New Compounds Departing Trifluoromethoxylation Station

Significance: The strongly electron-withdrawing trifluoromethoxy group (OCF$_3$) has attracted increasing attention as a unique substituent in biologically active compounds and organic materials; however, synthetic methods for installing OCF$_3$ directly remain rare, due in part to the fact that many of the available sources of or precursors to the trifluoromethoxide anion (−OCF$_3$) show limited stability or require specialized equipment for handling. Herein, the authors demonstrate the use of trifluoromethyl benzoate (TFBz) as a stable, liquid reagent for various direct trifluoromethoxylation reactions, acting as a precursor to −OCF$_3$, which is generated in situ by treatment of TFBz with a fluoride salt.

Comment: The use of TFBz was showcased in the trifluoromethoxylation-bromination of arynes. Crown ether 1 and KF were the best combination to generate both the aryne intermediate and −OCF$_3$ in situ, while several reagents could be employed as “Br$^+$” sources to afford the trifluoromethoxylation-bromination products 2. These conditions were successfully adapted to aryne trifluoromethoxylation-chlorination and trifluoromethoxylation-iodination (products 3 and 4, respectively). Various reactions using TFBz were also surveyed, including the synthesis of alkyl trifluoromethoxides 5 from the corresponding alkyl halides or pseudo-halides. Finally, other perfluoroalkyl benzoate esters 6 were synthesized from the requisite perfluorinated carbonyl compounds and shown to undergo analogous reactivity to TFBz.