In-catalyzed C-F bond transformation via oxymetalation/*β*-fluorine elimination to access fluorinated isocoumarins

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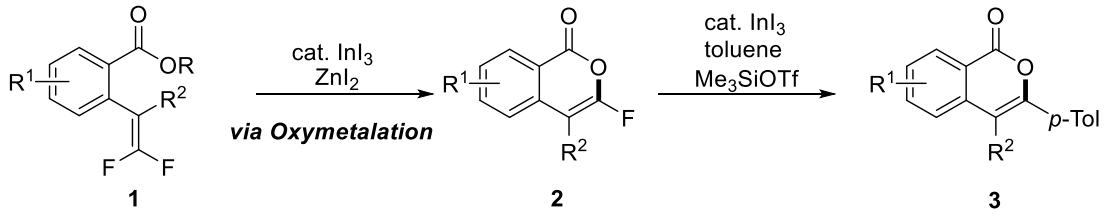
The introduction of fluorine group or fluorine-containing structural motifs into small molecules often brings about desirable properties in their bioactivity and provides unique chemical and physical properties. Fluorinated heterocycles have found widespread use in numerous bioactive compounds and drugs. Thus, the assembly of fluorinated heterocycles has been a topic of ongoing interest.[1] Despite the fact that isocoumarine derivatives are an important class of oxygen-containing heterocycles that possess a variety of biological properties, a synthetic strategy for fluorinated isocoumarins has not been established yet. Therefore, the exploration of new synthetic methods for the synthesis of fluorine-containing isocoumarin derivatives is highly desirable. Our group reported the intramolecular oxymetalation of alkynes using indium salts as a π-electrophilic Lewis acid.[2] Herein, we report indium-catalyzed C-F bond transformation of *β*,*β*-difluorostyrene derivatives bearing ester groups to give various fluorinated isocoumarins.

When difluorostyrene derivative **1** was treated with a catalytic amount of InI_3 and ZnI_2 under the optimized conditions, fluorinated isocoumarin **2** was efficiently obtained. This novel synthetic strategy allows access to a wide variety of fluorinated isocoumarins. DFT calculation clarified that the path through oxymetalation/*β*-fluorine elimination is adapted for C-F bond transformation of a *gem*-difluoroalkene moiety. Furthermore, by using toluene as a solvent in the presence of InI_3 and Me_3SiOTf, further transformation at the C-F bond of fluorinated isocoumarins **2** occurred to give aryl isocoumarin derivatives **3**.



1 **2** **3**

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