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$Mn(OAc)_3$-Mediated Addition Reactions of $NaSO_2CF_3$ and Perhalogenated Carboxylic Acids with Unactivated Alkenes Conjectured by a Single Electron Transfer and Halogen Abstraction Mechanism

Hui Sun, Guannan Cui, Huijian Shang, and Bin Cui*

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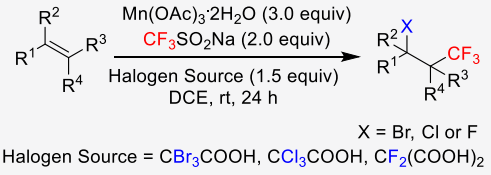
ABSTRACT: A free-radical halotrifluoromethylation of olefins by using $Mn(OAc)_3{\cdot}2H_2O$, CF_3SO_2Na, and perhalogenated carboxylic acids has been achieved. Perhalogenated carboxylic acids act as a halogen source and CF_3SO_2Na acts as a CF_3 source. The reaction displayed good tolerance of functional groups in the substrates under mild conditions. The radical clock experiment and TEMPO inhibition experiment support a radical process. The halogen reagent competition experiment shows that the last step of halogenation process is mainly through a halogen abstraction mechanism.



INTRODUCTION

The importance of trifluoromethyl group provides an increasing driving force for development of efficient and mild strategy for direct installation of trifluoromethyl group into organic molecules. The introduction of trifluoromethyl groups with strong electron-withdrawing and hydrophobic properties can significantly improve the bioavailability, lipophilicity, metabolic stability, and binding selectivity of organic compounds.[1] In recent years, regarding the development of new drugs containing trifluoromethyl groups, the trifluoromethyl structural fragments of new drugs have gradually changed from a $C(sp^2)-CF_3$ bond to $C(sp^3)-CF_3$ bond. A growing number of approved new drugs or investigated new drugs in clinical trial contained the $C(sp^3)-CF_3$ bond, such as Elexacaftor,[2] Alpelisib,[3] Agerafenib[4] and VX-659[5] (Scheme 1). However, the structural fragments containing the $C(sp^3)-CF_3$ bond in new drugs are poor. So, new synthesis methods of $C(sp^3)-CF_3$ bond can better guarantee the development of new drugs.

Among the variety of synthetic methods developed, halotrifluoromethylation of alkenes has been proven to be one of the most effective accesses to the incorporation of $C(sp^3)-CF_3$ bond.[6] Halogen groups can undergo a variety of chemical transformations, greatly enriching the drug structures containing the $C(sp^3)-CF_3$ bond.[7] In the field of halotrifluoromethylation reaction, Haszeldine reported on iodotrifluoromethylation of alkenes in 1949. The reaction was carried out with CF_3I as a trifluoromethyl source and iodide source, which was relatively corrosive and difficult to handle (gas).[8] In 1989, Kamigata and co-workers reported on chlorotrifluoromethylation of alkenes using $ClSO_2CF_3$ as a trifluoromethyl source and chlorine source in the presence of $RuCl_2(PPh_3)_3$ catalyst.[9] Comparable with CF_3I, $ClSO_2CF_3$ has the advantages of high reactivity and easy operation, although it could be problematic on a bigger scale (bp: 29−32 °C).[10] Subsequently, a few halotrifluoromethylation methologies were proposed, among which trifluoromethyl reagents and halogenated reagents used include $NaSO_2CF_3$[11] and I_2O_5[12]/$NaBrO_3$[7,13]/NCP(*N*-halophthalimide)[14]/$MgCl_2$,[10,15] Togni's reagent and KI[16]/LiCl[16b]/SOX_2,[17] Umemoto's reagent and CuX[18]/CsX[19]/TMSCl,[19] PPFR,[20] $TMSCF_3$ and selectfluor,[21] etc. Generally, the mechanism of these reactions was that the trifluoromethyl reagent releases a CF_3 radical through an oxidation−reduction process, the CF_3 radical adds to an alkene, and the carbon radical intermediate is formed. The carbon radical intermediate is followed by halo anion nucleophilic attack or halogen abstraction process to give the final product (Scheme 2). Although the mechanisms of trifluoromethylation of olefins are relatively thorough, using one type of method that can achieve hydrotrifluoromethylation, fluorotrifluoromethylation, chlorotrifluoromethylation, and bromotrifluoromethylation just by changing halogenated reagents is rarely reported and a great challenge. On the one hand, halogenated reagents have the limitation of synthesis and activity, such as CF_3SO_2X reagents that are mainly used in the chlorotrifluoromethylation reaction with CF_3SO_2Cl, but fluorotrifluoromethylation with CF_3SO_2F and hydrotrifluoromethylation reaction with CF_3SO_2H cannot

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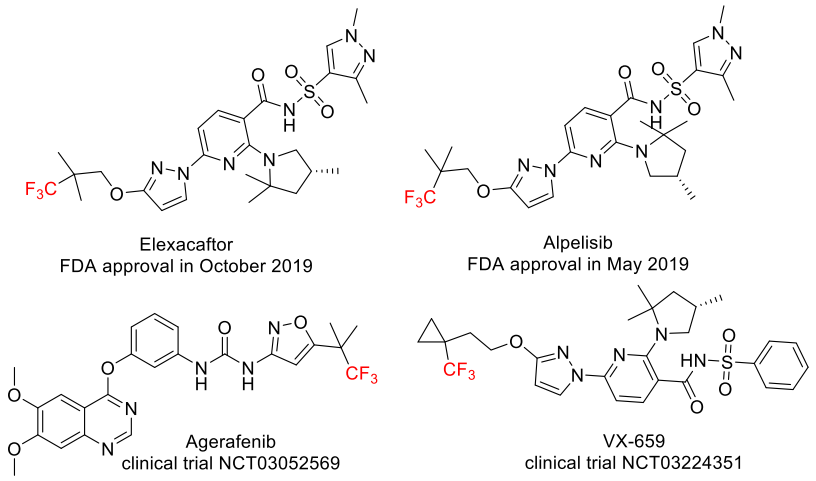
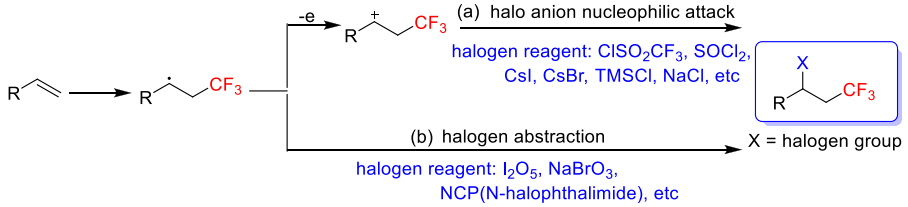
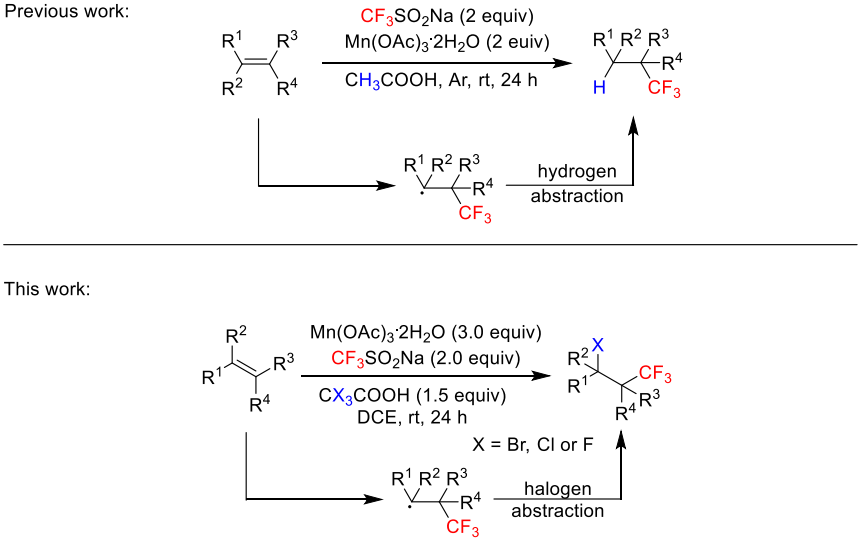
Scheme 1. Approved or Investigated New Drugs Containing the $C(sp^3)-CF_3$ bond



Scheme 2. Mechanism of Halogenation Reactions



Scheme 3. $Mn(OAc)_3{\cdot}2H_2O$-Mediated Trifluoromethylation of Alkenes



be achieved. On the other hand, the Gibbs free energy of bifunctional trifluoromethylation reaction processes is very different, especially the fluorotrifluoromethylation reaction and hydrotrifluoromethylation reaction (DFT calculation is explained in detail later). In a word, using one kind of simple and easy-to-obtain reagent that can realize hydrotrifluoromethylation, fluorotrifluoromethylation, chlorotrifluoromethylation, and bromotrifluoromethylation under similar reaction conditions is a great challenge.

Recently, we have shown that $Mn(OAc)_3$-mediated hydrotrifluoromethylation of alkenes using CF_3SO_2Na as the trifluoromethylating agent and the α-H proton of CH_3COO^- as the H source according to hydrogen abstraction to achieve the last step of hydrogenation process (Scheme 3).[22] We anticipated that the hydrogen abstraction process in the final product was driven by the oxidation of CH_3COOH using $Mn(OAc)_3{\cdot}2H_2O$, and the halotrifluoromethylation reaction may be realized by halogen abstraction if CH_3COOH was used instead of CF_3COOH, CCl_3COOH, or CBr_3COOH. Due to the stable properties and easy availability of perhalogenated carboxylic acid, it has certain advantages in the synthesis of compounds containing trifluoromethyl (Scheme 3). Moreover, this is the first article to use perhalogenated reagents as halogenated reagents to achieve halogenated trifluoromethylation through the halogen abstraction mechanism. We herein report a $Mn(OAc)_3{\cdot}2H_2O$-mediated halotrifluoromethylation

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of alkenes by halogen abstraction to achieve the last step of halogenation process as a continuation of our program on $Mn(OAc)_3$-mediated trifluoromethylation reactions.

To test this assumption, DFT calculations were carried out to study the energy of C−X bond breaking in CX_3COOH and Gibbs free energy of **1d**$^{\bullet}$ to transition states in Table 1 and Scheme 4. Previous work on the hydrotrifluoromethylation reaction indicated that the last step of hydrogenation process requires the participation of $Mn(OAc)_3$.[22] Calculation results indicated that the energies of C−X bond breaking in CCl_3COOH and CBr_3COOH were 61.4 and 45.8 kcal/mol, respectively, which were both lower than that in CH_3COOH. Therefore, we speculated that CCl_3COOH and CBr_3COOH could be used as halogen reagents to achieve the last step of halogenation process on $Mn(OAc)_3$-mediated halotrifluoromethylation reactions. (Table 1, entries 1 vs 3−4). The energy needed to break the C−F bond from CF_3COOH was higher than that needed to break the C−H bond from CH_3COOH, which showed that it was difficult to achieve the fluorotrifluoromethylation reaction according to this method (Table 1, entries 1 vs 2). As illustrated in Scheme 4, α-C−H bond abstraction of CH_3COOH with **1d**$^{\bullet}$ via the transition state **TS-H** required to overcome barriers of 22.4 kcal/mol to afford the desired product, which could be achieved with $Mn(OAc)_3\cdot 2H_2O$ under mild conditions (previous work, Scheme 4a).[22] Chlorotrifluoromethylation and bromotrifluoromethylation via **TS-Cl** ($\Delta G^{\ddagger}$ = 18.3 kcal/mol, **1d**$^{\bullet}$ → **TS-Cl**) and **TS-Br** ($\Delta G^{\ddagger}$ = 15.0 kcal/mol, **1d**$^{\bullet}$ → **TS-Br**) were more favorable than hydrotrifluoromethylation via **TS-H** ($\Delta G^{\ddagger}$ = 22.4 kcal/mol, **1d**$^{\bullet}$ → **TS-H**), leading to chlorotrifluoromethylated products and bromotrifluoromethylated products being much easier to achieve than hydrotrifluoromethylated products (Scheme 4b,c). Subsequently, a path through α-C−F bond abstraction of CF_3COOH with **1d**$^{\bullet}$ via **TS-F** required to surpass a barrier of 50.1 kcal/mol (**1d**$^{\bullet}$ → **TS-F**), which was 27.7 kcal/mol higher than **1d**$^{\bullet}$ through **TS-H** (Scheme 4d). So, the fluorotrifluoromethylation reaction with CF_3COOH was much more difficult to achieve than the hydrotrifluoromethylation reaction with CH_3COOH. In order to reduce the energy of the transition state of fluorotrifluoromethylation reaction, we calculated a series of compounds similar in structure to CF_3COOH and found that $CF_2(COOH)_2$ instead of CF_3COOH provided a considerably low energy, which was more promising to realize the reaction (Table 1, entries 2 vs 5; Scheme 4e). Based on the results of DFT calculations, we plan to use $CF_2(COOH)_2$, CCl_3COOH, and CBr_3COOH as halogen sources to realize the halotrifluoromethylation reaction involving $Mn(OAc)_3\cdot 2H_2O$.

