Electronic Supplementary Information

Chemoselective Direct Reductive Trifluoromethylation of Amides: A Flexible Access to Functionalized \( \alpha \)-Trifluoromethylamines

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1. General methods and General procedure

General methods

$^1$H NMR, $^{19}$F NMR and $^{13}$C NMR spectra were recorded on a spectrometer at 400, 376 and 100 MHz, respectively. Chemical shifts (δ) of $^1$H NMR and $^{13}$C NMR respectively referenced to an internal standard (Me$_4$Si, 0 ppm for $^1$H NMR and CDCl$_3$, 77.0 ppm for $^{13}$C NMR). $^{19}$F NMR used PhCF$_3$ as external standard. Mass spectra were obtained on a mass spectrometer in the ESI mode. Silicagel (300-400 mesh) was used for flash column chromatography (FC), eluting (unless otherwise stated) with ethyl acetate/ hexane mixture. Trifluoromethanesulfonic anhydride (Tf$_2$O) was distilled over phosphorous pentoxide and was stored for no more than a week before re-distillation. Dry dichloromethane and acetonitrile were distilled over calcium hydride under argon. Dimethylformamide was distilled under vacuum from P$_2$O$_5$ and stored over 4Å MS. Other commercially available chemicals were used without further purification. All reactions were carried out under an argon atmosphere.

General procedure A: One-pot Preparation of Trifluoromethylated Amines from Secondary Amides by Direct Reductive Nucleophilic Trifluoromethylation

To a solution of secondary amide (0.25 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (1.0 mL, 0.25 M), 2-fluoropyridine (24 μL, 0.28 mmol, 1.1 equiv) and trifluoromethanesulfonic anhydride (Tf$_2$O) (47 μL, 0.28 mmol, 1.1 equiv) was successively added dropwise via a syringe at 0 °C under Ar atmosphere, and the reaction was stirred for 30 min. To the resulting mixture, 1,1,3,3-tetramethyldisiloxane [(Me$_2$SiH)$_2$O] (31 μL, 0.18 mmol, 0.7 equiv) was added dropwise at 0 °C, and the reaction mixture was stirred for 30 min. Then, the reaction was allowed to warm up to room temperature and continually stirred for 5 h. CH$_2$Cl$_2$ was evaporated under reduced pressure. To the residue, KHF$_2$ (49 mg, 0.63 mmol, 2.5 equiv) and 4 Å MS powder (1.0 g/mmol) was added. Then MeCN (5.0 mL, 0.05 M) and DMF (60 μL, 0.75 mmol, 3.0 equiv) was added at −78 °C under Ar atmosphere, and the mixture was warmed up to room temperature and stirred for 10 mins. Again the reaction mixture was cooled to −78 °C. TMSCF$_3$ (120 ul, 0.75 mmol, 3.0 equiv) was added via a syringe The mixture was allowed to warmed up to room temperature and stirred for 18 h. The reaction was quenched with a saturated aqueous Na$_2$CO$_3$ (1.0 mL) and the mixture was stirred for 3 min, diluting with water (8.0 mL), and extracted with diethyl ether/hexane (1:3, 3×15 mL). The combined organic phases were dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give the corresponding trifluoromethylated amine.

General procedure B: One-pot Preparation of Trifluoromethylated Amines from Secondary Amides by Direct Reductive Nucleophilic Trifluoromethylation

To a solution of secondary amide (0.25 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (1.0 mL, 0.25 M), 2-fluoropyridine (24 μL, 0.28 mmol, 1.1 equiv) and trifluoromethanesulfonic anhydride (Tf$_2$O) (47 μL, 0.28 mmol, 1.1 equiv) was successively added dropwise via a syringe at 0 °C under Ar atmosphere, and the reaction was stirred for 30 min. To the resulting mixture, 1,1,3,3-tetramethyldisiloxane [(Me$_2$SiH)$_2$O] (31 μL, 0.18 mmol, 0.7 equiv) was
added dropwise at 0 °C, and the reaction mixture was stirred for 30 min. Then, the reaction was allowed to warm up to room temperature and continually stirred for 5 h. CH₂Cl₂ was evaporated under reduced pressure. To the residue, KHF₂ (68 mg, 0.88 mmol, 3.5 equiv) and 4 Å MS powder (1.0 g/mmol) was added. Then MeCN (5.0 mL, 0.05 M), DMF (100 uL, 1.25 mmol, 5.0 equiv) and TFA (19 uL, 0.25 mmol, 1.0 equiv) was added at –78 °C under Ar atmosphere, and the mixture was warmed up to room temperature and stirred for 10 mins. Again the reaction mixture was cooled to –78 °C. TMSCF₃ (185 uL, 1.25 mmol, 5.0 equiv) was added via a syringe. The mixture was allowed to warmed up to room temperature and stirred for 18 h. The reaction was quenched with a saturated aqueous Na₂CO₃ (1.0 mL) and the mixture was stirred for 3 min, diluting with water (8.0 mL), and extracted with diethyl ether/hexane (1:3, 3×15 mL). The combined organic phases were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give the corresponding trifluoromethylated amine.
2. Table S1. Optimization of reaction temperature and time.\textsuperscript{a}

