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Free-Radical Bromotrifluoromethylation of Olefin via Single-Electron Oxidation of $NaSO_2CF_3$ by $NaBrO_3$

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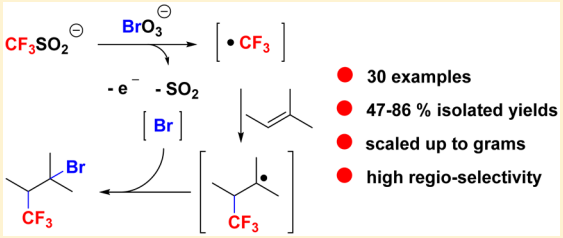
Supporting Information

ABSTRACT: A free-radical bromotrifluoromethylation of olefin by using $NaSO_2CF_3$ and $NaBrO_3$ has been achieved. Sodium bromate acts not only as a single-electron oxidant but also as a bromine source. A radical-clock experiment and electron-spin-resonance detection support a radical process.

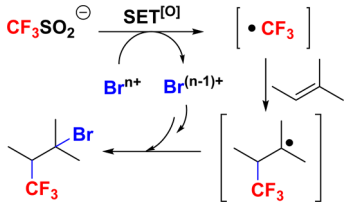


INTRODUCTION

The importance of organofluorine compounds provides an increasing driving force for development of efficient strategy for direct installation of fluorine atom into organic molecules.[1] Among these synthetic methods, halotrifluoromethylation of alkenes represents one of the most effective accesses to fluorinated compounds.[2] Along with the trifluoromethyl (CF_3) group,[3−5] introduction of a halogen atom allows versatile transformations for further manipulations. Therefore, various strategies for halotrifluoromethylation have been explored in the past decades.[6] However, most of these studies focus on iodotrifluoromethylation.[7] Only a few protocols have been successfully achieved to introduce halogen atoms such as Cl and Br. Traditional halotrifluoromethylation suffers from complex operations with gaseous $BrCF_3$ and/or CF_3SO_2Br[8] and ICF_3.[9] Hence, more convenient and practical strategies for halotrifluoromethylation are highly desirable.

Recently, we developed an efficient iodotrifluoromethylation by using sodium trifluoromethanesulfinate ($NaSO_2CF_3$, Langlois reagent) and iodine pentoxide (I_2O_5).[10] The radical CF_3 is generated through single-electron oxidation of $NaSO_2CF_3$ by a safe and cheap I(V) reagent (I_2O_5), which also acts as a donor of iodine atom. A wide range of molecules such as alkenes, alkynes, and enynes have been successfully iodotrifluoromethylated via this strategy. In continuation of this work, we began to envision whether a proper hypervalent bromide could not only oxidize CF_3-derivatived anion to CF_3 radical but also supply a bromine atom, and subsequently, an efficient radical bromotrifluoromethylation of alkenes would be achieved (Scheme 1). Fortunately, we found this hypervalent bromide reagent and explored an efficient approach for bromotrifluoromethylation of alkenes.

Scheme 1. Hypotheses of Radical Bromotrifluoromethylation



RESULTS AND DISCUSSION

In order to test the hypotheses, a series of optimizing experiments were carried out (Table 1). Several bromides were screened, and sodium bromate ($NaBrO_3$) was found to be the most effective reagent (entries 1−3). Then the amount of $NaSO_2CF_3$ and the oxidant, the temperature, and the solvent were examined (entries 4−8). Finally, the corresponding product was isolated in 85% yield through careful modification (entry 7).

As depicted in Table 2, a wide range of unactivated alkenes can give β-CF_3 alkyl bromate as the major products in moderate to high yields under the typical reaction conditions. Various functional groups such as halogens (Cl, Br), NO_2, sulfonate, sulfamide, carboxylate, aldehyde, ether, carbonyl, hydroxyl, and epoxides can be well-tolerated in this system (**1**−**19**). It is noteworthy that the bromotrifluoromethylation occurs selectively at the less hindered and relatively electron-rich position (**16** and **17**). Additionally, nonterminal alkenes are also compatible with this approach (**20** and **21**). In the case of a trisubstituted olefin, the desired product was isolated with

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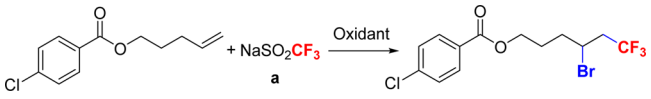
Table 1. Modification of the Typical Reaction Conditions[a]



entry	a (equiv)	oxid (equiv)	T (°C)	sol (mL) DCM/H2O	yield[b] (%)
1	3	$NaBrO_3$(1.5)	90	2.5/1(3.5)	45
2	3	$KBrO_3$ (1.5)	90	2.5/1(3.5)	45
3	3	NaBrO(1.5)	90	2.5/1(3.5)	NR
4	3	$NaBrO_3$ (3)	90	2.5/1(3.5)	57
5	3	$NaBrO_3$(1.5)	110	4/1(3.5)	60
6	3	$NaBrO_3$(2.5)	110	4/1(3.5)	69
7	**5**	**$NaBrO_3$(2.5)**	**110**	**4/1(10)**	**85**
8	5	$NaBrO_3$(2.5)	100	4/1(10)	70

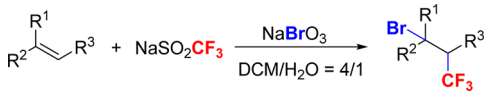
[a]Reaction conditions: pent-4-en-1-yl 4-chlorobenzoate (1 equiv, 0.2 mmol), 24 h, sealed tube. [b]Isolated yields.

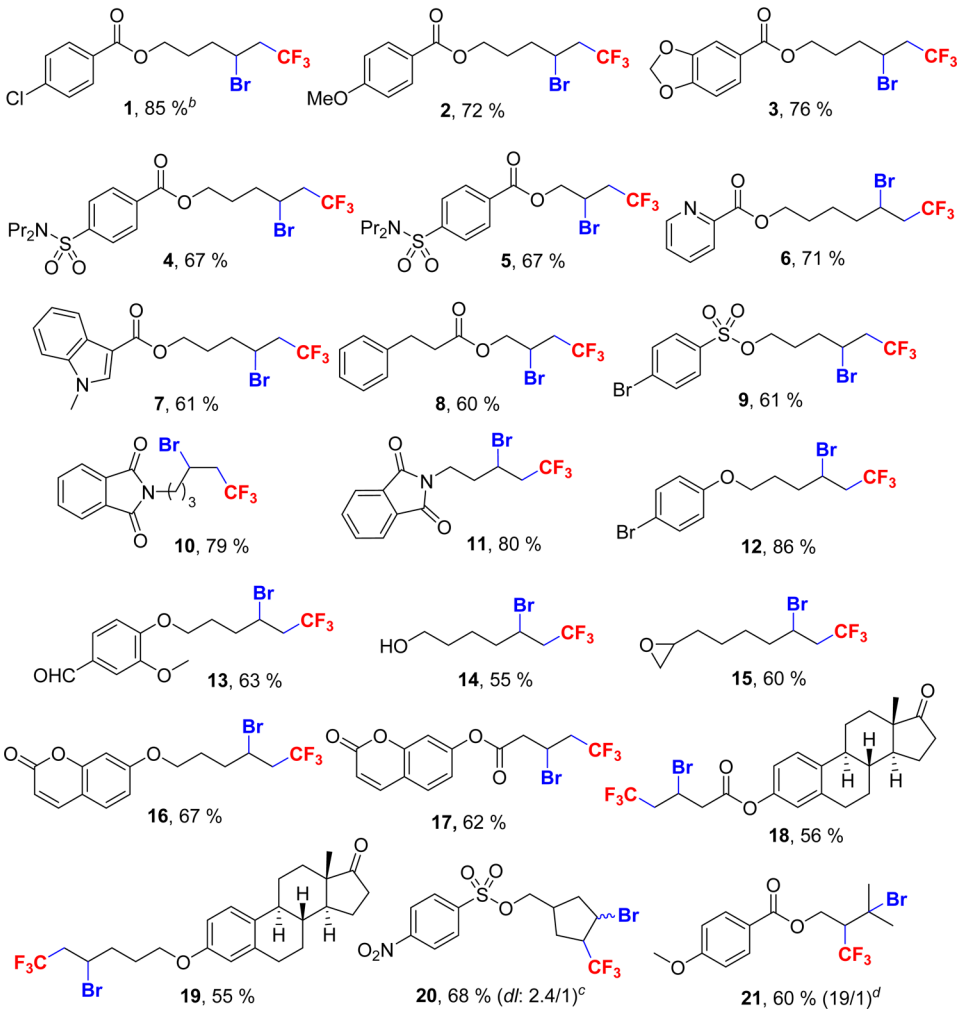
excellent regioselectivity (**21**), which should be due to the stability of the radical intermediate and steric effect.