Table 1. Energy Needed to Break the α-C−X Bond of CH_3COOH/Halogenated Carboxylic Acids

entry	reaction	energy (kcal/mol)
1	C−H bond breaking in CH_3COOH	97.4
2	C−F bond breaking in CF_3COOH	116.0
3	C−Cl bond breaking in CCl_3COOH	61.4
4	C−Br bond breaking in CBr_3COOH	45.8
5	C−F bond breaking in $CF_2(COOH)_2$	101.0

RESULTS AND DISCUSSION

On the basis of DFT calculation results and our understanding of Mn-mediated reactions, bromotrifluoromethylation of olefin substrate **1a** was carried out with CBr_3COOH as a Br source. To our delight, 87% of **1a** was converted to the desired **2a** under the standard conditions (Table 2, entry 1). Studies subsequently showed that DCE was better than other solvents such as MeOH, DMF, MeCN, acetone, or THF (Table 2, entries 1 vs 2−6). Reducing $Mn(OAc)_3\cdot 2H_2O$ from 3.0 equiv to 1.5 equiv resulted in a decrease in reaction conversions (Table 2, entries 1, 7−9). The bromotrifluoromethylation reactions with other bromide agents such as NaBr and KBr afforded poor yields (Table 2, entries 10 and 11), but the substrate **1a** with TMSBr under the standard reaction conditions was converted to **2a** in 78% yield. Later, comparing with Ar conditions, air conditions had little effect on the reaction when CBr_3COOH was used as a bromide reagent. However, a side reaction occurred under TMSBr with air conditions (Table 2, entry 14). Two major products were identified after careful analysis of the reaction mixtures: one was the desired bromotrifluoromethylation product **2a**, and the other was the dibromide product formed possibly via oxygen oxidation of Br anion. Therefore, the optimized conditions of bromotrifluoromethylation reaction was carried out in the presence of 3.0 equiv of $Mn(OAc)_3\cdot 2H_2O$, 2.0 equiv of

Scheme 4. Hydrogen/Halogen Abstraction of 1d$^{\bullet}$ with CH_3COOH/Halogenated Carboxylic Acids in Dichloroethane

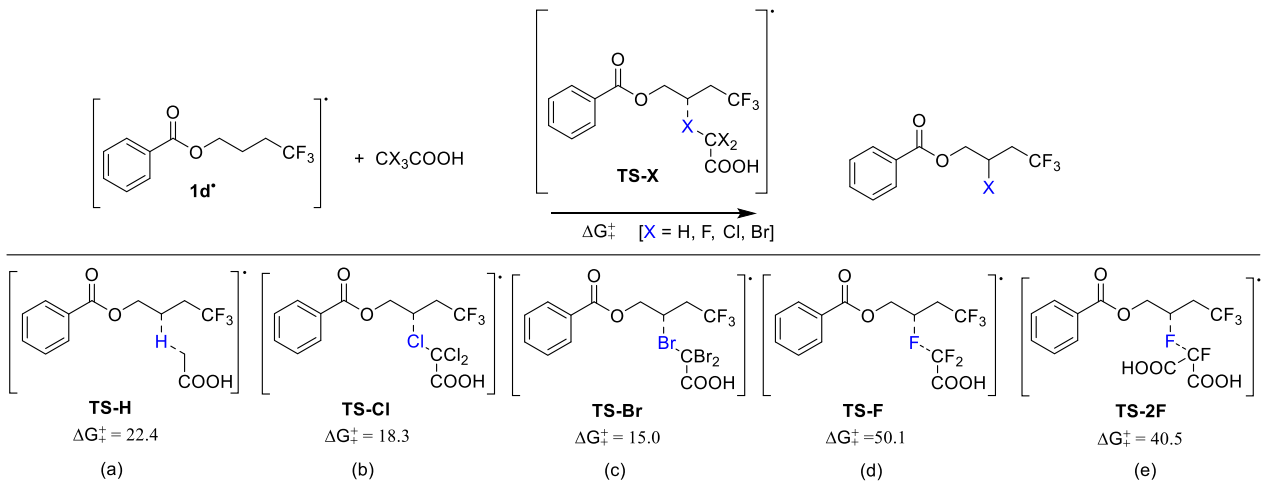

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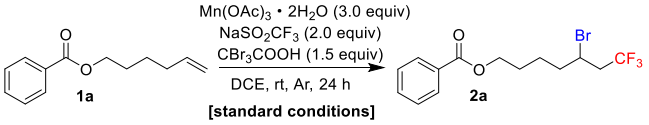
Table 2. Optimization of Reaction Conditions[a]



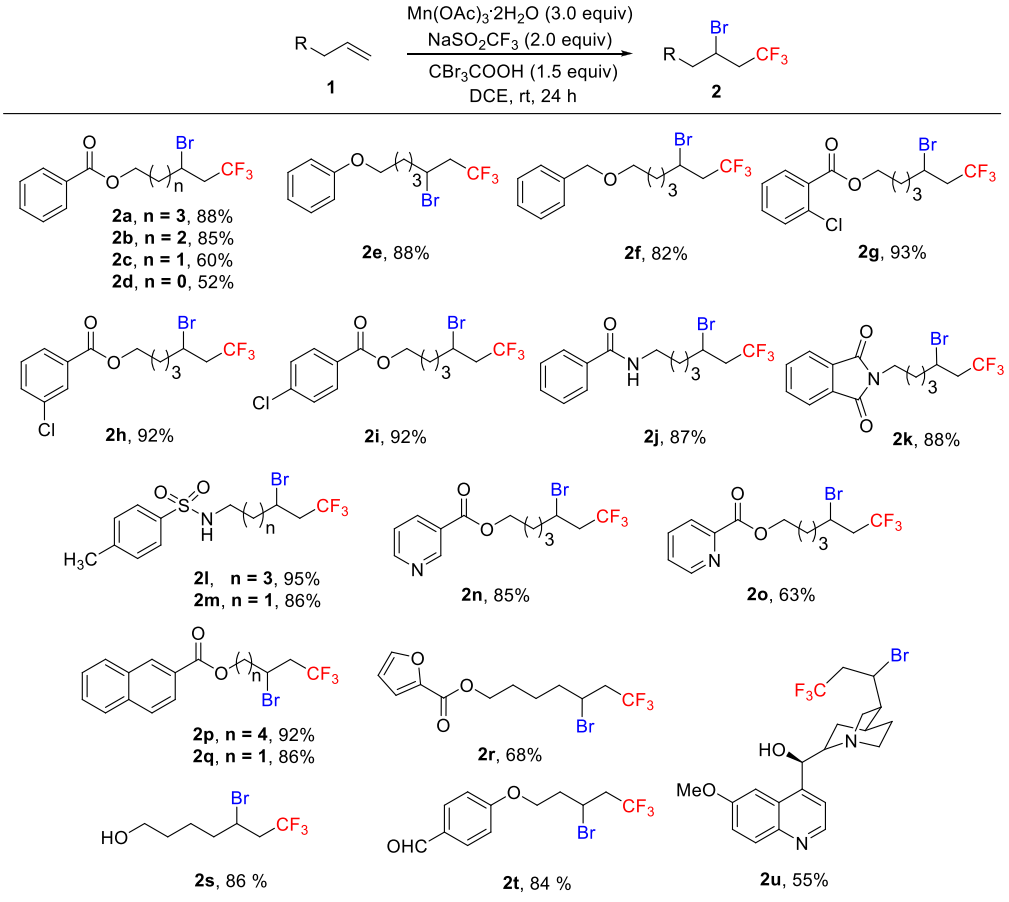
entry	deviation from standard conditions	yield(%)[b]
1		87
2	MeOH instead of DCE	81
3	DMF instead of DCE	50
4	MeCN instead of DCE	82
5	acetone instead of DCE	trace
6	THF instead of DCE	35
7	$Mn(OAc)_3{\cdot}2H_2O$ (2.5 equiv)	71
8	$Mn(OAc)_3{\cdot}2H_2O$ (2.0 equiv)	66
9	$Mn(OAc)_3{\cdot}2H_2O$ (1.5 equiv)	50
10	NaBr instead of CBr_3COOH	trace
11	KBr instead of CBr_3COOH	trace
12	TMSBr instead of CBr_3COOH	78
13	without argon protection	88
14	TMSBr instead of CBr_3COOH, without argon protection	30

[a]Reactions conditions: **1a** (0.50 mmol), $Mn(OAc)_3{\cdot}2H_2O$ (1.5 mmol), CBr_3COOH (0.75 mmol), CF_3SO_2Na (1.0 mmol), DCE (6 mL), room temperature, argon protection, 24 h; see table for deviations. [b]Isolated yields.

CF_3SO_2Na, 1.5 equiv of CBr_3COOH, and DCE (6 mL) for 24 h under an air atmosphere.

With the optimized reaction conditions established, we explored the substrate scope of the reaction by using various unactivated terminal monosubstituted alkenes **1a**−**1u**, and the results are summarized in Scheme 5. A wide range of substrates and functional groups were tolerated, including esters, amides, protected and unprotected alcohols, protected amines, halogen atoms, sulfonamides, alkyl groups, (hetero)arenes, and aldehydes. We found that the carbon chain length of terminal monosubstituted alkenes had little influence on the reaction process (Scheme 5; **2a**−**2d**, **2l**−**2m**, and **2p**−**2q**). In a similar vein, electronic properties on aromatic rings of the substituents also had little impact on the bromotrifluoromethylation reactions (Scheme 5; **2a**, **2i**, **2l**, and **2t**). The chlorine substituent at the *ortho* (**1g**), *meta* (**1h**), and *para* (**1i**) position of benzene rings did not affect this transformation significantly and the corresponding products (**2g**−**2i**) were obtained in excellent yields. We then tested substrate **1s** with unprotected hydroxyl group without aryl group. Interestingly, bromotrifluoromethylation was not affected and obtained the corresponding product **2s** in 86% yield under the optimized conditions. The reaction of **1t** containing an aldehyde group proceeded smoothly to afford **2t** in 84% yield. It was glad to find that quinine **1u** could be bromotrifluoromethylated under our optimized conditions with 55% isolated yield (**2u**). To prove the scalability of the current protocol, substrate **1a** was

Scheme 5. Unactivated Terminal Monosubstituted Alkenes Participated in the Bromotrifluoromethylation[a]



[a]Reactions conditions: **1** (0.50 mmol), $Mn(OAc)_3{\cdot}2H_2O$ (1.5 mmol), CF_3SO_2Na (1.0 mmol), CBr_3COOH (0.75 mmol), DCE (6 mL), room temperature, 24 h, isolated yields.

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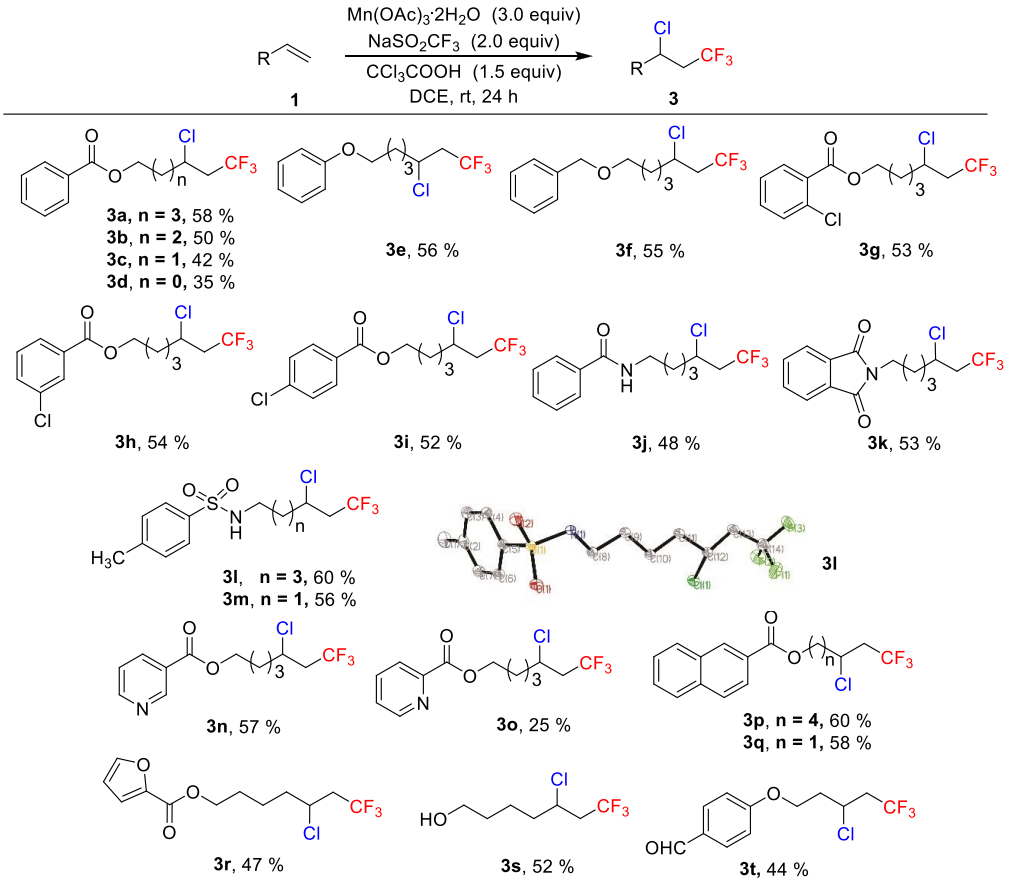
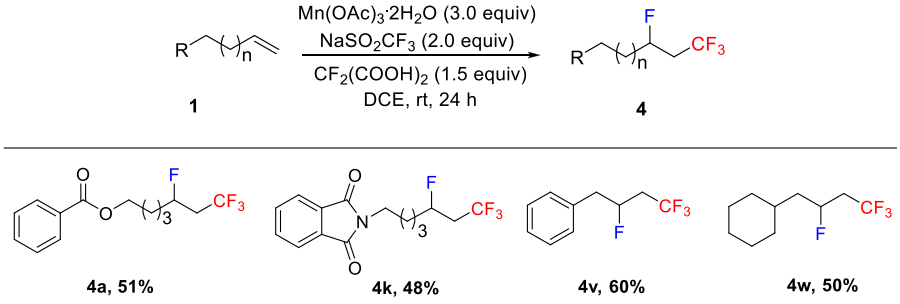
Scheme 6. Unactivated Terminal Monosubstituted Alkenes Participated in the Chlorotrifluoromethylation[a]



[a]Reactions conditions: **1** (0.50 mmol), $Mn(OAc)_3{\cdot}2H_2O$ (1.5 mmol), CF_3SO_2Na (1.0 mmol), CCl_3COOH (0.75 mmol), DCE (6 mL), room temperature, 24 h, isolated yields.

