Metal-free alkene oxy- and amino-perfluoroalkylations via carbocation formation by using perfluoro acid anhydrides: unique reactivity between styrenes and perfluoro diacyl peroxides

Elena Valverde,¹ Shintaro Kawamura,¹,² Daisuke Sekine,² and Mikiko Sodeoka*¹,²

¹Synthetic Organic Chemistry Laboratory, RIKEN Cluster for Pioneering Research, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan
²RIKEN Center for Sustainable Resource Science, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan
1. General Experimental

General: Reactions were conducted in a dry vessel under a positive pressure of nitrogen gas by using a nitrogen-filled balloon. Analytical thin-layer chromatography (TLC) was performed on glass plates coated with 0.25 mm 230–400 mesh silica gel (Merck, Silica gel 60 F254) containing a fluorescent indicator. Visualization was accomplished by means of ultraviolet irradiation at 254 nm and/or by spraying an ethanolic solution of 12-molybdo(VI)phosphoric acid as a developing agent. Flash column chromatography was performed using Silica gel N-60 (spherical, neutral, 40–50 µm, Kanto Chemical Co., Inc. (Kanto)) as described by Still et al.1

Instrumentation:

NMR analysis
NMR spectra were recorded at room temperature on a JEOL JNM-ECS-400 NMR spectrometer at 400 MHz for $^1$H, 100 MHz for $^{13}$C, and 376 MHz for $^{19}$F. The proton chemical shift values are reported in parts per million (ppm, δ scale) downfield from tetramethysilane and referenced to the proton resonance of CHCl$_3$ (δ 7.26). The carbon chemical shift values are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and referenced to the carbon resonance of CDCl$_3$ (δ 77.16). The fluorine chemical shift values are reported in parts per million (ppm, δ scale) with CFCl$_3$ (δ 0.00) as an external standard. J values are reported in hertz (Hz). The data are presented in the following order: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances, and br = broad), coupling constant and signal area integration in natural numbers.

IR analysis
Infrared spectra were measured on a Thermo Nicolet iS5. Only diagnostic absorptions are listed.

HRMS analysis
ESI-MS spectra were measured on a Bruker micrOTOF-QII-RSL. The samples were diluted with MeOH for measurement. EI-MS was taken on a JEOL JMS-T100GCV gas chromatograph time-of-flight mass spectrometer. The samples were diluted with CHCl$_3$ for measurement.

Solvents: Anhydrous dichloromethane was purchased from Kanto Chemical Co., Inc.

Materials: Reagents were purchased from Wako Pure Chemical Industries, Ltd. Tokyo

---

1W. C. Still, M. Kahn, A. Mitra, J. Org. Chem., 1978, 43, 2923.
Chemical Industry Co., Ltd. and Sigma-Aldrich Inc. Known alkenes 3a and 12 were prepared according to the cited literature.

2. Additional Results

Optimization of the reaction conditions

Table S1. Optimization of the conditions for the synthesis of 2a

| Entry | TFAA/urea·H₂O₂ (equiv.) | Temp. (°C) | Additive | Yield (%)* | Recovery of 1a (%)† |
|-------|-------------------------|------------|----------|------------|---------------------|
| 1     | 4.0/1.2                 | 0          | –        | 0          | 0                  |
| 2     | 4.0/1.2                 | 25         | –        | 38         | 3                   |
| 3     | 4.0/1.2                 | 40         | –        | 60         | 5                   |
| 4     | 6.0/1.2                 | 40         | –        | 44         | 4                   |
| 5     | 8.0/2.2                 | 40         | –        | 74         | 4                   |
| 6     | 8.0/2.2                 | 40         | TFA (0.4 equiv.) | 75     | 4                   |
| 7     | 8.0/2.2                 | 40         | TFA (1.0 equiv.) | 75     | 3                   |
| 8     | 10/2.5                  | 40         | –        | 85 (80)†   | 4                   |
| 9     | 12/3.0                  | 40         | –        | 81         | 3                   |
| 10    | 10/3.5                  | 40         | –        | 83         | 3                   |

*The reactions were conducted on 0.20 mmol scale. †The yields were estimated by means of 19F NMR analysis, with α,α,α-trifluorotoluene as an internal standard. ‡The recovery of 1a was estimated by means of 1H NMR analysis, with 1,1,2,2-tetrachloroethane as an internal standard. †Yield in parenthesis is the isolated yield.

19F NMR monitoring:

Trifluoroacetic anhydride (0.14 mL, 1.0 mmol) was slowly added to a suspension of urea·H₂O₂ (24 mg, 0.25 mmol) in CD₂Cl₂ (0.6 mL) in a Schlenk tube at 0 °C, and the mixture

L. Zhou, J. Chen, C. K. Tan, Y.-Y. Yeung, J. Am. Chem. Soc., 2011, 133, 9164.
Y. Arai, R. Tomita, G. Ando, T. Koike, M. Akita, Chem. Eur. J., 2016, 22, 1262.
was stirred for 1 h. The obtained colorless solution containing bis(trifluoroacetyl)peroxide (BTFAP) was transferred to a valve NMR tube containing \( \alpha,\alpha,\alpha \)-trifluorotoluene (13 mg, 0.09 mmol) as an internal standard under a \( \text{N}_2 \) atmosphere. The \(^{19}\text{F} \) NMR spectrum of the sample was measured at room temperature, and 0.21 mmol of the peroxide was found to have been formed. After the measurement, the NMR sample was warmed to 40 °C on an oil bath. After 30 min, \(^{19}\text{F} \) NMR measurement was conducted at room temperature (I) (Figure S1); and no change of the spectral signals or integration values was observed. Then, styrene \( 1\text{a} \) (14 mg, 0.10 mmol) was added to the sample solution at room temperature, and the mixture was warmed to 40 °C on an oil bath. After 30 min, the \(^{19}\text{F} \) NMR spectrum of the sample was measured at room temperature (II); the results indicated the presence of 0.09 mmol (86% yield based on \( 1\text{a} \)) of oxy-trifluoromethylation product \( 2\text{a} \) and 0.10 mmol of BTFAP. This shows that styrene is essential for decomposition of BTFAP and CF\(_3\) radical generation.

Figure S1. \(^{19}\text{F} \) NMR monitoring of the decomposition of BTFAP
Reaction of N-(2-vinylphenethyl)-p-toluenesulfonamide:

To a suspension of urea·H₂O₂ (47 mg, 0.50 mmol) in DCM (1 mL) trifluoroacetic anhydride (0.28 mL, 2.0 mmol) was slowly added at 0 °C. After stirring for 1 h, N-(2-vinylphenethyl)-p-toluenesulfonamide (60 mg, 0.20 mmol) was added. Then, the mixture was immediately warmed to 40 °C, further stirred for 3 h, then diluted with Et₂O (5 mL), quenched with saturated K₂CO₃ solution at 0 °C, again stirred for 20 min. The phases were separated and the aqueous layer was extracted with Et₂O (2 x 5 mL). The combined organic phase was dried over Na₂SO₄, filtered and concentrated in vacuo. Purification of the crude product by column chromatography on silica gel afforded N-(2-(3,3,3-trifluoro-1-hydroxypropyl)phenethyl)-p-toluenesulfonamide (63 mg, 81% yield) and 2-tosyl-1-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroisoquinoline (7 mg, 9%).

<N-(2-(3,3,3-trifluoro-1-hydroxypropyl)phenethyl)-p-toluenesulfonamide>

\(^1\)H NMR (400 MHz, CDCl₃)

2.28–2.43 (m, 2H), 2.40 (s, 3H), 2.56–2.72 (m, 1H), 2.80 (ddd, J = 14.0, 6.9, 6.7 Hz, 1H), 2.89 (ddd, J = 14.0, 7.0, 6.9 Hz, 1H), 3.14 (ddd, J = 13.0, 7.0, 6.9 Hz), 3.22 (ddd, J = 13.0, 6.9, 6.7 Hz, 1H), 4.85–5.10 (br, 1H), 5.24 (dd, J = 8.9, 3.3 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 7.18–7.29 (overlap, 4H), 7.41 (d, J = 7.5 Hz, 1H), 7.63 (d, J = 7.9 Hz, 2H)

\(^13\)C NMR (100 MHz, CDCl₃)

21.6, 32.2, 42.2 (q, J = 27 Hz), 44.2, 64.9 (q, J = 2.9 Hz), 126.0 (q, J = 277 Hz), 126.4, 127.1 (2C), 127.7, 128.7, 129.9 (2C), 130.3, 134.9, 136.8, 140.5, 143.7.

\(^19\)F NMR (376 MHz, CDCl₃)

-63.7 (t, J = 10.1 Hz)

IR (neat, cm⁻¹)

3287, 1325, 1260, 1156, 1093, 815, 761, 662.

HRMS-ESI (m/z)

[M+Na]⁺ calcd. for C₁₈H₂₉F₃NO₃SNa, 410.1008; found, 410.1009.

<2-Tosyl-1-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroisoquinoline>

\(^1\)H NMR (400 MHz, CDCl₃)

2.35 (s, 3H), 2.41–2.56 (m, 1H), 2.56–2.82 (m, 3H), 3.48 (ddd, J = 14.2, 10.3,
5.3 Hz, 1H), 3.77 (dddd, \(J = 14.2, 6.4, 3.7, 0.9\) Hz, 1H), 5.42 (dd, \(J = 8.4, 5.1\) Hz, 1H), 6.96 (d, \(J = 7.0\) Hz, 1H), 7.08 (dd, \(J = 7.0, 1.8\) Hz, 1H), 7.12–7.18 (m, 4H), 7.63 (d, \(J = 8.3\) Hz, 2H)

\(^{13}\text{C NMR} (100\text{ MHz, CDCl}_3)\)

21.6, 26.3, 39.3, 41.3 (q, \(J = 27\) Hz), 51.1 (q, \(J = 2.9\) Hz), 125.3 (q, \(J = 278\) Hz), 126.7, 127.0, 127.4 (2C), 127.8, 129.3, 129.6 (2C), 133.3, 134.4, 137.0, 143.6.

\(^{19}\text{F NMR} (376\text{ MHz, CDCl}_3)\)

–63.3 (t, \(J = 11.6\) Hz)

IR (neat, cm\(^{-1}\))

1339, 1266, 1165, 1091, 941, 815, 734, 659.

