Medicines, Organic electronic materials, Synthetic resins

Functionalization of perfluoroalkyl compounds by photocatalyst/organostannanes mediated C–F bond activation

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Abstract

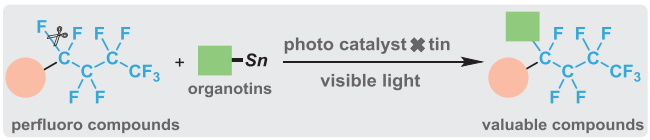
C–F bonds are extremely strong; hence, the transformation of them under mild conditions is difficult, and the selective activation of a specific C–F bond from among multiple C–F bonds in perfluorinated compounds has not been achieved. In this study, the world's first organic reaction that selectively converts a specific carbon–fluorine (C–F) bond in perfluorinated compounds to other functional groups. Experimental and theoretical results revealed the importance of the cooperation of a photocatalyst and organotin compounds in this transformation. Organofluorine compounds are attracting attention as pharmaceuticals, and this research is expected to lead to the rapid synthesis of fluorine-containing drugs from readily available perfluorinated compounds.

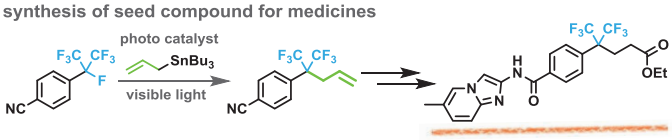
Background & Results

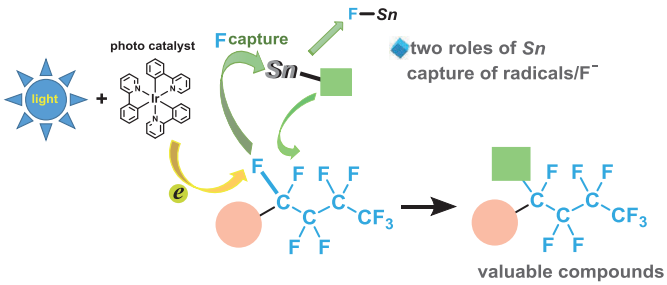
Fluorinated compounds are widely used in pharmaceuticals, agricultural chemicals, functional resins, and organic electronic materials. In particular, perfluorinated compounds are attracting attention because of their high thermal and chemical stability and various excellent properties such as water and oil repellency and chemical resistance. Since the carbon-fluorine bond is one of the strongest of chemical bonds, its activation is a challenging issue in organic chemistry and is being studied worldwide. In this research, the site-selective C–F bond transformation to carbon-functional groups has been accomplished by using a photocatalyst and organotin compounds under visible light irradiation. The establishment of the methodology to activate strong carbon-fluorine bonds under such mild conditions is the key to achieving the selective transformation of perfluorinated compounds. Both experimental and theoretical experiments revealed that the cooperative action of the photocatalyst and organotin compound are important in the progression of the reaction. In particular, it is noteworthy that the organotin compound plays the dual role of capturing unstable radical intermediates and scavenging fluorine as a Lewis acid, which is a very significant finding for future research on carbon-fluorine bond conversion reactions. Furthermore, we have succeeded in synthesizing fluorine-substituted analogues of a compound that show promise for pharmaceutical applications.

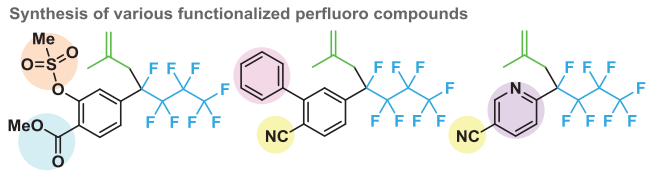
Significance of the research and Future perspective

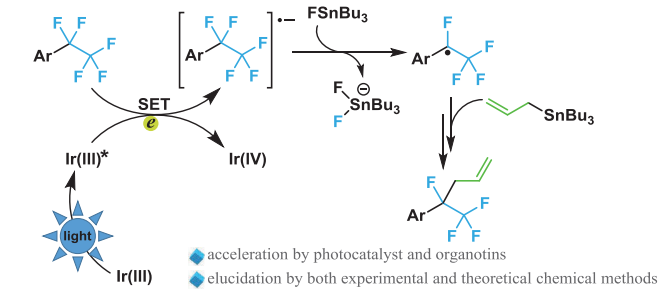
Fluorine is a significant element in pharmaceuticals because many small-molecule drugs contain fluorine atoms. It is expected that the field of fluorine-containing drugs will continue to grow. As a result of this research, high valuable perfluorinated compounds, which were impossible to synthesize in the past, can now be synthesized in a simple and short process, which is expected to lead to the expansion of the library of seed compounds for fluorine-containing drug discovery.











Patent

Treatise Sugihara, Naoki; Nishimoto, Yoshihiro; Yasuda, Makoto et al. Photoredox-Catalyzed C–F Bond Allylation of Perfluoroalkylarenes at the Benzylic Position. Journal of the American Chemical Society. 2021; 143(25): 9308-9313. doi: 10.1021/jacs.1c03760

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Keyword photocatalyst, stannane, fluorine compound, C–F bond activation