Furthermore, we found that styrene and its derivatives are also amenable to this system (Table 3). Substrates with both electron-donating and electron-withdrawing groups in the aromatic core gave a moderate to good yield of the corresponding products (**22**−**28**). An addition/elimination product was obtained with indene (**29**). Finally, a large-scale experiment was carried out, and we found that this reaction can be easily scaled up to a gram level (eq 1). It is interesting that the scaled-up reaction (5 mmol, 1.1 g, 7.5 h, 80% isolated yield) is even more efficient than that at the 0.2 mmol scale (44 mg, 24 h, 72% isolated yield, Table 2, **2**), which indicates that this method could be potentially applied in chemical industry.

As demonstrated in Figure 1, the products β-CF_3 alkyl bromates are useful synthons in synthetic organic chemistry. They can be easily converted into various different compounds such as azide, alkene, borate, alkane, etc.

Table 2. $NaBrO_3$-Promoted Bromotrifluoromethylation of Unactivated Alkenes[a]





[a]Reaction conditions: alkene (1 equiv, 0.2 mmol), $NaSO_2CF_3$ (5 equiv, 1.0 mmol), $NaBrO_3$ (2.5 equiv, 0.5 mmol), CH_2Cl_2/H_2O (4/1, 10 mL), 110 °C, sealed tube. [b]Isolated yields. [c]Obtained as a mixture of diastereoisomers. The ratio of the major two isomers was determined by ^{19}F NMR spectroscopy. [d]A regioselective isomer was obtained, and the ratio was determined by ^{19}F NMR spectroscopy.

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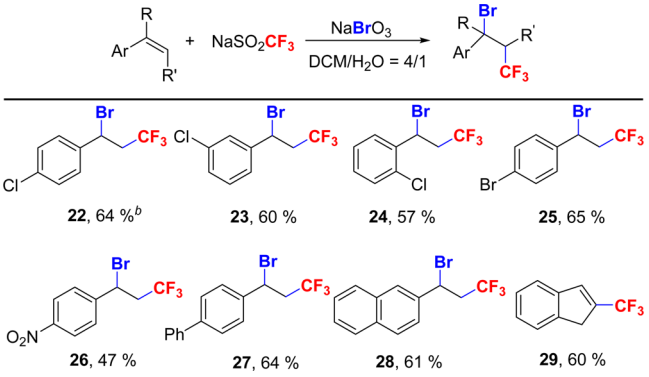
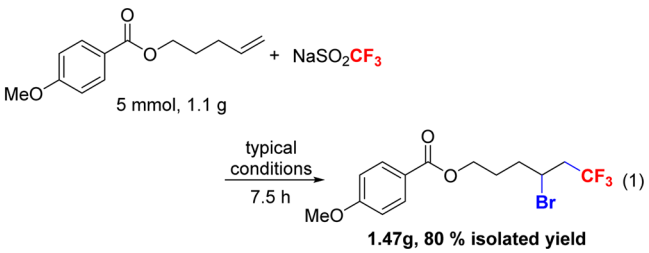
Table 3. $NaBrO_3$-Promoted Bromotrifluoromethylation of Styrenes[a]



[a]Reaction conditions: styrene (1 equiv, 0.2 mmol), $NaSO_2CF_3$ (5 equiv, 1.0 mmol), $NaBrO_3$ (2.5 equiv, 0.5 mmol), CH_2Cl_2/H_2O (4/1, 10 mL), 110 °C, sealed tube. [b]Isolated yields.



In order to investigate the mechanism, a set of mechanistic studies involving radical-clock experiments and electron-spin-resonance (ESR) detection combined with spin-trapping technology were carried out (Scheme 2 and Figure 2). It can be seen from Scheme 2 that (2-vinylcyclopropyl)methyl 4-chlorobenzoate gave the corresponding ring-opening product (**30**) in 72% yield. The CF_3 radical would be formed through one-electron oxidation of $NaSO_2CF_3$ by $NaBrO_3$. It adds to the double bond followed by ring opening of cyclopropane to generate a β-allylic C-centered radical. As expected, the ESR signal of the radical adduct of radical CF_3 to 2-methyl-2-nitrosopropane (MNP) was clearly recorded, which should belong to trifluoromethyl *tert*-butyl nitroxide (Figure 2a, g = 2.0074, $a_N = a_F$ = 12.25 G).[10a] Furthermore, the secondary β-CF_3 carbon-centered radical was also trapped by MNP, and the corresponding adduct was detected by ESR (Figure 2b, g = 2.0073, a_N = 14.65 G, a_H = 4.92 G).[10a] In fact, the last bromination step is not very clear at this point. One possible pathway is bromine atom abstraction by β-CF_3-C-centered radical from Br_2, which is observed in the system. However, another process involving one-electron oxidation of β-CF_3-C-centered radical to give a carbocation followed by Br anion addition cannot be ruled out, especially in the case of styrenes.

CONCLUSIONS

In summary, a radical bromotrifluoromethylation of alkenes by using two simple salts ($NaSO_2CF_3$ and $NaBrO_3$) was developed. Sodium bromate plays dual roles in this process. It not only acts as a one electron oxidant that converts the SO_2CF_3 anion to radical CF_3 but also provides the bromine atom. Through this strategy, two useful functional groups (CF_3 and Br) can be simultaneously installed into a wide range of organic molecules.

EXPERIMENTAL SECTION

General Information. All chemicals were commercially available and used as received without further purification. Reactions were monitored by thin-layer chromatography (TLC). ^1H, ^{13}C, and ^{19}F NMR spectra were recorded at 400, 100, and 375 MHz, respectively. Chemical shifts (δ) are given relative to internal TMS. The NMR data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constant J (Hz), and integration. HRMS spectra (ESI-TOF) were recorded in CH_2Cl_2 or acetonitrile. ESR data were measured on an X-band EPR spectrometer, and the calculated hyperfine splittings g values are obtained by using 2,2-diphenyl-1-picrylhydrazyl as a standard.