Scheme 7. Unactivated Terminal Monosubstituted Alkenes Participated in the Fluorotrifluoromethylation[a]



[a]Reactions conditions: **1** (0.50 mmol), $Mn(OAc)_3{\cdot}2H_2O$ (1.5 mmol), CF_3SO_2Na (1.0 mmol), $CF_2(COOH)_2$ (0.75 mmol), DCE (6 mL), room temperature, 24 h, isolated yields.

converted to **2a** on a gram scale under the optimized reaction conditions in 76% isolated yield.

After bromotrifluoromethylation of terminal mono-substituted alkenes, chlorotrifluoromethylation was also submitted to the reaction with CCl_3COOH instead of CBr_3COOH. The substrates **1** with CCl_3COOH under the standard reaction conditions were converted to the desired trifluoromethylation products in moderate isolated yields (Scheme 6). According to the DFT calculation results, the breaking energy of C−Cl bond was greater than that of C−Br bond(61.4 kcal/mol vs 45.8 kcal/mol) and the Gibbs free energy of chlorotrifluoromethylation via **TS-Cl** ($\Delta G+$ + = 18.3 kcal/mol, **1d**$^{\cdot}$ → **TS-Cl**) was higher than Gibbs free energy of bromotrifluoromethylation via **TS-Br** ($\Delta G+$ + = 15.0 kcal/mol, **1d**$^{\cdot}$ → **TS-Br**). Therefore, the yield of chlorotrifluoromethylation was lower than that of bromotrifluoromethylation. Compound **3l** was subjected to X-ray diffraction experiments to determine the skeleton of the product. The ORTEP drawing clearly confirmed the trifluoromethylation structure.[23]

Fluorotrifluoromethylation of monosubstituted unactivated alkenes **1** was generally carried out with $CF_2(COOH)_2$ under standard reaction conditions, and the reaction results are summarized in Scheme 7. Ester, amide, allylbenzene, and aliphatic alkene proceeded smoothly to afford the desired products, and 48%−60% isolated yields were obtained.

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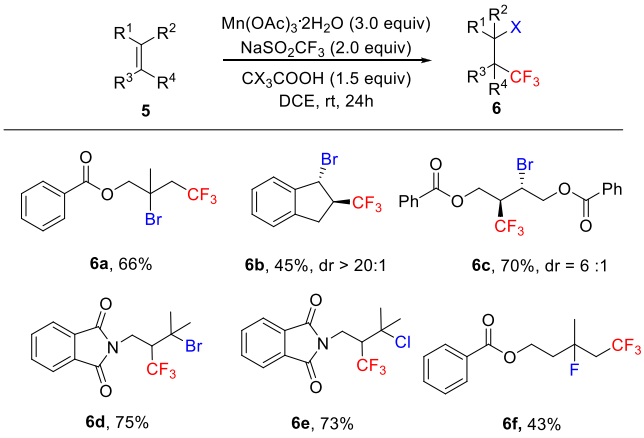
Once we had demonstrated the halotrifluoromethylation of monosubstituted unactivated alkenes, we next investigated the substrate scope of di- and tri-substituted unactivated alkenes and the results are summarized in Scheme 8. We found that

Scheme 8. Halotrifluoromethylation of Di- and Tri-substituted Unactivated Alkenes[a]



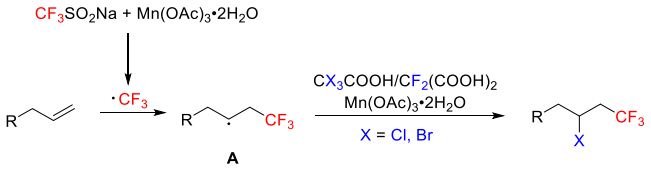
[a]Reactions conditions: **5** (0.50 mmol), $Mn(OAc)_3{\cdot}2H_2O$ (1.5 mmol), CF_3SO_2Na (1.0 mmol), $CX_3COOH/CF_2(COOH)_2$ (0.75 mmol), DCE (6 mL), room temperature, 24 h, isolated yields.

gem-disubstituted alkenes (**5a** and **5f**) could be reacted by our method and the corresponding products were isolated in acceptable yield (66% for **6a** and 43% for **6f**). 1,2-Disubstituted acyclic and cyclic internal alkenes were subjected to the reaction, and bromotrifluoromethylation products were obtained in good yields (45% for **6b** and 70% for **6c**). Similar to mono- and di-substituted alkenes, 1,2,2-trisubstituted alkenes were well tolerated under our optimized conditions, and the corresponding products were obtained (75% for **6d** and 73% for **6e**).

We initially hypothesized that the mechanism of halotrifluoromethylation reaction was similar to the mechanism of hydrotrifluoromethylation with $Mn(OAc)_3{\cdot}2H_2O$. The halotrifluoromethylation reaction proceeded by a pathway involving an *in situ* generated CF_3 radical species with subsequent radical addition and halogen abstraction to eventually afford the desired halotrifluoromethylation product. To figure out whether the CF_3 radical intermediate was involved in the reaction, the inhibition experiment of olefin **1a** was conducted with the addition of TEMPO (6.0 equiv). The capture product of CF_3 radical was detected by ^{19}F NMR (Scheme 9a). Furthermore, a radical clock reaction of substrate **7** was carried out under the standard reaction conditions and the product **8** was obtained in 73% yield (Scheme 9b).[15a] The radical clock experiment suggest that the involvement of an alkyl radical species was possible under the current reaction conditions. In order to prove that the halogenate reaction was through the halogen abstraction process, rather than the nucleophilic substitution reaction, we added $NaCl/CBr_3COOH$ and $NaBr/CCl_3COOH$ to the standard reaction condition separately and found that the halogenated reagent of the reaction was mainly perhalogenated carboxylic acids rather than sodium salts. The result indicates that the halotrifluoromethylated reaction was mainly realized through the process of halogen abstraction (Scheme 9c,d). Moreover, Snider reported that $Mn(OAc)_3$ will not oxidize isolated secondary radicals to cations.[24]

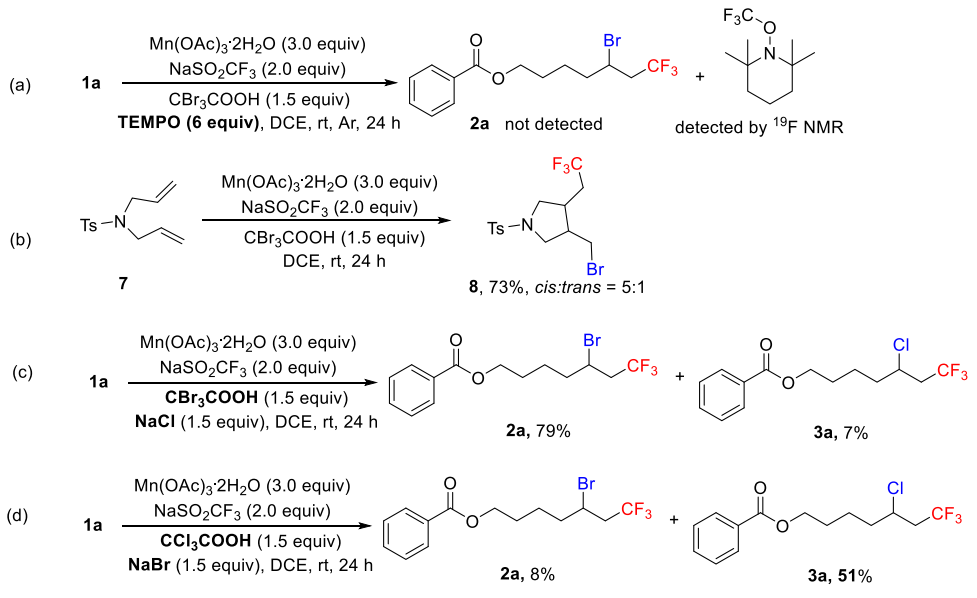
The proposed mechanism for the $Mn(OAc)_3{\cdot}2H_2O$-promoted halotrifluoromethylation of alkenes was proposed in Scheme 10. $Mn(OAc)_3{\cdot}2H_2O$ oxidized CF_3SO_2Na to

Scheme 10. Proposed Mechanism



generate the CF_3 radical through the single-electron transfer mechanism. The C=C double bond of the substrate was added by the CF_3 radical to form radical species **A**. Ultimately,

Scheme 9. Mechanistic Experiments



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radical species **A** undergo halogen abstraction from perhalogenated carboxylic acids (CBr_3COOH, CCl_3COOH, and $CF_2(COOH)_2$) to obtain the corresponding halotrifluoromethylation product.

CONCLUSIONS

In summary, on the basis of hydrotrifluoromethylation reaction with $Mn(OAc)_3{\cdot}2H_2O$, a $Mn(OAc)_3$-mediated free-radical halotrifluoromethylation of unactivated alkenes was developed by using CF_3SO_2Na and perhalogenated carboxylic acids. The mild reaction conditions allowed to effectively obtain difunctional halotrifluoromethylation products bearing a wide range of functional groups. TEMPO trapping experiments, radical clock experiments, and competition experiments revealed the reaction mechanism. Further studies on synthetic application of the reaction and a better understanding of $Mn(OAc)_3$-mediated oxidative radical reactions are ongoing.

EXPERIMENTAL SECTION

General Experimental Information. This halotrifluoromethylation reactions were performed at room temperature (25 °C). Reagents were purchased and used without further purification. ^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker DRX 500 spectrometer and a Bruker DRX 400 spectrometer at 298 K using deuterated chloroform as a solvent and TMS as an internal reference. Reactions were monitored by thin-layer chromatography (TLC) on silica gel plates (GF 254) using a mixture of iodine and silica gel as the visualizing agent, unless otherwise noted. Flash column chromatography was performed using a silica gel (200−400 meshes). Infrared (IR) spectra were recorded with a KBr pellet, and wavenumbers are given in cm^{-1}. HRMS analyses were carried out with Varian FTICR-MS 7.0T. Melting points were obtained on a Mettler Toledo MP50 apparatus.

General Procedure for Halotrifluoromethylation. Alkenes (0.50 mmol), CF_3SO_2Na (1.00 mmol, 156.1 mg), $Mn(OAc)_3{\cdot}2H_2O$ (1.50 mmol, 402.2 mg), CBr_3COOH (0.75 mmol, 222.6 mg)/CCl_3COOH (0.75 mmol, 122.6 mg)/$CF_2(COOH)_2$ (0.75 mmol, 105.0 mg), and DCE (6 mL) were added into a round-bottom flask (25 mL). The mixture was stirred vigorously at room temperature for 24 h. Then, the reaction mixture was poured into a beaker and sodium thiosulfate solution was added. The mixture was neutralized with solid $NaHCO_3$ and extracted with CH_2Cl_2 (50 mL, three times). Finally, the organic mixture was dried with anhydrous magnesium sulfate, concentrated *in vacuo*, and separated with flash column chromatography.

Gram-Scale Bromotrifluoromethylation. The gram-scale bromotrifluoromethylation was carried out with **1a** (2.04 g), $Mn(OAc)_3{\cdot}2H_2O$ (8.03 g), CBr_3COOH (4.45 g), CF_3SO_2Na (3.12 g), and DCE (50 mL) in a round-bottom flask (100 mL). After stirring vigorously at room temperature for 24 h, the reaction mixture was poured into a beaker and sodium thiosulfate solution was added. Then, the mixture was added slowly with $NaHCO_3$ and extracted with CH_2Cl_2 (60 mL, three times). The organic mixture was dried with anhydrous magnesium sulfate, concentrated *in vacuo*, and separated with flash column chromatography to obtain **2a** (2.68 g, 76% yield, light yellow oil).