HRMS-ESI (m/z)

[M+H]\(^+\) calcd. for C\(_{18}\)H\(_{19}\)F\(_3\)NO\(_2\)S, 370.1083; found, 370.1090.
Figure S2. NMR spectra of $N$-(2-(3,3,3-trifluoro-1-hydroxypropyl)phenethyl)-$p$-toluenesulfonamide
Figure S3. NMR spectra of 2-Tosyl-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydro-isoquinoline
3. Experimental procedures

Preparation of aminoalkene 3b

Substrate 3b was synthesized according to the literature procedure for preparing 3a.2 A solution of carboxylic acid S-1 (2.0 g, 12 mmol) in dry Et2O (15 mL) was added dropwise to a suspension of lithium aluminum hydride (0.9 g, 24 mmol) in dry Et2O (35 mL) at 0 °C. The mixture was stirred at room temperature for 2 h, and then the reaction was quenched by careful and sequential addition of H2O (7 mL) and 2 M NaOH solution (7 mL) at 0 °C. The resulting suspension was filtered through a Celite pad and the filtrate was dried over Na2SO4, filtered and concentrated in vacuo to provide S-2 (1.5 g, 84% yield) as a yellow oil. Methanesulfonyl chloride (0.97 mL, 13 mmol) was added dropwise to a solution of S-2 (1.5 g, 10 mmol) and triethylamine (1.9 mL, 14 mmol) in dry DCM (30 mL) at 0 °C. The solution was stirred at 0 °C for 10 min, then warmed to room temperature, and stirred further for 1 h. The reaction mixture was diluted with DCM (10 mL) and washed with 1 M HCl aqueous solution (40 mL), saturated NaHCO3 solution (40 mL) and brine (40 mL). The organic phase was dried over Na2SO4, filtered and concentrated in vacuo. Purification by means of column chromatography (SiO2; EtOAc/hexane = 20/80) provided S-3 (2.2 g, 93% yield) as a yellow oil. A solution of p-toluenesulfonamide (4.4 g, 26 mmol) and potassium hydroxide (1.4 g, 26 mmol) in dry DMF (70 mL) was heated to 100 °C for 0.5 h. Then a solution of S-3 (2.1 g, 13 mmol) in dry DMF (40 mL) was added dropwise. The mixture was stirred at 100 °C for 2 h, cooled to room temperature, quenched with water (80 mL), and extracted with Et2O (3 x 60 mL). The combined organic phase was washed with water (60 mL) and brine (60 mL), dried over Na2SO4, filtered and concentrated in vacuo. Purification of the residue by means of column chromatography (SiO2; EtOAc/hexane = 20/80) provided 3b (2.0 g, 64% yield) as a colorless oil, whose spectroscopic data matched reported values.4

---

4J. Ciesielski, G. Dequirez, P. Retailleau, V. Gandon, P. Dauban, Chem. Eur. J. 2016, 22, 9338.
Preparation of aminoalkene 3c

\[
\begin{array}{c}
\text{S-4} \\
\text{TsCl, Et3N} \\
\text{DCM} \\
0 \, \text{°C to rt, 13 h} \\
\end{array}
\begin{array}{c}
\text{3c} \\
83\% \\
\end{array}
\]

\(p\)-Toluenesulfonyl chloride (0.46 mg, 2.4 mmol) was added to a solution of S-4\(^*\) (0.50 g, 2.2 mmol) and triethylamine (0.6 mL, 4.4 mmol) in dry DCM (9 mL) at 0 °C. The reaction mixture was stirred at room temperature overnight, then diluted with DCM (10 mL) and washed with 1 M HCl aqueous solution (2 x 15 mL). The organic phase was dried over Na\(_2\)SO\(_4\), filtered and concentrated \textit{in vacuo} to give a yellow oil. Purification by column chromatography (SiO\(_2\); EtOAc/hexane = 10/90) provided 3c (0.70 g, 83% yield) as a white solid.

\(^1\)H NMR (400 MHz, CDCl\(_3\))

1.21–1.45 (overlap, 10H), 2.42 (s, 3H), 2.49 (s, 2H), 2.50 (d, \(J = 7.6\) Hz, 2H), 3.93 (t, \(J = 7.6\) Hz, 1H), 5.03 (d, \(J = 1.6\) Hz, 1H), 5.17 (d, \(J = 1.6\) Hz, 1H), 7.22 (d, \(J = 8.4\) Hz, 2H), 7.27–7.33 (overlap, 5H), 7.39 (d, \(J = 8.4\) Hz, 2H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\))

21.5 (2C), 21.6, 26.1, 33.9 (2C), 37.6, 42.5, 48.6, 118.0, 126.5 (2C), 127.0 (2C), 127.7, 128.9 (2C), 129.6 (2C), 136.9, 143.1, 143.8, 146.0.

IR (neat, cm\(^{-1}\))

3284, 1454, 1415, 1325, 1161, 1093, 1071, 906, 813, 779, 705, 662.

HRMS-ESI (\textit{m/z})

[M+Na]\(^+\) calcd. for C\(_{23}\)H\(_{29}\)NO\(_2\)SNa, 406.1817; found, 406.1818.

Oxy- and amino-perfluoroalkylation of alkenes: general procedure

To a suspension of urea-H\(_2\)O\(_2\) (47 mg, 0.50 mmol) in DCM (1 mL) perfluoro acid anhydride (2.0 mmol) was slowly added at 0 °C. After stirring for 1 h, styrene (0.20 mmol) was added. Then, the mixture was immediately warmed to 40 °C, further stirred for 1 h, then diluted with Et\(_2\)O (5 mL), quenched with saturated K\(_2\)CO\(_3\) solution at 0 °C, again stirred for 20 min. The phases were separated and the aqueous layer was extracted with Et\(_2\)O (2 x 5 mL).\(^6\) The combined organic phase was dried over Na\(_2\)SO\(_4\), filtered and

---

\(^3\)J.-S. Lin, P. Yu, L. Huang, P. Zhang, B. Tan, X.-Y. Liu, \textit{Angew. Chem. Int. Ed.}, 2015, \textbf{54}, 7847.

\(^4\)The combined organic phase was checked with XploSens PS\(^*\) to confirm the absence of peroxide, and the water phase was treated with saturated Na\(_2\)S\(_2\)O\(_3\) to decompose H\(_2\)O\(_2\).

---

S10
concentrated *in vacuo*. Purification of the crude product by column chromatography on silica gel afforded the target compound.

**Synthesis of 1-(4-chlorophenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2a):**

![Chemical structure of 2a]

The reaction was carried out according to the general procedure. The target compound 2a was obtained as a colorless oil (51 mg, 80% yield) after purification by column chromatography (SiO$_2$; 100% hexane).

$^1$H NMR (400 MHz, CDCl$_3$)

2.62 (dq, $J = 15.7$, 10.1, 2.8 Hz, 1H), 2.95 (m, 1H), 6.18 (dd, $J = 7.6$, 2.8 Hz, 1H), 7.33 (d, $J = 6.8$ Hz, 2H), 7.41 (d, $J = 6.8$ Hz, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$)

40.1 (q, $J = 29$ Hz), 73.0 (q, $J = 2.9$ Hz), 114.4 (q, $J = 285$ Hz), 124.7 (q, $J = 277$ Hz), 128.0 (2C), 129.7 (2C), 134.5, 136.1, 156.2 (q, $J = 43$ Hz).

$^{19}$F NMR (376 MHz, CDCl$_3$)

–64.3 (t, $J = 10.1$ Hz, 3F), –75.2 (s, 3F).

IR (neat, cm$^{-1}$)

1793, 1495, 1392, 1378, 1338, 1323, 1283, 1253, 1226, 1143, 1130, 1096, 1064, 1016, 828, 819, 668.

HRMS-EI (m/z)

[M] calcd. for C$_{11}$H$_7$ClF$_6$O$_2$, 320.0039; found, 320.0027.

**Synthesis of 1-(4-fluorophenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2b):**

![Chemical structure of 2b]

The reaction was carried out according to the general procedure. The target compound 2b was obtained as a yellow oil (54 mg, 88% yield) after purification by column chromatography (SiO$_2$; 100% hexane).

Procedure for gram-scale synthesis: To a suspension of urea·H$_2$O$_2$ (3.9 g, 41 mmol) in DCM (82 mL), trifluoroacetic anhydride (23.1 mL, 164 mmol) was slowly added at 0 °C. After stirring for 1 h, 4-fluorostyrene (2.0 g, 16 mmol) was added. The mixture was immediately warmed to 40 °C and stirred for further 1 h. After dilution with DCM (50 mL), the reaction was quenched with saturated K$_2$CO$_3$ solution at 0 °C for 20 min. The phases were separated and the aqueous layer was extracted with DCM (2 x 50 mL). The
combined organic phase was dried over Na₂SO₄, filtered and concentrated in vacuo to give pure 2b (4.7 g, 93%) as a yellow oil.

¹H NMR (400 MHz, CDCl₃)
2.62 (dqd, J = 15.5, 10.1, 3.6 Hz, 1H), 2.96 (m, 1H), 6.20 (dd, J = 9.6, 3.6 Hz, 1H), 7.12 (m, 2H), 7.39 (m, 2H).

¹³C NMR (100 MHz, CDCl₃)
40.2 (q, J = 29 Hz), 73.1 (q, J = 2.8 Hz), 114.4 (q, J = 285 Hz), 116.5 (d, J = 22 Hz, 2C), 124.7 (q, J = 277 Hz), 128.7 (d, J = 8.6 Hz, 2C), 132.0 (d, J = 3.9 Hz), 156.2 (q, J = 43 Hz), 163.5 (d, J = 249 Hz).

¹⁹F NMR (376 MHz, CDCl₃)
–64.3 (t, J = 10.1 Hz, 3F), –75.2 (s, 3F), –110.6 (m, 1F).

IR (neat, cm⁻¹)
1791, 1515, 1340, 1229, 1129, 1098, 1064, 831, 771, 735.

HRMS-EI (m/z)
[M] calcd. for C₁₁H₇F₇O₂, 304.0334; found, 304.0312.

Synthesis of 1-(4-bromophenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2c):

The reaction was carried out according to the general procedure. The target compound 2c was obtained as a colorless oil (56 mg, 77% yield) after purification by column chromatography (SiO₂; 100% hexane).

¹H NMR (400 MHz, CDCl₃)
2.62 (dqd, J = 15.6, 10.1, 3.6 Hz, 1H), 2.95 (m, 1H), 6.17 (dd, J = 9.6, 3.6 Hz, 1H), 7.27 (d, J = 8.4 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H).

¹³C NMR (100 MHz, CDCl₃)
40.1 (q, J = 29 Hz), 73.1 (q, J = 3.8 Hz), 114.4 (q, J = 285 Hz), 124.2, 124.7 (q, J = 277 Hz), 128.2 (2C), 132.7 (2C), 135.1, 156.2 (q, J = 43 Hz).

¹⁹F NMR (376 MHz, CDCl₃)
–64.3 (t, J = 10.1 Hz, 3F), –75.2 (s, 3F).

IR (neat, cm⁻¹)
1791, 1491, 1377, 1338, 1253, 1225, 1129, 1102, 1075, 1013, 816, 735, 668.

HRMS-EI (m/z)
[M] calcd. for C₁₁H₇BrF₆O₂, 363.9534; found, 363.9506.
Synthesis of 1-(4-acetoxyphenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2d):

The reaction was carried out according to the general procedure. The target compound 2d was obtained as a colorless oil (69 mg, quantitative yield) after purification by column chromatography (SiO$_2$; EtOAc/hexane = 5/95).

$^1$H NMR (400 MHz, CDCl$_3$)

2.31 (s, 3H), 2.62 (dqd, $J = 15.6, 10.1, 3.2$ Hz, 1H), 2.96 (m, 1H), 6.23 (dd, $J = 10.0, 3.2$ Hz, 1H), 7.16 (d, $J = 8.4$ Hz, 2H), 7.41 (d, $J = 8.4$ Hz, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$)

21.2, 40.2 (q, $J = 29$ Hz), 73.0 (q, $J = 3.0$ Hz), 114.4 (q, $J = 285$ Hz), 122.7 (2C), 124.8 (q, $J = 277$ Hz), 127.8 (2C), 133.6, 151.7, 156.2 (q, $J = 43$ Hz), 169.3.

