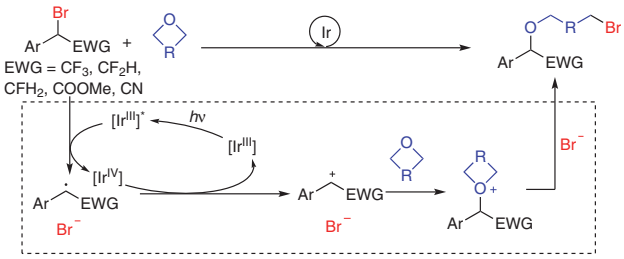
Synthesis C. Kuang et al. Feature

Photoredox-Catalyzed Ring-Opening Addition Reaction between Benzyl Bromides and Cyclic Ethers

Cuiwen Kuang[a]
Chuanfa Ni[a]
Yucheng Gu[b]
Jinbo Hu[*a]

[a] Key Laboratory of Organofluorine Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Shanghai 200032, P. R. of China
jinbohu@sioc.ac.cn
[b] Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire RG42 6EY, U.K.



Received: 21.09.2021
Accepted: 18.10.2021
Published online: 18.10.2021
DOI: 10.1055/a-1671-6856; Art ID: ss-2021-z0566-fa

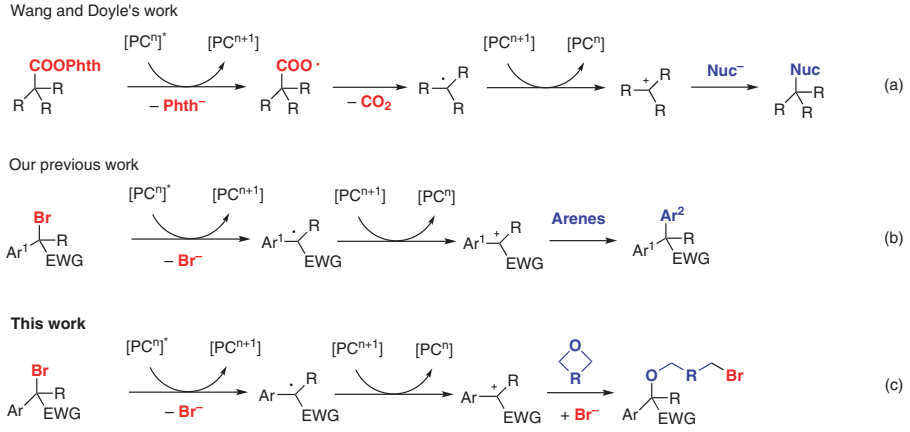
Abstract A novel nucleophilic reaction between cyclic ethers and benzyl bromides is achieved under photoredox catalysis. The reaction proceeds through a single-electron-transfer (SET) pathway rather than a common S_N2 mechanism. By two steps of reduction and oxidation, a benzyl bromide heterolyzes to give a carbocation and bromide ion under mild conditions, and then a cyclic ether captures both the carbocation and bromide ion to afford the addition product.

Key words photoredox catalysis, carbocation, cyclic ether, benzyl bromide, ring-cleavage addition reaction, fluorine

The last decade has witnessed a rapid progress in the visible-light-promoted photoredox-catalyzed reactions, which enable single-electron-transfer (SET) processes under mild conditions. The radical intermediates generated under photoredox catalysis can react with metal complexes,[1] alkenes,[2] and other radical acceptors,[3] which vastly enriches the radical chemistry. On the other hand, the generation of a carbocation from a radical (via an oxidation step) under photoredox catalysis is rare.

Recently, the groups led by Wang[4] and Doyle[5] reported the redox-neutral generation of carbocations from *N*-hydroxyphthalimide esters via two SET processes under photoredox catalysis (Scheme 1a). Although carboxylate radicals generated through single-electron reduction of the *N*-hydroxyphthalimide esters are difficult to be oxidized to carboxylate cations, the carbon-centered radicals generated by further decarboxylation could be oxidized smoothly to carbocations.[1b,5,6]

Previously, we reported the generation of carbocations from substituted benzyl bromides by two consecutive reduction and oxidation processes under photoredox catalysis[7] (Scheme 1b). In this reaction, the bromide ion (leaving group) was generated along with the generation of a carbocation. We envisaged that both bromide ion (as a nucleo-



Scheme 1 Two redox-neutral patterns to form carbocation under photoredox catalysis conditions

phile) and carbocation (as an electrophile) could add to one molecule (like cyclic ethers), thus affording a new product with high atom economy (Scheme 1c). Indeed, the ring-opening reaction between alkyl bromides and cyclic ethers is rare,[8,9] although the reaction between acyl halides and cyclic ethers under Lewis acid catalysis has been systematically studied.[10]

Biographical Sketches

Cuiwen Kuang was born in Hubei (P. R. of China) in 1994. He received his B.S. degree in chemistry from Huazhong University of Science and Technology in 2015 and received his Ph.D. in 2020 from Shanghai Institute of Organic Chemistry, Chinese Academy of Science (SIOC, CAS) under the supervision of Professor Jinbo Hu. His doctoral research interests are focused on fluorine-containing radical chemistry.

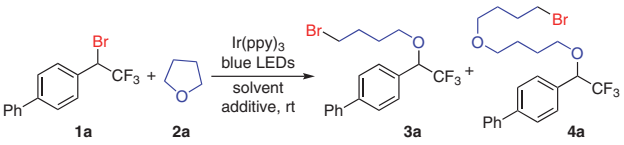
Chuanfa Ni obtained his Ph.D. in chemistry from Shanghai Institute of Organic Chemistry (SIOC) in 2009 under the supervision of Professor Jinbo Hu. After his postdoctoral work (2009–2012) at the University of Southern California (USA) under the supervision of Professor G. K. Surya Prakash, he joined SIOC as an associate research professor. His research interest is the development of new methodologies for the synthesis of fluorinated molecules.

Yu-Cheng Gu received his BSc from Hebei Medical University in 1984 and worked there as a teaching assistant for two years. He then went to China Academy of Traditional Chinese Medicine and graduated in 1989 with a MSc degree under the supervision of Professor Youyou Tu. He joined the China Japan Friendship Hospital as a research associate. In 1994 he went to the UK and received his PhD at Edinburgh Napier University in Scotland in 1998 followed by a postdoc at Huddersfield University in England for three years. In 2002, he joined Syngenta as a natural products chemist and is now a principal technical specialist. His research interests are natural products, biological active compounds, and their applications with over 470 publications in the chemistry and bioscience areas. He has been awarded honorary and visiting professorships from the Chinese Academy of Sciences, Peking Union Medical College and Chinese Academy of Medical Sciences, China Academy of Traditional Chinese Medicine, Hebei Medical University, Nanjing Agricultural University, Central China Normal University, Jilin University, Wuhan Polytechnic University, Hubei Academy of Agricultural Sciences, Shanghai Southern Pesticide Research Centre, and Huanghe University of Science and Technology.

Jinbo Hu was born in Zhejiang (P. R. of China) in 1973. After he completed his B.S. (Hangzhou University) and M.S. (Chinese Academy of Sciences) degrees, he did his Ph.D. work from 1997 to 2002 at the University of Southern California (USA). After postdoctoral work at the same univeristy, he joined Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences (SIOC, CAS) in early 2005 as a research professor. He served as the Head of the CAS Key Laboratory of Organofluorine Chemistry during 2010–2020. He is the recipient of RSC Fluorine Prize 2009, Novartis Chemistry Lectureship 2015, IOCF Lectureship 2019, and ACS Award for Creative Work in Fluorine Chemistry (2022). His current research interests include organofluorine chemistry and functional materials.

At the onset of our investigation, we chose 4-(1-bromo-2,2,2-trifluoroethyl)-1,1′-biphenyl (**1a**) and THF as model reaction partners, and $Ir(ppy)_3$ (5 mol%) as the photoredox catalyst. The reactants and catalyst were dissolved in acetonitrile and stirred at room temperature for 24 hours under irradiation by blue LEDs; the product **3a** was formed in 63% yield (determined by ^{19}F NMR spectroscopy; Table 1, entry 1). Solvent screening showed that neither less polar solvents (CH_2Cl_2 and toluene) nor more polar solvents (DMF and DMSO) were suitable for the reaction (entries 2–4). Although acetonitrile can sometimes react with carbocation intermediates (such as in Ritter reaction), it was still the optimal solvent for the present reaction (entries 1–5). It was found that the addition of $ZnBr_2$ (as additive) promoted the yield, and the equivalents of THF (**2a**) have influence on the yield (entries 6–9). The control experiments without either $Ir(ppy)_3$ catalyst or blue light irradiation demonstrated the necessity of the visible light promoted photoredox catalysis (entries 10, 11). Although the addition of $ZnBr_2$ was beneficial for the yield of desired product **3a**, it also brought about the side product **4a** (entry 12). Obviously, **4a** was generated by the further reaction of carbocation intermediate (as shown in Scheme 1c) with another molecule of THF. Since bromide ions could be trapped by $ZnBr_2$, the concentration of bromide ions decreased so that they were not able to efficiently react with carbocation intermediates. Therefore, we added external bromide ion source (NaBr) into the reaction mixture, and **3a** was obtained in 84% isolated yield (entry 13). It should be noted that, when **3a** was subjected to the $Ir(ppy)_3$-catalyzed photoredox reaction condition with THF, **4a** was not observed and **3a** was recovered quantitatively (Scheme 3a, vide infra). This result suggests that the formation of **4a** does not proceed through **3a** and is likely via carbocationic intermediates.

Table 1 Optimization of Reaction Conditions[a]



Entry	**2a** (equiv)	Additive (equiv)	Solvent	Yield (%)[b]
1	5	none	CH_3CN	63 (**3a**)
2	5	none	DMF	0
3	5	none	DMSO	0
4	5	none	toluene	0
5	5	none	CH_2Cl_2	0
6	5	$ZnBr_2$ (1)	CH_3CN	83[c]
7	4	$ZnBr_2$ (1)	CH_3CN	81[c]
8	3	$ZnBr_2$ (1)	CH_3CN	74[c]
9	2	$ZnBr_2$ (1)	CH_3CN	64[c]
10[d]	5	$ZnBr_2$ (1)	CH_3CN	0
11[e]	5	$ZnBr_2$ (1)	CH_3CN	0
12[f]	5	$ZnBr_2$ (0.5)	CH_3CN	89[c] (51) (**3a**) + (34) (**4a**)
13[f]	5	$ZnBr_2$ (0.5) + NaBr (0.45)	CH_3CN	89[c] (84) (**3a**)

[a] Reaction conditions: unless otherwise mentioned, a mixture of **1a** (0.2 mmol), **2a**, $Ir(ppy)_3$ (1 mol%), additive, and solvent (2 mL) was stirred under irradiation with blue LEDs at rt for 24 h.
[b] Yields were determined by ^{19}F NMR spectroscopy with $PhOCF_3$ as internal standard. Isolated yields are shown in parentheses.
[c] Total yield of **3a** and **4a**.
[d] Without $Ir(ppy)_3$.
[e] Without blue LEDs.
[f] 0.5 mmol scale; 0.5 mol% of $Ir(ppy)_3$ was used.