Procedure for TEMPO Experiments. A round-bottom flask (25 mL) equipped with a rubber septum and magnetic stir bar was charged with **1a** (0.50 mmol), CF_3SO_2Na (1.00 mmol, 156.1 mg), $Mn(OAc)_3{\cdot}2H_2O$ (1.50 mmol, 402.2 mg), CBr_3COOH (0.75 mmol, 222.6 mg), and TEMPO (3.00 mmol, 468.72 mg). DCE (10 mL) was added with a syringe under Ar protection, and the mixture was stirred vigorously at room temperature for 24 h. Then, the reaction mixture was concentrated *in vacuo* after filtration. Product **2a** was not obtained. As shown in Figure S2, there is significant formation of TEMPO−CF_3 (−53.2 ppm) adduct.[22]

Procedure for Radical Clock Experiments. The operation was the same as the general procedure for halotrifluoromethylation, except that the substrate was changed to **7**.

Procedure for Competition Experiments. A round-bottom flask (25 mL) equipped with a rubber septum and magnetic stir bar was charged with **1a** (0.50 mmol), CF_3SO_2Na (1.00 mmol, 156.1 mg), $Mn(OAc)_3{\cdot}2H_2O$ (1.50 mmol, 402.2 mg), CBr_3COOH (0.75 mmol, 222.6 mg)/CCl_3COOH (0.75 mmol, 122.6 mg), and NaCl (0.75 mmol, 43.8 mg)/NaBr (0.75 mmol, 77.2 mg). The subsequent operation was the same as the general procedure for halotrifluoromethylation.

*5-Bromo-7,7,7-trifluoroheptyl Benzoate (**2a**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1a** (0.50 mmol, 102.1 mg) reacted to **2a** (155.4 mg, 88% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 70:1). Reaction time: 24 h. ^1H NMR (500 MHz, $CDCl_3$) δ 8.00−7.95 (m, 2H), 7.53−7.45 (m, 1H), 7.37 (t, J = 7.6 Hz, 2H), 4.27 (t, J = 5.9 Hz, 2H), 4.14−4.04 (m, 1H), 2.81−2.68 (m, 1H), 2.68−2.56 (m, 1H), 1.95−1.64 (m, 5H), 1.61−1.49 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 166.3, 132.7, 130.0, 129.3, 128.2, 125.2 (q, ^1J(C, F) = 264.2 Hz), 64.2, 44.5 (q, ^3J(C, F) = 2.9 Hz), 42.9 (q, ^2J(C, F) = 28.6 Hz), 37.7, 27.6, 23.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.8 (t, ^3J(F, H) = 10.2 Hz).[18]

*4-Bromo-6,6,6-trifluorohexyl Benzoate (**2b**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1b** (0.50 mmol, 95.1 mg) reacted to **2b** (144.1 mg, 85% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 30:1). Reaction time: 24 h. ^1H NMR (500 MHz, $CDCl_3$) δ 8.06−8.02 (m, 2H), 7.59−7.54 (m, 1H), 7.44 (t, J = 6.2 Hz, 2H), 4.39−4.34 (m, 2H), 4.25−4.18 (m, 1H), 2.86−2.76 (m, 1H), 2.76−2.66 (m, 1H), 2.18−2.04 (m, 2H), 2.04−1.90 (m, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 166.5, 133.0, 130.1, 129.6, 128.4, 125.2 (q, ^1J(C, F) = 278.0 Hz), 63.9, 44.6 (q, ^3J(C, F) = 3.4 Hz), 42.5 (q, ^2J(C, F) = 28.6 Hz), 34.9, 26.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.8 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2963, 2361, 2342, 1719, 1453, 1389, 1278, 1149, 1118, 714, 595 cm^{-1}. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{13}H_{14}BrF_3O_2$, 339.0208; found: 339.0206.

*3-Bromo-5,5,5-trifluoropentyl Benzoate (**2c**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1c** (0.50 mmol, 88.1 mg) reacted to **2c** (97.5 mg, 60% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^1H NMR (500 MHz, $CDCl_3$) δ 8.05−8.00 (m, 2H), 7.60−7.55 (m, 1H), 7.45 (t, J = 7.7 Hz, 2H), 4.61−4.55 (m, 1H), 4.53−4.46 (m, 1H), 4.38−4.31 (m, 1H), 2.94−2.83 (m, 1H), 2.83−2.73 (m, 1H), 2.50−2.40 (m, 1H), 2.27−2.18 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 166.3, 133.2, 129.8, 129.6, 128.5, 125.2 (q, ^1J(C, F) = 278.1 Hz), 62.3, 43.2 (q, ^2J(C, F) = 28.8 Hz), 40.8 (q, ^3J(C, F) = 3.1 Hz), 37.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2964, 2361, 2342, 1719, 1603, 1453, 1275, 1114, 712, 606 cm^{-1}. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{12}H_{12}BrF_3O_2$, 325.0051; found: 325.0054.

*2-Bromo-4,4,4-trifluorobutyl Benzoate (**2d**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1d** (0.50 mmol, 81.0 mg) reacted to **2d** (80.9 mg, 52% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 7.7 Hz, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 4.63−4.57 (m, 1H), 4.57−4.52 (m, 1H), 4.43−4.36 (m, 1H), 2.97−2.85 (m, 1H), 2.85−2.73 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 165.7, 133.6, 129.9, 129.4, 128.7, 125.3 (q, ^1J(C, F) = 277.7 Hz), 67.1, 39.9 (q, ^2J(C, F) = 29.5 Hz), 39.3 (q, ^3J(C, F) = 3.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.0 Hz). IR (KBr): 3068, 2358, 2330, 1728, 1452, 1427, 1272, 1195, 1154, 711, 664 cm^{-1}. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{11}H_{10}BrF_3O_2$, 310.9895; found: 310.9899.

*((5-Bromo-7,7,7-trifluoroheptyl)oxy)benzene (**2e**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1e** (0.50 mmol, 88.1 mg) reacted to **2e** (143.1 mg, 88%

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yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 250:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30−7.24 (m, 2H), 6.93 (t, J = 7.3 Hz, 1H), 6.89 (d, J = 7.9 Hz, 2H), 4.20−4.13 (m, 1H), 3.96 (t, J = 6.0 Hz, 2H), 2.84−2.72 (m, 1H), 2.72−2.61 (m, 1H), 2.03−1.71 (m, 5H), 1.68−1.58 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.0, 129.5, 125.4 (q, ^1J(C, F) = 278.0 Hz), 120.7, 114.5, 67.4, 44.8 (q, ^3J(C, F) = 2.9 Hz), 43.1 (q, ^2J(C, F) = 28.4 Hz), 38.3, 28.5, 24.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.3 Hz). IR (KBr): 2947, 2361, 2341, 1498, 1390, 1247, 1147, 756, 692 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{13}H_{16}BrF_3O$, 325.0415; found: 325.0419.

*(((5-Bromo-7,7,7-trifluoroheptyl)oxy)methyl)benzene (**2f**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1f** (0.50 mmol, 95.1 mg) reacted to **2f** (139.1 mg, 82% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 150:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.32 (m, 4H), 7.30−7.25 (m, 1H), 4.50 (s, 2H), 4.17−4.10 (m, 1H), 3.48 (t, J = 5.8 Hz, 2H), 2.82−2.72 (m, 1H), 2.71−2.61 (m, 1H), 1.94−1.81 (m, 2H), 1.72−1.52 (m, 4H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 138.5, 128.4, 127.7, 127.6, 125.4 (q, ^1J(C, F) = 278.0 Hz), 73.0, 69.9, 44.9 (q, ^3J(C, F) = 2.9 Hz), 43.1 (q, ^2J(C, F) = 28.4 Hz), 38.3, 28.9, 24.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.8 (t, ^3J(F, H) = 10.2 Hz).[19]

*5-Bromo-7,7,7-trifluoroheptyl 2-chlorobenzoate (**2g**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1g** (0.50 mmol, 119.4 mg) reacted to **2g** (180.2 mg, 93% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 120:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (dd, J = 7.7, 1.7 Hz, 1H), 7.47−7.39 (m, 2H), 7.35−7.29 (m, 1H), 4.36 (t, J = 6.2 Hz, 2H), 4.20−4.13 (m, 1H), 2.87−2.76 (m, 1H), 2.74−2.64 (m, 1H), 2.01−1.74 (m, 5H), 1.67−1.60 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.8, 133.6, 132.5, 131.3, 131.1, 130.4, 126.6, 125.3 (q, ^1J(C, F) = 278.0 Hz), 65.0, 44.6 (q, ^3J(C, F) = 2.9 Hz), 43.1 (q, ^2J(C, F) = 28.4 Hz), 38.0, 27.8, 23.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 3075, 2342, 1732, 1593, 1436, 1253, 1142, 749, 651 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{14}H_{15}BrClF_3O_2$, 386.9974; found: 386.9973.

*5-Bromo-7,7,7-trifluoroheptyl 3-Chlorobenzoate (**2h**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1h** (0.50 mmol, 119.4 mg) reacted to **2h** (178.3 mg, 92% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 110:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (t, J = 1.9 Hz, 1H), 7.94−7.90 (m, 1H), 7.55−7.50 (m, 1H), 7.38 (t, J = 7.9 Hz, 1H), 4.37−4.32 (m, 2H), 4.20−4.14 (m, 1H), 2.86−2.76 (m, 1H), 2.74−2.65 (m, 1H), 2.00−1.72 (m, 5H), 1.67−1.57 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.3, 134.5, 133.0, 132.1, 129.7, 129.6, 127.7, 125.3 (q, ^1J(C, F) = 278.1 Hz), 64.9, 44.7 (q, ^3J(C, F) = 2.9 Hz), 43.1 (q, ^2J(C, F) = 28.5 Hz), 38.0, 27.9, 23.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 3073, 2360, 2342, 1722, 1575, 1428, 1390, 1257, 1147, 750, 675, 596 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{14}H_{15}BrClF_3O_2$, 386.9974; found: 386.9973.

*5-Bromo-7,7,7-trifluoroheptyl 4-Chlorobenzoate (**2i**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1i** (0.50 mmol, 119.4 mg) reacted to **2i** (178.3 mg, 92% yield, reddish brown oil), which was purified by silica gel chromatography (PE/EA = 120:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99−7.95 (m, 2H), 7.43−7.39 (m, 2H), 4.36−4.31 (m, 2H), 4.20−4.13 (m, 1H), 2.86−2.75 (m, 1H), 2.75−2.64 (m, 1H), 2.02−1.71 (m, 5H), 1.66−1.58 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.7, 139.4, 131.0, 128.7, 125.3 (q, ^1J(C, F) = 278.2 Hz), 64.7, 44.7 (q, ^3J(C, F) = 2.9 Hz), 43.1 (q, ^2J(C, F) = 28.5 Hz), 38.0, 27.9, 23.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz).[14a]

*N-(5-Bromo-7,7,7-trifluoroheptyl)benzamide (**2j**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1j** (0.50 mmol, 101.6 mg) reacted to **2j** (153.2 mg, 87% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 6:1). Reaction time: 24 h. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74−7.66 (m, 2H), 7.41−7.34 (m, 1H), 7.32−7.27 (m, 2H), 6.84 (t, J = 5.8 Hz, 1H), 4.05−3.97 (m, 1H), 3.37−3.29 (m, 2H), 2.74−2.51 (m, 2H), 1.86−1.66 (m, 2H), 1.58−1.46 (m, 3H), 1.44−1.33 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166. 8, 133.6, 130.3, 127.5, 125.9, 124.3 (q, ^1J(C, F) = 278.0 Hz), 43.8 (q, ^3J(C, F) = 3.0 Hz), 42.0 (q, ^2J(C, F) = 28.4 Hz), 38.7, 37.0, 27.7, 23.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 3307, 2943, 2361, 2342, 1637, 1541, 1256, 1147, 1077, 695 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{14}H_{17}BrF_3NO$, 352.0524; found: 352.0527.

*2-(5-Bromo-7,7,7-trifluoroheptyl)isoindoline-1,3-dione (**2k**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1k** (0.50 mmol, 114.6 mg) reacted to **2k** (166.4 mg, 88% yield, white solid, m.p. = 53−54 °C), which was purified by silica gel chromatography (PE/EA = 12:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, J = 5.4, 3.1 Hz, 2H), 7.72 (dd, J = 5.4, 3.0 Hz, 2H), 4.18−4.08 (m, 1H), 3.71 (t, J = 7.1 Hz, 2H), 2.85−2.74 (m, 1H), 2.74−2.63 (m, 1H), 2.02−1.93 (m, 1H), 1.93−1.83 (m, 1H), 1.80−1.62 (m, 3H), 1.57−1.47 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.4, 134.0, 132.1, 125.3 (q, ^1J(C, F) = 278.1 Hz), 123.2, 44.6 (q, ^3J(C, F) = 3.0 Hz), 43.1 (q, ^2J(C, F) = 28.4 Hz), 37.9, 37.5, 27.7, 24.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2944, 2367, 2325, 1710, 1398, 1370, 1256, 1150, 1103, 1034, 723, 529 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{15}H_{15}BrF_3NO_2$, 378.0317; found: 378.0319.