1. General Procedure for the Synthesis of (2-Vinylcyclopropyl)methyl 4-Chlorobenzoate. *1.1. General procedure for the synthesis of (Z)-4-Hydroxybut-2-en-1-yl 4-chlorobenzoate.* To a solution of 2-Butene-1,4-diol (1.76 g, 20.0 mmol, 2.0 equiv) in dry CH_2Cl_2 was added Et_3N (2.09 mL, 15.0 mmol, 1.5 equiv) and DMAP (122.2 mg, 1.0 mmol, 0.1 equiv) at 0 °C. After subsequent addition of commercially available 4-chlorobenzoyl chloride (1.75 g, 10.0 mmol, 1.0 equiv), the solution was stirred for 3 h at 0 °C. The reaction was quenched with satd $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (hexane/EtOAc = 5/1) to afford (Z)-4-hydroxybut-2-en-1-yl 4-chlorobenzoate (**A**) (70%, 3.16 g) as a white solid.

(Z)-4-Hydroxybut-2-en-1-yl 4-Chlorobenzoate. ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H),

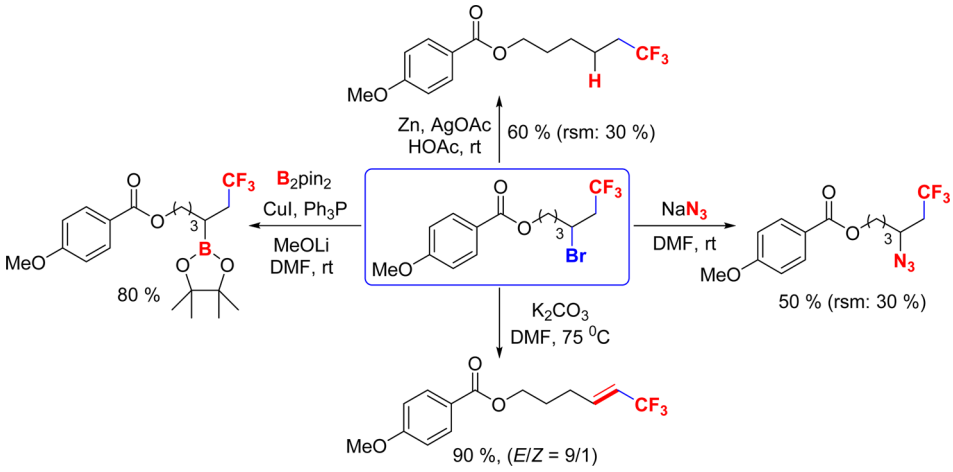


Figure 1. Functional group transformation of the products.

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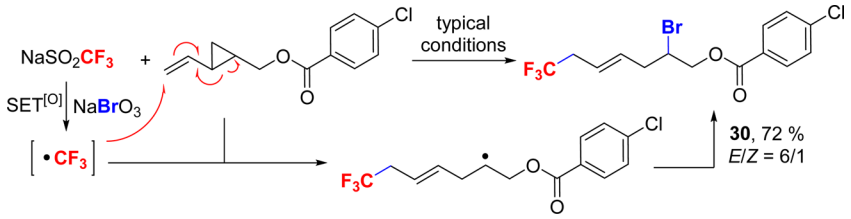
Scheme 2. Radical-Clock Experiment



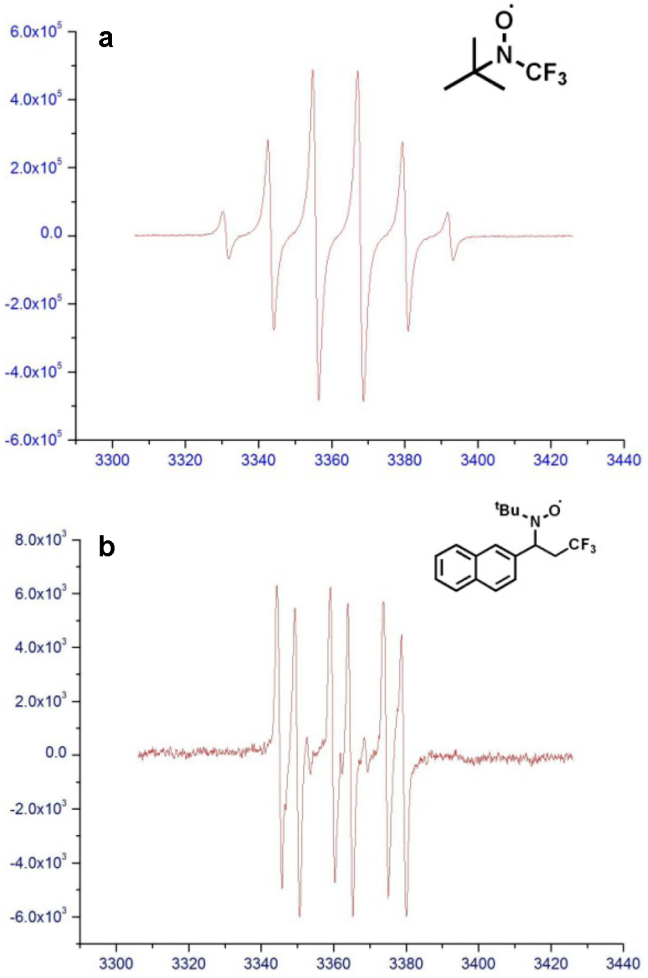


Figure 2. (a) ESR signal of radical trifluoromethyl *tert*-butyl nitroxide radical (g = 2.0074, $a_N = a_F$ = 12.25 G). (b) ESR signal of radical *N*-*tert*-butyl-*N*-(3,3,3-trifluoro-1-(naphthalen-2-yl)propyl) nitroxide (g = 2.0073, a_N = 14.65 G, a_H = 4.92 G).

5.94−5.88 (m, 1H), 5.77−5.70 (m, 1H), 4.92 (d, J = 7.2 Hz, 1H), 4.32 (d, J = 4.8 Hz, 2H), 2.24−2.14 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.8, 139.6, 133.7, 131, 128.7, 128.4, 125.3, 60.8, 58.5. MS(EI): m/z 111 (19.27), 139 (100), 141 (31.34), 223 (16.35), 225 (5.18), 240 (0.69).

1.2. General Procedure for the Synthesis of (2-(Hydroxymethyl)-cyclopropyl)methyl 4-Chlorobenzoate. A solution of **A** (2.26 g, 10.0 mmol) in dry DCM was stirred for 10 min beforea solution of diethylzinc (1 M in hexanes, 100.0 mL) and diiodomethane (8.04 mL, 100.0 mmol) was added dropwise at −10 °C under N_2, the solution was stirred at −10 °C for 60 min, and then the mixture was stirred at 0 °C for 4 h. Saturated aqueous NH_4Cl was added, and the mixture was extracted with brine and DCM. The organic phase was dried over $MgSO_4$ and filtered. The crude product (2-(hydroxymethyl)-cyclopropyl)methyl 4-chlorobenzoate (**B**) was obtained (50%, 1.20 g) as a light yellow oil.

(2-(Hydroxymethyl)cyclopropyl)methyl 4-Chlorobenzoate. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 8.6 Hz, 2H), 7.38 (d, J = 8.6 Hz, 2H), 4.59 (dd, J = 11.9, 5.8 Hz, 1H), 4.13 (dd, J = 11.9, 8.9 Hz, 1H), 3.84 (dd, J = 11.9, 5.7 Hz, 1H), 3.51 (dd, J = 11.8, 8.5 Hz, 1H), 2.33 (s, 1H), 1.41−1.31 (m, 2H), 0.90−0.85 (m, 1H), 0.29 (q, J = 5.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.7, 139.4, 130.9, 128.7, 128.5, 65.4, 62.3, 18.6, 14.4, 7.8. MS(EI): m/z 111 (19.27), 139 (100), 141 (31.34), 223 (16.35), 225 (5.18), 240 (0.69).