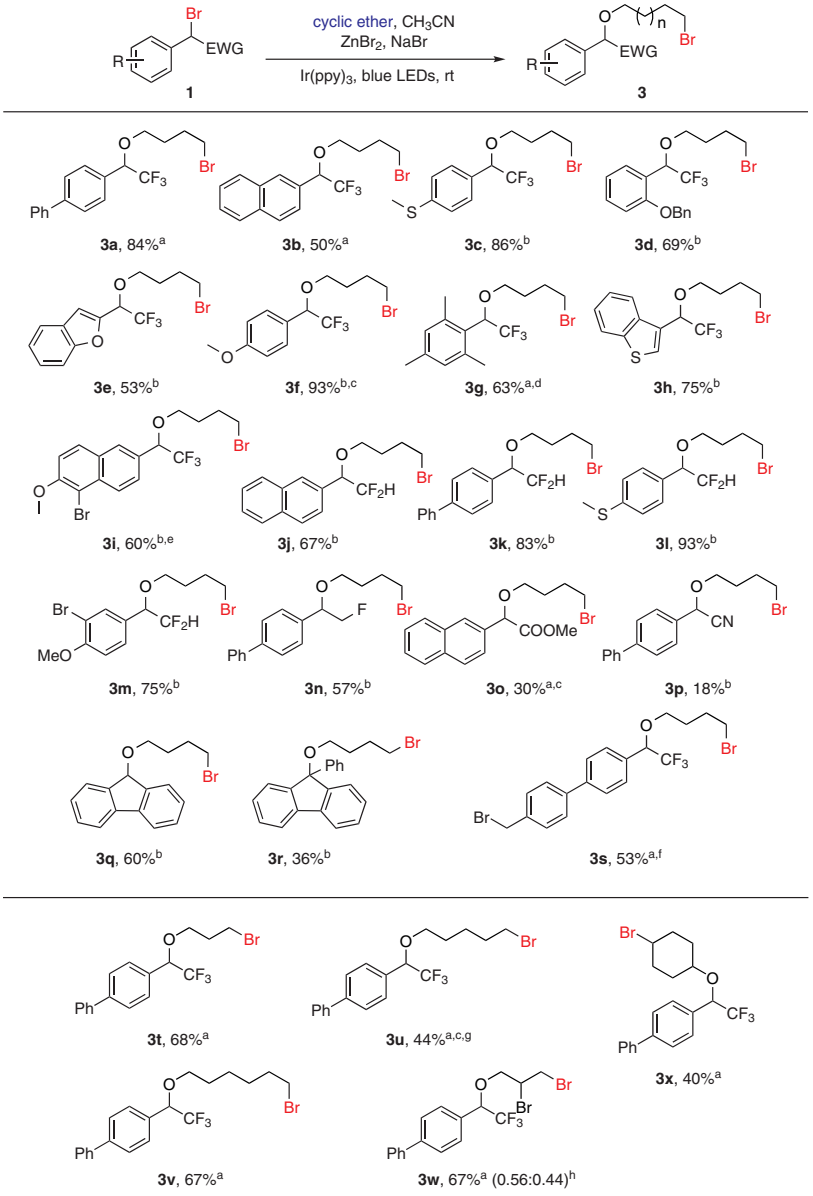
With the optimized reaction conditions (Table 1, entry 13) in hand, we examined the scope of this photoredox-catalyzed ring-opening addition reaction between benzyl bromides and cyclic ethers. The results are summarized in Scheme 2. It was found that a variety of structurally diverse α-trifluoromethylbenzyl bromides are amenable to this reaction, giving the corresponding products in good yields (Scheme 2). However, when compound **1t** (bearing a methanesulfonyl group) was subjected to the standard reaction conditions, no ring-opening addition reaction occurred and only the homo-coupling product was formed in 84% yield (Scheme 3b). It is worthwhile to mention that besides the CF_3 group, α-CF_2H, CFH_2, CO_2Me, and CN-substituted benzyl bromides **1j–p** were also suitable substrates for the ring-opening addition reaction (see **3j–p**). 9-Bromofluoren and its analogue **1q** and **1r** could also react with THF to give the corresponding products **3q** and **3r** in moderate yields. In the case of substrate **1s**, the generation of **3s** suggests that the CF_3-substituted benzyl bromide is more reactive than simple benzyl bromide under the current reaction conditions.[7] In addition to THF, other 4-, 6-, 7-membered or bridged oxacycles are also applicable to the current redox catalyzed ring-opening addition reaction (see **3t–w**). However, a cyclic amine (such as *N*-methylpyrrolidine) could not serve as reaction partner in this reaction,[11] and only homo-coupling product of **1a** was obtained (Scheme 3c). Furthermore, we found that α-Cl and α-OTs substituted benzyl bromides **1u** and **1v** were inert under the current reaction conditions (Schemes 3d and 3e).

To demonstrate the synthetic applications of products **3**, further elaboration of **3a** was carried out (Scheme 4). The benzylic hydrogen atom was deprotonated by NaH, and the resulting carbanion underwent intramolecular S_N2 reaction with the alkyl bromide to give **4b** in 96% yield (Scheme 4a). In addition, the bromine atom can be substituted by external nucleophile (such as sodium phenoxide) to give product **4c** in 62% yield (Scheme 4b). In the latter case, the side product was mainly **4b**, since sodium phenoxide could also serve as a weak base to promote the intramolecular S_N2 reaction.

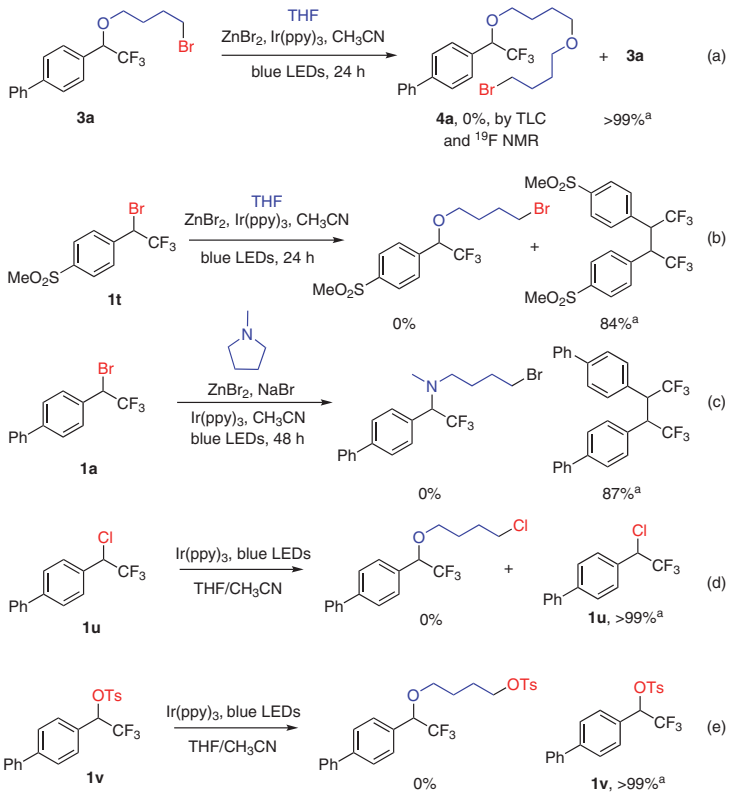
To gain mechanistic insights into the reaction, we performed some additional experiments. It was found that al-

cohol or fluoride anion (instead of a cyclic ether) could serve as the reaction partner of **1a**, affording the corresponding products **4d** and **4e** (Scheme 4c and 4d).[7] When TEMPO was added in reaction system in the presence of THF, TEMPO-quenched product **4f** was obtained in 88% yield, suggesting that a benzylic radical intermediate was formed during the reaction. Furthermore, the reaction did not proceed (with substrate **1a** being recovered) in the absence of either $Ir(ppy)_3$ catalyst or blue LEDs (Table 1, entries 10, 11).

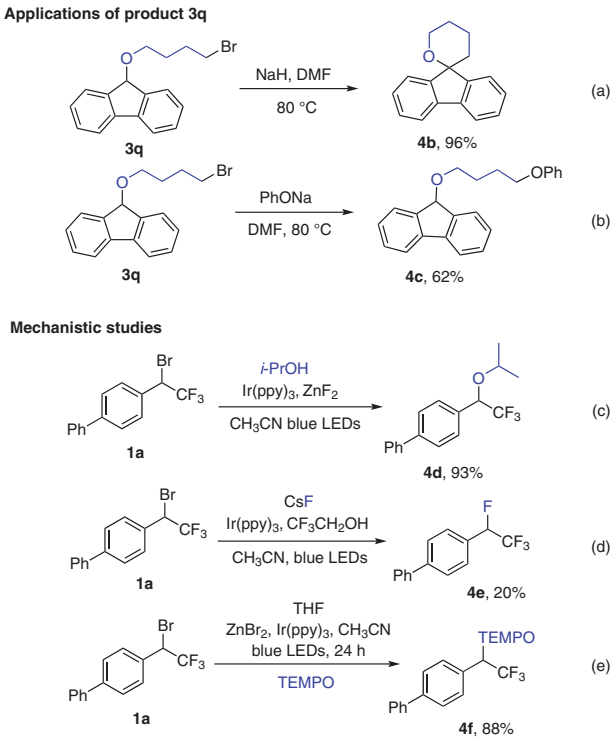
Based on the aforementioned experimental results and our previous work,[7] we propose a plausible reaction mechanism as shown in Scheme 5. Under blue light irradiation and catalysis by $Ir(ppy)_3$, substrate **1** is reduced to radical anion **5**, and then followed by oxidation to give the ion-pair intermediate **6**. The latter species reacts with solvent THF to give a new ion pair species **7**, which undergoes nucleophilic ring-opening reaction to give the desired product **3**. When the reaction is carried out in polar solvent such as CH_3CN, the solvent effect will enhance the ion-pair lifetime, which is beneficial for the nucleophilic reaction; while in non-



Scheme 2 Scope of the substrates. [a] Unless otherwise mentioned, the reaction conditions are as follows: **1** (0.5 mmol), $ZnBr_2$ (0.5 equiv), NaBr (0.45 equiv), cycllic ethers (5 equiv), $Ir(ppy)_3$ (0.5 mol%) in CH_3CN (5 mL) for 24 h. [b] **1** (0.5 mmol), $Ir(ppy)_3$ (1 mol%), CH_3CN (2.5 mL)/THF (2.5 mL) for 48 h. [c] 7 days. [d] 0.4 equiv of NaBr, 3 days. [e] 0.4 mmol scale. [f] NaBr (0.4 equiv), THF (10 equiv), $Ir(ppy)_3$ (1 mol%) in CH_3CN (5 mL) for 48 h. [g] 1 mol% $Ir(ppy)_3$. [h] Ratio of diastereoisomers, determined by ^{19}F NMR spectroscopy.

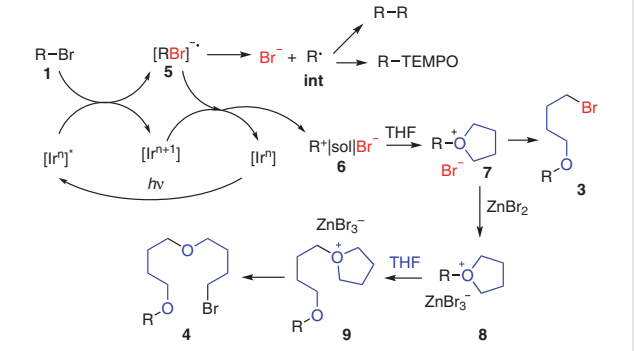


Scheme 3 Additional experiments. [a] Yield determined by ^{19}F NMR spectroscopy.



Scheme 4 Applications of product **3q** and mechanistic studies.

polar solvents such as toluene and dichloromethane, no desired product is formed (Table 1, entries 4, 5). When DMF or DMSO is used as solvent, due to the nucleophilicity of solvent the carbocationic intermediates are captured by solvent and no desired product is formed (Table 1, entries 2, 3). The Lewis acid $ZnBr_2$ interacts with benzyl bromides **1** to promote the reaction, and at the same time $ZnBr_2$ also decreases the nucleophilicity of bromide ion. Therefore, the addition of NaBr facilitates the formation of the desired product **3** and suppresses the generation of **4a** (Scheme 5).



Scheme 5 Proposed mechanism

In conclusion, we have developed an unprecedented photoredox-catalyzed ring-opening reaction between cyclic ethers and substituted benzyl bromides. The reaction proceeds through a single-electron-transfer (SET) pathway rather than a common S_N2 mechanism. By two steps of reduction and oxidation, a benzyl bromide heterolyzes to give a carbocation and bromide ion under mild conditions, and then a cyclic ether captures both the carbocation and bromide ion to afford the addition product.

Unless otherwise mentioned, all solvents and reagents were purchased from commercial sources and used as received. CH_2Cl_2, DMF, THF, CH_3CN, and toluene were dried by passing through a solvent purification system. In all cases, the fac isomer of $Ir(ppy)_3$ (ppy = phenylpyridine) was used. All the melting points were uncorrected. ^1H NMR spectra were recorded at 400 MHz. ^{19}F NMR spectra were recorded at 376 MHz. ^{13}C NMR spectra were recorded at 100 MHz. ^1H NMR chemical shifts were determined relative to internal TMS at δ = 0.00 or to the signal of the residual protonated solvent: $CDCl_3$ at δ = 7.26. ^{19}F NMR chemical shifts were determined relative to internal or external $CFCl_3$ at δ = 0.00. ^{13}C NMR chemical shifts were determined relative to the signal of the solvent: $CDCl_3$ at δ = 77.16. Mass spectra were obtained on a mass spectrometer. High-resolution mass data were recorded on a high-resolution mass spectrometer.

Benzyl Bromides 1a–v; General Procedure

*Method A for **1a**, **1c–e**, **1g–i**, **1t**:*[12,13] The respective aldehyde (10 mmol, 1 equiv), DMF (20 mL), and $TMSCF_3$ (1.2 equiv) were added to K_2CO_3 (1.2 mol%) in a Schlenk tube under N_2 atmosphere. After stirring the mixture for 3 h at rt, aq HCl (3 mol/L, 8 mL) was added. The mixture was stirred for another 3 h at rt. H_2O (20 mL) was added to the solution, and the aqueous layer was extracted with Et_2O (3 × 20 mL). Then the combined organic extracts were washed with brine (3 × 20 mL), dried (Na_2SO_4) and concentrated in vacuo. The product was used in the next step without purification, or it can be purified by flash column chromatography (PE/EtOAc 10:1) to give the corresponding trifluoromethylbenzyl alcohols.

