the organic framework are highly sought due to the influence of these units on physicochemical and pharmacological properties of molecules. However, the introduction of these synthons requires the use of prefunctionalized starting materials or a surrogate at the beginning of the synthesis. To address this limitation, perfluorocarboxylic anhydrides can be selected as perfect precursors because they are abundant sources of fluorine building blocks and possess varied reactivity. Herein, we report a visible light-mediated photoredox activation of trifluoroacetic anhydride (TFAA) that occurs through a trifluoroacyl radical mechanism. Remarkably, this radical can be stabilized under a CO atmosphere, and in the presence of olefines, delivers the corresponding α,β-unsaturated trifluoromethyl ketone derivatives. This method can also be diversified into a trifluoromethylation protocol by simply changing the reaction parameters. Furthermore, we developed a mild and operationally simple strategy to access gem-difluoro compounds using chlorodifloroacetic anhydride (CDFAA) as a low-cost and readily available reagent. In this case photoredox activation selectively triggers pseudo-mesolytic cleavage of a C−Cl bond generating an α,α-difluorinated radical, that acts as an exceptional bifunctional intermediate in reaction with alkenes. The reactivity of this radical is further determined by the solvent effect, detailed mechanistic studies of which have shown to occur by three distinct pathways, delivering in a single chemical step α,α-difluoro-γ-lactams, γ-lactones, or difunctionalized compounds. These methodologies are flow and batch scalable, possess excellent chemo- and regioselectivity, as well as practical for late-stage diversification of biorelevant molecules.



[1] K. Zhang, Dr. D. Rombach, N. Y. Nötel, Prof. Dr. G. Jeschke. D. Katayev *Angew. Chem. Int. Ed.* **2021**, *60*, 22487 (*Highlighted in SYNFACTS,* **2021**).

[2] R. Giri, I. Mosiagin, I. Franzoni, N. Y. Nötel, S. Patra, D. Katayev *Manuscript in preparation* **2022**.