\begin{figure}
\centering
\includegraphics[width=0.8\textwidth]{image}
\caption{Reaction pathway for the optimization of temperature and time.}
\end{figure}

<table>
<thead>
<tr>
<th>Entry</th>
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<th>Time</th>
<th>Yield (%)\textsuperscript{b}</th>
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<tr>
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<tr>
<td>3</td>
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<tr>
<td>10</td>
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<td>18 h</td>
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</table>

\textsuperscript{a} Reaction conditions: i) 1a-i (0.25 mmol), Tf\textsubscript{2}O (0.28 mmol), 2-F-Pyr. (0.28 mmol), CH\textsubscript{2}Cl\textsubscript{2} (0.25 M); ii) TMDS (0.18 mmol); iii) KHF\textsubscript{2} (0.63 mmol), TMSCF\textsubscript{3} (0.75 mmol), 4 Å MS (1.0 g/mmol), MeCN (0.05 M), DMF (0.75 mmol). \textsuperscript{b} Yields were determined by \textsuperscript{19}F NMR using PhCF\textsubscript{3} as an internal standard.
3. Data of α-trifluoromethylamines 2a–2i and 2l-2w

N-(2,2,2-Trifluoro-1-phenylethyl)cyclohexanamine (2a)

Following general procedure, the reductive trifluoromethylation of amide 1a (51 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: hexane), trifluoromethylated amine 2a (53 mg, yield: 82%) as a light yellow oil. IR (film): 3344, 3067, 3033, 2929, 2855, 1496, 1453, 1373, 1264, 1168, 1121, 890, 875, 845, 781, 709, 612 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.00-1.23 (m, 5H), 1.45-1.60 (m, 2H), 1.63-1.78 (m, 3H), 1.91-1.99 (m, 1H), 2.31-2.43 (m, 1H), 4.26 (q, J = 7.7 Hz, 1H), 7.33-7.42 (m, 5H); ¹³C NMR (100 MHz, CDCl₃): δ 24.6, 24.9, 25.9, 32.7, 34.2, 53.8, 61.5 (q, J = 28.5 Hz), 125.5 (q, J = 280.0 Hz), 128.4 (2C), 128.6 (2C), 128.7, 135.4; ¹⁹F NMR (376 MHz, CDCl₃): δ -74.2 (d, J = 8.2 Hz). HRMS-ESI calcd for [C₁₄H₁₉F₃N]+ (M+H⁺): 258.1464; found: 258.1473.

N-(2,2,2-Trifluoro-1-phenylethyl)cyclopentanamine (2b)

Following general procedure, the reductive trifluoromethylation of amide 1b (47 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: hexane), trifluoromethylated amine 2b (49 mg, 81%) as a light yellow oil. IR (film): 3337, 3062, 3030, 2956, 2870, 1696, 1472, 1456, 1363, 1262, 1164, 1107, 863, 845, 761, 703, 631 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.26-1.44 (m, 3H), 1.44-1.57 (m, 2H), 1.68-1.74 (m, 1H), 1.67 (br s, 1H), 1.74-1.85 (m, 2H), 2.98-3.07 (m, 1H), 4.17 (q, J = 7.7 Hz, 1H), 7.38-7.44 (m, 5H); ¹³C NMR (100 MHz, CDCl₃): δ 23.70, 23.72, 32.5, 33.6, 57.2, 63.4 (q, J = 28.7 Hz), 125.5 (q, J = 281.6 Hz), 128.4 (2C), 128.6 (2C), 128.8, 135.1; ¹⁹F NMR (376 MHz, CDCl₃): δ -74.3 (d, J = 7.0 Hz). HRMS-ESI calced for [C₁₃H₁₇F₃N]+ (M+H⁺): 244.1308; found: 244.1312.