$P(OPh)_3$ (20 mmol) was added to the above prepared trifluoromethylbenzyl alcohol (obtained from the previous step) and NBS (20 mmol) in CH_2Cl_2 (20 mL) in a reaction flask. The mixture was stirred for 6 h under reflux, cooled down to rt, and the CH_2Cl_2 was evaporated in vacuo. To the residue was added Et_2O to dissolve the product and filtered over a pad of Celite and washed by Et_2O. The organic layer was concentrated in vacuo. The products were purified by flash column chromatography (PE) to give the respective trifluoromethylbenzyl bromides **1**.

4-(1-Bromo-2,2,2-trifluoroethyl)-1,1′-biphenyl (1a)[13]

White solid; yield: 2.18 g (69% over 2 steps); mp 85–86 °C.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.65–7.59 (m, 6 H), 7.48 (t, *J* = 7.4 Hz, 2 H), 7.43–7.39 (m, 1 H), 5.20 (q, *J* = 7.4 Hz, 1 H).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –70.80 (d, *J* = 7.4 Hz, 3 F).

MS (EI): *m*/*z* = 314.0 $[M]^+$.

[4-(1-Bromo-2,2,2-trifluoroethyl)phenyl](methyl)sulfane (1c)[14]

Colorless liquid; yield: 1.8 g (63% over 2 steps).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 8.0 Hz, 2 H), 7.24 (d, *J* = 8.2 Hz, 2 H), 5.13 (q, *J* = 7.3 Hz, 1 H), 2.47 (s, 3 H).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –70.86 (d, *J* = 6.1 Hz, 3 F).

MS (EI): *m*/*z* = 283.9 $[M]^+$.

1-(Benzyloxy)-2-(1-bromo-2,2,2-trifluoroethyl)benzene (1d)

Colorless liquid; yield: 4.3 g (66% over 2 steps).

IR (film): 3066, 3035, 3004, 2877, 1602, 1587, 1491, 1454, 1351, 1293, 1247, 1160, 1114, 1051, 1021, 872, 858, 835, 751, 696 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.69 (dq, *J* = 7.9, 1.4 Hz, 1 H), 7.47–7.30 (m, 6 H), 7.04 (td, *J* = 7.6, 1.1 Hz, 1 H), 6.95 (dd, *J* = 8.4, 1.1 Hz, 1 H), 5.95 (q, *J* = 7.7 Hz, 1 H), 5.13 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.75, 136.36, 131.26, 130.52, 128.86, 128.36, 127.44, 123.97 (q, *J* = 277.8 Hz), 121.91, 121.56, 112.38, 70.71, 39.64 (q, *J* = 34.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –70.36 (d, *J* = 7.7 Hz, 3 F).

MS (DART): *m*/*z* = 362 $[M + NH_4]^+$.

HRMS (DART): *m*/*z* $[M + NH_4]^+$ calcd for $C_{15}H_{16}BrF_3NO^+$: 362.0362; found: 362.0354.

2-(1-Bromo-2,2,2-trifluoroethyl)benzofuran (1e)

Colorless liquid; yield: 1.2 g (43% over 2 steps).

IR (film): 3083, 2983, 1622, 1583, 1452, 1377, 1313, 1166, 1111, 969, 956, 861, 744 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 7.8 Hz, 1 H), 7.53 (d, *J* = 8.3 Hz, 1 H), 7.44–7.33 (m, 1 H), 7.34–7.25 (m, 1 H), 6.97 (s, 1 H), 5.42 (q, *J* = 6.9 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.26, 147.41 (q, *J* = 1.7 Hz), 127.41, 126.05, 123.60, 122.48 (q, *J* = 278.0 Hz), 121.77, 111.70, 108.28 (q, *J* = 1.4 Hz), 38.84 (q, *J* = 36.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –70.15 (d, *J* = 6.9 Hz, 3 F).

MS (EI): *m*/*z* = 278 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{10}H_6BrF_3O^+$: 277.9549; found: 277.9556.

2-(1-Bromo-2,2,2-trifluoroethyl)-1,3,5-trimethylbenzene (1g)

Colorless liquid; yield: 2.06 g (73% over 2 steps).

IR (film): 3028, 2984, 2954, 2933, 2881, 1611, 1455, 1384, 1350, 1299, 1263, 1220, 1198, 1158, 1110, 1032, 851, 814, 674 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.92 (s, 1 H), 6.87 (s, 1 H), 5.74 (q, *J* = 8.9 Hz, 1 H), 2.53 (s, 3 H), 2.37 (s, 3 H), 2.26 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.71, 139.70, 137.60, 132.17, 129.44, 125.66, 123.94 (d, *J* = 279.1 Hz), 42.32 (q, *J* = 35.8 Hz), 21.40 (q, *J* = 4.4 Hz), 21.17, 20.86.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –66.84 (d, *J* = 8.6 Hz, 3 F).

MS (EI): *m*/*z* = 280 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{11}H_{12}BrF_3^+$: 280.0069; found: 280.0070.

3-(1-Bromo-2,2,2-trifluoroethyl)benzo[*b*]thiophene (1h)

Colorless liquid; yield: 1.65 g (56% over 2 steps).

IR (film): 3111, 3072, 1482, 1385, 1313, 1258, 1112, 790, 760, 732, 710, 648 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.85 (m, 2 H), 7.78 (s, 1 H), 7.48 (ddd, *J* = 8.1, 7.1, 1.3 Hz, 1 H), 7.44–7.40 (m, 1 H), 5.60 (q, *J* = 7.3 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.07, 136.62, 128.61, 126.85, 125.21, 124.81, 123.54 (q, *J* = 277.9 Hz), 123.06, 121.76, 40.01 (q, *J* = 35.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –69.78 (d, *J* = 7.4 Hz, 3 F).

MS (EI): *m*/*z* = 294 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{10}H_6BrF_3S^+$: 293.9320; found: 293.9329.

3-Bromo-6-(1-bromo-2,2,2-trifluoroethyl)-2-methoxynaphthalene (1i)

White solid; yield: 2.4 g (60% over 2 steps from 6-methoxy-2-naphthaldehyde); mp 102–104 °C.

IR (film): 2977, 2933, 2844, 1627, 1600, 1499, 1357, 1320, 1274, 1110, 1067, 882, 818, 798, 720, 686 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 (d, *J* = 8.9 Hz, 1 H), 7.88 (s, 1 H), 7.83 (d, *J* = 9.0 Hz, 1 H), 7.68 (d, *J* = 8.9 Hz, 1 H), 7.32 (d, *J* = 9.0 Hz, 1 H), 5.29 (q, *J* = 7.4 Hz, 1 H), 4.04 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.93, 133.63, 129.37, 129.12, 128.94, 128.49, 127.48, 127.38, 123.45 (q, *J* = 277.9 Hz), 114.31, 108.54, 57.01, 47.11 (q, *J* = 34.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –70.62 (d, *J* = 7.3 Hz, 3 F).

MS (DART): *m*/*z* = 396 $[M]^+$.

HRMS (DART): *m*/*z* $[M]^+$ calcd for $C_{13}H_9Br_2F_3O^+$: 395.8967; found: 395.8962.

1-(1-Bromo-2,2,2-trifluoroethyl)-4-(methanesulfonyl)benzene (1t)

White solid; yield: 5.0 g (32% over 2 steps); mp 100–101 °C.

IR (film): 3000, 2919, 2854, 1323, 1306, 1290, 1253, 1151, 1111, 1092, 965, 824, 767, 736, 697, 659, 556, 543, 530 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.5 Hz, 2 H), 7.72 (d, *J* = 8.3 Hz, 2 H), 5.17 (q, *J* = 7.2 Hz, 1 H), 3.07 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.11, 138.48, 130.32, 128.03, 123.06 (q, *J* = 278.4 Hz), 45.53 (q, *J* = 34.6 Hz), 44.38.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –70.71 (d, *J* = 7.2 Hz, 3 F).

MS (EI): *m*/*z* = 316 $[M]^+$.

HRMS (DART): *m*/*z* $[M + NH_4]^+$ calcd for $C_9H_{12}BrF_3NO_2S^+$: 333.9719; found: 333.9719.

Method B for ***1b***, ***1f***:[12,15] The respective aldehyde (10 mmol, 1 equiv), DMF (20 mL), and $TMSCF_3$ (1.2 equiv) were added to K_2CO_3 (1.2 mol%) in a Schlenk tube under N_2 atmosphere. After stirring the mixture for 3 h at rt, aq HCl (3 mol/L, 8 mL) was added. The mixture was stirred for another 3 h at rt. H_2O (20 mL) was added to the solution, and the aqueous layer was extracted with Et_2O (3 × 20 mL). Then the combined organic extracts were washed with brine (3 × 20 mL), dried (Na_2SO_4) and concentrated in vacuo. The product was used without purification in the next step, or it can be purified by flash column chromatography (PE/EtOAc 10:1) to give the corresponding trifluoromethylbenzyl alcohols.

Toluene (20 mL) was added to the above prepared trifluoromethylbenzyl alcohol (obtained from the previous step), PPh_3 (15 mmol), and CBr_4 (15 mmol) in a Schlenk tube under N_2 atmosphere. The mixture was stirred for 10 h at 60 °C, cooled down to rt, and filtered over a plug of Celite washing with Et_2O. The organic layer was washed with sat. aq $NaHCO_3$, dried (Na_2SO_4) and concentrated in vacuo. The products were purified by flash column chromatography (PE) to give the respective trifluoromethylbenzyl bromides **1**.

2-(1-Bromo-2,2,2-trifluoroethyl)naphthalene (1b)

White solid; yield: 2.51 g (86% over 2 steps); mp 68–70 °C.

IR (film): 3071, 2984, 1596, 1507, 1378, 1319, 1206, 1177, 1109, 911, 820, 774, 752, 733, 478 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (s, 1 H), 7.84–7.89 (m, 3 H), 7.63 (d, *J* = 8.3 Hz, 1 H), 7.57–7.52 (m, 2 H), 5.31 (q, *J* = 7.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.79, 132.77, 130.05, 129.13, 129.06, 128.31, 127.80, 127.48, 126.95, 125.65, 123.57 (q, *J* = 278 Hz), 77.39, 77.07, 76.75, 47.56 (q, *J* = 34.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –70.57 (d, *J* = 7.4 Hz, 3 F).

MS (EI): *m*/*z* = 288 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_8BrF_3^+$: 287.9756; found: 287.9766.

1-(1-Bromo-2,2,2-trifluoroethyl)-4-methoxybenzene (1f)[15]

Colorless liquid; yield: 4.8 g (66% over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$): δ =7.42 (d, *J* = 8.7 Hz, 2 H), 6.91–6.88 (m, 2 H), 5.10 (q, *J* = 7.5 Hz, 1 H), 3.81 (s, 3 H).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –71.13 (d, *J* = 7.1 Hz, 3 F).

MS (EI): *m*/*z* = 268 $[M]^+$.

Method C for ***1j–m***:[12,16] DMF (40 mL) and $TMSCF_2H$ (2 equiv) were added to CsF (13 mol%) and the respective aldehyde (20 mmol, 1 equiv) in a Schlenk flask under N_2 atmosphere. After stirring the mixture for 12 h at rt, aq HCl (3 mol/L, 8 mL) was added. The mixture was stirred for another 6 h at rt. H_2O (20 mL) was added to the solution, and the aqueous layer was extracted with Et_2O (3 × 20 mL). Then the combined organic extracts were washed with brine (3 × 20 mL), dried (Na_2SO_4) and concentrated in vacuo. The product was used without further purification in the next step or it can be purified by flash column chromatography (PE/EtOAc 10:1) to give the corresponding difluoromethylbenzyl alcohols.

$P(OPh)_3$ (40 mmol) was added to the above prepared trifluoromethylbenzyl alcohol (obtained from the previous step) and NBS (40 mmol) in CH_2Cl_2 (20 mL) in a reaction flask. The mixture was stirred for 6 h under reflux, cooled, and the CH_2Cl_2 was evaporated in vacuo. Et_2O was added to dissolve the product and filtered over a plug of Celite washing with Et_2O. The organic layer was concentrated in vacuo. The products were purified by flash column chromatography (PE) to give the corresponding trifluoromethylbenzyl bromides **1**.

2-(1-Bromo-2,2-difluoroethyl)naphthalene (1j)

White solid; yield: 3.5 g (81% over 2 steps); mp 77–79 °C.

IR (film): 3066, 2972, 1594, 1397, 1362, 1109, 1070, 1045, 866, 824, 772, 756, 720, 479 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.84 (m, 4 H), 7.57–7.52 (m, 3 H), 6.13 (td, *J* = 55.7, 4.3 Hz, 1 H), 5.16 (td, *J* = 11.6, 4.3 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.58, 132.91, 131.35 (t, *J* = 2.7 Hz), 128.98, 128.67, 128.19, 127.76, 127.20, 126.83, 125.73, 114.24 (t, *J* = 247.0 Hz), 50.38 (t, *J* = 25.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –117.01 to –118.85 (m, 2 F).

