Supporting Information

Highly Efficient and Versatile Synthesis of Difluoro-γ-lactams via Aminodifluoroalkylation of Alkenes

Hongtai Chen, Xiaoyang Wang, Wentao Zhao, Minjie Guo, Xiangyang Tang, and Guangwei Wang

1. General Information

All reactions were carried out under Ar atmosphere with dry solvents in flame-dried glassware unless otherwise noted. Anhydrous CH$_3$CN and N,N,N',N''-pentamethyldiethylenetriamine and CuI were purchased commercial from sources and used as received. Chromatographic separations were carried out on 200-300 mesh silica gel. Reactions were monitored by TLC or HPLC analysis of reaction aliquots. HPLC analysis was performed on an Agilent 1260 Liquid Chromatography using a ZORBAX SB-C18 column (4.6 × 150 mm, 5-micron). $^1$H, $^{19}$F and $^{13}$C NMR spectra were recorded in CDCl$_3$ on a Bruker AVANCE III spectrometer. Melting points were recorded with a micro melting point apparatus on a Beijing Tech Instrument X-6. High resolution spectra (HRMS) were recorded on a QTOF mass analyzer with electrospray ionization (ESI) through a Bruker Daltonic miorOTOF-QII.
2. Typical Procedure for Amino-difluoroalkylation of Alkenes

![Chemical structure](image)

**Synthesis of 3,3-difluoro-1,5-diphenylpyrrolidin-2-one (3aa)**[1] **Representative Procedure I.** To a mixture of 2-bromo-2,2-difluoro-N-phenylacetamide 2a (250.0 mg, 1.0 mmol), CuI (19.0 mg, 0.1 mmol) in CH$_3$CN (2.0 mL) were added N,N,N',N''-Pentamethyldiethylenetriamine (313 µL, 1.5 mmol) and styrene 1a (230 µL, 2 mmol) successively. The resultant mixture was stirred at 80 °C for 10 h and monitored by TLC. The reaction was quenched with ethyl acetate and water, and then extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over anhydrous Na$_2$SO$_4$. After filtration, the filtrate was concentrated in vacuum and the residue was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1) to give the desired product 3aa (240.5 mg) in 90% yield as white solid, m.p. 144.4-144.6 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.46-7.43 (m, 2H), 7.35-7.24 (m, 7H), 7.16 (t, $J$ = 7.4 Hz, 1H), 5.37-5.34 (m, 1H), 3.20-3.07 (m, 1H), 2.62-2.49 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.23 (t, $J$ = 30.3 Hz, 1C), 138.57, 136.37, 129.30 (2C), 129.05 (2C), 128.69, 126.65, 126.38 (2C), 122.90 (2C), 117.50 (t, $J$ = 249.1 Hz, 1C), 58.29 (t, $J$ = 3.4 Hz, 1C), 39.11 (t, $J$ = 21.8 Hz, 1C); $^{19}$F NMR (377 MHz, CDCl$_3$) δ -101.22 (d, $^2$J$_{FF}$ = 270.6 Hz), -104.32 (d, $^2$J$_{FF}$ = 270.6 Hz).

![Chemical structure](image)

**3,3-Difluoro-5-(4-fluorophenyl)-1-phenylpyrrolidin-2-one (3ba)**[1] The title compound was prepared according to Representative Procedure I except that 4-fluorostyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 91%, 264.81 mg, white solid, m.p. 114.5-115.1 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.26 (d, $J$ = 9.3 Hz, 3H), 7.14-7.11 (m, 2H), 6.87-6.84 (m, 2H), 6.76-6.73 (m, 2H), 6.67-6.64 (m, 2H), 2.99-2.91 (m, 2H), 2.49-2.41 (m, 2H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.93 (t, $J$ = 30.3 Hz, 1C), 138.36, 136.39, 129.26 (2C), 129.07 (2C), 128.68, 126.64, 126.36 (2C), 122.89 (2C), 117.51 (t, $J$ = 249.1 Hz, 1C), 58.28 (t, $J$ = 3.4 Hz, 1C), 39.10 (t, $J$ = 21.8 Hz, 1C); $^{19}$F NMR (377 MHz, CDCl$_3$) δ -101.12 (d, $^2$J$_{FF}$ = 270.6 Hz), -104.31 (d, $^2$J$_{FF}$ = 270.6 Hz).
2H), 7.19-6.89 (m, 5H), 6.82 (d, J = 9.5, 7.7 Hz, 2H), 5.22-5.21 (m, 1H), 2.98-2.94 (m, 1H), 2.41-2.32 (m, 1H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 163.04 (t, \(J = 31.1\) Hz, 1C), 162.49 (d, \(J = 247.8\) Hz, 1C), 136.05, 134.28, 129.04 (2C), 128.25 (d, \(J = 8.4\) Hz, 1C), 126.75, 123.00 (2C), 117.49 (t, \(J = 250.48\) Hz, 1C), 116.19 (d, \(J = 21.9\) Hz, 1C), 57.56 (t, \(J = 3.3\) Hz, 1C), 138.86 (t, \(J = 21.9\) Hz, 1C); \(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -100.85 (d, \(2J_{FF} = 270.6\) Hz, \(3J_{HF} = 15.8, 12.5\) Hz), -104.55 (d, \(2J_{FF} = 270.5\) Hz, \(3J_{HF} = 17.1, 13.1\) Hz), -112.79.