N-(2,2,2-Trifluoro-1-phenylethyl)butan-2-amine (±2c)

Following general procedure, the reductive trifluoromethylation of amide 1c (44 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: hexane), trifluoromethylated amine (±)-2c (38 mg, 66%) as a mixture containing two inseparable diastereomers (d.r. = 1.6:1,
determined by $^1$H NMR). IR (film): 3349, 3068, 3034, 2966, 2932, 2977, 1498, 1456, 1379, 1332, 1166, 1171, 1117, 1031, 860, 850, 761, 703, 607, 601 cm$^{-1}$; Major diastereomer: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.92 (t, $J$ = 7.4 Hz, 3H), 1.10 (d, $J$ = 6.3 Hz, 3H), 1.35-1.53 (m, 3H), 2.49-2.59 (m, 1H), 4.28 (q, $J$ = 7.7 Hz, 1H), 7.39-7.46 (m, 5H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 10.2, 19.2, 30.4, 51.5, 62.1 (q, $J$ = 28.8 Hz), 125.7 (q, $J$ = 281.0 Hz), 128.5 (2C), 128.6 (2C), 128.8, 135.1; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -74.2 (d, $J$ = 7.8 Hz). Minor diastereomer: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.96 (t, $J$ = 7.4 Hz, 3H), 1.07 (d, $J$ = 6.4 Hz, 3H), 1.53-1.62 (m, 3H), 2.63-2.73 (m, 1H), 4.32 (q, $J$ = 7.5 Hz, 1H), 7.46-7.51 (m, 5H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 9.4, 20.4, 28.5, 52.0, 62.2 (q, $J$ = 28.5 Hz), 125.8 (q, $J$ = 281.0 Hz), 128.4 (2C), 128.64 (2C), 128.76, 135.7; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -74.1 (d, $J$ = 7.6 Hz). HRMS-ESI calcd for [C$_{12}$H$_{17}$F$_3$N]+ (M+H$^+$): 232.1308; found: 232.1309.

**N-(2,2,2-Trifluoro-1-phenylethyl)propan-2-amine (2d)**

![N-(2,2,2-Trifluoro-1-phenylethyl)propan-2-amine (2d)](image)

Following general procedure, the reductive trifluoromethylation of amide 1d (41 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: hexane), trifluoromethylated amine 2d (36 mg, 67%) as a light yellow oil (volatile). IR (film): 3337, 3068, 3034, 2966, 2931, 2871, 1497, 1456, 1375, 1358, 1264, 1179, 1115, 882, 851, 761, 703, 627 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.01-1.18 (m, 6H), 1.53 (br s, 1H), 2.73-2.85 (m, 1H), 4.25 (q, $J$ = 7.5 Hz, 1H), 7.34-7.52 (m, 5H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 21.9, 23.7, 46.0, 62.1 (q, $J$ = 28.6 Hz), 125.6 (q, $J$ = 281.3 Hz), 128.4 (2C), 128.6 (2C), 128.8, 135.2; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -74.2 (d, $J$ = 7.9 Hz). HRMS-ESI calcd for [C$_{12}$H$_{17}$F$_3$N]+ (M+H$^+$): 218.1146; found: 218.1153.

**N-(2,2,2-Trifluoro-1-phenylethyl)butan-1-amine (2e)**

![N-(2,2,2-Trifluoro-1-phenylethyl)butan-1-amine (2e)](image)

Following general procedure, the reductive trifluoromethylation of amide 1e (44mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: hexane), the trifluoromethylated amine 2e (36 mg, 62%) as a light yellow oil. IR (film): 3347, 3067, 3034, 2960, 2931, 2861, 1496, 1380, 1357, 1263, 1171, 1116, 1030, 878, 847, 760, 704, 608, 601 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.87 (t, $J$ = 7.3 Hz, 3H), 1.26-1.37 (m, 2H), 1.39-1.51 (m, 2H), 1.58 (br s, 1H), 2.55 (m, 2H), 4.11 (q, $J$ =7.6 Hz, 1H), 7.32-7.42 (m, 5H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 13.8, 20.2, 32.1, 47.5, 64.8 (q, $J$ = 28.6 Hz), 125.3 (q, $J$ = 281.4 Hz), 128.5 (2C), 128.6 (2C), 128.9, 134.8; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -74.5 (d, $J$ = 7.2 Hz). HRMS-ESI calcd for [C$_{12}$H$_{17}$F$_3$N]+ (M+H$^+$): 232.1308; found: 232.1313.