$^{19}$F NMR (376 MHz, CDCl$_3$)

–64.5 (t, $J = 10.1$ Hz, 3F), –75.2 (s, 3F).

IR (neat, cm$^{-1}$)

1791, 1770, 1374, 1341, 1258, 1216, 1199, 1130, 1104, 1064, 1018, 913, 800, 774, 631.

HRMS-EI (m/z)

[M] calcd. for C$_{13}$H$_{10}$F$_6$O$_4$, 344.0483; found, 344.0447.

Synthesis of 3,3,3-trifluoro-1-phenylpropyl 2,2,2-trifluoroacetate (2e):

The reaction was carried out according to the general procedure. The target compound 2e was obtained as a colorless oil (90% yield based on $^1$H and $^{19}$F NMR).$^7$ The crude product was purified by column chromatography (SiO$_2$; 100% hexane) to obtain an analytical sample (11 mg).

$^1$H NMR (400 MHz, CDCl$_3$)

2.63 (dqd, $J = 15.5, 10.1, 3.2$ Hz, 1H), 2.98 (m, 1H), 6.23 (dd, $J = 9.6, 3.2$ Hz, 1H), 7.37–7.45 (overlap, 5H).

$^{13}$C NMR (100 MHz, CDCl$_3$)

40.3 (q, $J = 29$ Hz), 73.7 (q, $J = 2.9$ Hz), 114.5 (q, $J = 284$ Hz), 124.8 (q, $J =

$^7$Compound 2e appeared to be volatile, hampering full isolation.
(2C), 129.9, 136.2, 156.3 (q, $J = 44$ Hz).

$^{19}$F NMR (376 MHz, CDCl$_3$)

\[ \text{–64.4 (d, } J = 10.1 \text{ Hz, 3F), –75.2 (s, 3F).} \]

IR (neat, cm$^{-1}$)

1791, 1347, 1332, 1254, 1226, 1129, 1077, 1062, 773, 763, 734, 698, 668, 609.

HRMS-EI ($m/z$)

[M] calcd. for C$_{11}$H$_8$F$_6$O$_2$, 286.0428; found, 286.0417.

Synthesis of 1-(4-methylphenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2f):

The reaction was carried out according to the general procedure. The target compound 2f was obtained as a colorless oil (43 mg, 72% yield) after purification by column chromatography (SiO$_2$; 100% hexane).

$^1$H NMR (400 MHz, CDCl$_3$)

\[ \begin{align*}
2.37 (s, 3H), & \ 2.61 (dqd, J = 15.6, 10.1, 3.6 \text{ Hz, } 1H), \\
2.96 (m, 1H), & \ 6.19 (dd, J = 9.6, 3.6 \text{ Hz, } 1H), \\
7.22 (m, 2H), & \ 7.27 (m, 2H). 
\end{align*} \]

$^{13}$C NMR (100 MHz, CDCl$_3$)

\[ \begin{align*}
21.4, & \ 40.2 (q, J = 29 \text{ Hz}), \ 73.7 (q, J = 3.8 \text{ Hz}), \ 114.5 (q, J = 285 \text{ Hz}), \\
124.9 (q, J = 277 \text{ Hz}), & \ 126.5 (2C), \ 130.0 (2C), \ 133.2, \ 140.1, \ 156.3 (q, J = 43 \text{ Hz}). 
\end{align*} \]

$^{19}$F NMR (376 MHz, CDCl$_3$)

\[ \text{–64.4 (t, } J = 10.1 \text{ Hz, 3F), –75.2 (s, 3F).} \]

IR (neat, cm$^{-1}$)

1791, 1378, 1324, 1254, 1227, 1130, 1058, 813, 733, 668, 652.

HRMS-EI ($m/z$)

[M] calcd. for C$_{12}$H$_{10}$F$_6$O$_2$, 300.0585; found, 300.0566.

Synthesis of 1-(2-(chloromethyl)phenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2g):

The reaction was carried out according to the general procedure. The target compound 2g was obtained as a colorless oil (50 mg, 75% yield) after purification by column chromatography (SiO$_2$; 100% hexane).
\( ^1 \text{H NMR (400 MHz, CDCl}_3 \) \\
2.62 (dq, \( J = 15.6, 10.1, 3.5 \text{ Hz, 1H})\), 2.96 (m, 1H), 4.59 (s, 2H), 6.22 (dd, \( J = 9.7, 3.5 \text{ Hz, 1H})\), 7.38 (d, \( J = 8.4 \text{ Hz, 2H})\), 7.46 (d, \( J = 8.4 \text{ Hz, 2H})\).

\( ^{13} \text{C NMR (100 MHz, CDCl}_3 \) \\
40.2 (q, \( J = 29 \text{ Hz})\), 45.5, 73.3 (q, \( J = 2.9 \text{ Hz})\), 114.4 (q, \( J = 284 \text{ Hz})\), 124.8 (q, \( J = 277 \text{ Hz})\), 126.9 (2C), 129.6 (2C), 136.3, 139.4, 156.2 (q, \( J = 43 \text{ Hz})\).

\( ^{19} \text{F NMR (376 MHz, CDCl}_3 \) \\
–64.3 (t, \( J = 10.1 \text{ Hz, 3F})\), –75.1 (s, 3F).

IR (neat, cm\(^{-1}\))
1791, 1340, 1314, 1275, 1254, 1227, 1130, 1063, 832, 789, 734, 684, 668, 658.

HRMS-EI (m/z)
[M] calcd. for \( \text{C}_{12}\text{H}_9\text{ClF}_6\text{O}_2 \), 334.0195; found, 334.0179.

Synthesis of \( 1\)-\((4\)-(tert-butyl)phenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2h):

The reaction was carried out according to the general procedure. The target compound \( 2h \) was obtained as a colorless oil (60 mg, 87% yield) after purification by column chromatography (SiO\(_2\); 100% hexane).

\( ^1 \text{H NMR (400 MHz, CDCl}_3 \) \\
1.32 (s, 9H), 2.61 (dq, \( J = 15.6, 10.1, 3.2 \text{ Hz, 1H})\), 2.97 (m, 1H), 6.23 (dd, \( J = 9.6, 3.2 \text{ Hz, 1H})\), 7.31 (d, \( J = 8.4 \text{ Hz, 2H})\), 7.43 (d, \( J = 8.4 \text{ Hz, 2H})\).

\( ^{13} \text{C NMR (100 MHz, CDCl}_3 \) \\
31.3 (3C), 34.9, 40.2 (q, \( J = 29 \text{ Hz})\), 73.6 (q, \( J = 2.9 \text{ Hz})\), 114.5 (q, \( J = 285 \text{ Hz})\), 124.9 (q, \( J = 277 \text{ Hz})\), 126.2 (2C), 126.3 (2C), 133.2, 153.2, 156.3 (q, \( J = 43 \text{ Hz})\).

\( ^{19} \text{F NMR (376 MHz, CDCl}_3 \) \\
–64.5 (t, \( J = 10.1 \text{ Hz, 3F})\), –75.2 (s, 3F).

IR (neat, cm\(^{-1}\))
1791, 1394, 1367, 1340, 1253, 1224, 1132, 1063, 830, 820, 774, 733, 639.

HRMS-EI (m/z)
[M] calcd. for \( \text{C}_{15}\text{H}_{16}\text{F}_6\text{O}_2 \), 342.1054; found, 342.1029.

S15
Synthesis of 1-(4-methoxyphenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2i):

To a suspension of urea·H₂O₂ (47 mg, 0.50 mmol) in DCM (1 mL), trifluoroacetic anhydride (0.28 mL, 2.0 mmol) was slowly added at 0 °C. After stirring for 1 h, Cs₂CO₃ (326 mg, 1.0 mmol) was added, followed by styrene 1i (27 mg, 0.20 mmol). The mixture was stirred for further 10 min. After addition of Et₂O (5 mL), the reaction was quenched with saturated K₂CO₃ solution at 0 °C for 20 min. The phases were separated and the aqueous layer was extracted with Et₂O (2 x 5 mL). The combined organic phase was dried over Na₂SO₄, filtered and concentrated in vacuo. Purification of the crude product by column chromatography on silica gel (SiO₂; EtOAc/hexane = 10/90) afforded the target product 2i as a colorless oil (24 mg, 38% yield).

¹H NMR (400 MHz, CDCl₃)

2.61 (dq, J = 15.5, 10.1, 3.6 Hz, 1H), 2.96 (m, 1H), 3.82 (s, 3H), 6.18 (dd, J = 9.5, 3.6 Hz, 1H), 6.93 (d, J = 8.8 Hz, 2H), 7.32 (d, J = 8.8 Hz, 2H).

¹³C NMR (100 MHz, CDCl₃)

40.1 (q, J = 29 Hz), 55.5, 73.6 (q, J = 2.9 Hz), 114.5 (q, J = 286 Hz), 114.7 (2C), 124.9 (q, J = 277 Hz), 128.1, 128.3 (2C), 156.3 (q, J = 43 Hz), 160.8.

¹⁹F NMR (376 MHz, CDCl₃)

–64.4 (t, J = 10.1 Hz, 3F), –75.2 (s, 3F).

IR (neat, cm⁻¹)

2924, 2853, 1791, 1617, 1506, 1308, 1279, 1226, 1131, 1063, 1033, 829.

HRMS-EI (m/z)

[M] calcd. for C₁₂H₁₀F₆O₃, 316.0534; found, 316.0544.

Synthesis of 1-(3-(trifluoromethyl)phenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2j):

The reaction was carried out in DCE at 60 °C for the second step, but otherwise according to the general procedure. The target compound 2j was obtained as a colorless oil (52 mg, 74% yield) after purification by column chromatography (SiO₂; 100% hexane).
\(^{1}\)H NMR (400 MHz, CDCl\(_3\))

2.66 (dqd, \(J = 15.5, 10.1, 3.6\) Hz, 1H), 2.99 (m, 1H), 6.27 (dd, \(J = 9.6, 3.6\) Hz, 1H), 7.59 (m, 2H), 7.64 (br, 1H), 7.69 (m, 1H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\))

40.2 (q, \(J = 29\) Hz), 72.9 (q, \(J = 2.9\) Hz), 114.4 (q, \(J = 285\) Hz), 123.6 (q, \(J = 272\) Hz), 123.3 (q, \(J = 3.8\) Hz), 124.6 (q, \(J = 277\) Hz), 126.9 (q, \(J = 3.7\) Hz), 129.9, 130.2, 132.0 (q, \(J = 32\) Hz), 137.1, 156.2 (q, \(J = 43\) Hz).

\(^{19}\)F NMR (376 MHz, CDCl\(_3\))

–62.8 (s, 3F), –64.2 (t, \(J = 10.1\) Hz, 3F), –75.1 (s, 3F).

IR (neat, cm\(^{-1}\))

1793, 1330, 1252, 1203, 1128, 1094, 1076, 805, 777, 736, 702, 668.

HRMS-EI (m/z)

[M] calcd. for C\(_{12}\)H\(_7\)F\(_9\)O\(_2\), 354.0302; found, 354.0283.

Synthesis of 1-(3-fluorophenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2k):

The reaction was carried out in DCE at 60 °C for the second step, but otherwise according to the general procedure. The target compound 2k was obtained as a colorless oil (47 mg, 78% yield) after purification by column chromatography (SiO\(_2\); 100% hexane).