\[\text{5-(4-Chlorophenyl)-3,3-difluoro-1-phenylpyrrolidin-2-one (3ca)}\] The title compound was prepared according to Representative Procedure I except that 4-chlorostyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 80%, 196.5 mg, white solid, m.p. 128.2-129.0 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.43-7.41 (m, 2H), 7.31-7.26 (m, 4H), 7.19-7.17 (m, 3H), 5.38-5.34 (m, 1H), 3.19-3.06 (m, 1H), 2.56-2.44 (m, 1H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 162.96 (t, \(J = 31.2\) Hz, 1C), 137.15, 136.05, 134.40, 129.43 (2C), 129.09 (2C), 127.81 (2C), 126.78, 122.84 (2C), 117.38 (t, \(J = 249.6\) Hz, 1C), 57.55 (t, \(J = 3.3\) Hz, 1C), 38.68 (t, \(J = 22.0\) Hz, 1C); \(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -100.71 (d, \(2J_{FF} = 270.7\) Hz, \(3J_{HF} = 16.2, 12.8\) Hz), -104.51 (d, \(2J_{FF} = 274.6\) Hz, \(3J_{HF} = 17.1, 13.1\) Hz).

\[\text{5-(4-Bromophenyl)-3,3-difluoro-1-phenylpyrrolidin-2-one (3da)}\] The title compound was prepared according to Representative Procedure I except that 4-bromostyrene was used instead of styrene. The product was purified by silica gel
column chromatography (petroleum ether/EtOAc = 5/1). Yield, 86%, 303.5 mg, white solid, m.p. 134.9-135.5 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.45-7.45 (m, 4H), 7.32-7.28 (m, 2H), 7.19-7.11 (m, 3H), 5.35-5.29 (m, 1H), 3.19-3.06 (m, 1H), 2.56-2.44 (m, 1H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 163.06 (t, \(J = 31.2\) Hz, 1C), 137.66, 136.07, 132.46 (2C), 129.17 (2C), 128.10 (2C), 126.84, 122.82 (2C), 122.63, 117.31 (t, \(J = 249.6\) Hz, 1C), 57.66 (t, \(J = 3.4\) Hz, 1C), 38.81 (t, \(J = 22.0\) Hz, 1C); \(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -100.83 (d, \(2J_{FF} = 271.0\) Hz, \(3J_{HF} = 16.1, 12.8\) Hertz), -104.54 (d, \(2J_{FF} = 271.0\) Hz, \(3J_{HF} = 17.0, 13.1\) Hertz).

3,3-Difluoro-1-phenyl-5-(p-tolyl) pyrrolidin-2-one (3ea).\(^{[1]}\) The title compound was prepared according to Representative Procedure I except that 4-methylstyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 82%, 182.8 mg, white solid, m.p. 127.7-128.5 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.47-7.45 (m, 2H), 7.31-7.27 (m, 2H), 7.15-7.14 (m, 5H), 5.35-5.31 (m, 1H), 3.18-3.05 (m, 1H), 2.60-2.47 (m, 1H), 2.30 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 163.17 (t, \(J = 31.2\) Hz, 1C), 138.45, 136.41, 135.54, 129.90 (2C), 128.95 (2C), 126.53, 126.27 (2C), 122.92 (2C), 117.58 (t, \(J = 249.4\) Hz, 1C), 58.05 (t, \(J = 3.4\) Hz, 1C), 39.10 (t, \(J = 21.7\) Hz, 1C), 21.03 (1C); \(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -101.13 (d, \(2J_{FF} = 270.4\) Hz, \(3J_{HF} = 16.0, 12.3, 3.4\) Hertz), -104.54 (d, \(2J_{FF} = 270.4\) Hz, \(3J_{HF} = 17.0, 13.1\) Hertz).