MS (EI): *m*/*z* = 270 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_9BrF_2^+$: 269.9850; found: 269.9863.

4-(1-Bromo-2,2-difluoroethyl)-1,1′-biphenyl (1k)

White solid; yield: 2.2 g (74% over 2 steps); mp 82–84 °C.

IR (film): 3094, 3033, 2966, 1961, 1919, 1883, 1569, 1412, 1133, 1107, 1060, 1042, 969, 840, 738, 692 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.56 (m, 4 H), 7.50 (d, *J* = 8.3 Hz, 2 H), 7.45–7.42 (m, 2 H), 7.38–7.34 (m, 1 H), 6.05 (td, *J* = 55.7, 4.3 Hz, 1 H), 5.01 (td, *J* = 11.7, 4.3 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.55, 140.10, 132.97, 129.43, 128.92, 127.86, 127.64, 127.19, 114.20 (t, *J* = 247.0 Hz), 49.77 (t, *J* = 24.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –118.09 (dd, *J* = 55.7, 11.8 Hz, 2 F).

MS (EI): *m*/*z* = 296 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{11}BrF_2^+$: 296.0007; found: 296.0011.

[4-(1-Bromo-2,2-difluoroethyl)phenyl](methyl)sulfane (1l)

White solid; yield: 851 mg (32% over 2 steps); mp 39–41 °C.

IR (film): 2983, 2938, 1597, 1495, 1438, 1409, 1366, 1135, 1091, 1065, 968, 848, 820, 753, 550 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.35 (d, *J* = 8.5 Hz, 2 H), 7.23 (d, *J* = 8.5 Hz, 2 H), 6.00 (td, *J* = 55.7, 4.2 Hz, 1 H), 4.94 (td, *J* = 11.8, 4.2 Hz, 1 H), 2.48 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.91, 130.39, 129.32, 126.26, 114.09 (t, *J* = 246.9 Hz), 49.71 (t, *J* = 24.9 Hz), 15.29.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –118.19 (ddd, *J* = 55.8, 19.2, 11.8 Hz, 2 F).

MS (EI): *m*/*z* = 266 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_9H_9BrF_2S^+$: 265.9571; found: 265.9581.

2-Bromo-4-(1-bromo-2,2-difluoroethyl)-1-methoxybenzene (1m)

Colorless liquid; yield: 2.6 g (79% over 2 steps from 4-methoxybenzaldehyde).

IR (film): 2971, 2946, 2841, 1601, 1502, 1369, 1290, 1055, 898, 781, 740, 608 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ =7.65 (d, *J* = 2.3 Hz, 1 H), 7.36 (dd, *J* = 8.5, 2.3 Hz, 1 H), 6.88 (d, *J* = 8.6 Hz, 1 H), 5.98 (td, *J* = 55.7, 4.1 Hz, 1 H), 4.90 (td, *J* = 11.9, 4.1 Hz, 1 H), 3.90 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.76, 133.85, 129.38, 127.35 (t, *J* = 2.6 Hz), 113.95 (t, *J* = 247.1 Hz), 111.95, 111.82, 56.36, 48.72 (t, *J* = 25.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –111.21 to – 119.43 (m, 2 F).

MS (EI): *m*/*z* = 328 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_9H_8Br_2F_2O^+$: 327.8904; found: 327.8918.

4-(1-Bromo-2-fluoroethyl)-1,1′-biphenyl (1n)

Method D: CH_3CN (100 mL) and H_2O (20 mL) were added to 4-phenylstyrene (3.6 g, 20 mmol) and Selectfluor (7.8 g, 22 mmol, 1.1 equiv) in a reaction flask. After stirring the mixture for 12 h at 80 °C, CH_3CN was evaporated in vacuo. The suspension was filtered and the solid was purified by flash column chromatography (PE/EtOAc 3:1) to give the intermediate alcohol as a yellow solid; yield: 2.88 g (67%).

PBr_3 (1.9 mL, 20 mmol, 1.5 equiv) was added to the yellow solid (2.88 g, 13.3 mmol) and CH_2Cl_2 (40 mL) in a reaction flask under 0 °C. The mixture was stirred for 3 h and brought to rt. Then it was stirred for 12 h at rt. H_2O (20 mL) was added to the solution and stirred for 5 min. The aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with aq $NaHCO_3$ (3 × 20 mL), dried (Na_2SO_4), filtered over a plug of Celite, and concentrated in vacuo. The product was purified by flash column chromatography (PE); yield: 1.74 g (47% over 2 steps); white solid; mp 59–61 °C.

IR (film): 3030, 2970, 2359, 2341, 1075, 1006, 992, 839, 765, 733, 693 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.56 (m, 4 H), 7.52–7.48 (m, 2 H), 7.46–7.42 (m, 2 H), 7.38–7.34 (m, 1 H), 5.16 (dt, *J* = 10.8, 7.0 Hz, 1 H), 4.92–4.71 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.16, 140.25, 136.09 (d, *J* = 3.2 Hz), 128.87, 128.40, 127.71, 127.67, 127.14, 84.60 (d, *J* = 180.0 Hz), 49.59 (d, *J* = 22.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –204.61 (td, *J* = 46.9, 10.8 Hz, 1 F).

MS (EI): *m*/*z* = 278 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{12}BrF^+$: 278.0101; found: 278.0106.

Methyl 2-Bromo-2-(naphthalen-2-yl)acetate (1o)

Method E: MeOH (20 mL) and $SOCl_2$ (6 mL, 80 mmol, 4 equiv) were added to 2-naphthylacetic acid (3.72 g, 20 mmol) in a reaction flask under 0 °C. After the mixture was brought to rt, it was stirred for another 3 h at rt. Aq Na_2CO_3 was added until no more bubbles were formed. The mixture was extracted with Et_2O (3 × 20 mL) and the combined organic extracts were dried (Na_2SO_4). After filtering over a plug of Celite, the solution was concentrated in vacuo. The solid ester formed was used in the next step without further purification.

CCl_4 (50 mmol) was added to the above prepared methyl 2-naphthylacetate (20 mmol), BPO (484 mg, 2 mmol, 0.1 equiv), and NBS (3.5 g, 20 mmol, 1 equiv) in a reaction flask. The mixture was stirred for 4 h at 90 °C. After the mixture was brought to rt, it was filtered over a plug of Celite and the filtrate was concentrated in vacuo. The product was purified by flash column chromatography (PE/EtOAc 50:1) to give **1o** (4.7 g, 84%) containing some impurity. After recrystallization twice from the mixture, the pure product was obtained as a white solid; yield: 1.2 g (22% over 2 steps); mp 46–48 °C.

IR (film): 3056, 3004, 2951, 2366, 1745, 1598, 1433, 1368, 1314, 1270, 1204, 1141, 1001, 955, 858, 750, 475 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (s, 1 H), 7.87–7.82 (m, 3 H), 7.69 (dd, *J* = 8.6, 1.6 Hz, 1 H), 7.52–7.50 (m, 2 H), 5.54 (s, 1 H), 3.80 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.74, 133.46, 132.95, 132.89, 128.90, 128.20, 127.95, 127.71, 127.06, 126.67, 125.83, 53.42, 46.98.

MS (EI): *m*/*z* = 278 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{11}BrO_2^+$: 277.9937; found: 277.9934.

2-([1,1′-Biphenyl]-4-yl)-2-bromoacetonitrile (1p)

Method F: CCl_4 (50 mmol) was added to 4-biphenylacetonitrile (3.86 g, 20 mmol), BPO (484 mg, 2 mmol, 0.1 equiv), and NBS (3.5 g, 20 mmol, 1 equiv) in a reaction flask. The mixture was stirred for 4 h at 90 °C. After the mixture was brought to rt, it was filtered over a plug of Celite and the filtrate was concentrated in vacuo. The product was purified by flash column chromatography (PE/EtOAc 50:1) to give **1p** containing some impurity. After recrystallization from the mixture, **1p** was obtained as a slight yellow solid; yield: 1.2 g (22%); mp 101–103 °C.

IR (film): 3074, 3029, 2966, 2361, 2242, 1914, 1484, 1448, 1412, 1182, 1148, 1112, 1071, 1007, 973, 840, 765, 731, 659, 548 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67–7.58 (m, 6 H), 7.48–7.45 (m, 2 H), 7.41–7.37 (m, 1 H), 5.55 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.41, 139.64, 132.25, 128.99, 128.26, 128.18, 128.15, 127.18, 116.24, 27.36.

MS (EI): *m*/*z* = 271 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{10}BrN^+$: 270.9991; found: 271.0003.

4-(1-Bromo-2,2,2-trifluoroethyl)-4′-(bromomethyl)-1,1′-biphenyl (1s)

Method G: Toluene (30 mL) was added to 4-tolylboronic acid (4.08 g, 30 mmol, 1.5 equiv), 4-bromobenzaldehyde (3.7 g, 20 mmol), $Pd(PPh_3)_4$ (460 mg, 0.8 mmol, 4 mol%), and Na_2CO_3 (3.18 g, 30 mmol, 1.5 equiv) under N_2 atmosphere. The reaction mixture was stirred for 8 h under reflux. After cooling down to rt, it was concentrated in vacuo, and the residue was purified by flash column chromatography to give the intermediate aldehyde; yield: 2.3 g (59%).

The above aldehyde (2.3 g, 11.8 mmol), DMF (20 mL), and $TMSCF_3$ (2.1 mL, 14.2 mmol, 1.2 equiv) were added to K_2CO_3 (18.8 mg, 0.14 mmol, 1.2 mol%) in a Schlenk tube under N_2 atmosphere. After stirring the mixture for 3 h at rt, aq HCl (3 mol/L, 8 mL) was added. The mixture was stirred for another 3 h at rt. H_2O (20 mL) was added to the solution, and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with brine (3 × 20 mL), dried (Na_2SO_4) and concentrated in vacuo. The corresponding trifluoromethylbenzyl alcohol obtained was used without purification in the next step.

$P(OPh)_3$ (5.9 mL, 23.6 mmol, 2 equiv) was added to the above prepared trifluoromethylbenzyl alcohol (11.8 mmol) and NBS (4.01 g, 23.6 mmol, 2 equiv) in CH_2Cl_2 (20 mL) in a reaction flask. The mixture was stirred for 6 h under reflux. After cooling down to rt, the CH_2Cl_2 was evaporated in vacuo. The residue was dissolved in Et_2O and filtered over a plug of with Celite and washed with Et_2O. The organic layer was concentrated in vacuo. The product was purified by flash column chromatography (PE) to give the corresponding trifluoromethylbenzyl bromide; yield: 2.5 g (64% over 2 steps).

CCl_4 (20 mL) was added to the above prepared trifluoromethylbenzyl bromide (2.36 g, 7.2 mmol), BPO (174 mg, 0.72 mmol, 10 mol%), and NBS (1.41 g, 7.92 mmol, 1.1 equiv). The mixture was stirred for 8 h under reflux. After cooling down to rt, it was concentrated in vacuo and the residue was purified by flash column chromatography to give the crude product (2.55 g, 6.25 mmol). Recrystallization from CH_2Cl_2/PE gave the pure product **1s**; yield: 1.78 g (22% over 4 steps); white solid; mp 76–78 °C.

IR (film): 3042, 1918, 1495, 1421, 1403, 1307, 1157, 1108, 1005, 817, 671, 608 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61–7.55 (m, 6 H), 7.48 (d, *J* = 8.0 Hz, 2 H), 5.17 (q, *J* = 7.4 Hz, 1 H), 4.54 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.17, 140.06, 137.51, 131.98, 129.64, 129.62, 127.58, 127.55, 123.41 (q, *J* = 278.0 Hz), 46.82 (q, *J* = 34.2 Hz), 33.08.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –70.82 (d, *J* = 7.4 Hz, 3 F).

MS (EI): *m*/*z* = 406 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{11}H_{15}Br_2F_3^+$: 405.9174; found: 405.9178.

4-(1-Chloro-2,2,2-trifluoroethyl)-1,1′-biphenyl (1u)

Method H: The respective aldehyde (10 mmol), DMF (20 mL), and $TMSCF_3$ (1.8 mL, 12 mmol, 1.2 equiv) were added to K_2CO_3 (16 mg, 0.12 mmol, 1.2 mol%) in a Schlenk tube under N_2 atmosphere. After stirring the mixture for 3 h at rt, aq HCl (3 mol/L, 8 mL) was added. The mixture was stirred for another 3 h at rt. H_2O (20 mL) was added to the solution, and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with brine (3 × 20 mL), dried (Na_2SO_4) and concentrated in vacuo. The corresponding trifluoromethylbenzyl alcohol obtained was used in the next step without further purification.

$SOCl_2$ (1.44 mL, 20 mmol, 2 equiv), pyridine (0.2 mL), and toluene (40 mL) were added to the above prepared trifluoromethylbenzyl alcohol (10 mmol) in a reaction flask. The mixture was stirred for 3 h at 70 °C. After completion of the reaction, it was concentrated in vacuo. The product was purified by flash column chromatography (PE) to give **1u** as a white solid; yield: 2.71 g (99% over 2 steps); mp 82–83 °C.