1.3. General Procedure for the Synthesis of (2-Formylcyclopropyl)methyl 4-Chlorobenzoate. To a solution of **B** (1.20 g, 5.0 mmol) in dry DCM was added sodium bicarbonate (840 mg, 10.0 mmol) at 0 °C. After addition of Dess−Martin periodinane (4.24 g, 10.0 mmol), the solution was stirred for 4 h at 0 °C. The mixture was purified by silica gel chromatography (hexane/EtOAc = 5/1) to afford (2-formylcyclopropyl)methyl 4-chlorobenzoate (**C**, 70%, 1.0 g) as a light yellow oil.

(2-Formylcyclopropyl)methyl 4-Chlorobenzoate. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.63 (d, J = 4.0 Hz, 1H), 7.93 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 4.77 (dd, J = 12.0, 6.1 Hz, 1H), 4.18 (dd, J = 12.0, 9.2 Hz, 1H), 2.17−2.11 (m, 1H), 2.05−1.95 (m, 1H), 1.43 (dd, J = 11.8, 5.6 Hz, 1H), 1.37−1.33 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 199.8, 165.4, 139.5, 131.0, 128.7, 128.3, 63.2, 26.6, 22.5, 12.9. MS(EI): m/z 111 (21.75), 139 (100), 141 (33.32), 236 (7.36), 238 (2.32).

1.4. General Procedure for the Synthesis of (2-Vinylcyclopropyl)-methyl 4-Chlorobenzoate. A solution of methyltriphenylphosphonium bromide (1.50 g, 4.4 mmol) in anhydrous THF was placed in a flask flushed with nitrogen at −78 °C. To the flask was slowly added 1.75 mL (4.4 mmol) of 2.5 M *n*-butyllithium with stirring. After addition, the reaction mixture was stirred for an additional 30 min, **C** (1.00 g, 3.5 mmol) was added, and the solution was stirred for several hours at 0 °C. The mixture was quenched slowly with saturated aqueous NH_4Cl. The organic and aqueous layers were separated, and the aqueous layer was washed with ether. The ether solutions were combined and dried over anhydrous magnesium sulfate. The crude product (2-vinylcyclopropyl)methyl 4-chlorobenzoate (**D**, 50%, 413 mg) was obtained as a colorless oil.

(2-Vinylcyclopropyl)methyl 4-Chlorobenzoate. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 5.75−5.66 (m, 1H), 5.22−5.18 (m, 1H), 5.08 (dd, J = 10.4, 1.2 Hz, 1H), 4.48 (dd, J = 11.7, 6.9 Hz, 1H), 4.16 (dd, J = 11.7, 8.5 Hz, 1H), 1.78−1.71 (m, 1H), 1.58−1.48 (m, 1H), 1.08−1.03 (m, 1H), 0.63 (q, J = 5.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.8, 139.2, 136.2, 131.0), 128.9, 128.6, 115.7, 65.7, 19.7, 16.8, 10.6. MS(EI): m/z 111 (21.00), 139 (100), 141 (33.78), 196 (1.91), 236 (7.32).

2. Transformation of the Products.

To a solution of the alkyl bromide (1 equiv, 0.20 mmol) in dry DMF was added NaN_3 (8 equiv, 4 times), and the mixture was stirred for 4 h. The reaction mixture was then diluted with DMF, filtered through silica gel with copious washings, concentrated, and purified by column chromatography (hexane/AcOEt = 20/1) to give the corresponding product (50% yield).

*4-Azido-6,6,6-trifluorohexyl 4-Methoxybenzoate (**E**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 50%, 35.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 4.35−4.32 (m, 2H), 3.86 (s, 3H), 3.75−3.69 (m, 1H), 2.41−2.26 (m, 2H), 2.01−1.87 (m, 2H), 1.85−1.68 (m, 2H); ^{19}F NMR (376 MHz,

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$CDCl_3$): δ −64.05 (t, J = 10.5 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.2, 163.5, 131.6, 125.6 (q, J = 277.1 Hz), 122.4, 113.6, 63.7, 56.5 (q, J = 2.7 Hz), 55.4, 38.6 (q, J = 28.3 Hz), 31.4, 25.1. HRMS (ESI, m/z): calcd for $C_{14}H_{16}N_3F_3O_3Na_1$ $(M + Na)^+$ 354.1036, found 354.1032.
To a solution of the alkyl bromide (1 equiv, 0.25 mmol) in dry DMF was added potassium carbonate (2 equiv, 0.5 mmol), and the mixture was stirred at 75 °C for 4 h. The reaction was washed with DCM and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by silica gel chromatography (hexane/AcOEt = 20/1) gave the corresponding product (90% yield).

*(E)-6,6,6-Trifluorohex-4-en-1-yl 4-Methoxybenzoate (**F**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 90%, 51.8 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 6.46−6.41 (m, 1H), 5.72−5.64 (m, 1H), 4.32 (t, J = 6.3 Hz, 2H), 3.86 (s, 3H), 2.34−2.32 (m, 2H), 1.96−1.88 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −58.20 (d, J = 8.6 Hz, 1F), −64.05 (dd, J = 6.3, 2.3 Hz, 9F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.2, 163.4, 139.5 (q, J = 6.5 Hz), 131.5, 122.9 (q, J = 269.2 Hz), 122.5, 119.1 (q, J = 33.4 Hz), 113.6, 63.5, 55.3, 28.1, 27.2. HRMS (ESI, m/z): calcd for $C_{14}H_{15}F_3O_3H_1$ $(M + H)^+$ 289.1046, found 289.1050.
The alkyl bromide (1 equiv, 0.25 mmol), Zn (4 equiv, 65 mg), and AgOAc (0.03 mmol, 5 mg) were mixed together in HOAc (0.5 mL) under vigorous stirring. A 0.05 mL portion of concentrated HCl (37%) was added dropwise over a 1 min period. The mixture was further stirred for 5 min and then filtered. The reaction mixture was then diluted with DCM, filtered through silica gel with copious washings (DCM), concentrated, and purified by column chromatography (hexane/AcOEt = 20/1) to give the corresponding product (60% yield).

*6,6,6-Trifluorohexyl 4-Methoxybenzoate (**G**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 60%, 34.8 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 4.29 (t, J = 6.4 Hz, 2H), 3.86 (s, 3H), 2.16−2.04 (m, 2H), 1.82−1.75 (m, 2H), 1.68−1.60 (m, 2H), 1.56−1.48 (m, 1H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −66.36 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.3, 163.3, 131.5, 127.1 (q, J = 277.3 Hz), 122.6, 113.6, 64.2, 55.4, 33.6 (q, J = 28.4 Hz), 28.4, 25.3, 21.7 (q, J = 2.9 Hz). HRMS (ESI, m/z): calcd for $C_{14}H_{18}F_3O_3$ $(M + H)^+$ 291.1203, found 291.1199.
In air, CuI (4.8 mg, 0. 025 mmol), PPh_3 (8.6 mg, 0.033 mmol), LiOMe (20 mg, 0.5 mmol), and bis(pinacolato)diboron (96.5 mg, 0.38 mmol) were added to a Schlenk tube equipped with a stir bar. The vessel was evacuated and filled with argon (three cycles). DMF (0.5 mL) and the alkyl bromide (0.25 mmol) were added in turn by syringe under an argon atmosphere. The resulting reaction mixture was stirred vigorously at 25 °C for 18 h. The reaction mixture was then diluted with EtOAc, filtered through silica gel with copious washings (Et_2O or EtOAc), concentrated, and purified by column chromatography (hexane/AcOEt = 20/1) to give the corresponding product (80% yield).