3,3-Difluoro-5-(4-methoxyphenyl)-1-phenylpyrrolidin-2-one (3fa).\(^{[1]}\) The title compound was prepared according to Representative Procedure I except that
4-methoxystyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 83%, white solid, m.p. 101.5-102.1 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.42-7.40 (m, 2H), 7.31-7.27 (m, 2H), 7.16-7.14 (m, 3H), 6.84-6.82 (m, 2H), 5.31-5.27 (m, 1H), 3.74 (s, 3H), 3.13-3.03 (m, 1H), 2.59-2.50 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 163.14 (t, J = 31.2 Hz, 1C), 159.73, 136.35, 130.33, 129.00 (2C), 127.73 (2C), 126.65, 123.17 (2C), 117.62 (t, J = 249.4 Hz, 1C), 114.63 (2C), 57.93 (t, J = 3.4 Hz), 55.26 (3C), 39.19 (t, J = 21.6 Hz, 1C); ¹⁹F NMR (377 MHz, CDCl₃) δ -101.33 (d, 2J_FF = 271.4 Hz, 3J_HF = 16.1, 12.8 Hz), -104.51 (d, 2J_FF = 271.4 Hz, 3J_HF = 17.5, 14.3 Hz). HRMS (ESI), m/z [M+Na⁺] calcd for C₁₄H₁₀ClNNaO₂⁺, 326.0963, found, 326.0956.

3,3-Difluoro-5-(4-nitrophenyl)-1-phenylpyrrolidin-2-one (3ga). The title compound was prepared according to Representative Procedure I except that 4-nitrostyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 76%, 254 mg, white solid, m.p. 139-140 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.19-8.17 (m, 2H), 7.46-7.41 (m, 4H), 7.34-7.30 (m, 2H), 7.21-7.17 (m, 1H), 5.53-5.49 (m, 1H), 3.24-3.18 (m, 1H), 2.60-2.48 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 162.98 (t, J = 31.3 Hz, 1C), 148.11, 145.82, 135.94, 129.43 (2C), 127.48 (2C), 127.13, 124.65 (2C), 122.58 (2C), 117.00 (t, J = 250.1 Hz, 1C), 57.48 (t, J = 3.4 Hz, 1C), 38.64 (t, J = 22.4 Hz, 1C); ¹⁹F NMR (377 MHz, CDCl₃) δ -101.33 (d, 2J_FF = 271.8 Hz, 3J_HF = 16.2, 13.4 Hz), -104.81 (d, 2J_FF = 271.8 Hz, 3J_HF = 16.4, 12.3 Hz). HRMS (ESI), m/z [M+Na⁺] calcd for C₁₄H₁₀ClNNaO₂⁺, 341.0708, found, 341.0710.
3,3-Difluoro-5-(3-chlorophenyl)-1-phenylpyrrolidin-2-one (3ha). The title compound was prepared according to Representative Procedure I except that 3-chlorostyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 82%, 251.74 mg, white solid, m.p. 121.9-123.6 °C. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.33-7.31 (m, 2H), 7.23-7.20 (m, 2H), 7.18-7.14 (m, 3H), 7.09-7.07 (m, 1H), 7.03-7.01 (m, 1H), 5.23-5.20 (m, 1H), 3.07-2.98 (m, 1H), 2.46-2.38 (m, 1H); $^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 163.12 (t, $J = 31.2$ Hz, 1C), 140.76, 136.11, 135.26, 130.75, 129.26 (2C), 129.03, 126.90, 126.68, 124.44, 122.76 (2C), 117.22 (t, $J = 249.15$ Hz, 1C), 57.72 (t, $J = 3.3$ Hz, 1C), 38.92 (t, $J = 22.1$ Hz, 1C); $^{19}$F NMR (565 MHz, CDCl$_3$) $\delta$ -100.93 (d, $^2J_{FF} = 271.5$ Hz, $^3J_{HF} = 16.1$, 12.9 Hz), -104.47 (d, $^2J_{FF} = 275.2$ Hz, $^3J_{HF} = 16.9$, 12.9 Hz). HRMS (ESI), m/z [M+Na$^+$] calcd for C$_{16}$H$_{12}$ClF$_2$NNaO$^+$, 330.0468, found, 330.0468.