**2,2,2-Trifluoro-N-methyl-1-phenylethanamine (2f)**
Following general procedure, the reductive trifluoromethylation of amide 1f (34 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (elucent: EtOAc/hexane = 1/20), trifluoromethylated amine 2f (27 mg, 57%) as a light yellow oil (volatile). IR (film): 3349, 2959, 2925, 2854, 1730, 1600, 1461, 1379, 1262, 1206, 1153, 1119, 1070, 1021, 801, 703 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.69 (br s, 1H), 2.29 (s, 3H), 3.92 (q, \(J = 7.5\) Hz, 1H), 7.14-7.39 (m, 5H); \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 34.6, 66.5 (q, \(J = 28.6\) Hz), 125.4 (q, \(J = 281.4\) Hz), 128.5 (2C), 128.7 (2C), 129.0, 134.2; \(^19\)F NMR (376 MHz, CDCl\(_3\)): \(\delta\) -74.2 (d, \(J = 7.0\) Hz). HRMS-ESI calcd for [C\(_9\)H\(_{11}\)F\(_3\)N\(^+\) (M+H\(^+\))]: 190.0838; found: 190.0846.

### 2,2,2-Trifluoro-N-phenethyl-1-phenylethanamine (2g)

Following general procedure B, the reductive trifluoromethylation of amide 1g (56 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (elucent: hexane), the known trifluoromethylated amine 2g (70 mg, 71%) as a yellow oil. IR (film): 3341, 3064, 3030, 2927, 2852, 1506, 1473, 1455, 1355, 1264, 1167, 1122, 1065, 752, 701, 630, 551 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.68 (br s, 1H), 2.73-2.92 (m, 4H), 4.14 (q, \(J = 7.4\) Hz, 1H), 7.12-7.41 (m, 10H); \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 36.2, 48.8, 64.6 (q, \(J = 28.8\) Hz), 125.3 (q, \(J = 281.4\) Hz), 128.3, 128.52 (2C), 128.64 (2C), 128.68 (2C), 128.9, 134.4, 139.3; \(^19\)F NMR (376 MHz, CDCl\(_3\)): \(\delta\) -74.2 (d, \(J = 7.3\) Hz). HRMS-ESI calcd for [C\(_{16}\)H\(_{16}\)F\(_3\)N\(^+\) (M+H\(^+\))]: 280.1303; found: 280.1308.

### 2,2,2-Trifluoro-N-phenethyl-1-phenylethanamine (2h)

Following general procedure B, the reductive trifluoromethylation of amide 1h (53 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (elucent: hexane), the known trifluoromethylated amine 2h (66 mg, 46%) as a light yellow oil. IR (film): 3345, 3088, 3065, 3031, 2925, 2852, 1604, 1496, 1455, 1375, 1339, 1263, 1172, 1124, 1029, 973, 880, 851, 739, 701, 637, 566, 512 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.93 (br s, 1H), 3.74 (d, \(J = 13.5\) Hz, 1H), 3.90 (q, \(J = 13.5\) Hz, 1H), 4.22 (q, \(J = 7.6\) Hz, 1H), 7.31-7.58 (m, 10H); \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 51.1, 64.5 (q, \(J = 28.8\) Hz), 125.5 (q, \(J = 281.4\) Hz), 127.4, 128.2 (2C), 128.6 (2C), 128.7 (2C), 128.8 (2C), 129.0, 134.3, 139.0; \(^19\)F NMR (376 MHz, CDCl\(_3\)): \(\delta\) -73.8 (d, \(J = 7.3\) Hz). MS(ESI) \(m/z\) 265 (M+H\(^+\)).
N-(2,2,2-Trifluoro-1-phenylethyl)prop-2-en-1-amine (2i)

Following general procedure B, the reductive trifluoromethylation of amide 1i (40 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: EtOAc/hexane = 1/30), trifluoromethylated amine 2i (54 mg, 60%) as a yellow oil (volatile). IR (film): 3343, 3069, 3034, 2925, 2851, 1645, 1456, 1365, 1264, 1171, 1123, 994, 925, 845, 761, 704, 626 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.67 (br s, 1H), 3.10-3.15 (m, 2H), 4.09-4.25 (m, 1H), 5.09-5.25 (m, 2H), 5.78-5.95 (m, 1H), 7.29-7.53 (m, 5H); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 49.8, 63.5 (q, \(J = 28.7\) Hz), 117.0, 125.5 (q, \(J = 282.0\) Hz), 128.6 (2C), 128.7 (2C), 129.0, 134.5, 135.7; \(^19\)F NMR (376 MHz, CDCl\(_3\)): \(\delta\) \(-74.0\) (d, \(J = 7.0\) Hz). HRMS-ESI calcd for [C\(_{11}\)H\(_{12}\)F\(_3\)NNa]\(^+\) (M+Na\(^+\)): 238.1587; found: 238.1594.