*6,6,6-Trifluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-hexyl 4-Methoxybenzoate (**H**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 80%, 66.5 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 8.9 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 4.27 (t, J = 6.4 Hz, 2H), 3.84 (s, 3H), 2.39−2.25 (m, 1H), 2.17−2.04 (m, 1H), 1.82−1.74 (m, 2H), 1.69−1.53 (m, 2H), 1.38−1.23 (m, 1H), 1.23 (s, 12H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.94 (t, J = 11.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.3, 163.3, 131.5, 127.4 (q, J = 277.0 Hz), 122.8, 113.5, 83.6, 64.5, 55.3, 35.0 (q, J = 28.0 Hz), 27.8, 27.3, 24.7, 24.6. HRMS (ESI, m/z): calcd for $C_{20}H_{29}B_1F_3O_5$ $(M + H)^+$ 417.2055, found 417.2060.

Typical Experimental Procedure for the Synthesis of 1−30. A mixture of alkene (1 equiv, 0.2 mmol), $NaSO_2CF_3$ (5 equiv, 1.0 mmol), $NaBrO_3$ (2.5 equiv, 0.5 mmol), and CH_2Cl_2/H_2O (4/1, 10 mL) was heated in a sealed tube at 110 °C for 24 h. After the reaction was complete, it was abstracted by CH_2Cl_2 (3 × 5 mL). The organic layer was dried with anhydrous Na_2SO_4, and the filtrate was evaporated under vacuum and purified by column chromatography to afford the desired product.

*4-Bromo-6,6,6-trifluorohexyl 4-Chlorobenzoate (**1**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 85%, 63.4 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.6 Hz, 2H), 7.41 (d, J = 8.6 Hz, 2H), 4.36 (t, J = 5.6 Hz, 2H), 4.25−4.19 (m, 1H), 2.90−2.64 (m, 2H), 2.14−2.04 (m, 2H), 2.01−1.91 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.79 (t, J = 10.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.6, 139.5, 130.9, 128.7, 128.5, 125.2 (q, J = 278.1 Hz), 64.0, 44.2 (q, J = 3.1 Hz), 43.1 (q, J = 28.5 Hz), 35.0, 26.5. HRMS (ESI, m/z): calcd for $C_{13}H_{13}Br_1Cl_1F_3O_2Na_1$ $(M + Na)^+$ 394.9632, found 394.9631.

*4-Bromo-6,6,6-trifluorohexyl 4-Methoxybenzoate(**2**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 72%, 53.1 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 4.32 (t, J = 5.5 Hz, 2H), 4.24−4.19 (m, 1H), 3.85 (s, 3H), 2.87−2.67(m, 2H), 2.13−2.03 (m, 2H), 2.01−1.90 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.79 (t, J = 10.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.2, 163.4, 131.5, 125.2 (q, J = 278.0 Hz), 122.5, 113.6, 67.9, 63.4, 55.4, 44.3 (q, J = 3.1 Hz), 43.1 (q, J = 28.5 Hz), 35.1, 26.6. HRMS (ESI, m/z): calcd for $C_{14}H_{16}Br_1F_3O_3Na_1$ $(M + Na)^+$ 391.0127, found 391.0135.

*4-Bromo-6,6,6-trifluorohexyl Benzo[d][1,3]dioxole-5-carboxylate (**3**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 76%, 58.2 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, J = 8.2 Hz, 1H), 7.44 (s, 1H), 6.83 (d, J = 8.2 Hz, 1H), 6.03 (s, 2H), 4.32 (t, J = 5.4 Hz, 2H), 4.24−4.18 (m, 1H), 2.89−2.64 (m, 2H), 2.12−2.02 (m, 2H), 1.98−1.89 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.79 (t, J = 10.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.8, 151.7, 147.7, 125.3, 125.2 (q, J = 278.1 Hz), 124.0, 109.4, 108.0, 101.8, 63.7, 44.3 (q, J = 3.1 Hz), 43.1 (q, J = 28.5 Hz), 35.0, 26.6. HRMS (ESI, m/z): calcd for $C_{14}H_{14}Br_1F_3O_4Na_1$ $(M + Na)^+$ 404.9920, found 404.9930.

*4-Bromo-6,6,6-trifluorohexyl 4-(N,N-Dipropylsulfamoyl)benzoate (**4**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 67%, 67.2 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H), 4.40−4.39 (m, 2H), 4.23−4.21 (m, 1H), 3.11−3.07 (m, 4H), 2.86−2.69 (m, 2H), 2.13−2.08 (m, 2H), 1.99−1.93 (m, 2H), 1.57−1.49 (m, 4H), 0.86 (t, J = 7.4 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.76 (t, J = 10.2 Hz, 3F). ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.1, 144.4, 133.3, 130.2, 127.0, 125.1 (q, J = 278.7 Hz), 64.4, 49.9, 44.1, 43.0 (q, J = 28.1 Hz), 34.9, 26.5, 21.9, 11.1. HRMS (ESI, m/z): calcd for $C_{19}H_{28}Br_1F_3O_4N_1S_1$ $(M + H)^+$ 502.0869, found 502.0862.

*2-Bromo-4,4,4-trifluorobutyl 4-(N,N-Dipropylsulfamoyl)benzoate (**5**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 67%, 63.3 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J = 8.5 Hz, 2H), 7.90 (d, J = 8.5 Hz, 2H), 4.64−4.62 (m, 2H), 4.46−4.40 (m, 1H), 3.12−3.08 (m, 4H), 2.96−2.79 (m, 2H), 1.60−1.52 (m, 4H), 0.87 (t, J = 7.4 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.94 (t, J = 10.0 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.4, 144.9, 132.4, 130.4, 127.2, 125.0 (q, J = 277.8 Hz), 67.4, 49.9, 39.9 (q, J = 29.6 Hz), 38.9 (q, J = 3.1 Hz), 21.9, 11.1. HRMS (ESI, m/z): calcd for $C_{17}H_{24}Br_1F_3O_4N_1S_1$ $(M + H)^+$ 474.0556, found 474.0562.

*5-Bromo-7,7,7-trifluoroheptyl Picolinate (**6**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 71%, 50.2 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.75 (d, J = 4.1 Hz, 1H), 8.11 (d, J = 7.8 Hz, 1H), 7.83 (td, J = 7.8, 1.6 Hz, 1H), 7.48−7.45 (m, 1H), 4.42 (t, J = 6.7 Hz, 2H), 4.17−4.10 (m, 1H), 2.82−2.63 (m, 2H), 2.01−1.80 (m, 4H), 1.79−1.53 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.81 (t, J = 10.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.1, 150.0, 148.0, 137.0, 125.2 (q, J = 278.0 Hz), 127.0, 125.1, 65.4, 44.5 (q, J = 3.1 Hz), 43.0 (q, J = 28.5 Hz), 37.9, 28.0, 23.7. HRMS (ESI, m/z): calcd for $C_{13}H_{16}Br_1F_3N_1O_2$ $(M + H)^+$ 354.0311, found 354.0314.