IR (film): 3083, 3055, 1411, 1256, 1169, 1121, 825, 761, 697, 680 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.55 (m, 6 H), 7.47–7.43 (m, 2 H), 7.39–7.36 (m, 1 H), 5.16 (q, *J* = 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.09, 140.00, 131.01, 129.15, 128.91, 127.91, 127.52, 127.19, 123.44 (q, *J* = 279.3 Hz), 58.54 (q, *J* = 34.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –73.63 (d, *J* = 6.8 Hz, 3 F).

MS (EI): *m*/*z* = 270 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{10}ClF_3^+$: 270.0418; found: 270.0421.

1-([1,1′-Biphenyl]-4-yl)-2,2,2-trifluoroethyl 4-Methylbenzenesulfonate (1v)

Method I: The respective aldehyde (36 mmol), DMF (50 mL), and $TMSCF_3$ (6.54 mL, 43.2 mmol, 1.2 equiv) were added to K_2CO_3 (58.1 mg, 0.432 mmol, 1.2 mol%) in a Schlenk tube under N_2 atmosphere. After stirring the mixture for 3 h at rt, aq HCl (3 mol/L, 15 mL) was added. The mixture was stirred for another 3 h at rt. H_2O (20 mL) was added to the solution, and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with brine (3 × 20 mL), dried (Na_2SO_4) and concentrated in vacuo. The residual solid was recrystallized from the mixture to give the corresponding trifluoromethylbenzyl alcohol as a white solid, which was directly used in the next step.

Et_2O (50 mL) was added to NaH (60% in mineral oil; 2.3 g, 57.6 mmol, 1.6 equiv) in a reaction flask. After adding the above prepared trifluoromethylbenzyl alcohol (obtained from the previous step), the mixture was stirred for 30 min at 0 °C. Then a solution of TsCl (6.8 g, 36 mmol, 1 equiv) in Et_2O (20 mL) was added. The mixture was stirred for 2 h at 0 °C. Et_2O (30 mL) was added to the white solid (36 mmol) formed. The mixture was stirred for 12 h at rt and H_2O was added. The solid tosylate formed was collected by filtration. Recrystallization from the mixture gave **1v** as a white solid; yield: 13 g (89% over 2 steps); mp 157–159 °C.

IR (film): 3447, 1636, 1385, 1352, 1279, 1175, 1128, 980, 889, 847, 814, 763, 724, 692, 554 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.3 Hz, 2 H), 7.55–7.50 (m, 4 H), 7.47–7.44 (m, 2 H), 7.40–7.36 (m, 3 H), 7.21 (d, *J* = 8.1 Hz, 2 H), 5.71 (q, *J* = 6.3 Hz, 1 H), 2.37 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.36, 143.23, 139.99, 133.10, 129.72, 128.91, 128.59, 128.49, 127.97, 127.93, 127.33, 127.12, 122.27 (q, *J* = 281.2 Hz), 77.99 (q, *J* = 34.5 Hz), 21.63.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –76.45 (d, *J* = 6.2 Hz, 3 F).

MS (DART): *m*/*z* = 424 [M + NH_4]$^+$.

HRMS (EI): *m*/*z* [M + NH_4]$^+$ calcd for $C_{21}H_{21}F_3NO_3S^+$: 424.1189; found: 424.1176.

Photoredox-Catalyzed Ring-Opening Reaction Between Cyclic Ethers and Substituted Benzyl Bromides; General Procedures

Procedure A: THF (205 μL, 2.5 mmol, 5 equiv) and CH_3CN (5 mL) were added to **1** (0.5 mmol), $ZnBr_2$ (56.3 mg, 0.25 mmol, 0.5 equiv), NaBr (23.3 g, 0.225 mmol, 0.45 equiv), and Ir(ppy)$_3$ (1.5 mg, 2.5 μmol, 0.5 mol%) in a bulb under N_2 atmosphere and the bulb was sealed. The mixture was stirred for 24 h at rt under blue LEDs. After completion of the reaction, the mixture was concentrated in vacuo. The product was purified by flash column chromatography (PE) to give **3**.

Procedure B: THF (2.5 mL), CH_3CN (2.5 mL), and **1** (0.5 mmol) were added to Ir(ppy)$_3$ (3 mg, 5 μmol, 1 mol%) in a bulb under N_2 atmosphere and the bulb was sealed. The mixture was stirred for 48 h at rt under blue LEDs. After completion of the reaction, the mixture was concentrated in vacuo. The product was purified by flash column chromatography (PE/EtOAc 100:1) to give **3**.

Slight changes from Procedure A and Procedure B for some substrates are shown in Scheme 2.

4-[1-(4-Bromobutoxy)-2,2,2-trifluoroethyl]-1,1′-biphenyl (3a)

Procedure A; colorless liquid; yield: 163.3 mg (84%).

IR (film): 3038, 2950, 2883, 1487, 1271, 1173, 1131, 827, 765, 696 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63–7.58 (m, 4 H), 7.49–7.42 (m, 4 H), 7.38–7.34 (m, 1 H), 4.62 (q, *J* = 6.6 Hz, 1 H), 3.56 (t, *J* = 6.1 Hz, 2 H), 3.42 (t, *J* = 6.7 Hz, 2 H), 2.02–1.94 (m, 2 H), 1.82–1.75 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.56, 136.45, 127.91, 124.96, 124.64, 123.77, 123.42, 123.26, 119.95 (q, *J* = 281.9 Hz), 75.86 (q, *J* = 31.1 Hz), 65.82, 29.57, 25.43, 24.25.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –77.06 (d, *J* = 6.7 Hz, 3 F).

MS (DART): *m*/*z* = 404 [M + NH_4]$^+$.

HRMS (DART): *m*/*z* [M + NH_4]$^+$ calcd for $C_{18}H_{22}BrF_3NO^+$: 404.0831; found: 404.0827.

2-[1-(4-Bromobutoxy)-2,2,2-trifluoroethyl]naphthalene (3b)

Procedure A; colorless liquid; yield: 90.5 mg (50%).

IR (film): 3061, 2955, 2872, 1363, 1170, 1130, 818, 747 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.85 (m, 4 H), 7.54–7.51 (m, 3 H), 4.74 (q, *J* = 6.7 Hz, 1 H), 3.58–3.55 (m, 2 H), 3.44–3.40 (m, 2 H), 2.02–1.95 (m, 2 H), 1.83–1.78 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.85, 132.91, 130.32, 128.56, 128.29, 128.16, 127.80, 126.86, 126.57, 124.81, 123.91 (d, *J* = 282.0 Hz), 80.18 (q, *J* = 31.1 Hz), 69.68, 33.47, 29.34, 28.14.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –76.82 (d, *J* = 6.8 Hz, 3 F).

MS (DART): *m*/*z* = 378 [M + NH_4]$^+$.

HRMS (DART): *m*/*z* [M + NH_4]$^+$ calcd for $C_{16}H_{20}BrF_3NO^+$: 378.0675; found: 378.0671.

{4-[1-(4-Bromobutoxy)-2,2,2-trifluoroethyl]phenyl}(methyl)-sulfane (3c)

Procedure B; colorless liquid; yield: 153.2 mg (86%).

IR (film): 2927, 2866, 2372, 1597, 1500, 1444, 1358, 1275, 1172, 1132, 1109, 810, 681 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ =7.32 (d, *J* = 8.2 Hz, 2 H), 7.26 (d, *J* = 8.3 Hz, 2 H), 4.53 (q, *J* = 6.6 Hz, 1 H), 3.52 (t, *J* = 6.1 Hz, 2 H), 3.41 (t, *J* = 6.6 Hz, 2 H), 2.48 (s, 3 H), 2.00–1.92 (m, 2 H), 1.79–1.71 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.50, 129.37, 128.52, 126.16, 123.74 (q, *J* = 282.0 Hz), 79.58 (q, *J* = 31.2 Hz), 69.59, 33.45, 29.31, 28.11, 15.40.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –77.20 (d, *J* = 6.7 Hz, 3 F).

MS (DART): *m*/*z* = 374 [M + NH_4]$^+$.

HRMS (DART): *m*/*z* [M + NH_4]$^+$ calcd for $C_{13}H_{20}BrF_3NOS^+$: 374.0396; found: 374.0392.

1-(Benzyloxy)-2-[1-(4-bromobutoxy)-2,2,2-trifluoroethyl]-benzene (3d)

Procedure B; colorless liquid; yield: 137.4 mg (69%).

IR (film): 3066, 3044, 2938, 2877, 1602, 1490, 1454, 1245, 1173, 1134, 1093, 1022, 755 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 7.6 Hz, 1 H), 7.39–7.30 (m, 6 H), 7.02 (t, *J* = 7.5 Hz, 1 H), 6.96 (d, *J* = 8.3 Hz, 1 H), 5.29 (q, *J* = 6.6 Hz, 1 H), 5.09 (d, *J* = 2.4 Hz, 2 H), 3.53–3.43 (m, 2 H), 3.38 (t, *J* = 6.6 Hz, 2 H), 1.97–1.89 (m, 2 H), 1.73–1.67 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.01, 136.70, 130.45, 128.70, 128.66, 128.13, 127.33, 124.27 (q, *J* = 282.1 Hz), 121.87, 121.17, 112.10, 72.57 (q, *J* = 31.5 Hz), 70.44, 69.53, 33.55, 29.37, 28.18.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –76.99 (d, *J* = 6.6 Hz, 3 F).

MS (DART): *m*/*z* = 434 [M + NH_4]$^+$.

HRMS (DART): *m*/*z* [M + NH_4]$^+$ calcd for $C_{19}H_{24}BrF_3NO_2^+$: 434.0937; found: 434.0929.

2-[1-(4-Bromobutoxy)-2,2,2-trifluoroethyl]benzofuran (3e)

Procedure B; colorless liquid; yield: 93.3 mg (53%).

IR (film): 2950, 2888, 1453, 1271, 1177, 1139, 968, 820, 751 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 7.6 Hz, 1 H), 7.52 (d, *J* = 8.2 Hz, 1 H), 7.34 (t, *J* = 7.4 Hz, 1 H), 7.26 (t, *J* = 7.7 Hz, 1 H), 6.91 (s, 1 H), 4.83 (q, *J* = 6.3 Hz, 1 H), 3.66 (td, *J* = 6.1, 2.2 Hz, 2 H), 3.42 (t, *J* = 6.6 Hz, 2 H), 2.01–1.94 (m, 2 H), 1.82–1.77 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.24, 148.86 (q, *J* = 1.2 Hz), 127.40, 125.32, 123.30, 123.03 (d, *J* = 282.2 Hz), 121.57, 111.66, 107.79, 74.49 (q, *J* = 33.1 Hz), 70.28, 33.36, 29.19, 28.04.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –76.15 (d, *J* = 6.3 Hz, 3 F).

MS (DART): *m*/*z* = 368 [M + NH_4]$^+$.

HRMS (DART): *m*/*z* [M + NH_4]$^+$ calcd for $C_{14}H_{18}BrF_3NO_2^+$: 368.0468; found:368.0458.

1-[1-(4-Bromobutoxy)-2,2,2-trifluoroethyl]-4-methoxybenzene (3f)

Procedure B; colorless liquid; yield: 158.0 mg (93%).

IR (film): 3011, 2958, 2844, 1612, 1514, 1289, 1250, 1173, 1131, 1033, 825, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 8.6 Hz, 2 H), 6.93 (d, *J* = 8.7 Hz, 2 H), 4.52 (q, *J* = 6.7 Hz, 1 H), 3.82 (s, 3 H), 3.51 (t, *J* = 6.1 Hz, 2 H), 3.42 (t, *J* = 6.7 Hz, 2 H), 2.01–1.92 (m, 2 H), 1.79–1.71 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.49, 129.38, 124.78, 123.87 (q, *J* = 281.7 Hz), 113.99, 79.50 (q, *J* = 31.1 Hz), 69.30, 55.26, 33.46, 29.32, 28.09.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –77.39 (d, *J* = 6.7 Hz, 3 F).

MS (DART): *m*/*z* = 358 $[M + NH_4]^+$.

HRMS (DART): *m*/*z* $[M + NH_4]^+$ calcd for $C_{13}H_{20}BrF_3NO_2^+$: 358.0624; found:358.0615.

2-[1-(4-Bromobutoxy)-2,2,2-trifluoroethyl]-1,3,5-trimethylbenzene (3g)

Procedure A; colorless liquid; yield: 110.9 mg (63%).