N-(2,2,2-Trifluoro-1-(4-methoxyphenyl)ethyl)cyclohexanamine (2l)

Following general procedure, the reductive trifluoromethylation of amide 1l (58 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: EtOAc/hexane = 1/30), the trifluoromethylated amine 2l (58 mg, 81%) as a light yellow oil. IR (film): 3335, 2930, 2854, 1613, 1586, 1515, 1465, 1374, 1305, 1251, 1171, 1121, 1035, 857, 825, 695, 612, 584, 530 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.00-1.21 (m, 5H), 1.51-1.61 (m, 1H), 1.47 (br s, 1H), 1.63-1.80 (m, 3H), 1.88-1.98 (m, 1H), 2.32-2.42 (m, 1H), 3.82 (s, 3H), 4.23 (q, \(J = 7.8\) Hz, 1H), 6.89-6.94 (m, 2H), 7.29-7.35 (m, 2H); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 24.6, 24.9, 25.9, 32.7, 34.2, 53.8, 55.2, 61.4 (q, \(J = 28.6\) Hz), 114.0, 114.2, 121.4, 125.5 (q, \(J = 281.8\) Hz), 129.6, 137.0, 159.8; \(^19\)F NMR (376 MHz, CDCl\(_3\)): \(\delta\) \(-74.8\) (d, \(J = 7.8\) Hz). HRMS-ESI calcd for [C\(_{15}\)H\(_{21}\)F\(_3\)NO]\(^+\) (M+H\(^+\)): 288.1570; found: 288.1573.

N-(2,2,2-Trifluoro-1-(3-methoxyphenyl)ethyl)cyclohexanamine (2m)

Following general procedure, the reductive trifluoromethylation of amide 1m (58 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: EtOAc/hexane = 1/30), the trifluoromethylated amine 2m (57 mg, 80%) as a light yellow oil. IR (film): 3335, 2930, 2854, 1603, 1588, 1491, 1467, 1453, 1438, 1350, 1306, 1259, 1170, 1120, 1049, 937, 890, 851, 786, 714, 625, 568 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.00-1.22 (m, 5H), 1.51 (br s, 1H), 1.53-1.63 (m, 1H), 1.63-1.79 (m, 3H), 1.89-1.97 (m, 1H), 2.34-2.44 (m, 1H), 3.83 (s, 3H), 4.23 (q, \(J = 7.7\) Hz, 1H), 6.88-6.99 (m, 2H), 7.27-7.33 (m, 2H); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 24.7, 25.1,
26.1, 32.8, 34.3, 53.9, 55.4, 61.5 (q, \( J = 28.6 \) Hz), 114.1, 114.3, 120.8, 129.7, 137.1, 125.7 (q, \( J = 281.4 \) Hz), 160.0; \(^{19}F\) NMR (376 MHz, CDCl\(_3\)): \( \delta = -74.1 \) (d, \( J = 7.6 \) Hz). HRMS-ESI calcd for \([\text{C}_{15}\text{H}_{21}\text{F}_{3}\text{NO}]^{+}\) (M+H\(^{+}\)): 288.1570; found: 288.1569.

\( N-(2,2,2\text{-Trifluoro-1-(2-methoxyphenyl)ethyl})\text{cyclohexanamine (2n)} \)

Following general procedure, the reductive trifluoromethylation of amide \( 1n \) (58 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (elucent: EtOAc/hexane = 1/30), the trifluoromethylated amine \( 2n \) (59 mg, 82%) as a light yellow oil. IR (film): 3342, 3005, 2930, 2854, 698, 618 cm\(^{-1}\); \(^1H\) NMR (400 MHz, CDCl\(_3\)): \( \delta = 1.02-1.22 \) (m, 5H), 1.49-1.58 (m, 1H), 1.61-1.75 (m, 4H), 1.87-1.97 (m, 1H), 2.32-2.41 (m, 1H), 3.83 (s, 3H), 4.87 (q, \( J = 8.1 \) Hz, 1H), 6.91 (dd, \( J = 8.3, 0.8 \) Hz, 1H), 6.98 (td, \( J = 7.5, 1.0 \) Hz, 1H), 7.27-7.33 (m, 1H); 7.37 (d, \( J = 7.5 \) Hz, 1H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)): \( \delta = 24.6, 24.9, 26.0, 32.8, 34.1, 53.7 \) (q, \( J = 29.3 \) Hz), 54.1, 55.7, 111.1, 120.9, 124.2, 125.9 (q, \( J = 281.4 \) Hz), 128.2, 129.6, 157.8; \(^{19}F\) NMR (376 MHz, CDCl\(_3\)): \( \delta = -74.2 \) (d, \( J = 7.6 \) Hz). HRMS-ESI calcd for \([\text{C}_{15}\text{H}_{20}\text{F}_{3}\text{NNaO}]^{+}\) (M+Na\(^{+}\)): 310.1389; found: 310.1388.