3,3-Difluoro-5-(2-nitrophenyl)-1-phenylpyrrolidin-2-one (3ia). The title compound was prepared according to Representative Procedure I except that 2-nitrostyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 82%, white solid, m.p. 134-135 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.03 (d, $J = 8.1$ Hz, 1H), 7.51 (t, $J = 7.6$ Hz, 1H), 7.40 (t, $J = 7.3$ Hz, 3H), 7.30-7.21 (m, 3H), 7.09 (t, $J = 7.4$ Hz, 1H), 6.0-5.98 (m, 1H), 3.33-3.19 (m, 1H), 2.59-2.49 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.45 (t, $J = 31.3$ Hz, 1C), 147.82, 136.24, 134.68, 134.66, 129.63, 129.44 (2C), 127.30, 126.76, 125.88, 121.56 (2C), 117.10 (t, $J = 248.46$ Hz), 54.18 (d, $J = 6.3$ Hz, 1C), 38.25 (t, $J = 22.4$ Hz, 1C); $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -98.44 (d, $^2J_{FF} = 272.8$ Hz),
-105.25 (d, $^2J_{FF} = 272.8$ Hz). HRMS (ESI), m/z [M+Na$^+$] calcd for C$_{16}$H$_{12}$F$_2$N$_2$NaO$_3$$^+$, 341.0708, found, 341.0709.

3,3-Difluoro-5-(naphthalen-1-yl)-1-phenylpyrrolidin-2-one (3ja).\textsuperscript{[1]} The title compound was prepared according to Representative Procedure I except that 2-vinylnaphthalene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 90%, 325 mg, white solid, m.p. 157.4-158.3 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.73-7.63 (m, 3H), 7.60 (s, 1H), 7.40-7.36 (m, 4H), 7.21 (d, $J = 8.5$ Hz, 1H), 7.15 (t, $J = 7.9$ Hz, 2H), 7.00 (t, $J = 7.4$ Hz, 1H), 5.40-5.36 (m, 1H), 3.13-3.00 (m, 1H), 2.57-2.45 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.34 (t, $J = 31.2$ Hz), 136.44, 135.94, 133.29, 133.25, 129.74 (2C), 129.13, 128.00, 127.88, 126.89, 126.80, 126.74, 126.29, 123.07, 122.96 (2C), 117.51 (t, $J = 249.4$ Hz, 1C), 58.56 (t, $J = 3.4$ Hz, 1C), 39.12 (t, $J = 21.9$ Hz, 1C). $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -101.19 (d, $^2J_{FF} = 271.3$ Hz), -104.10 (d, $^2J_{FF} = 271.3$ Hz, $^3J_{HF} = 17.3$, 13.9 Hz).

3,3-Difluoro-1-phenyl-5-(pyridin-4-yl) pyrrolidin-2-one (3ka). The title compound was prepared according to Representative Procedure I except that 4-vinylpyridine was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 92%, 254.8 mg, white solid, m.p. 148.5-148.9 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.58 (d, $J = 5.3$ Hz, 2H), 7.43-7.41 (m, 2H), 7.38-7.25 (m, 2H), 7.18 (t, $J = 7.4$ Hz, 3H), 5.38-5.34 (m, 1H), 3.22-3.09 (m 1H), 2.57-2.45 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.01 (t, $J = 31.3$ Hz), 150.74 (2C), 147.84, 135.97, 129.38 (2C), 127.03, 122.36 (2C), 121.25,
116.94 (t, J = 250.1 Hz, 1C), 57.08 (t, J = 3.03 Hz, 1C), 38.34 (t, J = 22.5 Hz, 1C); \(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -100.63 (d, \(^2\)J\(_{FF}\) = 271.7 Hz), -104.75 (d, \(^2\)J\(_{FF}\) = 271.7 Hz, \(^3\)J\(_{HF}\) = 16.3, 11.6 Hz). HRMS (ESI), m/z [M+Na\(^+\)] calcd for C\(_{15}\)H\(_{12}\)F\(_2\)N\(_2\)NaO\(^+\), 297.0810, found, 297.0808.