\(^{1}\)H NMR (400 MHz, CDCl\(_3\))

2.63 (dqd, \(J = 15.6, 10.1, 3.2\) Hz, 1H), 2.95 (m, 1H), 6.20 (dd, \(J = 9.6, 3.2\) Hz, 1H), 7.11 (m, 2H), 7.17 (m, 1H), 7.41 (m, 1H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\))

40.2 (q, \(J = 29\) Hz), 72.9, 113.6 (d, \(J = 22\) Hz), 114.4 (q, \(J = 285\) Hz), 117.1 (d, \(J = 21\) Hz), 122.2 (d, \(J = 2.8\) Hz), 124.7 (q, \(J = 277\) Hz), 131.2 (d, \(J = 8.7\) Hz), 138.4 (d, \(J = 7.7\) Hz), 156.2 (q, \(J = 43\) Hz), 163.1 (d, \(J = 248\) Hz).

\(^{19}\)F NMR (376 MHz, CDCl\(_3\))

–64.3 (t, \(J = 10.1\) Hz, 3F), –75.1 (s, 3F), –110.6 (m, 1F).

IR (neat, cm\(^{-1}\))

1793, 1596, 1491, 1378, 1341, 1258, 1227, 1144, 1127, 1064, 876, 789, 779, 735, 696, 668.
HRMS-EI (m/z)

[M] calcd. for C\textsubscript{11}H\textsubscript{7}F\textsubscript{7}O\textsubscript{2}, 304.0334; found, 304.0314.

Synthesis of 1-(2-chlorophenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2l):

The reaction was carried out according to the general procedure. The target compound 2l was obtained as a colorless oil (43 mg, 67% yield) after purification by column chromatography (SiO\textsubscript{2}; 100% hexane).

\(^1^H\) NMR (400 MHz, CDCl\textsubscript{3})

2.64–2.90 (overlap, 2H), 6.64 (dd, J = 9.6, 2.8 Hz, 1H), 7.33–7.38 (overlap, 2H), 7.40–7.46 (overlap, 2H).

\(^{13}C\) NMR (100 MHz, CDCl\textsubscript{3})

39.2 (q, J = 29 Hz), 70.4 (q, J = 3.9 Hz), 114.5 (q, J = 285 Hz), 124.8 (q, J = 277 Hz), 126.6, 128.0, 130.4, 130.7, 132.0, 134.2, 156.0 (q, J = 43 Hz).

\(^{19}F\) NMR (376 MHz, CDCl\textsubscript{3})

–64.5 (t, J = 10.1 Hz, 3F), –75.1 (s, 3F).

IR (neat, cm\textsuperscript{−1})

1793, 1379, 1344, 1252, 1225, 1134, 1054, 1037, 757, 736, 711, 668, 612.

HRMS-EI (m/z)

[M] calcd. for C\textsubscript{11}H\textsubscript{7}ClF\textsubscript{6}O\textsubscript{2}, 320.0039; found, 320.0017.

Synthesis of 1-(2-bromophenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2m):

The reaction was carried out according to the general procedure. The target compound 2m was obtained as a colorless oil (54 mg, 74% yield) after purification by column chromatography (SiO\textsubscript{2}; 100% hexane).

\(^1^H\) NMR (400 MHz, CDCl\textsubscript{3})

2.63–2.88 (overlap, 2H), 6.60 (dd, J = 9.6, 2.8 Hz, 1H), 7.22–7.29 (m, 1H), 7.39–7.42 (overlap, 2H), 7.62 (d, J = 7.6 Hz, 1H).

\(^{13}C\) NMR (100 MHz, CDCl\textsubscript{3})

39.3 (q, J = 29 Hz), 72.6 (q, J = 2.8 Hz), 114.5 (q, J = 285 Hz), 121.6, 124.7 (q, J = 277 Hz), 126.7, 128.6, 131.0, 133.7, 135.9, 155.9 (q, J = 43 Hz).
$^{19}$F NMR (376 MHz, CDCl$_3$)

$-64.5$ (t, $J = 10.1$ Hz, 3F), $-75.1$ (s, 3F).

IR (neat, cm$^{-1}$)

1793, 1474, 1438, 1392, 1343, 1314, 1284, 1251, 1225, 1205, 1131, 1065, 1026, 843, 756, 736, 722, 691, 668, 611.

HRMS-EI ($m/z$)

[M] calcd. for C$_{11}$H$_7$BrF$_6$O$_2$, 363.9534; found, 363.9505.

**Synthesis of 1-(2-methylphenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2n):**

![Chemical structure](image)

The reaction was carried out according to the general procedure. The target compound 2n was obtained as a colorless oil (50 mg, 83% yield) after purification by column chromatography (SiO$_2$; 100% hexane).

$^1$H NMR (400 MHz, CDCl$_3$)

2.45 (s, 3H), 2.54 (dqd, $J = 15.7$, 10.1, 3.2, 1H), 2.92 (m, 1H), 6.43 (dd, $J = 9.6$, 3.2 Hz, 1H), 7.21 (m, 1H), 7.25-7.29 (overlap, 2H), 7.33 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$)

19.0, 39.9 (q, $J = 29$ Hz), 70.7 (q, $J = 2.8$ Hz), 114.5 (q, $J = 285$ Hz), 124.9 (q, $J = 277$ Hz), 125.5, 127.2, 129.6, 131.2, 134.9, 135.1, 156.3 (q, $J = 43$ Hz).

$^{19}$F NMR (376 MHz, CDCl$_3$)

$-64.8$ (t, $J = 10.1$ Hz, 3F), $-75.2$ (s, 3F).

IR (neat, cm$^{-1}$)

1792, 1333, 1252, 1222, 1133, 1099, 1064, 833, 761, 725, 615.

HRMS-EI ($m/z$)

[M] calcd. for C$_{12}$H$_{10}$F$_6$O$_2$, 300.0585; found, 300.0558.

**Synthesis of 1-(2,6-dichlorophenyl)-3,3,3-trifluoropropyl 2,2,2-trifluoroacetate (2o):**

![Chemical structure](image)

The reaction was carried out in DCE at 60 °C for the second step, but otherwise according to the general procedure. The desired compound 2o was obtained as a colorless oil (53 mg, 75% yield) after purification by column chromatography (SiO$_2$; 100% hexane).
\[ ^1H \text{NMR (400 MHz, CDCl}_3 \text{)} \]
\[
2.77 (\text{dqd, } J = 15.5, 10.1, 4.0 \text{ Hz, 1H}), 3.40 (\text{m, 1H}), 6.91 (\text{dd, } J = 8.8, 4.0 \text{ Hz, 1H}), 7.27 (\text{m, 1H}), 7.37 (\text{m, 2H}).
\]
\[ ^{13}C \text{NMR (100 MHz, CDCl}_3 \text{)} \]
\[
36.7 (\text{q, } J = 29 \text{ Hz}), 70.1 (\text{q, } J = 2.9 \text{ Hz}), 114.4 (\text{q, } J = 285 \text{ Hz}), 124.9 (\text{q, } J = 277 \text{ Hz}), 128.5, 130.7 (2\text{C}), 131.3 (2\text{C}), 135.6, 156.2 (\text{q, } J = 43 \text{ Hz}).
\]
\[ ^{19}F \text{NMR (376 MHz, CDCl}_3 \text{)} \]
\[
–64.8 (\text{d, } J = 10.1 \text{ Hz, 3F}), –74.7 (\text{s, 3F}).
\]
IR (neat, cm\(^{-1}\))
\[
1793, 1566, 1441, 1395, 1352, 1318, 1284, 1249, 1226, 1196, 1139, 1093, 1076, 832, 782, 774, 740, 622.
\]
HRMS-EI (m/z)
\[
[M] \text{calcd. for } C_{11}H_{6}Cl_{2}F_{6}O_{2}, 353.9649; \text{found, 353.9632.}
\]

**Synthesis of 3,3,3-trifluoro-2-methyl-1-phenylpropyl 2,2,2-trifluoroacetate (2p):**

The reaction was carried out according to the general procedure. The target compound 2p was obtained as a colorless oil (28 mg, 47% yield, \textit{anti}:\textit{syn} = 2:1) after purification by column chromatography (SiO\(_2\); 100% hexane).\(^8\)

\[ ^1H \text{NMR (400 MHz, CDCl}_3 \text{)} \]
\[
\textit{anti}-\text{isomer: } 1.22 (\text{d, } J = 7.2 \text{ Hz, 3H}), 2.68 (\text{m, 1H}), 6.36 (\text{d, } J = 3.2 \text{ Hz, 1H}), 7.29 (\text{m, 2H}), 7.35–7.44 (\text{overlap, 3H}).
\]
\[
\textit{syn}-\text{isomer: } 0.94 (\text{d, } J = 7.2 \text{ Hz, 3H}), 2.93 (\text{m, 1H}), 5.97 (\text{d, } J = 9.6 \text{ Hz, 1H}), 7.35–7.44 (\text{overlap, 5H}).
\]
\[ ^{13}C \text{NMR (100 MHz, CDCl}_3 \text{)} \]
\[
\textit{anti}-\text{isomer: } 7.0, 44.3 (\text{q, } J = 26 \text{ Hz}), 75.6 (\text{q, } J = 2.8 \text{ Hz}), 114.5 (\text{q, } J = 284 \text{ Hz}), 125.7 (2\text{C}), 126.5 (\text{q, } J = 279 \text{ Hz}), 129.1 (2\text{C}), 129.2, 135.8, 156.1 (\text{q, } J = 43 \text{ Hz}).
\]
\[
\textit{syn}-\text{isomer: } 10.7, 42.7 (\text{q, } J = 26 \text{ Hz}), 78.1, 114.5 (\text{q, } J = 284 \text{ Hz}), 126.7 (\text{q, } J = 279 \text{ Hz}), 127.6 (2\text{C}), 129.2 (2\text{C}), 129.9, 135.0, 156.1 (\text{q, } J = 43 \text{ Hz}).
\]

---

\(^8\)The stereochemistry was determined by comparison of \(^{19}F\) NMR signals to those reported for the alcohols after hydrolysis of the products. For 2p, 2r, 2t (a) Y. Yasu, T. Koike, M. Akita, \textit{Angew. Chem. Int. Ed.}, 2012, \textbf{51}, 9567; For 2s, (b) Y. Yang, Y. Liu, Y. Jiang, Y. Zhang, D. A. Vicic, \textit{J. Org. Chem.}, 2015, \textbf{80}, 6639.
\[ \text{IR (neat, cm}^{-1}) \]

1791, 1378, 1348, 1328, 1263, 1226, 1156, 1133, 1076, 1019, 773, 753, 732, 700, 668, 612.

\[ \text{HRMS-EI (m/z)} \]

[M] calcd. for C\textsubscript{12}H\textsubscript{10}F\textsubscript{6}O\textsubscript{2}, 300.0585; found, 300.0566.