\( N-(2,2,2\text{-Trifluoro-1-(3,4,5-trimethoxyphenyl)ethyl})\text{cyclohexanamine (2o)} \)

Following general procedure, the reductive trifluoromethylation of amide \( 1o \) (73 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (elucent: EtOAc/hexane = 1/5), the trifluoromethylated amine \( 2o \) (72 mg, 83%) as a light yellow oil. IR (film): 3327, 2930, 1593, 1508, 1484, 1423, 1327, 1242, 1152, 1130, 1009, 824, 713, 660, 535 cm\(^{-1}\); \(^1H\) NMR (400 MHz, CDCl\(_3\)): \( \delta = 1.00-1.23 \) (m, 5H), 1.47 (br s, 1H), 1.53-1.60 (m, 1H), 1.62-1.80 (m, 3H), 1.88-1.97 (m, 1H), 2.34-2.43 (m, 1H), 3.86 (s, 3H), 3.87 (s, 6H), 4.18 (q, \( J = 7.5 \) Hz, 1H), 6.62 (s, 2H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)): \( \delta = 24.6, 25.0, 25.9, 32.8, 34.3, 53.8, 56.2 \) (2C), 60.8, 61.7 (q, \( J = 28.5 \) Hz), 105.5 (2C), 125.5 (q, \( J = 281.5 \) Hz), 130.8, 138.4, 153.3 (2C); \(^{19}F\) NMR (376 MHz, CDCl\(_3\)): \( \delta = -74.2 \) (d, \( J = 7.5 \) Hz). HRMS-ESI calcd for \([\text{C}_{17}\text{H}_{25}\text{F}_{3}\text{NNaO}_3]^{+}\) (M+H\(^{+}\)): 370.1600; found: 370.1604.

\( N-(2,2,2\text{-Trifluoro-1-(3-methoxyphenyl)ethyl})\text{cyclohexanamine (2p)} \)
Following general procedure, the reductive trifluoromethylation of amide 1p (59 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: hexane), the trifluoromethylated amine 2p (36 mg, 50%) as a yellow oil. IR (film): 3339, 2929, 2655, 1588, 1493, 1450, 1412, 1351, 1261, 1169, 1123, 1093, 1016, 890, 853, 817, 730, 689, 611 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 0.99-1.21 (m, 5H), 1.49 (br s, 1H), 1.52-1.62 (m, 1H), 1.62-1.79 (m, 3H), 1.85-1.99 (m, 1H), 2.30-2.42 (m, 1H), 4.28 (q, J = 7.5 Hz, 1H), 7.33-7.39 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 24.5, 24.9, 25.9, 32.6, 34.2, 53.7, 60.9 (q, J = 28.7 Hz), 125.3 (q, J = 281.3 Hz), 128.8 (2C), 129.8 (2C), 133.8, 134.7; ¹⁹F NMR (376 MHz, CDCl₃): δ -74.4 (d, J = 7.5 Hz). HRMS-ESI calcd for [C₁₄H₁₈ClF₃N]⁺ (M+H⁺): 292.1074; found: 292.1080.

N-(1-(4-Bromophenyl)-2,2,2-trifluoroethyl)cyclohexanamine (2q)

Following general procedure, the reductive trifluoromethylation of amide 1q (71 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: hexane), the trifluoromethylated amine 2q (59 mg, 70%) as a yellow oil. IR (film): 3334, 2929, 2855, 1593, 1490, 1407, 1351, 1261, 1173, 1123, 1074, 1012, 890, 852, 814, 727, 685, 611 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 0.99-1.21 (m, 5H), 1.50 (br s, 1H), 1.53-1.62 (m, 1H), 1.62-1.79 (m, 3H), 1.85-1.94 (m, 1H), 2.28-2.39 (m, 1H), 4.25 (q, J = 7.5 Hz, 1H), 7.23-7.32 (m, 2H), 7.47-7.55 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 24.5, 24.9, 25.9, 32.6, 34.2, 53.7, 61.0 (q, J = 281.7 Hz), 130.1 (2C), 131.8 (2C), 134.4; ¹⁹F NMR (376 MHz, CDCl₃): δ -74.4 (d, J = 7.5 Hz). HRMS-ESI calcd for [C₁₄H₁₈BrF₃N]⁺ (M+H⁺): 336.0569; found: 336.0573.

