Bifunctional Activation of Feedstock Chemicals for Solvent-Controlled Switchable Synthesis

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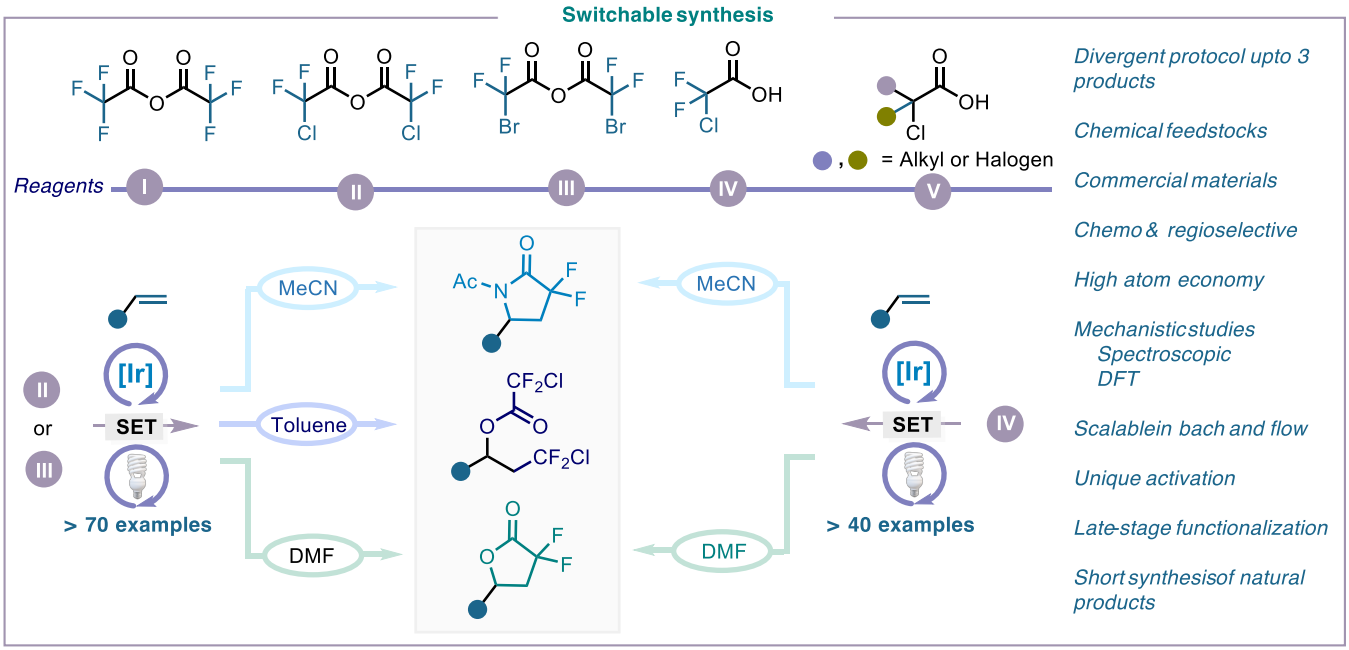
In the pharmaceutical industry, approximately 20-25% of drugs contain fluorine.[1] Synthetic chemists are currently engaged in active innovation to develop methods for the seamless integration of fluorine fragments into organic compounds. This branch of organofluorine chemistry is rapidly growing, focusing on generating fluorinated radicals from readily available functional group transfer reagents (FGTRs).[2] In this context, we found that fluorinated building blocks such as chlorodifloroacetic anhydride (CDFAA, II) as a promising precursor for bifunctional reagent and delivers a wide range of gem-difluorinated γ-lactams, γ-lactones, as well as promotes oxy-perfluoroalkylation under solvent-controlled reaction conditions.[3] Although most of anhydrides are prepared from the corresponding acids, developing a mild and operationally simple strategy to access gem-difluoro compounds using chlorodifloroacetic acid (CDFA, IV) can serve as beneficial entry for achieving step economic and practical synthesis of fluorinated cyclic scaffolds. These methodologies are flow and batch scalable, possess excellent chemo- and regioselectivity, and are useful for late-stage diversification of complex organic scaffolds as well as employed for concise synthesis of (±)-boivinianin A and epi-eupomatilone-6.[4]



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