**Synthesis of 3-oxo-1-phenyl-2-(trifluoromethyl)butyl 2,2,2-trifluoroacetate (2q):**

The reaction was carried out in DCE at 60 °C for the second step, but otherwise according to the general procedure. The target compound 2q was obtained as a yellow oil (26 mg, 38% yield, \( \text{anti/syn} = 2:1 \)) after purification by column chromatography (SiO\textsubscript{2}; EtOAc/hexane = 5/95).\(^9\)

\[ \text{\( ^{1}H\ NMR (400 MHz, CDCl}_3 \)} \]

- **anti-isomer:** 2.41 (s, 3H), 4.00 (m, 1H), 6.37 (d, \( J = 9.6 \) Hz, 1H), 7.42 (overlap, 5H).
- **syn-isomer:** 1.95 (s, 3H), 4.07 (m, 1H), 6.36 (d, \( J = 10.8 \) Hz, 1H), 7.42 (overlap, 5H).

\[ \text{\( ^{13}C\ NMR (100 MHz, CDCl}_3 \)} \]

- **anti-isomer:** 32.3, 59.9 (q, \( J = 25 \) Hz), 76.5 (q, \( J = 1.9 \) Hz), 114.3 (q, \( J = 285 \) Hz), 122.6 (q, \( J = 279 \) Hz), 127.4 (2C), 129.3 (2C), 130.3, 133.8, 155.3 (q, \( J = 43 \) Hz), 198.3.
- **syn-isomer:** 32.7, 60.0 (q, \( J = 25 \) Hz), 75.4, 114.3 (q, \( J = 285 \) Hz), 122.6 (q, \( J = 9.6 \) Hz).

\[^9\]The stereochemistry was determined by comparison of \(^{1}H\ NMR\) chemical shifts of the methyl groups due to magnetic shielding by the phenyl groups of each diastereomers, where the conformations were confirmed by NOESY correction as shown in the following scheme. In addition, relative chemical shifts of diastereomers of 2q are similar to those of diastereomers of 3,3,3-trifluoro-2-methyl-1-phenylpropanol (ref 8a).
= 279 Hz), 127.7 (2C), 128.5, 129.5 (2C), 130.5, 155.3 (q, J = 43 Hz), 198.1.

$^19$F NMR (376 MHz, CDCl$_3$)

*anti*-isomer: $-70.7$ (d, $J = 8.6$ Hz, 3F), $-74.9$ (s, 3F).
*syn*-isomer: $-66.0$ (d, $J = 8.6$ Hz, 3F), $-75.1$ (s, 3F).

IR (neat, cm$^{-1}$)

1799, 1734, 1363, 1344, 1328, 6171, 1171, 1143, 1017, 798, 698, 668.

HRMS-EI ($m/z$)

$[M]$ calcd. for C$_{13}$H$_{10}$F$_6$O$_3$, 328.0534; found, 328.0502.

**Synthesis of 2-(trifluoromethyl)-2,3-dihydro-1H-inden-1-yl 2,2,2-trifluoroacetate (2r):**

The reaction was carried out according to the general procedure. The target compound 2r was obtained as a colorless oil (38 mg, 60% yield, *trans:cis* = 8:1) after purification by column chromatography (SiO$_2$; 100% hexane).$^8$

$^1$H NMR (400 MHz, CDCl$_3$)

*trans*-isomer: 3.16 (dd, $J = 16.0$, 6.4 Hz, 1H), 3.35 (m, 1H), 3.43 (dd, $J = 16.0$, 8.8 Hz, 1H), 6.68 (d, $J = 4.8$ Hz, 1H), 7.30–7.37 (overlap, 3H), 7.41 (m, 1H).
*cis*-isomer: 3.16 (dd, $J = 15.3$, 7.8 Hz, 1H), 3.35 (m, 1H), 3.47 (dd, $J = 15.3$, 9.0 Hz, 1H), 6.53 (d, $J = 6.0$ Hz, 1H), 7.32–7.36 (overlap, 2H), 7.43 (m, 1H), 7.50 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$)

*trans*-isomer: 30.8 (q, $J = 1.9$ Hz), 49.1 (q, $J = 28$ Hz), 80.8 (q, $J = 2.9$ Hz), 114.6 (q, $J = 285$ Hz), 125.2, 125.4, 126.6 (q, $J = 277$ Hz), 128.3, 130.7, 137.0, 140.8, 157.2 (q, $J = 43$ Hz).
*cis*-isomer: 30.8 (q, $J = 1.9$ Hz), 46.7 (q, $J = 29$ Hz), 78.4 (q, $J = 1.9$ Hz), 114.5 (q, $J = 286$ Hz), 125.3, 125.5 (q, $J = 277$ Hz), 126.5, 128.2, 131.1, 136.8, 142.3, 157.0 (q, $J = 43$ Hz).

$^19$F NMR (376 MHz, CDCl$_3$)

*trans*-isomer: $-70.7$ (d, $J = 8.6$ Hz, 3F), $-74.9$ (s, 3F).
*cis*-isomer: $-66.0$ (d, $J = 8.6$ Hz, 3F), $-75.1$ (s, 3F).
HRMS-EI (m/z)
[M] calcd. for C_{12}H_{8}F_{6}O_{2}, 298.0428; found, 298.0401.

Synthesis of 2-(trifluoromethyl)-1,2,3,4-tetrahydronaphthalene-1-yl 2,2,2-trifluoroacetate (2s):

The reaction was carried out according to the general procedure. The target compound 2s was obtained as a colorless oil (46 mg, 73% yield, trans:cis = 2:1) after purification by column chromatography (SiO\(_2\); 100% hexane).\(^8\)

\(^{1}\)H NMR (400 MHz, CDCl\(_3\))

- **trans**-isomer: 1.90 (m, 1H), 2.31 (m, 1H), 2.81–3.02 (overlap, 3H), 6.50 (d, \(J = 8.0\) Hz, 1H), 7.17–7.20 (overlap, 2H), 7.24–7.32 (overlap, 2H).
- **cis**-isomer: 2.16 (m, 1H), 2.26 (m, 1H), 2.70 (m, 1H), 2.96 (m, 1H), 3.13 (dd, \(J = 17.6, 6.0\) Hz, 1H), 6.50 (d, \(J = 8.0\) Hz, 1H), 7.23 (d, \(J = 6.8\) Hz, 2H), 7.36 (m, 1H), 7.42 (d, \(J = 8.0\) Hz, 1H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\))

- **trans**-isomer: 21.3 (q, \(J = 2.9\) Hz), 27.3, 44.3 (q, \(J = 27\) Hz), 72.6 (q, \(J = 1.9\) Hz), 114.6 (q, \(J = 285\) Hz), 126.5 (q, \(J = 278\) Hz), 127.4, 128.2, 129.0, 129.4, 131.0, 137.3, 157.4 (q, \(J = 42\) Hz).
- **cis**-isomer: 17.1, 27.8, 43.4 (q, \(J = 28\) Hz), 70.8 (q, \(J = 2.8\) Hz), 114.6 (q, \(J = 285\) Hz), 126.5 (q, \(J = 278\) Hz), 127.2, 129.5, 130.4, 130.8 (2C), 136.6, 157.4 (q, \(J = 42\) Hz).

\(^{19}\)F NMR (376 MHz, CDCl\(_3\))

- **trans**-isomer: \(-71.0\) (d, \(J = 8.6\) Hz, 3F), \(-75.1\) (s, 3F).
- **cis**-isomer: \(-69.5\) (d, \(J = 8.6\) Hz, 3F), \(-75.2\) (s, 3F).

IR (neat, cm\(^{-1}\))

1787, 1324, 1263, 1224, 1148, 1128, 902, 830, 771, 750, 668.

HRMS-EI (m/z)

[M] calcd. for C_{13}H_{10}F_{6}O_{2}, 312.0585; found, 312.0563.
Synthesis of 1-phenyl-2-(trifluoromethyl)cyclohexyl 2,2,2-trifluoroacetate (2t):

The reaction was carried out according to the general procedure. The desired compound 2t was obtained as a colorless oil (40 mg, 59% yield, trans:cis = 1:2) after purification by column chromatography (SiO₂; 100% hexane).

¹H NMR (400 MHz, CDCl₃)

cis-isomer: 1.78 (m, 2H), 2.13–2.39 (overlap, 5H), 3.87–3.97 (overlap, 2H), 7.36–7.47 (overlap, 3H), 7.69 (m, 2H).

trans-isomer: 1.97 (m, 2H), 2.13-2.39 (overlap, 3H), 2.51 (m, 1H), 2.98 (m, 1H), 3.64 (m, 2H), 7.36–7.47 (overlap, 5H).

¹³C NMR (100 MHz, CDCl₃)

cis-isomer: 19.5, 21.6, 22.3, 23.1, 46.8 (q, J = 26 Hz), 87.1, 114.3 (q, J = 286 Hz), 125.4 (q, J = 278 Hz), 126.8 (2C), 128.2 (2C), 129.0, 134.4, 156.1 (q, J = 43 Hz).

trans-isomer: 21.0, 24.1, 27.5, 34.5, 46.1 (q, J = 24 Hz), 87.9, 114.4 (q, J = 286 Hz), 125.4 (q, J = 278 Hz), 126.4 (2C), 128.6 (2C), 129.2, 136.1, 156.1 (q, J = 43 Hz).

¹⁹F NMR (376 MHz, CDCl₃)

cis-isomer: –65.2 (d, J = 8.6 Hz, 3F), –75.6 (s, 3F).

trans-isomer: –64.2 (d, J = 7.1 Hz, 3F), –75.2 (s, 3F).

IR (neat, cm⁻¹)

1778, 1364, 1335, 1290, 1264, 1227, 1151, 1131, 1076, 986, 891, 838, 774, 764, 744, 706, 686, 638.

HRMS-EI (m/z)

[M] calcd. for C₁₅H₁₄F₆O₂, 340.0898; found, 340.0881.

Synthesis of 1-bromo-3,3,3-trifluoro-1-phenylpropyl 2,2,2-trifluoroacetate (2u):

The reaction was carried out according to the general procedure. The target compound 2u was obtained as a colorless oil (58 mg, 80% yield) after purification by column chromatography (SiO₂; 100% hexane).

¹H NMR (400 MHz, CDCl₃)
3.53 (dq, \( J = 15.6, 9.3 \) Hz, 1H), 4.18 (dq, \( J = 15.6, 9.3 \) Hz, 1H), 7.40–7.48 (overlap, 3H), 7.60 (m, 2H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\))

47.7 (q, \( J = 29 \) Hz), 87.0 (q, \( J = 1.9 \) Hz), 114.0 (q, \( J = 285 \) Hz), 123.2 (q, \( J = 278 \) Hz), 125.0 (2C), 129.0 (2C), 130.2, 139.2, 153.9 (q, \( J = 44 \) Hz).

\(^{19}\)F NMR (376 MHz, CDCl\(_3\))

–61.7 (t, \( J = 9.3 \) Hz, 3F), –75.2 (s, 3F).

IR (neat, cm\(^{-1}\))

1805, 1365, 1349, 1257, 1226, 1178, 1120, 874, 838, 799, 767, 735, 721, 690, 668, 624, 617.

HRMS-EI (m/z)

\([M]\) calcd. for C\(_9\)H\(_7\)F\(_3\)O (degradation product), 188.0449; found, 188.0432.

**Synthesis of 1-(4-fluorophenyl)-3,3,4,4,4-pentafluorobutyl 2,2,3,3,3-pentafluoropropanoate (2b’):**

The reaction was carried out according to the general procedure. The target compound 2b’ was obtained as a colorless oil (75 mg, 93% yield) after purification by column chromatography (SiO\(_2\); 100% hexane).