*N-(5-Bromo-7,7,7-trifluoroheptyl)-4-methylbenzenesulfonamide (**2l**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1l** (0.50 mmol, 126.6 mg) reacted to **2l** (191.1 mg, 95% yield, white solid, m.p. = 81−82 °C), which was purified by silica gel chromatography (PE/EA = 6:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 5.15 (t, J = 6.2 Hz, 1H), 4.08−4.01 (m, 1H), 2.94 (q, J = 6.3 Hz, 2H), 2.78−2.68 (m, 1H), 2.67−2.56 (m, 1H), 2.43 (s, 3H), 1.86−1.70 (m, 2H), 1.58−1.36 (m, 4H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 143.5, 136.9, 129.8, 127.1, 125.3 (q, ^1J(C, F) = 278.0 Hz), 44.6 (q, ^3J(C, F) = 2.9 Hz), 42.9 (q, ^2J(C, F) = 28.5 Hz), 42.8, 37.9, 28.7, 24.1, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 3273, 2946, 2866, 2360, 2342, 1600, 1434, 1321, 1268, 1159, 1086, 812, 687, 550 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{14}H_{19}BrF_3NO_2S$, 402.0350; found: 402.0353.

*N-(3-Bromo-5,5,5-trifluoropentyl)-4-methylbenzenesulfonamide (**2m**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1m** (0.50 mmol, 112.6 mg) reacted to **2m** (160.9 mg, 86% yield, white solid, m.p. = 61−62 °C), which was purified by silica gel chromatography (PE/EA = 8:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H), 5.10 (s, 1H), 4.20−4.12 (m, 1H), 3.21−3.10 (m, 2H), 2.80−2.69 (m, 1H), 2.69−2.57 (m, 1H), 2.43 (s, 3H), 2.17−2.08 (m, 1H), 1.96−1.86 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 143.8, 136.5, 129.9, 127.1, 125.1 (q, ^1J(C, F) = 278.1 Hz), 43.0 (q, ^2J(C, F) = 28.8 Hz), 41.6 (q, ^3J(C, F) = 2.9 Hz), 41.2, 38.2, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz).[18]

*5-Bromo-7,7,7-trifluoroheptyl Nicotinate (**2n**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1n** (0.50 mmol, 102.6 mg) reacted to **2n** (150.5 mg, 85% yield, yellow oil), which was purified by silica gel chromatography (PE/EA = 8:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.79 (s, 1H), 8.33−8.28 (m, 1H), 7.43−7.39 (m, 1H), 4.41−4.37 (m, 2H), 4.21−4.14 (m, 1H), 2.88−2.77 (m, 1H), 2.75−2.66 (m, 1H), 2.03−1.73 (m, 5H), 1.68−1.58 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.3, 153.5, 150.9, 137.0, 126.2, 125.3 (q, ^1J(C, F) = 278.1 Hz), 123.4, 64.9, 44.6 (q, ^3J(C, F) = 2.9 Hz), 43.1 (q, ^2J(C, F) = 28.5 Hz), 37.9, 27.9, 23.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2961, 2361, 2343, 1724, 1592, 1420, 1389, 1287, 1113, 1025, 802, 742, 703 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{13}H_{15}BrF_3NO_2$, 354.0317; found: 354.0320.

*5-Bromo-7,7,7-trifluoroheptyl Picolinate (**2o**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1o** (0.50 mmol, 102.6 mg) reacted to **2o** (111.6 mg, 63%

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yield, yellow oil), which was purified by silica gel chromatography (PE/EA = 6:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.79 (d, J = 4.8 Hz, 1H), 8.33−8.28 (m, 1H), 7.41 (dd, J = 7.9, 4.8 Hz, 1H), 4.42−4.36 (m, 2H), 4.21−4.15 (m, 1H), 2.88−2.78 (m, 1H), 2.77−2.66 (m, 1H), 2.03−1.74 (m, 5H), 1.69−1.59 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.2, 153.4, 150.8, 137.0, 126.1, 125.2 (q, ^1J(C, F) = 278.1 Hz), 123.3, 64.9, 44.6 (q, ^3J(C, F) = 2.9 Hz), 43.0 (q, ^2J(C, F) = 28.4 Hz), 37.9, 27.8, 23.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.8 (t, ^3J(F, H) = 10.2 Hz).[7]

*5-Bromo-7,7,7-trifluoroheptyl 2-Naphthoate (**2p**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1p** (0.50 mmol, 127.2 mg) reacted to **2p** (185.5 mg, 92% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.05 (dd, J = 8.6, 1.7 Hz, 1H), 7.94 (d, J = 8.1 Hz, 1H), 7.86 (dd, J = 8.3, 5.1 Hz, 2H), 7.59−7.49 (m, 2H), 4.41−4.36 (m, 2H), 4.20−4.14 (m, 1H), 2.84−2.74 (m, 1H), 2.73−2.63 (m, 1H), 2.01−1.74 (m, 5H), 1.68−1.59 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.7, 135.6, 132.5, 131.0, 129.4, 128.3, 128.2, 127.8, 127.6, 126.7, 125.4 (q, ^1J(C, F) = 278.0 Hz), 125.2, 64.6, 44.8 (q, ^3J(C, F) = 3.0 Hz), 43.1 (q, ^2J(C, F) = 28.5 Hz), 38.1, 28.0, 23.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2955, 2361, 2342, 1716, 1632, 1468, 1435, 1390, 1285, 1228, 1197, 1145, 1096, 779, 763, 475 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{18}H_{18}BrF_3O_2$, 403.0521; found: 403.0525.

*2-Bromo-4,4,4-trifluorobutyl 2-Naphthoate (**2q**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1q** (0.50 mmol, 106.1 mg) reacted to **2q** (155.3 mg, 86% yield, reddish brown solid, m.p. = 48−49 °C), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.05 (dd, J = 8.7, 1.7 Hz, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.89 (t, J = 7.8 Hz, 2H), 7.61 (t, J = 7.3 Hz, 1H), 7.56 (t, J = 7.4 Hz, 1H), 4.68 (dd, J = 11.9, 5.8 Hz, 1H), 4.62 (dd, J = 11.9, 5.8 Hz, 1H), 4.49−4.43 (m, 1H), 3.01−2.92 (m, 1H), 2.89−2.80 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 164.8, 134.7, 131.4, 130.4, 128.4, 127.6, 127.4, 126.8, 125.8, 125.3, 124.1 (q, ^1J(C, F) = 277.6 Hz), 124.0, 66.0, 38.7 (q, ^2J(C, F) = 29.4 Hz), 38.2 (q, ^3J(C, F) = 2.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.0 Hz). IR (KBr): 3064, 2957, 1724, 1283, 1195, 1154, 1132, 1097, 778, 668 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{15}H_{12}BrF_3O_2$, 361.0051; found: 361.0054.

*5-Bromo-7,7,7-trifluoroheptyl Furan-2-carboxylate (**2r**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1r** (0.50 mmol, 97.1 mg) reacted to **2r** (116.7 mg, 68% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 10:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.18 (d, J = 3.5 Hz, 1H), 6.52 (dd, J = 3.5, 1.7 Hz, 1H), 4.33 (t, J = 6.3 Hz, 2H), 4.19−4.13 (m, 1H), 2.85−2.76 (m, 1H), 2.74−2.66 (m, 1H), 2.00−1.70 (m, 5H), 1.65−1.56 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 158.7, 146.3, 144.7, 125.3 (q, ^1J(C, F) = 278.0 Hz), 117.9, 111.8, 64.4, 44.6 (q, ^3J(C, F) = 2.9 Hz), 43.1 (q, ^2J(C, F) = 28.5 Hz), 38.0, 27.9, 23.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.0 Hz). IR (KBr): 2955, 2360, 2342, 1730, 1581, 1475, 1398, 1298, 1181, 1122, 1014, 764, 596 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{12}H_{14}BrF_3O_3$, 343.0157; found: 343.0159.

*5-Bromo-7,7,7-trifluoroheptan-1-ol (**2s**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1s** (0.50 mmol, 50.1 mg) reacted to **2s** (107.1 mg, 86% yield, colorless oil), which was purified by silica gel chromatography (PE/EA = 10:1). Reaction time: 24 h. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.13−4.06 (m, 1H), 3.60 (t, J = 5.9 Hz, 2H), 2.80−2.68 (m, 1H), 2.68−2.58 (m, 1H), 1.92−1.77 (m, 2H), 1.64−1.44 (m, 5H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 124.3 (q, ^1J(C, F) = 278.1 Hz), 61.4, 43.9 (q, ^3J(C, F) = 3.1 Hz), 42.0 (q, ^2J(C, F) = 28.4 Hz), 37.2, 30.7, 22.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz).[7]

*4-((3-Bromo-5,5,5-trifluoropentyl)oxy)benzaldehyde (**2t**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1t** (0.50 mmol, 88.1 mg) reacted to **2t** (136.6 mg, 84% yield, yellow oil), which was purified by silica gel chromatography (PE/EA = 50:1). Reaction time: 24 h. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.75−7.71 (m, 2H), 6.94−6.89 (m, 2H), 4.38−4.31 (m, 1H), 4.19−4.13 (m, 2H), 2.82−2.68 (m, 2H), 2.42−2.33 (m, 1H), 2.19−2.09 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.7, 162.4, 131.0, 129.2, 124.2 (q, ^1J(C, F) = 278.1 Hz), 113.8, 64.4, 42.1 (q, ^2J(C, F) = 28.7 Hz), 40.1 (q, ^3J(C, F) = 3.2 Hz), 36.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2939, 2831, 2742, 2360, 1696, 1601, 1509, 1258, 1159, 832, 598 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{12}H_{12}BrF_3O_2$, 325.0051; found: 325.0054.

*(1R)-((1S,4S)-5-(1-Bromo-3,3,3-trifluoropropyl)quinuclidin-2-yl)(6-methoxyquinolin-4-yl)methanol (**2u**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1u** (0.50 mmol, 162.2 mg) reacted to **2u** (130.2 mg, 55% yield, yellow oil), which was purified by silica gel chromatography (ethyl acetate/methyl alcohol = 8:1). Reaction time: 24 h. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58−8.37 (m, 1H), 7.71 (t, J = 9.5 Hz, 1H), 7.62−7.51 (m, 1H), 7.13−7.06 (m, 1H), 6.95 (s, 1H), 6.11−5.97 (m, 1H), 4.32−4.08 (m, 1H), 3.84−3.64 (m, 4H), 3.55−3.44 (m, 1H), 3.34−3.21 (m, 1H), 3.08−2.95 (m, 1H), 2.94−2.80 (m, 1H), 2.67−2.50 (m, 2H), 2.50−2.28 (m, 1H), 2.23−2.04 (m, 3H), 1.94−1.88 (m, 1H), 1.79−1.65 (m, 1H), 1.20−1.11 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.9, 144.9, 144.5, 141.3, 129.0, 124.6, 124.0 (q, ^1J(C, F) = 279.1 Hz), 122.4, 117.9, 98.7, 65.1, 59.4, 59.2, 55.3, 55.2, 44.8, 42.7, 39.4 (q, ^2J(C, F) = 29.3), 28.7, 24.0, 19.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1(t, ^3J(F, H) = 10.4 Hz). IR (KBr): 3290, 2964, 2598, 1622, 1510, 1243, 1157, 1028, 832, 719, 639, 465 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{21}H_{24}BrF_3N_2O_2$, 473.1052; found: 473.1055.

*5-Chloro-7,7,7-trifluoroheptyl Benzoate (**3a**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1a** (0.50 mmol, 102.1 mg) reacted to **3a** (89.5 mg, 58% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 70:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.8 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 4.40−4.3 (m, 2H), 4.18−4.09 (m, 1H), 2.71−2.59 (m, 1H), 2.58−2.49 (m, 1H), 1.96−1.88 (m, 1H), 1.87−1.72 (m, 4H), 1.67−1.57 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.6, 133.0, 130.3, 129.6, 128.4, 125.3 (q, ^1J(C, F) = 277.5 Hz), 64.5, 53.9 (q, ^3J(C, F) = 2.8 Hz), 42.5 (q, ^2J(C, F) = 28.4 Hz), 37.6, 28.1, 22.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz).[18]

*4-Chloro-6,6,6-trifluorohexyl Benzoate (**3b**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1b** (0.50 mmol, 95.1 mg) reacted to **3b** (73.7 mg, 50% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 30:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08−7.99 (m, 2H), 7.58−7.54 (m, 1H), 7.44 (t, J = 7.8 Hz, 2H), 4.41−4.33 (m, 2H), 4.23−4.14 (m, 1H), 2.71−2.61 (m, 1H), 2.60−2.51 (m, 1H), 2.11−2.00 (m, 2H), 1.98−1.85 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.5, 133.0, 130.1, 129.6, 128.4, 125.2 (q, ^1J(C, F) = 277.7 Hz), 63.9, 53.7 (q, ^3J(C, F) = 3.1 Hz), 42.5 (q, ^2J(C, F) = 28.6 Hz), 34.7, 25.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2963, 2360, 2341, 1719, 1277, 1150, 1118, 713, 631 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{13}H_{14}ClF_3O_2$, 295.0713; found: 295.0714.

*3-Chloro-5,5,5-trifluoropentyl Benzoate (**3c**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1c** (0.50 mmol, 88.1 mg) reacted to **3c** (58.9 mg, 42% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 7.9 Hz, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 4.60−4.54 (m, 1H), 4.54−4.47 (m, 1H), 4.38−4.30 (m, 1H), 2.78−2.60 (m, 2H), 2.41−2.33 (m, 1H), 2.18−2.10 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.3, 133.2, 129.9, 129.6, 128.5, 125.1 (q, ^1J(C, F) = 277.7 Hz), 61.2, 50.7 (q, ^3J(C, F) = 3.0 Hz), 42.5 (q, ^2J(C, F) = 28.8 Hz), 37.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2969, 2359, 2341, 1722, 1277, 1151, 1117, 712, 633 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{12}H_{12}ClF_3O_2$, 281.0556; found: 281.0559.