*4-Bromo-6,6,6-trifluorohexyl 1-Methyl-1H-indole-3-carboxylate (**7**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 61%, 47.0 mg). ^1H NMR

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(400 MHz, $CDCl_3$): δ 8.14 (dd, J = 6.4, 2.6 Hz, 1H), 7.79 (s, 1H), 7.38−7.35 (m, 1H), 7.32−7.29 (m, 2H), 4.40−4.36 (m, 2H), 4.28−4.22 (m, 1H), 3.84 (s, 3H), 2.88−2.68 (m, 2H), 2.19−2.07 (m, 2H), 2.05−1.93 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.73 (t, J = 10.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.9, 137.2, 135.3, 126.5, 125.2 (q, J = 278.1 Hz), 122.8, 121.9, 121.5, 109.8, 106.7, 62.4, 44.5 (q, J = 3.1 Hz), 43.1 (q, J = 28.5 Hz), 35.2, 33.5, 26.8. HRMS (ESI, m/z): calcd for $C_{16}H_{17}Br_1F_3N_1O_2Na_1$ $(M + Na)^+$ 414.0287, found 414.0283.

*2-Bromo-4,4,4-trifluorobutyl 3-Phenylpropanoate (**8**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1, yield 60%, 40.6 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.33−7.29 (m, 2H), 7.24−7.21(m, 3H), 4.40−4.26 (m, 2H), 4.25−4.18 (m, 1H), 2.99 (t, J = 7.6 Hz, 2H), 2.74−2.57 (m, 4H); ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.00 (t, J = 10.1 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.0, 139.9, 128.6, 128.2, 126.4, 125.0 (q, J = 278.7 Hz), 66.4, 39.4 (q, J = 29.5 Hz), 38.9 (q, J = 3.2 Hz), 35.5, 30.7. HRMS (ESI, m/z): calcd for $C_{13}H_{14}Br_1F_3O_2Na_1$ $(M + Na)^+$ 361.0021, found 361.0018.

*4-Bromo-6,6,6-trifluorohexyl 4-Bromobenzenesulfonate (**9**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 61%, 55.4 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, J = 8.6 Hz, 2H), 7.71 (d, J = 8.6 Hz, 2H), 4.11−4.09 (m, 3H), 2.83−2.58(m, 2H), 2.01−1.98 (m, 2H), 1.84−1.81 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.76 (d, J = 4.1 Hz, 3F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 134.9, 132.6, 129.3, 129.1, 125.0 (q, J = 278.2 Hz), 69.7, 43.7, 43.0 (q, J = 28.6 Hz), 34.3, 26.8. HRMS (ESI, m/z): calcd for $C_{12}H_{13}Br_2F_3O_3Na_1$ $(M + Na)^+$ 474.8796, found 474.8802.

*2-(4-Bromo-6,6,6-trifluorohexyl)isoindoline-1,3-dione (**10**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 79%, 57.5 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 (dd, J = 5.4, 3.1 Hz, 2H), 7.71 (dd, J = 5.4, 3.1 Hz, 2H), 4.21−4.18(m, J = 7.5 Hz, 1H), 3.74−3.71 (t, J = 6.4 Hz, 2H), 2.83−2.56 (m, 2H), 2.02−1.90 (m, 2H), 1.89−1.82 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.82 (t, J = 10.1 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.3, 134.0, 132.0, 125.1 (q, J = 278.1 Hz), 123.26 (s), 43.9 (q, J = 3.1 Hz), 43.0 (q, J = 28.6 Hz), 36.8, 35.5, 26.4. HRMS (ESI, m/z): calcd for $C_{14}H_{13}Br_1N_1F_3O_2Na_1$ $(M + Na)^+$ 385.9974, found 385.9980.

*2-(3-Bromo-5,5,5-trifluoropentyl)isoindoline-1,3-dione (**11**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 80%, 56.0 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.85 (dd, J = 5.4, 3.0 Hz, 2H), 7.73 (dd, J = 5.4, 3.1 Hz, 2H), 4.19−4.12 (m, 1H), 3.98−3.83 (m, 2H), 2.89−2.71 (m, 2H), 2.40−2.31 (m, 1H), 2.26−2.16 (m, 1H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.60 (t, J = 10.1 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.1, 134.1, 131.9, 125.1 (q, J = 278.2 Hz), 123.4, 42.9 (q, J = 28.7 Hz), 41.0 (q, J = 3.2 Hz), 36.8, 36.1. HRMS (ESI, m/z): calcd for $C_{13}H_{11}Br_1F_3N_1O_2Na_1$ $(M + Na)^+$ 371.9817, found 371.9822.

*1-Bromo-4-((4-bromo-6,6,6-trifluorohexyl)oxy)benzene (**12**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 86%, 66.5 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, J = 9.2 Hz, 2H), 6.81 (d, J = 9.2 Hz, 2H), 4.26−4.19 (m, 1H), 3.99−3.96 (m, 2H), 2.88−2.66 (m, 2H), 2.19−2.03 (m, 2H), 1.98−1.91 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.77 (t, J = 10.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 157.3, 129.3, 125.7, 125.2 (q, J = 279.0 Hz), 115.7, 67.0, 44.5, 43.2 (q, J = 28.5 Hz), 35.2, 27.0. HRMS (ESI, m/z): calcd for $C_{12}H_{14}Br_2F_3O$ $(M + H)^+$ 388.9363, found 388.9365.

*4-((4-Bromo-6,6,6-trifluorohexyl)oxy)-3-methoxybenzaldehyde (**13**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 63%, 46.5 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 9.85 (s, 1H), 7.45−7.41 (m, 2H), 6.96 (d, J = 8.4 Hz, 1H), 4.31−4.25 (m, 1H), 4.20−4.10 (m, 2H), 3.92 (s, 3H), 2.88−2.65 (m, 2H), 2.20−2.11 (m, 2H), 2.07−1.97 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.76 (t, J = 10.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 190.9, 153.7, 149.9, 130.3, 126.6, 125.2 (q, J = 278.1 Hz), 111.6, 109.4, 68.0, 56.0, 44.5 (q, J = 3.2 Hz), 43.1 (q, J = 28.6 Hz), 35.2, 26.8. HRMS (ESI, m/z): calcd for $C_{14}H_{16}Br_1F_3O_3Na_1$ $(M + Na)^+$ 391.0127, found 391.0133.

*5-Bromo-7,7,7-trifluoroheptan-1-ol (**14**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1, yield 55%, 27.3 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 4.17−4.11 (m, 1H), 3.64 (t, J = 5.9 Hz, 2H), 2.85−2.61 (m, 2H), 1.93−1.80 (m, 3H), 1.69−1.47 (m, 4H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.85 (t, J = 9.9 Hz, 3F). ^{13}C NMR (151 MHz, $CDCl_3$): δ 125.3 (q, J = 278.7 Hz), 62.3, 44.9, 43.0 (q, J = 27.6 Hz), 38.2, 31.6, 29.6, 23.5, 22.5. MS(EI): m/z 77 (11.77), 81 (14.43), 87 (12.22), 111 (15.44), 131 (24.19), 151 (100.00), 152 (7.60), 247 (0.04), 249 (0.05). Characterization data matched those reported in the literature.[10a]

*2-(5-Bromo-7,7,7-trifluoroheptyl)oxirane (**15**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1, yield 60%, 33.0 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 4.19−4.12 (m, 1H), 2.94−2.91 (m, 1H), 2.87−2.59 (m, 3H), 2.48 (dd, J = 4.8, 2.8 Hz, 1H), 1.95−1.80 (m, 2H), 1.64−1.46 (m, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.82 (t, J = 10.0 Hz, 3F). ^{13}C NMR (151 MHz, $CDCl_3$): δ 125.2 (q, J = 279.0 Hz), 52.1, 47.0, 44.8, 43.0 (q, J = 28.8 Hz), 38.3, 32.19, 26.9, 25.2. HRMS (ESI, m/z): calcd for $C_9H_{14}Br_1F_3O_1Na_1$ $(M + Na)^+$ 297.0072, found 297.0069.

