Direct C–H Trifluoromethoxylation of Arenes Triggered by a Visible-Light-Mediated Redox Fragmentation of Pyridinium Reagents

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The incorporation of fluorine and fluorine-containing groups into organic frameworks is widely recognized as a key strategy for tailoring bioactivities in pharmaceuticals and agrochemicals. Owing to its lipophilic and conformational properties, the trifluoromethoxy (OCF_3) moiety has attracted growing attention by the synthetic and industrial community. However, access to trifluoromethyl aryl ethers has remained a major unsolved problem with classical approaches relying on harsh reaction conditions. Furthermore, development of a general trifluoromethoxylation method has been hampered by the inherent instability and poor nucleophilicity of the OCF_3 anion. In contrast to anionic-based approaches, the present work investigates the generation and reactivity of the largely unexplored trifluoromethoxy radical. Herein, we report a new bench-stable pyridinium reagent capable of undergoing N–O bond homolysis under photoredox conditions, thus providing access to late-stage diversification. A variety of arenes including a selection of biologically active compounds can undergo unselective C–H functionalization to afford trifluoromethyl aryl ethers as mixtures of regioisomers. Preliminary EPR and DFT studies support the involvement of a trifluoromethoxy radical but also reveal the presence of a pyridinium radical cation as a minor fragmentation pathway.