3,3-Difluoro-5-octyl-1-phenylpyrrolidin-2-one (3la). The title compound was prepared according to Representative Procedure I except that 1-decene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 86\%, 223.6 mg, white solid, m.p. 90.5-91.5 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.44-7.40 (m, 4H), 7.31-7.30 (m, 1H), 4.28-4.21 (m, 1H), 2.81-2.75 (m, 1H), 2.40-2.27 (m, 1H), 1.74-1.70 (m, 1H), 1.39-1.22 (m, 13H), 0.89-0.86 (m, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 162.63 (t, \(^1\)J = 31.4 Hz, 1C), 135.94, 129.32 (2C), 127.18, 123.93 (2C), 117.87 (t, J = 249.2 Hz, 1C), 54.44 (t, J = 3.0 Hz, 1C), 34.65 (t, J = 21.9 Hz), 33.08, 31.74, 29.28, 29.17, 29.05, 24.38, 22.59, 14.04; \(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -100.91 (d, \(^2\)J\(_{FF}\) = 270.2 Hz), -104.21 (d, \(^2\)J\(_{FF}\) = 270.1 Hz). HRMS (ESI), m/z [M+Na\(^+\)] calcd for C\(_{18}\)H\(_{25}\)F\(_2\)NNaO\(^+\), 332.1796, found,332.1785.

3,3-Difluoro-5-(3-hydroxypropyl)-1-phenylpyrrolidin-2-one (3ma). The title compound was prepared according to Representative Procedure I except that 4-penten-1-ol was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 84\%, 215.4 mg, colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.49-7.35 (m, 4H), 7.30 (t, J = 6.9 Hz, 1H), 4.32 (s, 1H), 3.58 (d, J = 5.1 Hz, 2H), 2.86-2.73 (m, 1H), 2.42-2.29 (m, 1H), 1.85 (t, J = 10.1 Hz, 1H), 1.59-1.49 (m, 5H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 162.74 (t, J = 31.3 Hz, 1C), 135.34, 129.25 (2C), 127.32, 123.91 (2C), 117.86 (t, J = 249.1 Hz, 1C), 61.36, 54.36, 34.20 (t, J = 21.9 Hz, 1C), 29.51, 27.01; \(^{19}\)F NMR (377 MHz,
CDCl₃) δ -100.75 (d, $^2J_{FF} = 271.4$ Hz), -104.11 (d, $^2J_{FF} = 271.4$ Hz). HRMS (ESI), m/z [M+Na⁺] calcd for C₁₃H₁₅F₂NNaO₂⁺, 278.0963, found, 278.0965.

Butyl 4,4-difluoro-5-oxo-1-phenylpyrrolidine-2-carboxylate (3na). The title compound was prepared according to Representative Procedure I except that butyl acrylate was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 86%, 257.3 mg, white solid, m.p. 89.8-90.5 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.52-7.50 (m, 2H), 7.43-7.39 (m, 2H), 7.29-7.26 (m, 1H), 4.87-4.83 (m, 1H), 4.13-4.09 (m, 2H), 2.97-2.93 (m, 1H), 2.74-2.68 (m, 1H), 1.52-1.47 (m, 2H), 1.25-1.18 (m, 2H), 0.83 (t, $J = 7.4$ Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 169.40, 162.51 (t, $J = 31.3$ Hz, 1C), 136.75, 129.34, 127.11, 121.95 (2C), 116.47 (t, $J = 250.3$ Hz, 1C), 66.31, 56.14 (d, $J = 2.8$ Hz, 1C), 33.61 (t, $J = 24.2$ Hz, 1C), 30.32, 18.81, 13.50; ¹⁹F NMR (377 MHz, CDCl₃) δ -102.09 (d, $^2J_{HF} = 271.4$ Hz), -104.59 (d, $^2J_{HF} = 271.4$ Hz, $^3J_{HF} = 15.8$, 8.7 Hz). HRMS (ESI), m/z [M+Na⁺] calcd for C₁₅H₁₇F₂NNaO₃⁺, 320.1069, found, 320.1062.