*7-((4-Bromo-6,6,6-trifluorohexyl)oxy)-2H-chromen-2-one (**16**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1, yield 67%, 49.0 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 9.4 Hz, 1H), 7.36 (d, J = 8.5 Hz, 1H), 6.83−6.78 (m, 2H), 6.23 (d, J = 9.4 Hz, 1H), 4.27−4.22 (m, 1H), 4.07−4.06 (m, 2H), 2.88−2.66 (m, 2H), 2.19−2.13 (m, 2H), 2.05−1.96 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.75 (t, J = 10.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.9, 161.1, 155.8, 143.4, 128.8, 125.2 (q, J = 278.0 Hz), 113.2, 112.8, 112.6, 101.3, 67.3, 44.4 (q, J = 3.1 Hz), 43.1 (q, J = 28.5 Hz), 35.1, 26.9. HRMS (ESI, m/z): calcd for $C_{15}H_{15}Br_1F_3O_3$ $(M + H)^+$ 379.0151, found 379.0154.

*2-Oxo-2H-chromen-7-yl 3-bromo-5,5,5-trifluoropentanoate (**17**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 62%, 46.7 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 9.6 Hz, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.16−7.14 (m, 1H), 7.09−7.07 (m, 1H), 6.41 (d, J = 9.6 Hz, 1H), 4.62−4.55 (m, 1H), 3.37 (dd, J = 16.7, 4.8 Hz, 1H), 3.21 (dd, J = 16.7, 8.8 Hz, 1H), 2.97−2.87 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.77 (t, J = 10.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.2, 160.1, 154.6, 152.5, 142.7, 128.7, 124.9 (q, J = 278.2 Hz), 118.2, 117.0, 116.4, 110.3, 43.1, 42.1 (q, J = 29.1 Hz), 36.69−36.63 (m). HRMS (ESI, m/z): calcd for $C_{14}H_{11}Br_1F_3O_4$ $(M + H)^+$ 378.9787, found 378.9790.

*(8R,9S,13S,14S)-13-Methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl 3-Bromo-5,5,5-trifluoropentanoate (**18**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1, yield 56%, 53.5 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, J = 8.4 Hz, 1H), 6.89−6.84 (m, 2H), 4.60−4.56 (m, 1H), 3.29 (dd, J = 16.5, 5.1 Hz, 1H), 3.17 (dd, J = 16.5, 8.4 Hz, 1H), 2.96−2.87 (m, 4H), 2.54−1.95 (m, 8H), 1.68−1.43 (m, 5H), 0.91 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.79 (t, J = 10.0 Hz, 3F). ^{13}C NMR (151 MHz, $CDCl_3$): δ 220.6, 168.1, 148.1, 138.2, 137.8, 126.5, 125.0 (q, J = 278.2 Hz), 121.3, 118.5, 50.4, 47.9, 44.1, 43.3, 42.1 (q, J = 29.1 Hz), 37.9, 37.0 (q, J = 3.2 Hz), 35.8, 31.5, 29.4, 26.3, 25.7, 21.6, 13.8. HRMS (ESI, m/z): calcd for $C_{23}H_{30}Br_1F_3N_1O_3$ $(M + NH_4)^+$ 504.1358, found 504.1362.

*(8R,9S,13S,14S)-3-((4-Bromo-6,6,6-trifluorohexyl)oxy)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]-phenanthren-17-one(**19**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1, yield 55%, 53.3 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.20 (d, J = 8.8 Hz, 1H), 6.71 (dd, J = 8.5, 2.2 Hz, 1H), 6.65 (s, 1H), 4.26−4.20 (m, 1H), 3.98 (t, J = 5.4 Hz, 2H), 2.92−2.87 (m, 2H), 2.84−2.68 (m, 2H), 2.54−2.47 (m, 1H), 2.42−2.38 (m, 1H), 2.28−2.23 (m, 1H), 2.19−1.89 (m, 9H), 1.71−1.39 (m, 5H), 0.91 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −63.70 (t, J = 10.2 Hz, 3F). ^{13}C NMR (151 MHz, $CDCl_3$): δ 220.1, 156.7, 137.7, 132.2, 126.3, 125.2 (q, J = 278.7 Hz), 114.5, 120.0, 66.6, 50.3, 47.9, 44.7, 43.9, 43.1 (q, J = 28.8 Hz), 38.9, 35.8,

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35.3, 31.5, 29.6, 27.1, 26.5, 25.9, 21.5, 13.8. HRMS (ESI, m/z): calcd for $C_{24}H_{31}Br_1F_3O_2$ $(M + H)^+$ 487.1454, found 487.1449.

*(3-Bromo-4-(trifluoromethyl)cyclopentyl)methyl 4-Nitrobenzenesulfonate (**20**).* Yellow solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 68%, 58.7 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, J = 8.8 Hz, 6.8H), 8.12 (dd, J = 8.9, 2.5 Hz, 6.8H), 4.43−4.40 (m, 1H), 4.24−4.18 (m, 2.4H), 4.14−4.10 (m, 6.8H), 3.17−3.11 (m, 1H), 3.05−2.98 (m, 2.4H), 2.84−2.80 (m, 1.2H), 2.59−2.42 (m, 5H), 2.31−2.21 (m, 2H), 2.07−1.97 (m, 3.49H), 1.93−1.84 (m, 5H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −71.06 (d, J = 9.2 Hz), −71.23 (d, J = 9.4 Hz). ^{13}C NMR (101 MHz, $CDCl_3$): δ 150.9, 141.5, 129.2, 126.7 (d, J = 278.9 Hz), 124.6, 72.8, 52.5 (q, J = 27.6 Hz), 42.8 (q, J = 2.6 Hz), 40.8, 37.3, 28.2. HRMS (ESI, m/z): calcd for $C_{13}H_{13}Br_1N_1F_3O_5S_1Na_1$ $(M + Na)^+$ 453.9542, found 453.9545.

*3-Bromo-3-methyl-2-(trifluoromethyl)butyl 4-Methoxybenzoate (**21**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1, yield 60%, 44.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 9.0 Hz, 2H), 6.93 (d, J = 9.0 Hz, 2H), 4.83 (dd, J = 12.4, 2.4 Hz, 1H), 4.71 (dd, J = 12.2, 5.8 Hz, 1H), 3.86 (s, 3H), 3.04−2.95 (m, 1H), 2.06 (s, 3H), 1.94 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.78 (d, J = 9.2 Hz), −72.88 (s). ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.6, 163.7, 131.7, 125.6 (q, J = 284.0 Hz), 121.9, 113.7, 62.1, 61.2, 55.4, 54.6 (q, J = 24.4 Hz), 34.8, 32.08. HRMS (ESI, m/z): calcd for $C_{14}H_{17}Br_1F_3O_3$ $(M + H)^+$ 369.0310, found 369.0308.