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*2-Chloro-4,4,4-trifluorobutyl Benzoate (**3d**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1d** (0.50 mmol, 81.0 mg) reacted to **3d** (46.7 mg, 35% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, J = 7.9 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 4.59−4.49 (m, 2H), 4.47−4.39 (m, 1H), 2.83−2.74 (m, 1H), 2.73−2.63 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.9, 133.7, 129.9, 129.3, 128.7, 125.2 (q, ^1J(C, F) = 277.2 Hz), 66.8, 50.4 (q, ^3J(C, F) = 3.0 Hz), 39.4 (q, ^2J(C, F) = 29.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.1 Hz).[25]

*((5-Chloro-7,7,7-trifluoroheptyl)oxy)benzene (**3e**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1e** (0.50 mmol, 88.1 mg) reacted to **3e** (78.6 mg, 56% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 250:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (t, J = 7.9 Hz, 2H), 6.93 (t, J = 7.3 Hz, 1H), 6.88 (d, J = 8.2 Hz, 2H), 4.18−4.07 (m, 1H), 3.96 (t, J = 6.1 Hz, 2H), 2.68−2.57 (m, 1H), 2.56−2.46 (m, 1H), 1.95−1.85 (m, 1H), 1.85−1.70 (m, 4H), 1.68−1.57 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.0, 129.5, 125.3 (q, ^1J(C, F) = 277.5 Hz), 120.7, 114.5, 67.4, 54.0 (q, ^3J(C, F) = 2.8 Hz), 42.5 (q, ^2J(C, F) = 28.4 Hz), 37.8, 28.6, 22.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2944, 2864, 2360, 2342, 1456, 1389, 1268, 1147, 1104, 736, 698, 631 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{13}H_{16}ClF_3O$, 281.0920; found: 281.0923.

*(((5-Chloro-7,7,7-trifluoroheptyl)oxy)methyl)benzene (**3f**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1f** (0.50 mmol, 95.1 mg) reacted to **3f** (81.0 mg, 55% yield, colorless oil), which was purified by silica gel chromatography (PE/EA = 150:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.31 (m, 4H), 7.30−7.25 (m, 1H), 4.49 (s, 2H), 4.13−4.06 (m, 1H), 3.48 (t, J = 5.8 Hz, 2H), 2.63−2.55 (m, 1H), 2.54−2.45 (m, 1H), 1.87−1.79 (m, 1H), 1.78−1.72 (m, 1H), 1.69−1.59 (m, 3H) 1.58−1.49 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 138.5, 128.4, 127.7, 127.6, 125.4 (q, ^1J(C, F) = 277.4 Hz), 73.0, 69.9, 54.1 (q, ^3J(C, F) = 2.9 Hz), 42.4 (q, ^2J(C, F) = 28.4 Hz), 37.9, 29.0, 22.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz).[26]

*5-Chloro-7,7,7-trifluoroheptyl 2-Chlorobenzoate (**3g**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1g** (0.50 mmol, 119.4 mg) reacted to **3g** (90.9 mg, 53% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 120:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 7.7 Hz, 1H), 7.48−7.38 (m, 2H), 7.35−7.29 (m, 1H), 4.36 (t, J = 6.2 Hz, 2H), 4.18−4.09 (m, 1H), 2.69−2.59 (m, 1H), 2.59−2.50 (m, 1H), 1.96−1.87 (m, 1H), 1.87−1.72 (m, 4H), 1.67−1.58 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.8, 133.6, 132.5, 131.3, 131.1, 130.3, 126.6, 125.2 (q, ^1J(C, F) = 277.7 Hz), 65.1, 53.9 (q, ^3J(C, F) = 2.9 Hz), 42.4 (q, ^2J(C, F) = 28.5 Hz), 37.6, 27.9, 22.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz).[14a]

*5-Chloro-7,7,7-trifluoroheptyl 3-Chlorobenzoate (**3h**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1h** (0.50 mmol, 119.4 mg) reacted to **3h** (92.7 mg, 54% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 110:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.92 (d, J = 7.7 Hz, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.38 (t, J = 7.9 Hz, 1H), 4.35 (t, J = 6.2 Hz, 2H), 4.17−4.10 (m, 1H), 2.70−2.60 (m, 1H), 2.60−2.51 (m, 1H), 1.97−1.88 (m, 1H), 1.87−1.69 (m, 4H), 1.65−1.57 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.4, 134.6, 133.1, 132.1, 129.8, 129.7, 127.8, 125.3 (q, ^1J(C, F) = 277.6 Hz), 65.0, 54.0 (q, ^3J(C, F) = 2.9 Hz), 42.6 (q, ^2J(C, F) = 28.5 Hz), 37.6, 28.1, 22.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz).[14a]

*5-Chloro-7,7,7-trifluoroheptyl 4-Chlorobenzoate (**3i**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1i** (0.50 mmol, 119.4 mg) reacted to **3i** (89.2 mg, 52% yield, yellow oil), which was purified by silica gel chromatography (PE/EA = 120:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00−7.93 (m, 2H), 7.45−7.35 (m, 2H), 4.36−4.31 (m, 2H), 4.18−4.04 (m, 1H), 2.71−2.60 (m, 1H), 2.59−2.47 (m, 1H), 1.96−1.88 (m, 1H), 1.87−1.70 (m, 4H), 1.65−1.55 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.7, 139.4, 131.0, 128.7, 125.2 (q, ^1J(C, F) = 277.5 Hz), 64.7, 53.9 (q, ^3J(C, F) = 2.8 Hz), 42.5 (q, ^2J(C, F) = 28.5 Hz), 37.5, 28.0, 22.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.8 (t, ^3J(F, H) = 10.2 Hz).[14a]

*N-(5-Chloro-7,7,7-trifluoroheptyl)benzamide (**3j**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1j** (0.50 mmol, 101.6 mg) reacted to **3j** (73.9 mg, 48% yield, colorless oil), which was purified by silica gel chromatography (PE/EA = 6:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) 7.80−7.76 (m, 2H), 7.50−7.45 (m, 1H), 7.39 (dd, J = 8.4, 6.9 Hz, 2H), 6.74 (t, J = 5.8 Hz, 1H), 4.12−4.04 (m, 1H), 3.47−3.39 (m, 2H), 2.64−2.55 (m, 1H), 2.55−2.46 (m, 1H), 1.87−1.79 (m, 1H), 1.79−1.70 (m, 1H), 1.67−1.56 (m, 3H), 1.54−1.44 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.8, 134.7, 131.4, 128.5, 127.0, 125.3 (q, ^1J(C, H) = 277.7 Hz), 54.0 (q, ^3J(C, F) = 2.9 Hz), 42.4 (q, ^2J(C, F) = 28.4 Hz), 39.7, 37.6, 28.9, 23.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 3308, 2943, 2361, 2342, 1637, 1542, 1270, 1242, 1147, 695, 668 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{14}H_{17}ClF_3NO$, 308.1029; found: 308.1031.

*2-(5-Chloro-7,7,7-trifluoroheptyl)isoindoline-1,3-dione (**3k**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1k** (0.50 mmol, 114.6 mg) reacted to **3k** (88.4 mg, 53% yield, white solid, m.p. = 59−60 °C), which was purified by silica gel chromatography (PE/EA = 12:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (dd, J = 5.3, 3.1 Hz, 2H), 7.73 (dd, J = 5.4, 3.0 Hz, 2H), 4.15−4.06 (m, 1H), 3.71 (t, J = 7.1 Hz, 2H), 2.68−2.58 (m, 1H), 2.58−2.49 (m, 1H), 1.95−1.86 (m, 1H), 1.84−1.58 (m, 4H), 1.56−1.45 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.3, 133.9, 132.1, 125.2 (q, ^1J(C, F) = 277.6 Hz), 123.2, 53.9 (q, ^3J(C, F) = 2.9 Hz), 42.4 (q, ^2J(C, F) = 28.4 Hz), 37.5, 37.5, 27.8, 23.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 3464, 2948, 1769, 1712, 1467, 1400, 1372, 1277, 1264, 1142, 1117, 1037, 893, 725, 625, 531 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{15}H_{15}ClF_3NO_2$, 334.0822; found: 334.0825.

*N-(5-Chloro-7,7,7-trifluoroheptyl)-4-methylbenzenesulfonamide (**3l**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1l** (0.50 mmol, 126.6 mg) reacted to **3l** (107.3 mg, 60% yield, white solid, m.p. = 76−77 °C), which was purified by silica gel chromatography (PE/EA = 6:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 5.22 (t, J = 6.0 Hz, 1H), 4.06−3.97 (m, 1H), 2.93 (q, J = 6.3 Hz, 2H), 2.62−2.45 (m, 2H), 2.42 (s, 3H), 1.80−1.71 (m, 1H), 1.70−1.61 (m, 1H), 1.56−1.36 (m, 4H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 143.5, 136.9, 129.7, 127.1, 125.3 (q, ^1J(C, F) = 277.6 Hz), 53.9 (q, ^3J(C, F) = 2.8 Hz), 42.8, 42.2 (q, ^2J(C, F) = 28.5 Hz), 37.4, 28.7, 22.9, 21.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 3272, 2948, 2868, 2362, 2343, 1915, 1599, 1433, 1318, 1159, 1084, 900, 813, 689, 570, 477 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{14}H_{19}ClF_3NO_2S$, 358.0855; found: 358.0853.

*Crystal Data for **3l**.* $C_{14}H_{19}ClF_3NO_2S$ (M = 357.81 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 5.1623(2) Å, b = 10.4648(3) Å, c = 30.1346(10) Å, β = 89.539(3)°, V = 1627.89(10) Å^3, Z = 4, T = 123.15 K, μ(MoKα) = 0.399 mm^{-1}, D_{calc} = 1.460 g/cm^3, 12,435 reflections measured (4.12° ≤ 2Θ ≤ 52.744°), 3334 unique (R_{int} = 0.0359, R_{sigma} = 0.0285), which were used in all calculations. The final R_1 was 0.0576 (I > 2σ(I)), and wR_2 was 0.1863 (all data).

*N-(3-Chloro-5,5,5-trifluoropentyl)-4-methylbenzenesulfonamide (**3m**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1m** (0.50 mmol, 112.6 mg) reacted to **3m** (92.3 mg, 56% yield, white solid, m.p. = 87−88 °C), which was purified by silica gel chromatography (PE/EA = 8:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 5.37 (t, J = 6.3 Hz, 1H), 4.21−4.12 (m, 1H), 3.18−3.10 (m, 2H), 2.63−2.53 (m, 1H), 2.53−2.44 (m, 1H), 2.43 (s,

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3H), 2.11−2.02 (m, 1H), 1.88−1.78 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 143.8, 136.5, 129.9, 127.1, 125.1 (q, ^1J(C, F) = 277.7 Hz), 51.2 (q, ^3J(C, F) = 3.1 Hz), 42.3 (q, ^2J(C, F) = 28.7 Hz), 40.0, 37.7, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz).[18]

*5-Chloro-7,7,7-trifluoroheptyl Nicotinate (**3n**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1n** (0.50 mmol, 102.6 mg) reacted to **3n** (88.3 mg, 57% yield, reddish brown oil), which was purified by silica gel chromatography (PE/EA = 8:1). Reaction time: 24 h. ^1H NMR (500 MHz, $CDCl_3$) δ 9.23 (d, J = 2.2 Hz, 1H), 8.79 (dd, J = 4.8, 1.8 Hz, 1H), 8.33−8.27 (m, 1H), 7.41 (dd, J = 7.9, 4.8 Hz, 1H), 4.42−4.36 (m, 2H), 4.19−4.10 (m, 1H), 2.71−2.61 (m, 1H), 2.61−2.51 (m, 1H), 1.98−1.89 (m, 1H), 1.89−1.71 (m, 4H), 1.68−1.58 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 165.2, 153.4, 150.9, 137.0, 126.1, 125.2 (q, ^1J(C, F)) = 277.6 Hz), 123.3, 64.9, 53.9 (q, ^3J(C, F) = 2.8 Hz), 42.4 (q, ^2J(C, F) = 28.4 Hz), 37.5, 27.9, 22.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2962, 2359, 2330, 1725, 1592, 1287, 1146, 1115, 1025, 804, 742, 703, 629 cm^{-1}. HRMS-ESI (*m*/*z*): $[M + H]^+$ calcd for $C_{13}H_{15}ClF_3NO_2$, 310.0822; found: 310.0820.