Methyl 4-(1-(cyclohexylamino)-2,2,2-trifluoroethyl)benzoate (2r)

Following general procedure B, the reductive trifluoromethylation of amide 1r (65 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: hexane), the trifluoromethylated amine 2r (55 mg, 70%) as a yellow oil. IR (film): 3338, 2930, 1727, 1614, 1579, 1450, 1437, 1418, 1350, 1283, 1169, 1116, 1021, 971, 890, 862, 842, 820, 771, 717, 686, 613 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.00-1.19 (m, 5H), 1.50-1.58 (m, 1H), 1.60 (br s, 1H), 1.63-1.77 (m, 3H), 1.86-1.94 (m, 1H), 2.29-2.39 (m, 1H), 3.92 (s, 3H), 4.33 (q, J = 7.5 Hz, 1H), 7.46-7.51 (m, 2H), 8.03-8.08 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 24.5, 24.8, 25.9, 32.6, 34.2, 52.1, 53.9, 61.3 (q, J = 28.8 Hz), 125.3 (q, J = 281.7 Hz), 128.5 (2C), 129.8 (2C), 130.7, 140.4, 166.6; ¹⁹F NMR (376 MHz, CDCl₃): δ -74.2 (d, J = 7.4 Hz). HRMS-ESI calcd for [C₁₆H₂₀F₃NNaO₂]⁺ (M+H⁺): 338.1339; found: 338.1340.

4-(1-(Cyclohexylamino)-2,2,2-trifluoroethyl)phenyl acetate (2s)
Following general procedure, the reductive trifluoromethylation of amide 1s (65 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: EtOAc/hexane = 1/10), the trifluoromethylated amine 2s (51 mg, 65%) as a light yellow oil. IR (film): 3340, 3040, 2930, 2855, 1762, 1609, 1474, 1450, 1422, 1371, 1309, 1262, 1205, 1121, 1018, 914, 863, 839, 691, 664, 612, 526 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 0.99-1.29 (m, 5H), 1.49 (br s, 1H), 1.52-1.66 (m, 1H), 1.62-1.78 (m, 3H), 1.91-2.01 (m, 1H), 2.34 (s, 3H), 2.38-2.47 (m, 1H), 4.32 (q, J = 7.6 Hz, 1H); 7.13-7.19 (m, 2H), 7.43-7.48 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 21.1, 24.5, 24.9, 25.9, 32.7, 34.2, 53.6, 60.8 (q, J = 28.6 Hz), 121.7 (2C), 125.4 (q, J = 280.9 Hz), 129.5 (2C), 151.0, 169.2; ¹⁹F NMR (376 MHz, CDCl₃): δ -74.4 (d, J = 7.6 Hz). HRMS-ESI calcd for [C₁₆H₂₁F₃NO₂]⁺ (M+H⁺): 316.1519; found: 316.1522.

1-(4-(1-(Cyclohexylamino)-2,2,2-trifluoroethyl)phenyl)ethanone (2t)

Following general procedure B, the reductive trifluoromethylation of amide 1t (61 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: EtOAc/hexane = 1/10), the trifluoromethylated amine 2t (46 mg, 61%) as a yellow oil. IR (film): 3343, 2929, 2855, 1687, 1610, 1560, 1450, 1416, 1360, 1265, 1166, 1124, 1017, 958, 890, 858, 822, 694, 617 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.03-1.25 (m, 5H), 1.50-1.57 (m, 2H), 1.65-1.78 (m, 3H), 1.89-1.97 (m, 1H), 2.32-2.42 (m, 1H), 2.64 (s, 3H), 4.37 (q, J = 7.6 Hz, 1H), 7.53 (d, J = 8.2 Hz, 2H), 8.00 (d, J = 8.3 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 24.5, 24.8, 25.9, 26.6, 32.7, 34.2, 53.9, 61.3 (q, J = 28.6 Hz), 125.2 (q, J = 281.3 Hz), 128.6 (2C), 128.7 (2C), 137.5, 140.5, 197.5; ¹⁹F NMR (376 MHz, CDCl₃): δ -74.4 (d, J = 7.9 Hz). HRMS-ESI calcd for [C₁₆H₂₀F₃NNaO]⁺ (M+Na⁺): 322.1389; found: 322.1389.