IR (film): 2924, 2877, 1611, 1458, 1438, 1268, 1167, 1131, 850, 694 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.88 (s, 1 H), 6.85 (s, 1 H), 5.11 (q, *J* = 8.0 Hz, 1 H), 3.52–3.46 (m, 2 H), 3.42 (td, *J* = 6.7, 1.4 Hz, 2 H), 2.45 (s, 3 H), 2.33 (s, 3 H), 2.26 (s, 3 H), 2.00–1.93 (m, 2 H), 1.79–1.73 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.88, 138.59, 138.09, 131.56, 129.25, 125.53, 125.01 (q, *J* = 283.1 Hz), 77.41 (q, *J* = 31.9 Hz), 69.66, 33.47, 29.40, 28.14, 20.91, 20.81, 20.38.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –74.14 (d, *J* = 8.1 Hz, 3 F).

MS (DART): *m*/*z* = 370 $[M + NH_4]^+$.

HRMS (DART): *m*/*z* $[M + NH_4]^+$ calcd for $C_{15}H_{24}BrF_3NO^+$: 370.0987; found: 370.0983.

3-[1-(4-Bromobutoxy)-2,2,2-trifluoroethyl]benzo[*b*]thiophene (3h)

Procedure B; colorless liquid; yield: 137.4 mg (75%).

IR (film): 3094, 2938, 2883, 1519, 1463, 1425, 1355, 1269, 1175, 1132, 840, 760, 735 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 7.7 Hz, 1 H), 7.89–7.87 (m, 1 H), 7.60 (s, 1 H), 7.44–7.37 (m, 2 H), 5.02 (q, *J* = 6.7 Hz, 1 H), 3.59 (t, *J* = 6.1 Hz, 2 H), 3.40 (t, *J* = 6.6 Hz, 2 H), 2.01–1.93 (m, 2 H), 1.81–1.75 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.56, 137.30, 128.08, 127.90, 124.83, 124.56, 123.85 (q, *J* = 282.2 Hz), 122.85, 122.59, 76.00 (q, *J* = 32.4 Hz), 69.82, 33.42, 29.28, 28.13.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –76.15 (d, *J* = 6.7 Hz, 3 F).

MS (DART): *m*/*z* = 384 $[M + NH_4]^+$.

HRMS (DART): *m*/*z* $[M + NH_4]^+$ calcd for $C_{14}H_{18}BrF_3NOS^+$: 384.0239; found: 384.0235.

1-Bromo-6-[1-(4-bromobutoxy)-2,2,2-trifluoroethyl]-2-methoxynaphthalene (3i)

Procedure B; colorless liquid; yield: 111.9 mg (60%).

IR (film): 2955, 2844, 1633, 1602, 1481, 1358, 1273, 1169, 1132, 1066, 880, 820, 802, 701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 8.8 Hz, 1 H), 7.85 (d, *J* = 9.1 Hz, 1 H), 7.83 (s, 1 H), 7.60 (d, *J* = 8.8 Hz, 1 H), 7.32 (d, *J* = 9.0 Hz, 1 H), 4.74 (q, *J* = 6.6 Hz, 1 H), 4.05 (s, 3 H), 3.60–3.54 (m, 2 H), 3.43 (t, *J* = 6.6 Hz, 2 H), 2.04–1.93 (m, 2 H), 1.84–1.76 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.50, 133.66, 129.24, 129.20, 128.82, 128.27, 126.88, 126.72, 123.85 (q, *J* = 282.0 Hz), 114.12, 108.55, 79.82 (q, *J* = 31.2 Hz), 69.77, 57.06, 33.43, 29.32, 28.13.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –76.90 (d, *J* = 6.4 Hz, 3 F).

MS (DART): *m*/*z* = 486 $[M + NH_4]^+$.

HRMS (DART): *m*/*z* $[M + NH_4]^+$ calcd for $C_{17}H_{21}Br_2F_3NO_2^+$: 485.9886; found:485.9880.

2-[1-(4-Bromobutoxy)-2,2-difluoroethyl]naphthalene (3j)

Procedure B; colorless liquid; yield: 114.9 mg (67%).

IR (film): 3055, 2955, 2883, 1605, 1511, 1441, 1386, 1248, 1108, 1069, 863, 820, 748, 478 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.82 (m, 4 H), 7.51–7.46 (m, 3 H), 5.85 (td, *J* = 55.7, 4.6 Hz, 1 H), 4.55 (td, *J* = 10.3, 4.6 Hz, 1 H), 3.50 (t, *J* = 6.1 Hz, 2 H), 3.41 (t, *J* = 6.8 Hz, 2 H), 2.01–1.92 (m, 2 H), 1.80–1.71 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.67, 133.09, 132.11–132.05 (m), 128.55, 128.07, 127.81, 127.76, 126.59, 126.49, 124.90, 115.22 (dd, *J* = 247.1, 244.2 Hz), 81.40 (dd, *J* = 25.5, 23.7 Hz), 68.96, 33.56, 29.48, 28.26.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –125.00 to –128.04 (m, 2 F).

MS (DART): *m*/*z* = 360 $[M + NH_4]^+$.

HRMS (DART): *m*/*z* $[M + NH_4]^+$ calcd for $C_{16}H_{21}BrF_2NO^+$: 360.0769; found: 360.0761.

4-[1-(4-Bromobutoxy)-2,2-difluoroethyl]-1,1′-biphenyl (3k)

Procedure B; colorless liquid; yield: 152.0 mg (83%).

IR (film): 3027, 2955, 2872, 1600, 1487, 1391, 1247, 1211, 1105, 1069, 1008, 858, 837, 765, 755, 698 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63–7.58 (m, 4 H), 7.46–7.42 (m, 4 H), 7.38–7.34 (m, 1 H), 5.80 (td, *J* = 55.7, 4.6 Hz, 1 H), 4.45 (td, *J* = 10.3, 4.6 Hz, 1 H), 3.55–3.49 (m, 2 H), 3.43 (t, *J* = 6.7 Hz, 2 H), 2.02–1.94 (m, 2 H), 1.81–1.73 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.99, 140.52, 133.54 (dd, *J* = 4.0, 1.1 Hz), 128.85, 128.33, 127.58, 127.38, 127.16, 115.16 (dd, *J* = 246.9, 244.1 Hz), 80.99 (dd, *J* = 25.4, 23.6 Hz), 68.98, 33.57, 29.48, 28.28.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –125.02 to –128.33 (m, 2 F).

MS (DART): *m*/*z* = 386 $[M + NH_4]^+$.

HRMS (DART): *m*/*z* $[M + NH_4]^+$ calcd for $C_{18}H_{23}BrF_2NO^+$: 386.0921; found: 386.0920.

2-Bromo-4-(1-(4-bromobutoxy)-2,2-difluoroethyl)-1-methoxybenzene (3m)

Procedure B; colorless liquid; yield: 150.8 mg (75%).

IR (film): 2944, 2872, 1603, 1498, 1441, 1291, 1258, 1110, 1053, 1020, 816, 675 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 2.1 Hz, 1 H), 7.27 (dd, *J* = 8.4, 1.9 Hz, 1 H), 6.92 (d, *J* = 8.4 Hz, 1 H), 5.73 (td, *J* = 55.7, 4.5 Hz, 1 H), 4.32 (td, *J* = 10.3, 4.4 Hz, 1 H), 3.91 (s, 3 H), 3.50–3.45 (m, 2 H), 3.42 (t, *J* = 6.6 Hz, 2 H), 2.00–1.92 (m, 2 H), 1.78–1.71 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.39, 132.71, 128.19, 128.03–127.98 (m), 114.86 (dd, *J* = 246.6, 244.2 Hz), 111.90, 111.85, 80.12 (t, *J* = 24.8 Hz), 68.92, 56.30, 33.51, 29.38, 28.17.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –125.02 to –128.78 (m, 2 F).

MS (DART): *m*/*z* = 418 $[M + NH_4]^+$.

HRMS (DART): *m*/*z* $[M + NH_4]^+$ calcd for $C_{13}H_{20}Br_2F_2NO_2^+$: 417.9823; found: 417.9818.

(4-(1-(4-bromobutoxy)-2,2-difluoroethyl)phenyl)(methyl)sulfane (3l)

Method B: Colorless liquid; yield: 157.8 mg (93%).

IR (film): 2961, 2927, 2861, 1600, 1493, 1438, 1380, 1104, 1069, 1019, 855, 817, 758.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.26 (s, 4H), 5.73 (td, *J* = 55.8, 4.5 Hz, 1H), 4.35 (td, *J* = 10.3, 4.5 Hz, 1H), 3.48 3.44 (m, 2H), 3.40 (t, *J* = 6.6 Hz, 2H), 1.98 1.88 (m, 2H), 1.77 1.68 (m, 2H).

^{19}F NMR (376 MHz, $CDCl_3$) δ = -125.03 -128.53 (m, 2F).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 139.76, 131.18, 128.37, 126.35, 115.06 (dd, *J* = 246.8, 244.0 Hz), 81.02 80.53 (m), 68.85, 33.61, 29.46, 28.23, 15.50.

MS (DART): m/z = 356 [M+NH_4]$^+$.

HRMS (DART): *m*/*z* [M+NH_4]$^+$ calcd for $C_{13}H_{21}BrF_2NOS^+$: 356.0490; Found: 356.0485.

4-[1-(4-Bromobutoxy)-2-fluoroethyl]-1,1′-biphenyl (3n)

Procedure B; colorless liquid; yield: 100.5 mg (57%).

IR (film): 3055, 3028, 2943, 2868, 1597, 1485, 1449, 1401, 1342, 1247, 1112, 1007, 837, 764, 697, 569, 515 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.48 (m, 4 H), 7.36–7.23 (m, 5 H), 4.54–4.25 (m, 3 H), 3.41–3.35 (m, 2 H), 3.32 (t, *J* = 6.7 Hz, 2 H), 1.93–1.84 (m, 2 H), 1.71–1.64 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.47, 140.62, 136.28 (d, *J* = 7.8 Hz), 128.87, 127.53, 127.49, 127.45, 127.14, 85.96 (d, *J* = 177.9 Hz), 80.74 (d, *J* = 19.4 Hz), 68.46, 33.73, 29.67, 28.48.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –219.87 (td, *J* = 47.3, 14.9 Hz, 1 F).

MS (DART): *m*/*z* = 368 [M + NH_4]$^+$.

HRMS (DART): *m*/*z* [M + NH_4]$^+$ calcd for $C_{18}H_{24}BrFNO^+$: 368.1020; found: 368.1016.

Methyl 2-(4-Bromobutoxy)-2-(naphthalen-2-yl)acetate (3o)

Procedure A; colorless liquid; yield: 53.3 mg (30%).

IR (film): 3055, 2950, 2872, 1751, 1434, 1247, 1167, 1126, 1112, 858, 819, 753 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (s, 1 H), 7.85–7.82 (m, 3 H), 7.55 (d, *J* = 8.5 Hz, 1 H), 7.50–7.48 (m, 2 H), 5.03 (s, 1 H), 3.71 (s, 3 H), 3.64–3.59 (m, 1 H), 3.54–3.50 (m, 1 H), 3.47–3.43 (m, 2 H), 2.05–1.98 (m, 2 H), 1.86–1.80 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.27, 133.86, 133.44, 133.12, 128.55, 128.12, 127.73, 126.69, 126.44, 126.37, 124.45, 81.19, 68.79, 52.32, 33.65, 29.51, 28.16.

MS (DART): *m*/*z* = 368 [M + NH_4]$^+$.

HRMS (DART): *m*/*z* [M + NH_4]$^+$ calcd for $C_{17}H_{23}BrNO_3^+$: 368.0856; found: 368.0847.

2-([1,1′-Biphenyl]-4-yl)-2-(4-bromobutoxy)acetonitrile (3p)

Procedure B; colorless liquid; yield: 31.7 mg (18%).

IR (film): 3038, 2925, 2871, 1716, 1611, 1486, 1406, 1278, 1248, 1187, 1087, 1008, 831, 763, 748, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.2 Hz, 2 H), 7.61–7.54 (m, 4 H), 7.47–7.44 (m, 2 H), 7.40–7.36 (m, 1 H), 5.29 (s, 1 H), 3.82–3.78 (m, 1 H), 3.68–3.63 (m, 1 H), 3.43 (t, *J* = 6.6 Hz, 2 H), 2.02–1.97 (m, 2 H), 1.86–1.81 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.86, 140.10, 132.33, 128.93, 127.87, 127.78, 127.72, 127.20, 117.25, 70.72, 69.03, 33.32, 29.34, 27.94.

MS (DART): *m*/*z* = 361 [M + NH_4]$^+$.

HRMS (DART): *m*/*z* [M + NH_4]$^+$ calcd for $C_{18}H_{22}BrN_2O^+$: 361.0910; found: 361.0907.

9-(4-Bromobutoxy)-9*H*-fluorene (3q)

Procedure B; yield: 94.4 mg (60%); white solid; mp 34–35 °C.

IR (film): 3065, 3041, 3020, 2938, 2867, 1608, 1476, 1450, 1303, 1246, 1192, 1155, 1108, 1070, 1029, 944, 765, 741, 675, 622 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 7.5 Hz, 2 H), 7.58 (d, *J* = 7.4 Hz, 2 H), 7.40–7.37 (m, 2 H), 7.33–7.30 (m, 2 H), 5.62 (s, 1 H), 3.37 (t, *J* = 6.8 Hz, 2 H), 3.18 (t, *J* = 6.1 Hz, 2 H), 1.96–1.90 (m, 2 H), 1.67–1.61 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.89, 140.80, 128.96, 127.53, 125.34, 119.96, 80.78, 63.40, 33.65, 29.60, 28.71.