*5-Chloro-7,7,7-trifluoroheptyl Picolinate (**3o**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1o** (0.50 mmol, 102.6 mg) reacted to **3o** (38.7 mg, 25% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 6:1). Reaction time: 24 h. ^1H NMR (500 MHz, $CDCl_3$) δ 8.77 (d, J = 3.5 Hz, 1H), 8.13 (d, J = 7.8 Hz, 1H), 7.88−7.83 (m, 1H), 7.51−7.46 (m, 1H), 4.45 (t, J = 6.7 Hz, 2H), 4.20−4.10 (m, 1H), 2.80−2.45 (m, 2H), 1.98−1.82 (m, 4H), 1.78−1.70 (m, 1H), 1.67−1.57 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 165.2, 149.9, 148.1, 137.0, 126.9, 125.2 (q, ^1J(C, F) = 277.5 Hz), 125.1, 65.4, 53.8 (q, ^3J(C, F) = 2.7 Hz), 42.4 (q, ^2J(C, F) = 28.4 Hz), 37.5, 23.7, 22.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.8 (t, ^3J(F, H) = 10.3 Hz). IR (KBr): 2958, 2361, 2342, 1717, 1585, 1437, 1392, 1245, 1136, 747, 707, 620 cm^{-1}. HRMS-ESI (*m*/*z*): $[M + H]^+$ calcd for $C_{13}H_{15}ClF_3NO_2$, 310.0822; found: 310.0820.

*5-Chloro-7,7,7-trifluoroheptyl 2-Naphthoate (**3p**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1p** (0.50 mmol, 127.2 mg) reacted to **3p** (107.6 mg, 60% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^1H NMR (500 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.05 (dd, J = 8.6, 1.7 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.86 (dd, J = 8.4, 4.7 Hz, 2H), 7.60−7.50 (m, 2H), 4.42−4.36 (m, 2H), 4.17−4.10 (m, 1H), 2.68−2.58 (m, 1H), 2.58−2.48 (m, 1H), 1.96−1.73 (m, 5H), 1.68−1.58 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 166.7, 135.6, 132.5, 131.0, 129.4, 128.3, 128.2, 127.8, 127.6, 126.7, 125.3 (q, ^1J(C, F) = 277.6 Hz), 125.2, 64.6, 54.0 (q, ^3J(C, F) = 2.8 Hz), 42.5 (q, ^2J(C, F) = 28.5 Hz), 37.6, 28.1, 22.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2957, 2361, 2342, 1716, 1632, 1468, 1436, 1390, 1285, 1229, 1197, 1146, 1097, 780, 763, 631, 475 cm^{-1}. HRMS-ESI (*m*/*z*): $[M + H]^+$ calcd for $C_{18}H_{18}ClF_3O_2$, 359.1026; found: 359.1024.

*2-Chloro-4,4,4-trifluorobutyl 2-Naphthoate (**3q**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1q** (0.50 mmol, 106.1 mg) reacted to **3q** (91.8 mg, 58% yield, white solid, m.p. = 47−48 °C), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^1H NMR (500 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.05 (dd, J = 8.6, 1.7 Hz, 1H), 7.98 (d, J = 8.1 Hz, 1H), 7.93−7.88 (m, 2H), 7.64−7.60 (m, 1H), 7.59−7.54 (m, 1H), 4.64−4.55 (m, 2H), 4.52−4.45 (m, 1H), 2.88−2.79 (m, 1H), 2.78−2.68 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 166.0, 135.8, 132.5, 131.5, 129.5, 128.6, 128.5, 127.8, 126.9, 126.4, 125.1, 125.1 (q, ^1J(C, F) = 277.5 Hz), 66.9, 50.4 (q, ^3J(C, F) = 3.1 Hz), 39.4 (q, ^2J(C, F) = 29.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.0 Hz). IR (KBr): 2960, 1714, 1629, 1390, 1288, 1264, 1232, 1196, 1135, 1095, 779, 765, 698 cm^{-1}. HRMS-ESI (*m*/*z*): $[M + H]^+$ calcd for $C_{15}H_{12}ClF_3O_2$, 317.0556; found: 317.0559.

*5-Chloro-7,7,7-trifluoroheptyl Furan-2-carboxylate (**3r**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1r** (0.50 mmol, 97.1 mg) reacted to **3r** (70.2 mg, 47% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 10:1). Reaction time: 24 h. ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.18 (d, J = 3.5 Hz, 1H), 6.52 (dd, J = 3.5, 1.7 Hz, 1H), 4.33 (t, J = 6.4 Hz, 2H), 4.16−4.10 (m, 1H), 2.70−2.60 (m, 1H), 2.60−2.50 (m, 1H), 1.97−1.87 (m, 1H), 1.86−1.68 (m, 4H), 1.65−1.55 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 158.8, 146.4, 144.8, 125.3 (q, ^1J(C, F) = 277.6 Hz), 118.0, 111.9, 64.5, 54.0 (q, ^3J(C, F) = 3.0 Hz), 42.5 (q, ^2J(C, F) = 28.5 Hz), 37.6, 28.1, 22.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2963, 2361, 2343, 1718, 1261, 1079, 1016, 800, 669 cm^{-1}. HRMS-ESI (*m*/*z*): $[M + H]^+$ calcd for $C_{12}H_{14}ClF_3O_3$, 299.0662; found: 299.0661.

*5-Chloro-7,7,7-trifluoroheptan-1-ol (**3s**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1s** (0.50 mmol, 50.1 mg) reacted to **3s** (53.2 mg, 52% yield, colorless oil), which was purified by silica gel chromatography (PE/EA = 10:1). Reaction time: 24 h. ^1H NMR (400 MHz, $CDCl_3$) δ 4.16−4.08 (m, 1H), 3.66 (t, J = 5.8 Hz, 2H), 2.70−2.48 (m, 2H), 1.92−1.74 (m, 2H), 1.68−1.50 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 125.3 (q, ^1J(C, F) = 277.5 Hz), 62.4, 54.1 (q, ^3J(C, F) = 3.1 Hz), 42.4 (q, ^2J(C, F) = 28.4 Hz), 37.8, 31.8, 22.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.3 Hz). IR (KBr): 3346, 2944, 2360, 2341, 1391, 1269, 1242, 1146, 1075, 666, 631 cm^{-1}. HRMS-ESI (*m*/*z*): $[M + H]^+$ calcd for $C_7H_{12}ClF_3O$, 205.0607; found: 205.0609.

*4-((3-Chloro-5,5,5-trifluoropentyl)oxy)benzaldehyde (**3t**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1t** (0.50 mmol, 88.1 mg) reacted to **3t** (61.7 mg, 44% yield, yellow oil), which was purified by silica gel chromatography (PE/EA = 50:1). Reaction time: 24 h. ^1H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 7.88−7.83 (m, 2H), 7.05−6.99 (m, 2H), 4.48−4.40 (m, 1H), 4.34−4.21 (m, 2H), 2.80−2.60 (m, 2H), 2.47−2.38 (m, 1H), 2.22−2.11 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 189.7, 162.4, 131.0, 129.3, 124.1 (q, ^1J(C, F) = 277.6 Hz), 113.7, 63.2, 49.7 (q, ^3J(C, F) = 3.3 Hz), 41.6 (q, ^2J = 28.7 Hz), 36.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2917, 2848, 2360, 2342, 1685, 1601, 1509, 1258, 1156, 830, 616 cm^{-1}. HRMS-ESI (*m*/*z*): $[M + H]^+$ calcd for $C_{12}H_{12}ClF_3O_2$, 281.0556; found: 281.0558.

*5,7,7,7-Tetrafluoroheptyl Benzoate (**4a**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1a** (0.50 mmol, 102.1 mg) reacted to **4a** (74.5 mg, 51% yield, colorless oil), which was purified by silica gel chromatography (PE/EA = 250:1). Reaction time: 24 h. ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 6.8 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 4.99−4.72 (m, 1H), 4.32 (t, J = 6.5 Hz, 2H), 2.51−2.43 (m, 1H), 2.43−2.28 (m, 1H), 2.00−1.59 (m, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 167.4, 133.7, 131.1, 130.3, 129.1, 126.2 (dd, ^1J(C, F) = 274.9, ^3J(C, F) = 3.2 Hz), 88.2 (dq, ^1J(C, F) = 171.3 Hz, ^3J(C, F) = 3.4 Hz), 65.2, 40.2 (dq, ^2J(C, F) = 28.3, ^3J(C, F) = 5.3 Hz), 35.4 (d, ^2J(C, F) = 21.0), 29.1, 22.1 (d, ^3J(C, F) = 4.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −64.1 (m, 3F), −182.4 (m, 1F).[21]

*2-(5,7,7,7-Tetrafluoroheptyl)isoindoline-1,3-dione (**4k**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1k** (0.50 mmol, 114.6 mg) reacted to **4k** (76.1 mg, 48% yield, white solid, m.p. = 94−95 °C), which was purified by silica gel chromatography (PE/EA = 250:1). Reaction time: 24 h. ^1H NMR (400 MHz, $CDCl_3$) δ 7.91−7.80 (m, 2H), 7.78−7.68 (m, 2H), 4.92−4.66 (m, 1H), 3.69 (t, J = 7.0 Hz, 2H), 2.64−2.43 (m, 1H), 2.43−2.16 (m, 1H), 1.86−1.44 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.4, 134.9, 133.0, 126.4 (qd, ^1J(C, F) = 276.2 Hz, ^3J(C, F) = 3.3 Hz), 124.2, 88.3(dq, ^1J(C, F) = 171.6 Hz, ^3J(C, F) = 3.4 Hz), 40.3 (qd, ^2J(C, F) = 27.7, ^2J(C, F) = 22.5 Hz), 38.5, 35.4 (d, ^2J(C, F) = 20.8 Hz), 29.1, 22.9 (d, ^3J(C, F) = 5.1 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ −64.04 to −64.32 (m, 3F), −181.94 to −182.73 (m, 1F).[21]

*(2,4,4,4-Tetrafluorobutyl)benzene (**4v**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1v** (0.50 mmol, 59.1 mg) reacted to **4v** (61.9 mg, 60% yield, colorless oil), which was purified by silica gel chromatography (PE/EA = 250:1). Reaction time: 24 h. ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J

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= 7.1 Hz, 2H), 7.28 (t, J = 7.2 Hz, 1H), 7.22 (t, J = 7.3 Hz, 2H), 5.13−4.93 (m, 1H), 3.16−2.84 (m, 2H), 2.58−2.21 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 135.1(d, ^3J(C, F) = 4.2 Hz), 129.2, 128.5, 127.0, 125.2 (qd, ^1J(C, F) = 273.7, ^3J(C, F) = 2.9 Hz), 87.5 (dq, ^1J(C, F) = 176.8, ^3J(C, F) = 3.4 Hz), 40.9 (d, ^2J(C, F) = 20.8 Hz), 38.3 (qd, ^2J(C, F) = 29.0, ^2J(C, F) = 23.0 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ −63.8 (td, ^3J(F, H) = 10.7, ^4J(F, F) = 7.6 Hz, 3F), −179.7 (m, 1F).[20]

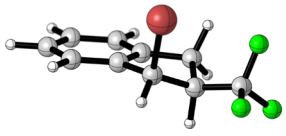
*(2,4,4,4-Tetrafluorobutyl)cyclohexane (**4w**).* Following the general procedure for halotrifluoromethylation described in this experiment, **1w** (0.50 mmol, 62.1 mg) reacted to **4w** (53.0 mg, 50% yield, colorless oil), which was purified by silica gel chromatography (PE/EA = 250:1). Reaction time: 24 h. ^1H NMR (400 MHz, $CDCl_3$) δ 5.07−4.76 (m, 1H), 2.68−2.39 (m, 1H), 2.36−2.11 (m, 1H), 1.86−0.82 (m, 13H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 125.5 (qd, ^1J(C, F) = 277.9, ^3J(C, F) = 3.2 Hz), 85.8 (dq, ^1J(C, F) = 171.8, ^3J(C, F) = 3.8 Hz), 42.7 (d, ^2J(C, F) = 22.6 Hz), 39.9 (qd, ^2J(C, F) = 28.3, ^2J(C, F) = 23.4 Hz), 33.8, 33.7 (d, ^3J(C, F) = 3.4 Hz), 32.6, 26.4, 26.2, 26.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ −63.92 to −64.16 (m, 3F), −181.18 to −181.70 (m, 1F).[20]

*2-Bromo-4,4,4-trifluoro-2-methylbutyl Benzoate (**6a**).* Following the general procedure for halotrifluoromethylation described in this experiment, **5a** (0.50 mmol, 88.1 mg) reacted to **6a** (107.3 mg, 66% yield, colorless oil), which was purified by silica gel chromatography (PE/EA = 250:1). Reaction time: 24 h. ^1H NMR (500 MHz, $CDCl_3$) δ 8.09−8.05 (m, 2H), 7.63−7.58 (m, 1H), 7.48 (t, J = 7.8 Hz, 2H), 4.58 (d, J = 12.0 Hz, 1H), 4.52 (d, J = 12.0 Hz, 1H), 3.04−2.97 (m, 1H), 2.97−2.89 (m, 1H), 1.98 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 165.5, 133.5, 129.7, 129.4, 128.6, 125.0 (q, ^1J(C, F) = 278.9 Hz), 71.4, 56.1 (q, ^3J(C, F) = 4.5 Hz), 45.0 (q, ^2J(C, F) = 28.4 Hz), 28.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 10.1 Hz). IR (KBr): 2982, 2360, 2341, 1728, 1453, 1380, 1365, 1263, 1144, 1113, 711, 581 cm^{-1}. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{12}H_{12}BrF_3O_2$, 325.0051; found: 325.0054.