3,3-Difluoro-5-(morpholine-4-carbonyl)-1-phenylpyrrolidin-2-one (3oa). The title compound was prepared according to Representative Procedure I except that 1-morpholinoprop-2-en-1-one was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 78%, 244.8 mg, white solid, m.p.174-175 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.39-7.29 (m, 4H), 7.29 (t, $J = 8.0$ Hz, 1H), 5.10 (d, $J = 6.3$ Hz, 1H), 3.66-3.39 (m, 8H), 2.91-2.78 (m, 1H), 2.67-2.52 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 166.71, 163.08 (t, $J = 31.3$ Hz, 1C), 136.56, 129.58, 127.78, 123.44, 116.75 (t, $J = 252.5$ Hz), 66.77, 66.42 53.46 (t, $J = 3.2$ Hz, 1C), 45.94, 42.92, 33.71 (t, $J = 24.0$ Hz, 1C); ¹⁹F NMR (377
MHZ, CDCl$_3$ $\delta$ -100.95 (d, $^2$J$_{FF}$ = 275.2 Hz), -104.27 (d, $^2$J$_{FF}$ = 275.2 Hz). HRMS (ESI), m/z [M+Na$^+$] calcd for C$_{15}$H$_{16}$F$_2$N$_2$NaO$_3^+$, 333.1021, found, 333.1027.

![Structure of 3,3-Difluoro-5-(2-hydroxybenzyl)-1-phenylpyrrolidin-2-one (3pa).](image)

**3,3-Difluoro-5-(2-hydroxybenzyl)-1-phenylpyrrolidin-2-one (3pa).** The title compound was prepared according to Representative Procedure I except that 2-allylphenol was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 86%, 260.8 mg, white solid, m.p. 105.1-106.2 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.11 (s, 1H), 7.48 (d, $J$ = 7.7 Hz, 2H), 7.27-7.25 (m, 2H), 7.10-6.96 (m, 3H), 6.79-4.42 (m, 1H), 6.57 (d, $J$ = 8.0 Hz, 1H), 4.94-4.92 (m, 1H), 3.30-3.24 (m, 1H), 2.85-2.79 (m, 1H), 2.74-2.60 (m, 1H), 2.48-2.36 (m, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 161.83 (t, $J$ = 28.0 Hz, 1C), 158.74, 136.12, 129.24 (2C), 128.30, 125.82, 125.68, 120.91, 120.51 (2C), 116.90 (t, $J$ = 254.7 Hz, 1C), 109.72, 76.73 (t, $J$ = 4.8 Hz, 1C), 39.96 (t, $J$ = 22.9 Hz, 1C), 35.94. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -102.30 (d, $^2$J$_{FF}$ = 256.3 Hz), -105.69 (d, $^2$J$_{FF}$ = 256.3 Hz). HRMS (ESI), m/z [M-H$^+$] calcd for C$_{17}$H$_{15}$F$_2$NO$_2^+$, 302.0998, found, 302.0995.

![Structure of (4S,5R)-3,3-Difluoro-4-methyl-1,5-diphenylpyrrolidin-2-one (3qa).](image)

**(4S,5R)-3,3-Difluoro-4-methyl-1,5-diphenylpyrrolidin-2-one (3qa).** The title compound was prepared according to Representative Procedure I except that 4-vinylpyridine was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 92%, 254.8 mg, white solid, m.p. 118-119 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.22 (d, $J$ = 8.0 Hz, 2H), 7.13 (m, 7H), 6.95 (t, $J$ = 7.4 Hz, 1H), 4.69 (d, $J$ = 7.3 Hz, 1H), 2.46-2.35 (m, 1H), 1.17 (d, $J$ = 6.9 Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.38 (t, $J$ = 31.3 Hz, 1C), 136.59, 135.89, 129.07 (2C), 128.77 (2C), 128.68 (2C), 126.94 (2C), 126.36, 123.23
(2C), 117.37 (t, $J = 249.37$ Hz, 1C), 65.48 (d, $J = 6.6$ Hz, 1C), 45.35 (t, $J = 20.7$ Hz, 1C), 8.32 (d, $J = 8.1$ Hz, 1C); $^{19}$F NMR (377 MHz, CDCl$_3$) δ -110.60 (d, $^2$J$_{FF}$ = 267.1 Hz), -118.63 (d, $^2$J$_{FF}$ = 267.1 Hz, $^3$J$_{HF}$ = 19.3 Hz).