MS (EI): *m*/*z* = 316 [M]$^+$.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{17}H_{17}BrO^+$: 316.0457; found: 316.0467.

9-(4-Bromobutoxy)-9-phenyl-9*H*-fluorene (3r)

Procedure B; yield: 70.4 mg (36%); white solid; mp 78–79 °C.

IR (film): 3061, 3021, 2937, 2869, 1488, 1449, 1285, 1247, 1174, 1155, 1074, 1031, 941, 895, 753, 733, 698, 648, 641 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 7.5 Hz, 2 H), 7.40–7.33 (m, 4 H), 7.27–7.20 (m, 7 H), 3.38 (t, *J* = 6.8 Hz, 2 H), 3.02 (t, *J* = 6.0 Hz, 2 H), 2.01–1.94 (m, 2 H), 1.69–1.62 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.41, 143.63, 140.73, 129.02, 128.19, 128.13, 127.14, 125.58, 125.23, 119.98, 88.51, 62.07, 33.82, 29.79, 28.65.

MS (EI): *m*/*z* = 392 [M]$^+$.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{23}H_{21}BrO^+$: 392.0770; found: 392.0780.

4-[1-(4-Bromobutoxy)-2,2,2-trifluoroethyl]-4′-(bromomethyl)-1,1′-biphenyl (3s)

Procedure A; colorless liquid; yield: 126.2 mg (53%).

IR (film): 3030, 2957, 2875, 1613, 1496, 1439, 1401, 1356, 1171, 1132, 814, 688, 607 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 8.3 Hz, 2 H), 7.56 (d, *J* = 8.2 Hz, 2 H), 7.47 (t, *J* = 8.9 Hz, 4 H), 4.62 (q, *J* = 6.7 Hz, 1 H), 4.53 (s, 2 H), 3.57 (t, *J* = 6.1 Hz, 2 H), 3.42 (t, *J* = 6.6 Hz, 2 H), 2.02–1.94 (m, 2 H), 1.82–1.76 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.67, 140.50, 137.26, 132.20, 129.62, 128.64, 127.58, 127.31, 123.85 (q, *J* = 282.0 Hz), 79.73 (q, *J* = 31.0 Hz), 69.81, 33.51, 33.26, 29.36, 28.18.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –77.02 (d, *J* = 6.7 Hz, 3 F).

MS (EI): *m*/*z* = 478 [M]$^+$.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{19}H_{19}Br_2F_3O^+$: 477.9755; found: 477.9760.

4-[1-(3-Bromopropoxy)-2,2,2-trifluoroethyl]-1,1′-biphenyl (3t)

Procedure A; colorless liquid; yield: 126.7 mg (68%).

IR (film): 3044, 2888, 1488, 1358, 1271, 1173, 1131, 1108, 1027, 916, 827, 765, 696 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63–7.58 (m, 4 H), 7.50–7.42 (m, 4 H), 7.36 (t, *J* = 7.3 Hz, 1 H), 4.65 (q, *J* = 6.6 Hz, 1 H), 3.69–3.64 (m, 2 H), 3.57–3.50 (m, 2 H), 2.18–2.11 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.56, 140.38, 131.60, 128.89, 128.58, 127.71, 127.38, 127.20, 123.82 (q, *J* = 281.9 Hz), 80.05 (q, *J* = 31.2 Hz), 68.08, 32.68, 30.02.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –77.07 (d, *J* = 6.7 Hz, 3 F).

MS (DART): *m*/*z* = 390 $[M + NH_4]^+$.

HRMS (DART): *m*/*z* $[M + NH_4]^+$ calcd for $C_{17}H_{20}BrF_3NO^+$: 390.0675; found: 390.0672.

4-{1-[(5-Bromopentyl)oxy]-2,2,2-trifluoroethyl}-1,1′-biphenyl (3u)

Procedure A; yield: 90.0 mg (44%); white solid; mp 30–31 °C.

IR (film): 3038, 2941, 2877, 1613, 1602, 1563, 1487, 1405, 1271, 1172, 1132, 1108, 1008, 826, 765, 745, 731, 697 cm–1.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63–7.58 (m, 4 H), 7.50–7.42 (m, 4 H), 7.36 (t, *J* = 7.3 Hz, 1 H), 4.62 (q, *J* = 6.7 Hz, 1 H), 3.54 (t, *J* = 6.3 Hz, 2 H), 3.39 (t, *J* = 6.8 Hz, 2 H), 1.90–1.83 (m, 2 H), 1.69–1.62 (m, 2 H), 1.58–1.51 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.43, 140.42, 131.98, 128.87, 128.58, 127.67, 127.32, 127.18, 123.90 (q, *J* = 281.9 Hz), 79.79 (q, *J* = 31.1 Hz), 70.49, 33.60, 32.45, 28.73, 24.68.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –77.06 (d, *J* = 6.7 Hz, 3 F).

MS (EI): *m*/*z* = 400 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{20}BrF_3O^+$: 400.0644; found: 400.0655.

4-{1-[(6-Bromohexyl)oxy]-2,2,2-trifluoroethyl}-1,1′-biphenyl (3v)

Procedure A; colorless liquid; yield: 138.0 mg (67%).

IR (film): 3055, 3038, 2938, 2864, 1613m 1487, 1406, 1355, 1271, 1171, 1132, 1008, 858, 826, 765, 745, 730, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63–7.58 (m, 4 H), 7.50–7.42 (m, 4 H), 7.35 (t, *J* = 7.3 Hz, 1 H), 4.62 (q, *J* = 6.7 Hz, 1 H), 3.53 (t, *J* = 6.4 Hz, 2 H), 3.38 (t, *J* = 6.8 Hz, 2 H), 1.88–1.81 (m, 2 H), 1.67–1.60 (m, 2 H), 1.45–1.39 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.39, 140.43, 132.08, 128.88, 128.60, 127.67, 127.30, 127.19, 123.95 (q, *J* = 281.9 Hz), 79.75 (q, *J* = 30.9 Hz), 70.66, 33.83, 32.69, 29.38, 27.88, 25.16.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –77.06 (d, *J* = 6.5 Hz, 3 F).

MS (EI): *m*/*z* = 414 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{22}BrF_3O^+$: 414.0801; found: 414.0803.

4-[1-(2,3-Dibromopropoxy)-2,2,2-trifluoroethyl]-1,1′-biphenyl (3w)

Procedure A; colorless liquid; yield: 151.7 mg (56:44) (67%).

IR (film): 3060, 3032, 2926, 2898, 1758, 1487, 1356, 1272, 1174, 1134, 1008, 825, 765, 731, 698, 574 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65–7.58 (m, 4 H), 7.54–7.51 (m, 2 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 7.37 (t, *J* = 7.3 Hz, 1 H), 4.79–4.73 (m, 1 H), 4.30–4.23 (m, 1 H), 4.03–3.96 (m, 1 H), 3.93–3.79 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.82, 142.78, 140.30, 140.28, 130.81, 130.78, 128.90, 128.90, 128.67, 128.65, 127.78, 127.77, 127.47, 127.44, 127.20, 127.20, 123.57 (q, *J* = 281.9 Hz), 123.55 (q, *J* = 281.9 Hz), 80.44 (q, *J* = 31.7 Hz), 80.31 (q, *J* = 31.6 Hz), 71.38, 71.22, 47.94, 47.84, 32.63, 32.57.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –76.99 (d, *J* = 6.3 Hz, 3 F × 0.44), -77.05 (d, *J* = 6.6 Hz, 3 F × 0.56).

MS (DART): *m*/*z* = 468 $[M + NH_4]^+$.

HRMS (DART): *m*/*z* $[M + NH_4]^+$ calcd for $C_{17}H_{19}Br_2F_3NO^+$: 467.9780; found: 467.9774.

4-{1-[(4-Bromocyclohexyl)oxy]-2,2,2-trifluoroethyl}-1,1′-biphenyl (3x)

Procedure A; yield: 81.2 mg (40%); white solid; mp 86–88 °C.

IR (film): 3044, 2945, 2901, 1487, 1453, 1359, 1272, 1235, 1169, 1130, 1095, 1007, 936, 828, 765, 747, 732, 695 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (t, *J* = 8.2 Hz, 4 H), 7.50 (d, *J* = 8.1 Hz, 2 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 7.39–7.35 (m, 1 H), 4.73 (q, *J* = 6.7 Hz, 1 H), 4.33–4.28 (m, 1 H), 3.60–3.56 (m, 1 H), 2.34–2.29 (m, 1 H), 2.26–2.20 (m, 1 H), 2.09–2.04 (m, 1 H), 1.97–1.91 (m, 1 H), 1.86–1.74 (m, 2 H), 1.69–1.64 (m, 1 H), 1.60–1.51 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.39, 140.38, 132.44, 128.85, 128.50, 127.66, 127.28, 127.16, 123.95 (q, *J* = 281.8 Hz), 77.08 (q, *J* = 30.9 Hz), 74.71, 51.95, 32.83, 32.68, 30.07, 28.28.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –77.35 (d, *J* = 6.7 Hz, 3 F).

MS (EI): *m*/*z* = 412 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{20}BrF_3O^+$: 412.0644; found: 412.0646.

4-{1-[4-(4-Bromobutoxy)butoxy]-2,2,2-trifluoroethyl}-1,1′-biphenyl (4a)

THF (205 μL, 2.5 mmol, 5 equiv) and CH_3CN (5 mL) were added to **1a** (157.5 mg, 0.5 mmol), $ZnBr_2$ (56.3 mg, 0.25 mmol, 0.5 equiv), and $Ir(ppy)_3$ (1.5 mg, 2.5 μmol, 0.5 mol%) in a blub under N_2 atmosphere and the bulb was sealed. The mixture was stirred for 24 h at rt under blue LEDs. After completion of the reaction, the mixture was concentrated in vacuo. The product was purified by flash column chromatography (PE); colorless liquid; yield: 76.7 mg (34%).

IR (film): 2955, 2877, 1597, 1486, 1361, 1269, 1175, 1130, 1005, 825, 765, 698 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (dd, *J* = 10.5, 7.9 Hz, 4 H), 7.50 (d, *J* = 8.1 Hz, 2 H), 7.45 (t, *J* = 7.7 Hz, 2 H), 7.36 (t, *J* = 7.3 Hz, 1 H), 4.63 (q, *J* = 6.7 Hz, 1 H), 3.56 (t, *J* = 5.9 Hz, 2 H), 3.43–3.40 (m, 6 H), 1.96–1.89 (m, 2 H), 1.72–1.64 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.36, 140.42, 132.05, 128.86, 128.59, 127.65, 127.27, 127.17, 123.92 (q, *J* = 282.0 Hz), 79.69 (q, *J* = 31.0 Hz), 70.62, 70.48, 69.78, 33.80, 29.75, 28.35, 26.42, 26.29.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –77.06 (d, *J* = 6.5 Hz, 3 F).

MS (DART): *m*/*z* = 459 $[M + H]^+$.

HRMS (DART): *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{27}BrF_3O_2^+$: 459.1141; found: 459.1132.

3′,4′,5′,6′-Tetrahydrospiro[fluorene-9,2′-pyran] (4b)

DMF (2 mL) was added to **3q** (63.4 mg, 0.2 mmol), NaH (60% in mineral oil; 13.2 mg, 0.33 mmol, 1.65 equiv) in a reaction flask. The mixture was stirred for 12 h at 80 °C. After completion of the reaction, H_2O (10 mL) was added, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with brine (3 × 10 mL), dried (Na_2SO_4) and concentrated in vacuo. The product **4b** was purified by flash column chromatography (PE); colorless liquid; yield: 45.1 mg (96%).

IR (film): 3066, 2935, 2870, 1477, 1447, 1300, 1213, 1040, 899, 755, 732 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 7.5 Hz, 2 H), 7.63 (d, *J* = 7.5 Hz, 2 H), 7.35 (t, *J* = 7.4 Hz, 2 H), 7.26 (t, *J* = 7.5 Hz, 2 H), 4.13–4.10 (m, 2 H), 2.13–2.07 (m, 2 H), 1.99–1.96 (m, 2 H), 1.92–1.87 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.29, 139.76, 128.79, 127.50, 125.01, 120.02, 82.21, 63.80, 33.71, 25.61, 19.58.

MS (EI): *m*/*z* = 236 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{16}O^+$: 236.1196; found: 236.1196.