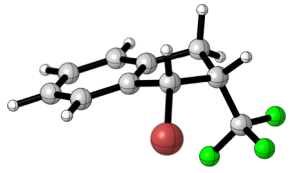
*1-Bromo-2-(trifluoromethyl)-2,3-dihydro-1H-indene (**6b**).* Following the general procedure for halotrifluoromethylation described in this experiment, **5b** (0.50 mmol, 58.1 mg) reacted to **6b** (59.6 mg, 45% yield, light yellow oil), which was purified by silica gel chromatography (PE/EA = 500:1). Reaction time: 24 h. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.34 (m, 1H), 7.25−7.21 (m, 2H), 7.18−7.14 (m, 1H), 5.53 (d, J = 4.7 Hz, 1H), 3.50−3.39 (m, 1H), 3.38−3.29 (m, 1H), 3.10 (dd, J = 16.5, 5.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.3, 138.5, 128.4, 127.0, 125.8 (q, ^1J(C, F) = 280.1 Hz), 124.8, 123.5, 52.6 (q, ^2J(C, F) = 27.6 Hz), 47.6 (q, ^3J(C, F) = 2.7 Hz), 30.5 (q, ^3J(C, F) = 2.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −70.8 (d, ^3J(F, H) = 8.3 Hz). IR (KBr): 2919, 2850, 1464, 1422, 1277, 1213, 1151, 731, 594 cm^{-1}. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{10}H_8BrF_3$, 264.9840; found: 264.9843.

The H vicinal to the CF_3 group of **6b** was found to have only small H,H couplings (<6 Hz), indicating that it is equatorial and the CF_3 group is therefore axial in the major product. All possible conformations were studied computationally, and the ground state energies of each conformation were determined. The results are shown below. The trans diaxial conformation was found to be the lowest energy conformation while the cis conformation bearing an axial CF_3 was found to be 2.64 kcal/mol higher in energy than the cis conformation in which the CF_3 was equatorial. These results support the assignment of the major product as trans.

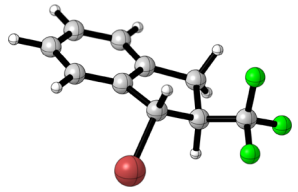
Cis Isomers. CF_3 equatorial: *E*rel,E+ZPE = 1.098 kcal/mol.



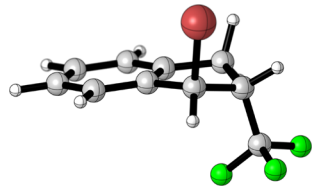
CF_3 axial: *E*rel,E+ZPE = 3.740 kcal/mol.



Trans Isomers. CF_3 equatorial: *E*rel,E+ZPE = 0.464 kcal/mol.



CF_3 axial: *E*rel,E+ZPE = 0.000 kcal/mol

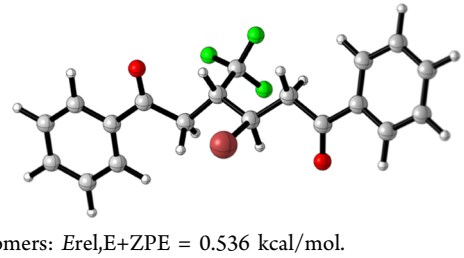


*2-Bromo-3-(trifluoromethyl)butane-1,4-diyl Dibenzoate (**6c**).* Following the general procedure for halotrifluoromethylation described in this experiment, **5c** (0.50 mmol, 148.2 mg) reacted to **6c** (155.8 mg, 70% yield, white solid, m.p. = 73−74 °C), which was purified by silica gel chromatography (PE/EA = 30:1). Reaction time: 24 h. ^1H NMR (400 MHz, $CDCl_3$) δ 8.02−7.97 (m, 4H), 7.61−7.54 (m, 2H), 7.43 (q, J = 7.5 Hz, 4H), 4.84−4.74 (m, 3H), 4.70−4.65 (m, 2H), 3.28−3.20 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 165.8, 165.5, 133.6, 133.5, 129.7, 129.7, 129.1, 129.0, 128.6, 125.3 (d, ^1J(C, F) = 282.8 Hz), 65.6, 60.5 (q, ^3J(C, F) = 2.0 Hz), 44.7 (q, ^2J(C, F) = 26.6 Hz), 43.1 (q, ^3J(C, F) = 2.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −65.4 (d, ^3J(F, H) = 8.5 Hz). IR (KBr): 2917, 1726, 1602, 1452, 1267, 1177, 1110, 709, 686 cm^{-1}. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{19}H_{16}BrF_3O_4$, 445.0262; found: 445.0264.

*Data of **6c′**.* ^1H NMR (400 MHz, $CDCl_3$) δ 8.09−7.99 (m, 4H), 7.63−7.55 (m, 2H), 7.49−7.40 (m, 4H), 4.82−4.71 (m, 4H), 4.71−4.62 (m, 1H), 3.39−3.25 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 165.8, 165.7, 133.6, 133.6, 129.8, 129.7, 129.1, 129.0, 128.6, 125.2 (d, ^1J(C, F) = 282.8 Hz), 65.8, 60.0 (q, ^3J(C, F) = 2.8 Hz), 46.8 (q, ^2J(C, F) = 26.2 Hz), 42.9 (d, ^3J(C, F) = 1.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −65.4 (d, ^3J(F, H) = 8.5 Hz). IR (KBr): 2926, 1724, 1602, 1452, 1266, 1175, 1108, 707, 688 cm^{-1}. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{19}H_{16}BrF_3O_4$, 445.0262; found: 445.0264.

Two possible conformations of **6c** and **6c′** were studied computationally, and the ground state energies were determined. The results are shown below. The **6c** conformation was found to be the lower energy conformation. These results support the assignment of the major product as **6c**.

6c isomers: *E*rel,E+ZPE = 0.000 kcal/mol.



6c′ isomers: *E*rel,E+ZPE = 0.536 kcal/mol.

https://dx.doi.org/10.1021/acs.joc.0c02086
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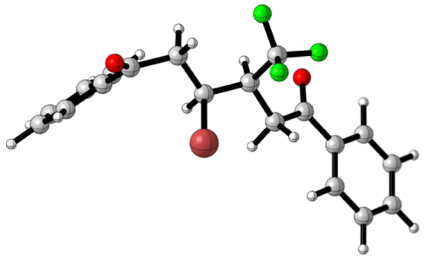

*2-(3-Bromo-3-methyl-2-(trifluoromethyl)butyl)isoindoline-1,3-dione (**6d**).* Following the general procedure for halotrifluoromethylation described in this experiment, **5d** (0.50 mmol, 107.6 mg) reacted to **6d** (136.6 mg, 75% yield, white solid, m.p. = 79−80 °C), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88−7.83 (m, 2H), 7.76−7.72 (m, 2H), 4.35 (dd, J = 14.8, 9.4 Hz, 1H), 4.05 (d, J = 14.7 Hz, 1H), 3.30−3.06 (m, 1H), 2.10 (s, 3H), 1.96 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.8, 134.3, 131.9, 125.9 (q, ^1J(C, F) = 283.9 Hz), 123.5, 60.7, 51.5 (q, ^2J(C, F) = 23.8 Hz), 37.5 (q, ^3J(C, F) = 2.7 Hz), 35.4, 32.3 (q, ^3J(C, F) = 2.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.6 (d, ^3J(F, H) = 6.6 Hz). IR (KBr): 2974, 2360, 2342, 1773, 1717, 1400, 1255, 1133, 724, 530 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{14}H_{13}BrF_3NO_2$, 364.0160; found: 364.0164.

*2-(3-Chloro-3-methyl-2-(trifluoromethyl)butyl)isoindoline-1,3-dione (**6e**).* Following the general procedure for halotrifluoromethylation described in this experiment, **5e** (0.50 mmol, 107.6 mg) reacted to **6e** (116.7 mg, 73% yield, white solid, m.p. = 69−70 °C), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, J = 5.5, 3.1 Hz, 2H), 7.74 (dd, J = 5.5, 3.1 Hz, 2H), 4.32 (dd, J = 14.8, 9.3 Hz, 1H), 4.08−4.02 (m, 1H), 3.25−3.15 (m, 1H), 1.90 (s, 3H), 1.78 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.7, 134.2, 131.8, 126.1 (q, ^1J(C, F) = 283.4 Hz), 123.4, 66.9, 50.9 (q, ^2J(C, F) = 23.8 Hz), 35.8, 33.5, 30.3 (q, ^3J(C, F) = 2.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (t, ^3J(F, H) = 6.6 Hz). IR (KBr): 2978, 2360, 2342, 1773, 1717, 1402, 1368, 1255, 1139, 725, 610 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{14}H_{13}ClF_3NO_2$, 320.0665; found: 320.0668.

*3,5,5,5-Tetrafluoro-3-methylpentyl benzoate (**6f**).* Following the general procedure for halotrifluoromethylation described in this experiment, **5f** (0.50 mmol, 95.1 mg) reacted to **6f** (59.8 mg, 43% yield, colorless liquid), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.2 Hz, 2H), 7.50 (t, J = 7.7 Hz, 1H), 7.39 (t, J = 7.7 Hz, 2H), 4.59−4.43 (m, 2H), 2.69−2.49 (m, 2H), 2.35−2.09 (m, 2H), 1.58 (d, J = 21.5 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.1, 134.9, 131.7, 131.3, 130.2, 126.8 (qd, ^1J(C, F) = 277.6, ^3J(C, F) = 8.0 Hz), 94.0 (dd, ^1J(C, F) = 172.2, ^3J(C, F) = 1.6 Hz), 61.7 (d, ^3J(C, F) = 6.6 Hz), 45.0 (qd, ^2J(C, F) = 28.5 Hz, ^2J(C, F) = 23.6 Hz), 40.3(d, ^2J(C, F) = 22.4 Hz), 26.4 (d, ^2J(C, F) = 24.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ −60.73 to −60.94 (m, 3F), −143.13 to −143.86 (m, 1F). The NMR data were in agreement with reported results.[21]

*(3S,4R)-3-(Bromomethyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-pyrrolidine (**8-cis**).* According to the procedure for radical clock experiments, **7** (0.50 mmol, 125.7 mg) reacted to the **8-*cis*** isomer (major) (122.1 mg, 61% yield, white solid, m.p. = 83−84 °C), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 7.9 Hz, 2H), 3.50−3.37 (m, 3H), 3.26−3.21 (m, 1H), 3.18−3.12 (m, 1H), 2.94 (t, J = 9.9 Hz, 1H), 2.64−2.57 (m, 1H), 2.55−2.48 (m, 1H), 2.44 (s, 3H), 2.25−2.15 (m, 1H), 2.00−1.89 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 144.1, 133.5, 130.0, 127.5, 126.3 (q, ^1J(C, F) = 277.1 Hz), 51.3, 51.0, 43.6, 35.6 (q, ^3J(C, F) = 2.9 Hz), 31.8 (q, ^2J(C, F) = 29.0 Hz), 29.9, 21.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ −64.6 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2964, 2923, 2866, 1930, 1597, 1337, 1262, 1159, 1109, 841, 806, 666, 593, 548 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{14}H_{17}BrF_3NO_2S$, 400.0194; found: 400.0198.

*(3R,4R)-3-(Bromomethyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-pyrrolidine (**8-trans**).* According to the procedure for radical clock experiments, **7** (0.50 mmol, 125.7 mg) reacted to the **8-*trans*** isomer (minor) (24.0 mg, 12% yield, white solid, m.p. = 65−66 °C), which was purified by silica gel chromatography (PE/EA = 35:1). Reaction time: 24 h. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 3.64−3.58 (m, 1H), 3.52−3.46 (m, 1H), 3.41−3.37(m, 1H), 3.37−3.31 (m, 1H), 3.25−3.18 (m, 1H), 3.14−3.08 (m, 1H), 3.02−2.96 (m, 1H), 2.46 (s, 3H), 2.33−2.14 (m, 2H), 2.05−1.94 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 143.9, 132.6, 129.8, 127.5, 125.8 (q, ^1J(C, F) = 277.2 Hz), 52.9, 51.4, 45.3, 36.6 (q, ^3J(C, F) = 2.9 Hz), 36.1 (q, ^2J(C, F) = 29.2 Hz), 32.4, 21.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.8 (t, ^3J(F, H) = 10.2 Hz). IR (KBr): 2919, 2850, 2352, 1732, 1600, 1338, 1270, 1156, 1106, 1027, 816, 670, 583, 549 cm^{-1}. HRMS-ESI (m/z): [M + H]$^+$ calcd for $C_{14}H_{17}BrF_3NO_2S$, 400.0194; found: 400.0198.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02086.

Screening of reaction conditions, DFT calculation results, and characterization data for the products (PDF)

Accession Codes

CCDC 1979206 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

Bin Cui − *College of Chemistry and Pharmaceutical Engineering, Hebei University of Science and Technology, Shijiazhuang 050018, People's Republic of China;* orcid.org/0000-0002-0782-1595; Email: cuibin1989@hebust.edu.cn

Authors

Hui Sun − *College of Chemistry and Pharmaceutical Engineering, Hebei University of Science and Technology, Shijiazhuang 050018, People's Republic of China;* orcid.org/0000-0002-9921-7773

Guannan Cui − *College of Chemistry and Pharmaceutical Engineering, Hebei University of Science and Technology, Shijiazhuang 050018, People's Republic of China*

Huijian Shang − *College of Chemistry and Pharmaceutical Engineering, Hebei University of Science and Technology, Shijiazhuang 050018, People's Republic of China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.0c02086

Notes

The authors declare no competing financial interest.

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