*1-(1-Bromo-3,3,3-trifluoropropyl)-4-chlorobenzene (**22**).* Colorless oil after purification by flash column chromatography (petroleum ether, yield 64%, 36.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, J = 8.5 Hz, 2H), 7.35 (d, J = 8.5 Hz, 2H), 5.14−5.10 (m, 1H), 3.17−3.03 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.09 (t, J = 9.6 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.6, 134.9, 129.2, 128.5, 124.6 (q, J = 278.3 Hz), 43.9 (q, J = 28.6 Hz), 42.4 (q, J = 3.2 Hz). MS(EI): m/z 103 (12.67), 138 (12.07), 143 (69.37), 145 (22.64), 151 (12.13), 207 (100.00), 209 (32.91), 286 (1.73), 288 (2.41). Characterization data matched those reported in the literature.[10a,11]

*1-(1-Bromo-3,3,3-trifluoropropyl)-3-chlorobenzene (**23**).* Colorless oil after purification by flash column chromatography (petroleum ether, yield 60%, 25.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (s, 1H), 7.32−7.28 (m, 3H), 5.10−5.05 (m, 1H), 3.15−3.02 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.13 (t, J = 9.7 Hz, 3F). ^{13}C NMR (151 MHz, $CDCl_3$): δ 142.0, 134.7, 130.2, 127.3, 126.5 (q, J = 278.7 Hz), 125.3, 123.7, 43.8 (q, J = 28.8 Hz), 42.1. MS(EI): m/z 103 (15.25), 142 (37.70), 143 (83.83), 145 (29.90), 174 (100), 207 (88.04), 209 (28.95). Characterization data matched those reported in the literature.[10a]

*1-(1-Bromo-3,3,3-trifluoropropyl)-2-chlorobenzene (**24**).* Colorless oil after purification by flash column chromatography (petroleum ether, yield 57%, 23.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (dd, J = 7.8, 1.4 Hz, 1H), 7.38 (dd, J = 7.8, 1.4 Hz, 1H), 7.32 (td, J = 7.6, 1.2 Hz, 1H), 7.28−7.23 (m, 1H), 5.70 (t, J = 7.2 Hz, 1H), 3.18−3.09 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.28 (t, J = 9.7 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.4, 132.5, 130.1, 130.1, 128.8, 127.6, 124.7 (q, J = 278.5 Hz), 42.8 (q, J = 28.8 Hz), 38.7 (q, J = 3.1 Hz). MS(EI): m/z 125 (17.48), 143 (54.81), 161 (16.06), 187 (22.90), 207 (100), 209 (31.60). Characterization data matched those reported in the literature.[10a]

*1-Bromo-4-(1-bromo-3,3,3-trifluoropropyl)benzene (**25**).* Colorless oil after purification by flash column chromatography (petroleum ether, yield 65%, 43.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 8.5 Hz, 2H), 7.28 (d, J = 8.5 Hz, 2H), 5.12−5.08 (m, 1H), 3.17−3.00 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.09 (t, J = 9.8 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.1, 132.2, 128.7, 124.6 (d, J = 278.5 Hz), 123.0, 43.9 (q, J = 28.6 Hz), 42.4 (q, J = 3.3 Hz). MS(EI): m/z 77 (17.53), 102 (11.14), 103 (15.64), 151 (20.87), 152 (14.86), 172 (15.41), 187 (61.03), 189 (57.46), 251 (100), 253 (87.76), 332 (3.94). Characterization data matched those reported in the literature.[10a,12]

*1-(1-Bromo-3,3,3-trifluoropropyl)-4-nitrobenzene (**26**).* Slight yellow solid after purification by flash column chromatography (petroleum ether, yield 47%, 27.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, J = 8.8 Hz, 2H), 7.59 (d, J = 8.7 Hz, 2H), 5.19−5.16 (m, 1H), 3.21−3.07 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.05 − −63.98 (m, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 148.0, 146.7, 128.2, 124.4 (q, J = 278.5 Hz), 124.2, 43.7 (q, J = 28.8 Hz), 41.0 (q, J = 3.4 Hz). HRMS (ESI, m/z): calcd for $C_9H_7Br_1F_3O_2N_1Na_1$ $(M + Na)^+$ 319.9504, found 319.9512.

*4-(1-Bromo-3,3,3-trifluoropropyl)-1,1′-biphenyl (**27**).* White solid after purification by flash column chromatography (petroleum ether, yield 64%, 42.2 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61−7.58 (m, 4H), 7.49−7.44 (m, 4H), 7.39−7.36 (m, 1H), 5.24−5.22 (m, 1H), 3.23−3.11 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.08 (t, J = 9.8 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 142.0, 140.1, 139.0, 128.8, 127.7, 127.6, 127.5, 127.1, 124.7 (q, J = 278.3 Hz), 43.8 (q, J = 28.4 Hz), 43.3 (q, J = 3.3 Hz). MS(EI): m/z 92 (10.79), 165 (19.85), 178 (18.57), 180 (16.30), 185 (9.86), 248 (19.87), 249 (100.00), 328 (2.67), 330 (2.41). Characterization data matched those reported in the literature.[10a,11]

*2-(1-Bromo-3,3,3-trifluoropropyl)naphthalene (**28**).* White solid after purification by flash column chromatography (petroleum ether, yield 61%, 37.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90−7.83 (m, 4H), 7.56−7.51 (m, 3H), 5.36 (t, J = 7.2 Hz, 1H), 3.28−3.19 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.09 (t, J = 9.7 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.2, 133.4, 132.9, 129.2, 128.1, 127.8, 126.9, 126.8, 126.1, 124.8 (q, J = 277.9 Hz), 124.3, 44.0 (q, J = 3.3 Hz), 43.8 (q, J = 28.4 Hz). MS(EI): m/z 152 (19.71), 153 (21.20), 154 (22.28), 159 (28.29), 183 (24.60), 223 (100.00), 302 (8.43), 304 (7.87). Characterization data matched those reported in the literature.[10a,11]

*2-(Trifluoromethyl)-1H-indene (**29**).* Colorless oil after purification by flash column chromatography (petroleum ether, yield 60%, 22.0 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53−7.49 (m, 2H), 7.36−7.33 (m, 2H), 7.32−7.30 (m, 1H), 3.63 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.08 (d, J = 1.0 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.0, 141.7, 134.9, 134.6 (q, J = 5.2 Hz), 127.1, 127.0, 124.2, 123.2 (q, J = 268.1 Hz), 122.9, 36.8. MS(EI): m/z 57 (100), 81 (47.52), 125 (29.99), 151 (16.10), 168 (18.57), 184 (72.17). Characterization data matched those reported in the literature.[10a,13]

*2-Bromo-7,7,7-trifluorohept-4-en-1-yl 4-Chlorobenzoate(**30**).* Colorless oil after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1, yield 72%, 55.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 8.5 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 5.83−5.54 (m, 2H), 4.58−4.49 (m, 2H), 4.29−4.23 (m, 2H), 2.91−2.75 (m, 3H), 2.71−2.64 (m, 1H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −65.97 (t, J = 10.7 Hz), −66.44 (t, J = 10.6 Hz). ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.0, 139.9, 132.9, 131.1, 128.9, 125.7(q, J = 277.1 Hz), 122.3, 67.5, 49.0, 38.2, 37.3(q, J = 29.9 Hz), 33.1. HRMS (ESI, m/z): calcd for $C_{14}H_{14}Br_1Cl_1F_3O_2$ $(M + H)^+$ 384.9815, found 384.9812.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02812.

^{1}H, ^{19}F, and ^{13}C NMR spectra for all reaction products (PDF)

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Notes

The authors declare no competing financial interest.

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