\(^1\)H NMR (400 MHz, CDCl\(_3\))

2.53 (m, 1H), 2.91 (m, 1H), 6.32 (dd, \( J = 9.6, 3.2 \) Hz, 1H), 7.12 (m, 2H), 7.39 (m, 2H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\))

37.1 (t, \( J = 21 \) Hz), 72.6 (br s), 100.0–130.0 (m, 4C),\(^{10}\) 116.5 (d, \( J = 22 \) Hz, 2C), 128.5 (d, \( J = 8.6 \) Hz, 2C), 132.4 (d, \( J = 3.8 \) Hz), 157.1 (t, \( J = 30 \) Hz), 163.5 (d, \( J = 249 \) Hz).

\(^{19}\)F NMR (376 MHz, CDCl\(_3\))

–82.6 (m, 3F), –85.7 (m, 3F), –110.4 (m, 1F), –117.4 (m, 2F), –121.7 (m, 2F).

IR (neat, cm\(^{-1}\))

1785, 1516, 1300, 1194, 1152, 1130, 1098, 1071, 1032, 838, 737, 668.

HRMS-EI (m/z)

\(^{10}\)The carbons of perfluoroalkyl groups could not be assigned because of low intensity of signals, their complex coupling, and overlap due to large \( J \) values.
Synthesis of 1-(4-acetoxyphenyl)-3,3,4,4,5,5,5-heptafluoropentyl 2,2,3,3,4,4,4-heptafluorobutyrate (2d”):

The reaction was carried out according to the general procedure. The desired compound 2d” was obtained as a white solid (105 mg, quantitative yield) after purification by column chromatography (SiO₂; EtOAc/hexane = 5/95).

\[
\text{[M] calcd. for C}_{13}\text{H}_{11}\text{F}_{11}\text{O}_{2}, \text{404.0270; found, 404.0248.}
\]

1H NMR (400 MHz, CDCl₃)

\[
\begin{align*}
2.31 \text{ (s, 3H),} & \ 2.57 \text{ (m, 1H),} \ 2.94 \text{ (m, 1H),} \ 6.36 \text{ (dd, } J = 9.6, 2.8 \text{ Hz, 1H),} \ 7.17 \text{ (d, } J = 8.8 \text{ Hz, 2H),} \\
7.42 \text{ (d, } J = 8.8 \text{ Hz, 2H).}
\end{align*}
\]

13C NMR (100 MHz, CDCl₃)

\[
\begin{align*}
21.2, & \ 37.1 \text{ (t, } J = 22 \text{ Hz),} \ 72.7, \ 100.0–130.0 \text{ (m, 6C),} \ 122.7 \text{ (2C),} \ 127.8 \text{ (2C),} \\
133.9, & \ 151.8, \ 157.1 \text{ (t, } J = 30 \text{ Hz),} \\
169.4. &
\end{align*}
\]

19F NMR (376 MHz, CDCl₃)

\[
\begin{align*}
–80.2 \text{ (m, 3F),} & \ –80.6 \text{ (m, 3F),} \ –114.4 \text{ (m, 2F),} \ –119.2 \text{ (m, 2F),} \ –126.7 \text{ (m, 2F),} \\
–127.7 \text{ (m, 2F).}
\end{align*}
\]

IR (neat, cm⁻¹)

\[
1783, \ 1354, \ 1301, \ 1217, \ 1147, \ 1117, \ 1083, \ 970, \ 939, \ 919, \ 725.
\]

HRMS-EI (m/z)

\[
\text{[M] calcd. for C}_{17}\text{H}_{10}\text{F}_{14}\text{O}_{4}, \text{544.0356; found, 544.0310.}
\]

Synthesis of 2-phenyl-1-tosyl-2-(2,2,2-trifluoroethyl)pyrrolidine (4a):

The reaction was carried out for 3 h at the second step, but otherwise according to the general procedure. The target compound 4a was obtained as a white solid (58 mg, 76% yield) after purification by column chromatography (SiO₂; EtOAc/hexane/Et₃N = 3/96/1).

1H NMR (400 MHz, CDCl₃)

\[
\begin{align*}
1.96 \text{ (m, 1H),} & \ 2.06 \text{ (m, 1H),} \ 2.38 \text{ (s, 3H),} \ 2.44 \text{ (m, 2H),} \ 3.44 \text{ (m, 2H),} \ 3.55 \text{ (m,} \\
3.71 \text{ (m, 1H),} & \ 7.10 \text{ (d, } J = 8.4 \text{ Hz, 2H),} \ 7.19–7.26 \text{ (overlap, 5H),} \ 7.30 \text{ (m,} \\
2H).&
\end{align*}
\]

13C NMR (100 MHz, CDCl₃)
21.6, 23.0, 41.1, 41.9 (q, J = 27 Hz), 49.6, 68.7 (q, J = 1.9 Hz), 126.1 (q, J = 277 Hz), 126.7 (2C), 127.0 (2C), 127.6, 128.3 (2C), 129.3 (2C), 137.5, 142.8, 142.9.

$^{19}$F NMR (376 MHz, CDCl$_3$)

-58.3 (t, J = 11.6 Hz).

IR (neat, cm$^{-1}$)

1379, 1338, 1304, 1262, 1223, 1154, 1136, 1092, 1040, 974, 912, 813, 757, 733, 699, 659, 614.

HRMS-ESI (m/z)

[M+Na]$^+$ calcd. for C$_{19}$H$_{20}$F$_{3}$NO$_2$SNa, 406.1065; found, 406.1067.

Synthesis of (2S,3R)-2-phenyl-1-tosyl-3-(trifluoromethyl)pyrrolidine (4b):

The reaction was carried out according to the general procedure. The target compound 4b was obtained as a colorless oil (28 mg, 37% yield) after purification by column chromatography (SiO$_2$; EtOAc/hexane/Et$_3$N = 10/89/1).

$^1$H NMR (400 MHz, CDCl$_3$)

1.96 (dddd, J = 13.6, 7.4, 4.5, 4.5 Hz, 1H), 2.22 (dddd, J = 13.6, 8.0, 8.0, 8.0 Hz, 1H), 2.43 (s, 3H), 2.76 (m, 1H), 3.52 (m, 1H), 3.74 (m, 1H), 4.87 (d, J = 3.6 Hz, 1H), 7.27–7.30 (overlap, 3H), 7.31–7.35 (overlap, 4H), 7.62 (d, J = 8.4 Hz, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$)

21.7, 24.5, 48.4, 52.7 (q, J = 27 Hz), 63.0 (q, J = 1.9 Hz), 126.2 (2C), 126.6 (q, J = 274 Hz), 127.7 (2C), 128.0, 128.9 (2C), 129.7 (2C), 134.4, 141.6, 143.9.

$^{19}$F NMR (376 MHz, CDCl$_3$)

-70.7 (d, J = 8.7 Hz).

IR (neat, cm$^{-1}$)

1394, 1351, 1268, 1236, 1161, 1128, 1097, 1024, 1012, 815, 801, 783, 756, 700, 668, 619.

HRMS-ESI (m/z)

$^{11}$The analytic and spectroscopic data matched reported values: Y. Wang, M. Jiang, J.-T. Liu, Adv. Synth. Catal., 2016, 358, 1322.
Synthesis of 3-phenyl-2-tosyl-3-(2,2,2-trifluoroethyl)-2-azaspiro[4.5]decane (4c):

The reaction was carried out for 3 h for the second step, but otherwise according to the general procedure, on a 0.10 mmol scale. The target compound 4c was obtained as a white solid (39 mg, 86% yield) after purification by column chromatography (SiO$_2$; EtOAc/hexane/ Et$_3$N = 5/94/1). An analytical sample was obtained by crystallization from EtOAc.

$^1$H NMR (400 MHz, CDCl$_3$)

1.27–1.61 (overlap, 10H), 2.36 (s, 3H), 2.39 (d, $J$ = 14.4 Hz, 1H), 2.46 (d, $J$ = 14.4 Hz, 1H), 3.07 (dq, $J$ = 16.1, 11.5 Hz, 1H), 3.14 (d, $J$ = 9.6 Hz, 1H), 3.56 (d, $J$ = 9.6 Hz, 1H), 4.01 (dq, $J$ = 16.0, 11.2 Hz, 1H), 7.06 (d, $J$ = 8.4 Hz, 2H), 7.14–7.22 (overlap, 5H), 7.32 (d, $J$ = 8.4 Hz, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$)

21.6, 23.3, 23.8, 25.8, 37.1, 37.5, 40.6, 44.1 (q, $J$ = 27 Hz), 51.6, 59.6, 69.0 (q, $J$ = 1.9 Hz), 125.7 (q, $J$ = 277 Hz), 127.0 (2C), 127.3 (2C), 127.6, 128.1 (2C), 129.2 (2C), 136.8, 142.2, 142.8.

$^{19}$F NMR (376 MHz, CDCl$_3$)

–56.3 (t, $J$ = 11.5 Hz).

IR (neat, cm$^{-1}$)

1448, 1340, 1257, 1212, 1156, 1121, 1090, 1054, 1034, 984, 925, 906, 813, 762, 732, 698, 661.

HRMS-ESI ($m/z$)

[M+Na]$^+$ calcd. for C$_{28}$H$_{28}$F$_3$NNaO$_2$S, 474.1691; found, 474.1689.

Synthesis of 2-phenyl-1-tosyl-2-(2,2,3,3,3-pentafluoropropyl)pyrrolidine (4a'):

The reaction was carried out for 3 h for the second step, but otherwise according to the general procedure. The target compound 4a' was obtained as a white solid (55 mg, 63% yield) after purification by column chromatography (SiO$_2$; EtOAc/hexane/ Et$_3$N = 3/96/1).
**Synthesis of 2-phenyl-1-tosyl-2-(2,2,3,3,3-pentafluoropropyl)pyrrolidine (4a”)**:

The reaction was carried out for 3 h for the second step, but otherwise according to the general procedure, on a 0.10 mmol scale. The target compound 4a” was obtained as a white solid (32 mg, 65% yield) after purification by column chromatography (SiO$_2$; EtOAc/hexane/Et$_3$N = 5/94/1).

**1H NMR (400 MHz, CDCl$_3$)**

1.99 (m, 1H), 2.09 (m, 1H), 2.37 (s, 3H), 2.53 (m, 2H), 3.20 (m, 1H), 3.63 (m, 1H), 3.73 (m, 1H), 7.08 (d, $J = 8.4$ Hz, 2H), 7.18–7.24 (overlap, 5H), 7.32 (m, 2H).

**13C NMR (100 MHz, CDCl$_3$)**

21.6, 23.3, 37.7 (t, $J = 19$ Hz), 41.1, 49.5, 69.3, 100.0–130.0 (m, 2C), 126.8 (2C), 126.9 (2C), 127.6, 128.3 (2C), 129.2 (2C), 137.5, 142.4, 142.9.

**19F NMR (376 MHz, CDCl$_3$)**

-79.9 (m, 3F), -110.2 (m, 2F), -127.4 (m, 2F).

**IR (neat, cm$^{-1}$)**

1340, 1224, 1174, 1155, 1133, 1112, 1092, 1035, 911, 813, 755, 735, 699, 687, 666.

