Acid-Mediated C–F/C–H Coupling of Fluorobenzofurans with Arenes

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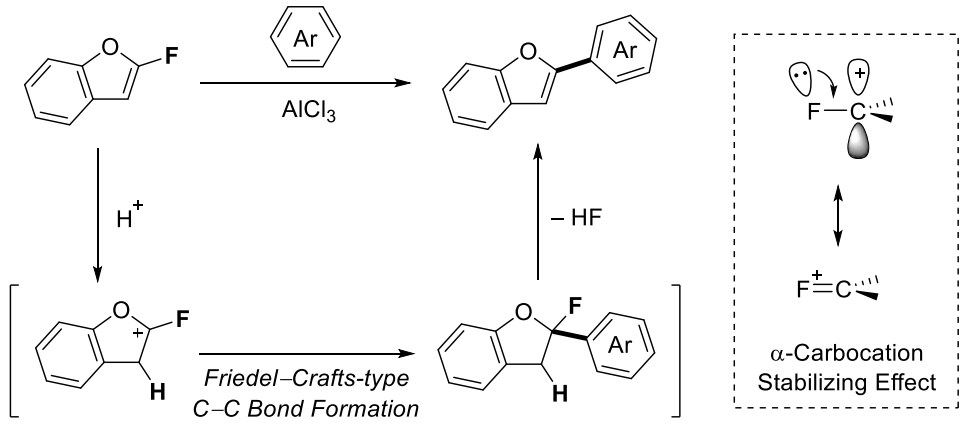
Although transition-metal-catalyzed intermolecular cross-coupling is one of the most notable achievements in the past half century, metal-free cross-coupling has been attracting much attention over the last decade. For example, aryl iodides and bromides undergo cross-coupling with arenes under appropriate conditions via the corresponding aryl radicals. In contrast, such a cross-coupling of aryl fluorides has been difficult so far. However, we have developed acid-mediated intramolecular cross-coupling of aryl fluorides via aromatic C–F bond activation, which is promoted by the α-carbocation stabilizing effect of a fluorine substituent. Herein, we report acid-mediated intermolecular C–F/C–H cross-coupling of 2-fluorobenzofurans with arenes, leading to the synthesis of 2-arylbenzofurans.

In the presence of $AlCl_3$, defluorinative cross-coupling of 2-fluorobenzofurans, readily prepared via 5-*endo-trig* cyclization of β,β-difluoro-*o*-hydroxystyrenes,[1] effectively proceeded with arenes to afford 2-arylbenzofurans. In this reaction, fluorine-stabilized cationic intermediates underwent Friedel–Crafts-type C–C bond formation with arenes, followed by HF elimination. 2-Fluorobenzofurans bearing a wide variety of substituents and several electron-rich arenes were applicable to the cross-coupling. Furthermore, we succeeded in a short-step synthesis of bioactive arylbenzofurans by using this protocol starting from readily available β,β-difluoro-*o*-hydroxystyrenes.



1) Morioka, R.; Fujita, T.; Ichikawa, J. *Helv. Chim. Acta* **2020**, *103*, e2000159.