N-(2,2,2-Trifluoro-1-(naphthalen-2-yl)ethyl)cyclohexanamine (2u)

Following general procedure, the reductive trifluoromethylation of amide 1u (63 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: hexane), the trifluoromethylated amine 2u (53 mg, 69%) as a light yellow oil. IR (film): 3336, 3058, 2929, 2854, 1510, 1499, 1371, 1350, 1267, 1164, 1120, 816, 747, 709; ¹H NMR (400 MHz, CDCl₃): δ 1.05-1.26 (m, 5H), 1.47-1.56 (m, 1H), 1.62 (br s, 1H), 1.63-1.79 (m, 3H), 1.95-2.09 (m, 1H), 2.32-2.48 (m, 1H), 4.43 (q, J = 7.7 Hz, 1H), 7.46-7.54 (m, 3H), 7.81-7.88 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 24.6, 25.0, 26.0, 32.7, 34.3, 53.8, 61.7 (q, J = 28.7 Hz), 125.5, 125.8 (q, J = 280.5 Hz), 126.4, 126.5,
127.8, 128.1, 128.2, 128.6, 132.8, 133.2, 133.6; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -73.9 (d, $J = 7.6$ Hz). HRMS-ESI calcd for [C$_{18}$H$_{20}$F$_3$N]$^+$ (M+H$^+$): 308.1621; found: 308.1626. 

$N$-(2,2,2-Trifluoro-1-(thiophen-2-yl)ethyl)cyclohexanamine (2v)

Following general procedure B, the reductive trifluoromethylation of amide 1v (52 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: hexane), the known trifluoromethylated amine 2v ($\infty$) (66 mg, 62%) as a yellow oil. IR (film): 3340, 2929, 2855, 1473, 1450, 1374, 1264, 1221, 1166, 1121, 858, 829, 705, 637 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.02-1.38 (m, 5H), 1.50 (br s, 1H), 1.53-1.64 (m, 1H), 1.66-1.81 (m, 3H), 1.89-1.97 (m, 1H), 2.47-2.57 (m, 1H), 4.55 (q, $J = 7.3$ Hz, 1H); 6.99-7.12 (m, 2H), 7.30-7.35 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 24.5, 24.9, 25.9, 32.7, 34.0, 54.0, 57.2 (q, $J = 30.3$ Hz), 125.0 (q, $J = 281.1$ Hz), 125.9, 126.89, 126.92, 138.7; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -75.0 (d, $J = 7.3$ Hz). MS(ESI) m/z 264 (M+H$^+$).

$N$-(1,1,1-Trifluorotridecan-2-yl)cyclohexanamine (2w)

Following general procedure B, the reductive trifluoromethylation of amide 1w (67 mg, 0.25 mmol) gave, after flash column chromatography on silica gel (eluent: hexane), the trifluoromethylated amine 2w (80 mg, 61%) as a light yellow oil. IR (film): 3441, 2927, 2855, 1640, 1466, 1451, 1377, 1263, 1147, 1110, 846, 700, 595 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.88 (t, $J = 7.0$ Hz, 3H), 0.94-1.41 (m, 22H), 1.44-1.55 (m, 1H), 1.56-1.63 (m, 1H), 1.63-1.77 (m, 3H), 1.78-1.91 (m, 2H), 2.52-2.63 (m, 1H), 2.95-3.07 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 14.2, 22.8, 25.0, 25.1, 25.8, 26.2, 29.5, 29.58, 29.64, 29.7, 30.06 (2C), 32.1, 33.7, 34.6, 55.5, 56.7 (q, $J = 27.2$ Hz), 127.3 (q, $J = 283.8$ Hz); $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ -75.8 (d, $J = 7.0$ Hz). HRMS-ESI calcd for [C$_{19}$H$_{35}$F$_3$N]$^+$ (M+H$^+$): 322.2716; found: 322.2719.

References

\[ ^{19}\text{F}, \, ^{1}\text{H} \, \text{and} \, ^{13}\text{C} \, \text{NMR spectra of compound 2a} \]
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2b
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2c
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2d
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2e
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2f
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2g
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2h
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2i
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2j
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2k
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2l
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2m
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2n
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2o
$^{19}F$, $^1H$ and $^{13}C$ NMR spectra of compound 2p
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2q
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2r
$^{19}\text{F}$, $^1\text{H}$ and $^{13}\text{C}$ NMR spectra of compound 2s
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2t
$^{19}$F, $^1$H and $^{13}$C NMR spectra of compound 2u