**HRMS-ESI (m/z)**

[M+Na]$^+$ calcd. for C$_{20}$H$_{20}$F$_5$NO$_2$SNa, 456.1033; found, 456.1032.
[M+Na]$^+$ calcd. for C$_{21}$H$_{20}$F$_7$NaO$_2$S, 506.1001; found, 506.0999.

**Synthesis of 1-(4-fluorophenyl)-3,3,3-trifluoropropan-1-ol (5b):**

![](image)

A solution of 2b (100 mg, 0.33 mmol) in DME (1 mL) was cooled to 0 °C. 1,8-Diazabicyclo[5.4.0]undec-5-ene (DBU) (54 μL, 0.36 mmol) was added dropwise and the solution was stirred for 10 min at 0 °C.$^{12}$ The reaction mixture was then quenched with saturated NH$_4$Cl solution (2 mL) and extracted with Et$_2$O (3 x 5 mL). Filtration of the combined organic phase through a silica pad, followed by evaporation *in vacuo* gave a colorless oil. The crude product was purified by column chromatography (SiO$_2$; EtOAc/hexane = 10/90), providing the target compound 5b as a colorless oil (41 mg, 96% yield).

**$^1$H NMR (400 MHz, CDCl$_3$)**

2.14 (br s, 1H), 2.43 (m, 1H), 2.62 (m, 1H), 5.08 (dd, $J = 8.8, 3.6$ Hz, 1H), 7.07 (t, $J = 8.8$ Hz, 2H), 7.36 (m, 2H).

**$^{13}$C NMR (100 MHz, CDCl$_3$)**

43.1 (q, $J = 27$ Hz), 68.3 (q, $J = 2.9$ Hz), 115.9 (d, $J = 22$ Hz, 2C), 125.9 (q, $J = 277$ Hz), 127.6 (d, $J = 8.6$ Hz, 2C), 138.2 (d, $J = 2.9$ Hz), 162.7 (d, $J = 246$ Hz).

**$^{19}$F NMR (376 MHz, CDCl$_3$)**

–63.6 (t, $J = 10.1$ Hz, 3F), –113.5 (m, 1F).

**IR (neat, cm$^{-1}$)**

3404, 1607, 1511, 1431, 1375, 1326, 1259, 1227, 1202, 1131, 1093, 1015, 860, 841, 827, 800, 669, 652.

**HRMS-EI (m/z)**

[M] calcd. for C$_9$H$_8$F$_4$O, 208.0511; found, 208.0503.

---

$^{12}$Moisture in DBU and/or DME may participate in the reaction.
Synthesis of (E)-β-trifluoromethyl-3-fluorostyrene (6b):

To a 0.07 M THF solution of KHMDS (0.4 mmol) was added 2b (30.4 mg, 0.1 mmol) at −78 °C. The reaction mixture was stirred for 3.5 h, then quenched with saturated NH₄Cl solution (2 mL), and extracted with Et₂O (3 x 5 mL). The combined organic phase was dried over Na₂SO₄ and gently evaporated under vacuum (200 mmHg, 20 °C). The crude product was purified by means of column chromatography (SiO₂; 100% hexane) providing the desired compound 6b as a colorless oil (12 mg, 63% yield).¹³

¹H NMR (400 MHz, CDCl₃)

6.13 (dq, J = 16.1, 6.5 Hz, 1H), 7.05–7.16 (m, 3H), 7.42–7.47 (m, 2H).

¹³C NMR (100 MHz, CDCl₃)

115.8 (q, J = 32 Hz), 116.2 (d, J = 34.6 Hz, 2C), 123.7 (q, J = 269 Hz), 129.5 (d, J = 8.7 Hz, 2C), 129.8 (d, J = 3.9 Hz), 136.6 (q, J = 6.7 Hz), 163.9 (d, J = 250 Hz).

¹⁹F NMR (376 MHz, CDCl₃)

−63.2 (d, J = 6.5 Hz, 3F), −110.2 (m, 1F).

Synthesis of 1-(3,3,3-trifluoro-1-(4-fluorophenyl)propyl)naphthalene-2-ol (7b):

2-Naphthol (47 mg, 0.33 mmol) and trifluoromethanesulfonic acid (3 μL, 20 mol%) were added to a solution of 2b (50 mg, 0.16 mmol) in HFIP (1.6 mL) under nitrogen in a Schlenk tube. The resulting solution was stirred at room temperature for 4 h, and then evaporated in vacuo. Purification by column chromatography (SiO₂; EtOAc/hexane = 10/90) provided the target compound 7b as a white solid (37 mg, 68% yield).

¹H NMR (400 MHz, CDCl₃)

2.96 (m, 2H), 4.44 (t, J = 7.2 Hz, 1H), 4.91 (br, 1H), 6.99 (t, J = 8.8 Hz, 2H), 7.08–7.11 (overlap, 2H), 7.22–7.26 (overlap, 3H), 7.60–7.62 (overlap, 2H),

¹³The spectroscopic data obtained were in agreement with literature data: L. He, X. Yang, G. C. Tsui, J. Org. Chem., 2017, 82, 6192.
7.71 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$)

39.7 (q, $J = 27$ Hz), 44.3 (q, $J = 2.8$ Hz), 109.5, 115.7 (d, $J = 22$ Hz, 2C), 118.3, 125.6, 126.4 (q, $J = 277$ Hz), 126.7, 127.3, 129.0, 129.3 (d, $J = 8.7$ Hz, 2C), 129.9, 133.6, 137.8, 138.5 (d, $J = 2.8$ Hz), 153.6, 161.8 (d, $J = 245$ Hz).

$^{19}$F NMR (376 MHz, CDCl$_3$)

–63.4 (t, $J = 10.1$ Hz, 3F), –115.9 (m, 1F).

IR (neat, cm$^{-1}$)

3340, 1607, 1508, 1379, 1265, 1226, 1174, 1160, 1133, 1107, 1088, 861, 833, 820, 668, 653.

HRMS-EI (m/z)

[M] calcd. for C$_{19}$H$_{14}$F$_4$O, 334.0981; found, 334.0969.

Synthesis of 1,4-dimethyl-2-(3,3,3-trifluoro-1-(4-fluorophenyl)propyl)benzene (8b):

$p$-Xylene (31 µL, 0.25 mmol) and trifluoromethanesulfonic acid (1.5 µL, 20 mol%) were added to a solution of 2b (25 mg, 0.08 mmol) in HFIP (0.8 mL) under nitrogen in a Schlenk tube. The resulting solution was stirred at room temperature for 3 h, and then evaporated in vacuo. Purification by column chromatography (SiO$_2$; 100% hexane) provided the target compound 8b as a colorless oil (22 mg, 92% yield).

$^1$H NMR (400 MHz, CDCl$_3$)

2.27 (s, 3H), 2.34 (s, 3H), 2.84 (m, 2H), 4.51 (t, $J = 7.2$ Hz, 1H), 6.95–7.01 (overlap, 3H), 7.03–7.05 (overlap, 2H), 7.20 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$)

19.4, 21.4, 39.9, 40.0 (q, $J = 27$ Hz), 115.5 (d, $J = 21$ Hz, 2C), 126.6 (q, $J = 277$ Hz), 127.0, 127.7, 129.6 (d, $J = 7.7$ Hz, 2C), 131.0, 132.7, 135.9, 138.0 (d, $J = 2.9$ Hz), 140.5, 161.6 (d, $J = 245$ Hz).

$^{19}$F NMR (376 MHz, CDCl$_3$)

–63.6 (t, $J = 10.1$ Hz, 3F), –116.1 (m, 1F).

IR (neat, cm$^{-1}$)

1605, 1509, 1441, 1376, 1318, 1290, 1263, 1229, 1159, 1133, 1085, 1015, 837,
Synthesis of 1-fluoro-4-(1,1,1-trifluorohex-5-en-3-yl)benzene (9b):

Allyltrimethylsilane (78 μL, 0.49 mmol) and 2b (100 mg, 0.33 mmol) were added to a solution of tris(pentafluorophenyl)borane (17 mg, 10 mol%) in DCM (1 mL) under nitrogen. The resulting solution was stirred at room temperature for 48 h, then passed through a silica gel pad and concentrated under vacuo. Purification of the residue by column chromatography (SiO₂; 100% hexane) provided the target compound 9b as a colorless oil (48 mg, 63% yield).

$^1$H NMR (400 MHz, CDCl₃)

2.29–2.55 (overlap, 4H), 3.02 (m, 1H), 5.02 (overlap, 2H), 5.60 (m, 1H), 7.00 (t, $J = 8.8$ Hz, 2H), 7.13 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl₃)

39.0 (q, $J = 1.9$ Hz), 39.5 (q, $J = 27$ Hz), 41.1, 115.5 (d, $J = 21$ Hz, 2C), 117.8, 126.7 (q, $J = 277$ Hz), 128.9 (d, $J = 7.6$ Hz, 2C), 135.1, 138.6 (d, $J = 2.9$ Hz), 161.8 (d, $J = 244$ Hz).

$^{19}$F NMR (376 MHz, CDCl₃)

–63.5 (t, $J = 10.1$ Hz, 3F), –116.0 (m, 1F).

IR (neat, cm⁻¹)

1606, 1512, 1378, 1256, 1226, 1161, 1143, 1122, 1093, 1053, 1015, 994, 920, 830, 742, 723, 668, 644, 626.

HRMS-EI (m/z)

[M] calcd. for C₁₂H₁₂F₄, 232.0875; found, 232.0866.
Synthesis of methyl 5,5,5-trifluoro-3-(4-fluorophenyl)-2,2-dimethylpentanoate (10b):

Methyl trimethylsilyl dimethylketene acetal (100 μL, 0.49 mmol) and 2b (50 mg, 0.16 mmol) were added to a solution of tris(pentafluorophenyl)borane (8.4 mg, 10 mol%) in DCM (0.6 mL). The resulting solution was stirred at reflux for 6 h, passed through a silica gel pad and concentrated in vacuo. Purification of the residue by column chromatography (SiO2; EtOAc/hexane = 1/99) provided the target compound 10b as a colorless oil (24 mg, 52% yield).

1H NMR (400 MHz, CDCl3)

1.08 (s, 3H), 1.15 (s, 3H), 2.42 (m, 1H), 2.62 (m, 1H), 3.27 (dd, J = 11.2, 2.0 Hz, 1H), 3.67 (s, 3H), 7.00 (t, J = 8.8 Hz, 2H), 7.14 (m, 2H).

13C NMR (100 MHz, CDCl3)

21.5, 24.4, 35.7 (q, J = 27 Hz), 46.3 (q, J = 1.9 Hz), 46.6, 52.2, 115.2 (d, J = 21 Hz, 2C), 126.8 (q, J = 277 Hz), 130.7 (d, J = 7.7 Hz, 2C), 134.5 (d, J = 3.8 Hz), 162.2 (d, J = 245 Hz), 177.0.

19F NMR (376 MHz, CDCl3)

–64.0 (t, J = 10.1 Hz, 3F), –115.3 (m, 1F).

IR (neat, cm⁻¹)

1729, 1512, 1436, 1392, 1325, 1303, 1294, 1256, 1227, 1192, 1138, 1125, 1113, 1090, 1051, 1015, 840, 827, 799, 633.