9-(4-Phenoxybutoxy)-9*H*-fluorene (4c)

DMF (2 mL) was added to **3q** (63.4 mg, 0.2 mmol) and PhONa (25.5 mg, 0.22 mmol, 1.1 equiv) in a reaction flask. The mixture was stirred for 24 hours at 80 °C. After completion of the reaction, H_2O (10 mL) was added, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with brine (3 × 10 mL), dried (Na_2SO_4) and concentrated in vacuo. The product **4c** was purified by flash column chromatography (EA/PE = 1/100 v/v); yield: 40.4 mg (62%); white solid; mp 85–86 °C.

IR (film): 3077, 3038, 2944, 2869, 1599, 1585, 1496, 1450, 1301, 1245, 1192, 1070, 742, 691 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 7.4 Hz, 2 H), 7.61 (d, *J* = 7.4 Hz, 2 H), 7.39 (t, *J* = 7.3 Hz, 2 H), 7.31 (t, *J* = 7.4 Hz, 2 H), 7.25 (t, *J* = 7.7 Hz, 2 H), 6.91 (t, *J* = 6.9 Hz, 1 H), 6.85 (d, *J* = 8.6 Hz, 2 H), 5.64 (s, 1 H), 3.92 (t, *J* = 6.4 Hz, 2 H), 3.25 (t, *J* = 6.2 Hz, 2 H), 1.87–1.80 (m, 2 H), 1.73–1.66 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.02, 143.07, 140.81, 129.38, 128.92, 127.52, 125.42, 120.50, 119.94, 114.51, 80.84, 67.53, 64.29, 26.76, 26.09.

MS (EI): *m*/*z* = 330 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{23}H_{22}O_2^+$: 330.1614; found: 330.1618.

4-(2,2,2-Trifluoro-1-isopropoxyethyl)-1,1′-biphenyl (4d)

i-PrOH (121 μL, 2 mmol, 10 equiv) and CH_3CN (2 mL) were added to **1a** (63 mg, 0.2 mmol), ZnF_2 (10.3 mg, 0.1 mmol, 0.5 equiv), and $Ir(ppy)_3$ (0.6 mg, 0.5 mol%, 1 μmol) in a bulb under N_2 atmosphere and the bulb was sealed. The mixture was stirred for 24 h at rt under blue LEDs. After completion of the reaction, the mixture was concentrated in vacuo. The product was purified by flash column chromatography (EA/PE = 1/100 v/v); yield: 54.4 mg (93%); white solid; mp 73–75 °C.

IR (film): 3061, 2994, 1408, 1387, 1259, 1175, 1125, 1097, 931, 839, 815, 762, 742, 724, 692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (t, *J* = 7.6 Hz, 4 H), 7.51 (d, *J* = 8.1 Hz, 2 H), 7.44 (t, *J* = 7.6 Hz, 2 H), 7.35 (t, *J* = 7.3 Hz, 1 H), 4.72 (q, *J* = 6.8 Hz, 1 H), 3.73 (hept, *J* = 6.1 Hz, 1 H), 1.24 (d, *J* = 6.1 Hz, 3 H), 1.17 (d, *J* = 6.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.21, 140.51, 132.92, 128.84, 128.58, 127.60, 127.19, 127.18, 124.08 (q, *J* = 281.8 Hz), 77.12 (q, *J* = 30.8 Hz), 71.95, 22.88, 21.20.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –77.32 (d, *J* = 7.0 Hz, 3 F).

MS (EI): *m*/*z* = 294 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{17}F_3O^+$: 294.1226; found: 294.1225.

4-(1,2,2,2-Tetrafluoroethyl)-1,1′-biphenyl (4e)

CF_3CF_2OH (180 μL, 2.5 mmol, 5 equiv) and CH_3CN (5 mL) were added to **1a** (157.5 mg, 0.5 mmol), CsF (152 mg, 1 mmol, 2 equiv), and $Ir(ppy)_3$ (3 mg, 5 μmol, 1 mol%) in a bulb at N_2 atmosphere and the bulb was sealed. The mixture was stirred for 24 h at rt under blue LEDs. After completion of the reaction, the mixture was concentrated in vacuo. The product was purified by flash column chromatography (EA/PE = 0–1/20 v/v); yield: 24.8 mg (20%); white solid; mp 62–63 °C.

IR (film): 2922, 1861, 1575, 1409, 1272, 1178, 1141, 1059, 824, 764, 742, 724, 695 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8.0 Hz, 2 H), 7.61–7.59 (m, 2 H), 7.53 (d, *J* = 8.1 Hz, 2 H), 7.46 (t, *J* = 7.5 Hz, 2 H), 7.38 (t, *J* = 7.3 Hz, 1 H), 5.63 (dq, *J* = 44.1, 6.1 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.45, 140.09, 129.08 (d, *J* = 20.1 Hz), 128.92, 127.91, 127.65 (d, *J* = 6.6 Hz), 127.45, 127.40, 127.21, 122.26 (qd, *J* = 281.6, 29.3 Hz), 88.83 (dq, *J* = 186.4, 34.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –79.17 (dd, *J* = 13.3, 6.1 Hz, 3 F), –194.62 (dq, *J* = 44.1, 13.1 Hz, 1 F).

MS (EI): *m*/*z* = 254 $[M]^+$.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{10}F_4^+$: 254.0713; found: 254.0716.

1-[1-([1,1′-Biphenyl]-4-yl)-2,2,2-trifluoroethoxy]-2,2,6,6-tetramethylpiperidine (4f)

THF (82 μL, 1 mmol, 5 equiv) and CH_3CN (2 mL) were added to **1a** (63 mg, 0.2 mmol), $ZnBr_2$ (22.5 mg, 0.1 mmol, 0.5 equiv), NaBr (9.3 mg, 0.09 mmol, 0.45 equiv), $Ir(ppy)_3$ (0.6 mg, 1 μmol, 0.5 mol%) and TEMPO (46.8 mg, 0.3 mmol, 1.5 equiv) in a blub under N_2 atmosphere and the bulb was sealed. The mixture was stirred for 24 h at rt under blue LEDs. After completion of the reaction, the mixture was concentrated in vacuo. The product was purified by flash column chromatography (PE); yield: 68.8 mg (88%); white solid; mp 98–100 °C.

IR (film): 2975, 2934, 1483, 1364, 1257, 1168, 1129, 1054, 905, 829, 765, 746, 733, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.58 (m, 4 H), 7.48 (d, *J* = 8.1 Hz, 2 H), 7.43 (t, *J* = 7.7 Hz, 2 H), 7.34 (t, *J* = 7.3 Hz, 1 H), 5.13 (q, *J* = 6.9 Hz, 1 H), 1.48–0.60 (m, 18 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.80, 140.49, 133.89, 129.68, 128.81, 127.55, 127.13, 126.82, 124.41 (q, *J* = 284.3 Hz), 84.47 (q, *J* = 28.7 Hz), 61.30, 60.52, 40.83, 34.05, 33.45, 20.37, 17.01.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –72.12 (d, *J* = 7.2 Hz, 3 F).

MS (DART): *m*/*z* = 392 $[M + H]^+$.

HRMS (EI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{29}F_3NO^+$: 392.2196; found: 392.2194.

Conflict of Interest

The authors declare no conflict of interest.

Funding Information

This work was supported by the National Key Research and Development Program of China (2016YFB0101200), the National Natural Science Foundation of China (21632009), the Key Programs of the Chinese Academy of Sciences (KGZD-EW-T08), the Key Research Program of Frontier Sciences of CAS (QYZDJ-SSW-SLH049).

Acknowledgment

C. Kuang acknowledges Syngenta for sponsoring the Ph.D. student scholarship.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-1671-6856.

References

(1) (a) Skubi, K. L.; Blum, T. R.; Yoon, T. P. *Chem. Rev.* **2016**, *116*, 10035. (b) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322.
(2) (a) Marzo, L.; Pagire, S. K.; Reiser, O.; König, B. *Angew. Chem. Int. Ed.* **2018**, *57*, 10034. (b) Horibe, T.; Ishihara, K. *Chem. Lett.* **2020**, *49*, 107. (c) Herraiz, A. G.; Suero, M. G. *Synthesis* **2019**, *51*, 2821.
(3) Dagousset, G.; Carboni, A.; Masson, G.; Magnier, E. In *Modern Synthesis Processes and Reactivity of Fluorinated Compounds, Chap. 14*; Groult, H.; Leroux, F. R.; Tressaud, A., Ed.; Elsevier: Amsterdam, **2017**, 389.
(4) Shen, M.; Shen, Y.; Wang, P. *Org. Lett.* **2019**, *21*, 2993.
(5) Webb, W. W.; Park, J. B.; Cole, E. L.; Donnelly, D. J.; Bonacorsi, S. J.; Ewing, W. R.; Doyle, A. G. *J. Am. Chem. Soc.* **2020**, *142*, 9493.
(6) Wayner, D. D. M.; McPhee, D. J.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 132.
(7) Kuang, C.; Zhou, X.; Xie, Q.; Ni, C.; Gu, Y.; Hu, J. *Org. Lett.* **2020**, *22*, 8670.
(8) (a) Cloke, J. B.; Pilgrim, F. J. *J. Am. Chem. Soc.* **1939**, *61*, 2667. (b) Ahmad, S.; Iqbal, J. *Chem. Lett.* **1987**, *5*, 953. (c) Iqbal, J.; Mukhopadhyay, M.; Mandal, A. K. *Synlett* **1997**, 876. (d) Iqbal, J.; Srivastava, R. R. *Tetrahedron* **1991**, *47*, 3155. (e) Coles, S. J.; Costello, J. F.; Draffin, W. N.; Hursthouse, M. B.; Paver, S. P. *Tetrahedron* **2005**, *61*, 4447. (f) Yadav, J. S.; Reddy, B. V. S.; Reddy, P. M. K.; Dash, U.; Gupta, M. K. *J. Mol. Catal. A: Chem.* **2007**, *271*, 266. (g) Yadav, J. S.; Reddy, B. V. S.; Reddy, P. M. K.; Gupta, M. K. *Tetrahedron Lett.* **2005**, *46*, 8493. (h) Srinivas, K.; Suresh, P.; Babu, C. N.; Sathyanarayana, A.; Prabusankar, G. *RSC Adv.* **2015**, *5*, 15579. (i) Suresh, V.; Suryakiran, N.; Rajesh, K.; Selvam, J. J. P.; Srinivasulu, M.; Venkateswarlu, Y. *Synth. Commun.* **2008**, *38*, 92. (j) Enthaler, S.; Weidauer, M. *Catal. Lett.* **2012**, *142*, 168. (k) Pasha, M. A.; Manjula, K. *Synth. Commun.* **2007**, *37*, 927. (l) Bodduri, V. D. V.; Choi, K. M.; Vaidya, R. R.; Patil, K.; Chirumarry, S.; Jang, K.; Yoon, Y.; Falck, J. R.; Shin, D. *Tetrahedron Lett.* **2015**, *56*, 7089. (m) Umeda, R.; Kaiba, K.; Tanaka, T.; Takahashi, Y.; Nishimura, T.; Nishiyama, Y. *Synlett* **2010**, 3089. (n) Umeda, R.; Nishimura, T.; Kaiba, K.; Tanaka, T.; Takahashi, Y.; Nishiyama, Y. *Tetrahedron* **2011**, *67*, 7217. (o) Fitch, J. W.; Payne, W. G.; Westmoreland, D. *J. Org. Chem.* **1983**, *48*, 751. (p) Pri-Bar, I.; Stille, J. K. *J. Org. Chem.* **1982**, *47*, 1215. (q) Luzzio, F. A.; Bobb, R. A. *Tetrahedron* **1999**, *55*, 1851. (r) Guo, Q.; Miyaji, T.; Hara, R.; Shen, B.; Takahashi, T. *Tetrahedron* **2002**, *58*, 7327.
(9) Kosmrlj, B.; Sket, B. *J. Org. Chem.* **2000**, *65*, 6890.
(10) Garzelli, R.; Samaritani, S.; Malanga, C. *Tetrahedron* **2008**, *64*, 4183.
(11) (a) It was reported that amines can be oxidized to radical cation. For examples under photoredox catalysis, see: (b) Prier, C. K.; MacMillan, D. W. C. *Chem. Sci.* **2014**, *5*, 4173. (c) Ahn, D. K.; Kang, Y. W.; Woo, S. K. *J. Org. Chem.* **2019**, *84*, 3612.
(12) Emer, E.; Twilton, J.; Tredwell, M.; Calderwood, S.; Collier, T. L.; Liégault, B.; Taillefer, M.; Gouverneur, V. *Org. Lett.* **2014**, *16*, 6004.
(13) Okano, T.; Sugiura, H.; Fumoto, M.; Matsubara, H.; Kusukawa, T.; Fujita, M. *J. Fluorine Chem.* **2002**, *114*, 91.
(14) Richard, J. R. *J. Am. Chem. Soc.* **1989**, *111*, 1455.
(15) Yusuke, Y.; Shoji, H.; Hisanori, S. *Tetrahedron* **2010**, *66*, 473.
(16) Zhao, Y.; Huang, W.; Zheng, J.; Hu, J. *Org. Lett.* **2011**, *13*, 5342.