HRMS-EI (m/z)

[M] calcd. for C14H16F4O2, 292.1086; found, 292.1071.

TEMPO trapping test (Scheme 7b)

The reaction was carried out according to the general procedure with the addition of TEMPO (1 equiv. versus the styrene) before the substrate. For neutralization, saturated K2CO3 solution (1.5 mL) was added in addition to 0.5 M NaHCO3 solution in order to recover TEMPO derivatives completely. The yields of the oxytrifluoromethylated products shown in Scheme 7b were estimated based on 19F NMR analysis of the crude product.14

14The structures of 11 and 5a were identified by comparison of the spectral data with literature values after rough isolation by means of column chromatography: (a) Y. Li, A. Studer, Angew. Chem. Int. Ed., 2012, 51, 8221. (b) Y. Yasu, T. Koike, M. Akita, Angew. Chem. Int. Ed., 2012, 51, 9567.
Radical probe test using 12 (Scheme 8):

The reaction of 12 was carried out according to the general procedure (the $^{19}$F NMR spectrum of the crude product is shown in Figure S4). Compound 13 was isolated as a colorless oil (25 mg, 31% yield, $E/Z = 4/96$) after purification by column chromatography ($\text{SiO}_2$; EtOAc/hexane = 4/96). Stereochemistry of isomers was determined by means of a NOESY experiment.

$^1$H NMR (400 MHz, CDCl$_3$)

Z-isomer: 2.84 (m, 1H), 3.01 (m, 1H), 3.16–3.36 (m, 2H), 5.87 (t, $J = 7.9$ Hz, 1H), 6.00 (dd, $J = 7.9$, 5.8 Hz, 1H), 7.20–7.48 (m, 10H).

E-isomer: 2.52–2.63 (m, 1H), 2.65–2.77 (m, 1H), 3.08 (overlap, 2H), 5.68 (t, $J = 7.3$ Hz, 1H), 5.90 (overlap, 1H), 7.20–7.48 (m, 10H).

$^{13}$C NMR (100 MHz, CDCl$_3$; Z-isomer)

35.0 (q, $J = 29.9$ Hz), 36.0, 79.6, 114.6 (q, $J = 286$ Hz), 125.8 (q, $J = 278$ Hz), 126.5 (2C), 126.6 (2C), 127.9, 128.6, 128.7 (2C), 129.1 (2C), 129.3, 133.9 (q, $J = 2.9$ Hz), 137.4, 141.5, 156.8 (q, $J = 43$ Hz).

$^{19}$F NMR (376 MHz, CDCl$_3$)

Z-isomer: –63.4 (t, $J = 10.1$ Hz, 3F), –75.0 (s, 3F).

E-isomer: –64.4 (t, $J = 10.1$ Hz, 3F), –175.0 (s, 3F).

IR (neat, cm$^{-1}$)

3067, 1784, 1496, 1457, 1383, 1331, 1253, 1223, 1153, 1113, 759, 698.

HRMS-EI ($m/z$)

[M] calcd. for C$_{20}$H$_{16}$F$_6$O$_2$, 402.1054; found, 402.1061.
Figure S4. $^{19}\text{F}$ NMR spectrum of the crude product of the radical probe experiment using 12
4. 'H and ^{13}C NMR spectra of new compounds

(3c)

\[ \text{Ts} \quad \text{N} \quad \text{H} \quad \text{Ts} \quad \text{Ph} \]
(2a)
\[
\begin{align*}
\text{OCOCF}_3 \\
\text{CF}_3
\end{align*}
\]
(2r, anti-isomer)
2r, syn-isomer

\[
\begin{align*}
\text{OCOCF}_3 & \\
\text{CF}_3 & \\
\end{align*}
\]
(2s, diastereomixture)
OCOCF$_3$
\[ \text{CF}_3 \]
(2s, anti-isomer)
\[
\text{F}_3\text{CCOO}
\]

\[
\text{CF}_3
\]

(2t)
(4a)
5. Computational details:

DFT calculations were conducted with Gaussian 16 series\(^{13}\) of programs. The structures were optimized at the UB3LYP level of theory, and 6-31+G(d,p) basis set was used. The single-point energy calculation was performed using UMPWB1K/6-311+G(2df,2p), except that LanL2DZ was used for Cu. The CPCM solvation model (dichloromethane) was used to reflect the solvent effect. The free energies described in this work were estimated from the ZPEs from UMPWB1K with thermal corrections by using vibrational analysis at the UB3LYP level of theory. No imaginary frequencies for intermediates and one imaginary frequency for the transition state were observed. The reaction pathway from the transition state was confirmed by IRC calculation and the vibration mode of the imaginary frequency. DFT calculations were conducted according to the literature procedure reported by Houk and Buchwald.\(^{15}\) The activation energy (\(\Delta G^\ddagger\)) of SET was estimated according to the Marcus equation with parameters as shown in Scheme S1 (\(n = 1.424, \varepsilon = 8.93\) for CH\(_2\)Cl\(_2\)).

\[
\Delta^\ddagger G = \left(\frac{\lambda}{4}\right) \left(1 + \frac{\Delta G}{\lambda}\right)^2
\]

\[
\lambda \approx 332 \times \left(\frac{1}{2r_A} + \frac{1}{2r_B} - \frac{1}{R}\right) \left(\frac{1}{n^2} - \frac{1}{\varepsilon}\right); \text{ reorganization energy (kcal/mol)}
\]

\(\Delta G\); reaction energy (kcal/mol)

\(r\); radius of molecules (Å)

\(R = r_A + r_B\) (Å)

\(n\); index of refraction

\(\varepsilon\); dielectric constant

\(^{13}\)M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnensberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, *Gaussian 09*, Revision A.02; Gaussian, Inc.: Wallingford CT, 2009.

\(^{15}\)G. O. Jones, P. Liu, K. N. Houk, S. L. Buchwald, *J. Am. Chem. Soc.* **2010**, *132*, 6205.
Scheme S1. Estimation of activation energies of pathway b

**HOMO and LUMO levels**

**Table S2. HOMO levels of styrenes**

| R   | HOMO (eV) |
|-----|-----------|
| OMe | -5.90     |
| Me  | -6.20     |
| Cl  | -6.41     |
| CF₃ | -6.74     |
| Benzene | -7.90 |

**Table S3. LUMO levels of potential oxidants**

| Oxidant          | LUMO (eV) |
|------------------|-----------|
| BTFAP            | -2.35     |
| Cu⁰(O₂CCF₃)₂⁻⁻   | -6.26     |
|                  | -5.09     |

**Cartesian coordinates and energies**

\[
E (\text{UMPWB1K}) = -337.5780555
\]

Sum electronic and thermal free energies = -337.5930245
Charge = 0 Multiplicity = 2

| C   | 0.00027  | 0.00002  | 0.32655 |
| F   | -0.97128 | 0.80219  | -0.07254 |
| F   | -0.20919 | -1.24218 | -0.07256 |
| F   | 1.18029  | 0.43998  | -0.0726  |

\[
E (\text{UMPWB1K}) = -1106.7106645
\]

Sum electronic and thermal free energies = -1106.609694
Charge = 1 Multiplicity = 1

| C   | -0.29953 | 0.30696  | -0.27609 |
| C   | -1.17376 | 1.4372   | -0.11899 |
| C   | -2.52621 | 1.26734  | 0.02967  |
| C   | -3.04496 | -0.04189 | 0.02514  |
| C   | -2.22233 | -1.18008 | -0.12686 |
| C   | -0.87142 | -1.01036 | -0.2733  |
| H   | -0.748   | 2.4331   | -0.11909 |
| H   | 3.19105  | 2.1113   | 0.1505   |
| H   | 2.66637  | 2.16586  | -0.12209 |
| H   | -0.23909 | -1.88042 | -0.38431 |
| C   | 1.42252  | 0.23852  | 0.00001  |
| C   | 0.57961  | 1.39434  | 0.        |
| C   | -0.78631 | 1.27451  | 0.        |
| C   | -1.5533  | -0.01927 | 0.        |
| C   | -0.55418 | -1.18497 | 0.00001  |
| C   | 0.80961  | -1.0561  | 0.00002  |
| H   | 1.03617  | 2.3765   | -0.00001 |
| H   | -1.42954 | 2.14396  | -0.00001 |
| H   | -1.02559 | 2.15832  | 0.00001  |
| H   | 1.4217   | -1.9473  | 0.00002  |
| C   | 2.83359  | 0.43103  | 0.00001  |
| H   | 3.1796   | 1.45969  | 0.00005  |
| C   | 3.77812  | -0.56229 | -0.00003 |
| H   | 3.52819  | -1.61556 | -0.00006 |
| H   | 4.83112  | -0.31    | -0.00001 |
| Cl  | -3.05339 | -0.17904 | -0.00001 |

\[
E (\text{UMPWB1K}) = -769.2528712
\]

\[\Delta G^\ddagger = +6.2 \text{ kcal/mol}\]
\[\Delta G = -23.4 \text{ kcal/mol}\]
Sum electronic and thermal free energies =
-769.1628782
Charge = 0 Multiplicity = 1
C 3.39066 -0.48217 -0.23904
F 4.21128 -1.16372 0.55658
Charge = 0 Multiplicity = 2
C 1.43138 0.2244 0.
C 0.60427 1.35892 -0.00001
C -0.7848 1.25226 0.
C -1.36045 -0.01378 0.
C -0.57187 -1.16404 -0.00001
C 0.81241 1.25226 0.
H 1.05481 2.34574 -0.00001
H -1.40707 2.13801 0.00001
H -1.0352 -2.14251 0.
H 1.41268 -1.93972 0.
C 2.89089 0.40833 0.
H 3.2127 1.4475 0.
C 3.83258 -0.54305 0.00001
H 3.60103 -1.6251 0.00001
H 4.88375 -0.28021 0.00001
Cl -3.10878 -0.16926 0.

E (UMPWB1K) = -1106.9066534

Sum electronic and thermal free energies =
-1106.809183
Charge = 0 Multiplicity = 2
C -0.32724 0.29685 -0.08624
C -1.21224 1.41426 -0.04175
C -2.58472 1.25326 0.00583
C -3.12201 -0.03893 0.00909
C -2.29462 -1.16413 -0.03571
C -0.91979 -0.99918 -0.08256
H -0.79455 2.41505 -0.04432
H -3.24024 2.11419 0.04043
H -2.72835 -2.15615 -0.03425
H -0.29349 -1.88225 -0.11971
C 2.07819 -0.5953 -0.19484
H 2.07475 -1.09997 -1.17027
H 1.88767 -1.36999 0.55549
C 3.49338 -0.11023 0.0328
F 3.65503 0.46257 1.24566
F 4.37898 -1.12694 -0.03948
F 3.87861 0.80811 -0.88116
C 1.06597 0.50708 -0.1334
H 1.42628 1.52922 -0.15608
Cl -4.85924 -0.24858 0.06848

E (UMPWB1K) = -1106.830502
Sum electronic and thermal free energies =
-1106.739551
Charge = 0 Multiplicity = 2
C 0.97264 1.5888 0.42454
H 1.13352 2.45224 -0.2164
C 1.98636 1.20047 1.2261
H 2.89919 1.7809 1.27636
H 1.89439 0.38633 1.93578