![Chemical structure](image)

**3,3-Difluoro-1-(4-fluorophenyl)-5-phenylpyrrolidin-2-one (3ab)**[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-$N$-(4-fluorophenyl) acetamide was used instead of 2-bromo-2,2-difluoro-$N$-phenyl acetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 92%, 284.2 mg, white solid, m.p. 143-144 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.40-7.31 (m, 5H), 7.24-7.22 (m, 2H), 6.99-6.95 (m, 2H), 5.31-5.27 (m, 1H), 3.19-3.08 (m, 1H), 2.63-2.50 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.22 (t, $^1$J$_{CF}$ = 31.4 Hz, 1C), 160.67 (d, $^1$J$_{CF}$ = 247.2 Hz, 1C), 138.13, 132.23, 129.39 (2C), 128.89, 126.48 (2C), 124.96 (d, $^1$J$_{CF}$ = 8.4 Hz, 2C), 117.42 (t, $^1$J$_{CF}$ = 252.5 Hz, 1C), 116.00 (d, $^1$J$_{CF}$ = 22.8 Hz, 1C), 58.61 (t, $^1$J$_{HF}$ = 3.4 Hz, 1H), 39.04 (t, $^1$J$_{CF}$ = 21.9 Hz, 1C); $^{19}$F NMR (377 MHz, CDCl$_3$) δ -101.44 (d, $^2$J$_{FF}$ = 271.4 Hz), -104.37 (d, $^2$J$_{FF}$ = 271.4 Hz, $^3$J$_{HF}$ = 17.4, 14.4 Hz), -114.29.

![Chemical structure](image)

**1-(4-Chlorophenyl)-3,3-difluoro-5-phenylpyrrolidin-2-one (3ac)**[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-$N$-(4-chlorophenyl)-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-$N$-phenyl acetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 93%, 294.5 mg, white solid, m.p. 150-151 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.40-7.37 (m, 2H), 7.35-7.31 (m, 3H), 7.28-7.25 (m, 2H), 7.23-7.21 (m, 2H), 5.31-5.27 (m, 1H), 3.20-3.17 (m, 1H), 2.62-2.50 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.25 (t, $^1$J$_{CF}$ = 31.4 Hz, 1C), 138.15, 134.91, 132.10, 129.54 (2C), 129.28 (2C), 128.99, 126.35 (2C), 124.01 (2C), 117.26 (t, $^1$J$_{CF}$ = 249.47 Hz, 1C), 58.31 (t, $^1$J$_{CF}$ = 3.4 Hz, 1C), 39.21 (t, $^1$J$_{CF}$ = 21.9 Hz, 1C); $^{19}$F NMR
1-(4-Cromophenyl)-3,3-difluoro-5-phenylpyrrolidin-2-one (3ad). The title compound was prepared according to Representative Procedure I except that 2-bromo-N-(4-bromophenyl)-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-N-phenyl acetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 86%, 302.5 mg, white solid, m.p. 148.9-149.4 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40-7.29 (m, 7H), 7.24-7.22 (m, 2H), 5.36-5.32 (m, 1H), 3.20-3.07 (m, 1H), 2.61-2.48 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.14 (t, $J$ = 31.5 Hz, 1C), 138.10, 135.40, 132.08 (2C), 129.40 (2C), 128.84, 126.26 (2C), 124.25 (2C), 119.86, 117.33 (t, $J$ = 249.47 Hz, 1C), 58.10 (t, $J$ = 3.3 Hz, 1C), 38.94 (t, $J$ = 21.8 Hz, 1C); $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -101.22 (d, $^2$J$_{FF}$ = 271.1 Hz), -104.24 (d, $^2$J$_{FF}$ = 271.1 Hz, $^3$J$_{HF}$ = 17.1, 14.2 Hz).

3,3-Difluoro-5-phenyl-1-(p-tolyl) pyrrolidin-2-one (3ae). The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-N-(p-tolyl) acetamide was used instead of 2-bromo-2,2-difluoro-N-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 87%, 250.7 mg, white solid, m.p. 140.1-141.0 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.26-7.19 (m, 5H), 7.14 (d, $J$ = 7.1 Hz, 2H), 7.00 (d, $J$ = 8.3 Hz, 2H), 5.22-5.18 (m, 1H), 3.09-2.96 (m, 1H), 2.51-2.39 (m, 1H), 2.18 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.21 (t, $J$ = 31.0 Hz, 1C), 138.71, 136.64, 133.77, 129.72 (2C), 129.35 (2C), 128.74, 126.48 (2C), 122.92 (2C), 117.42 (t, $J$ = 252.5 Hz, 1C), 58.44 (t, $J$ = 3.4 Hz, 1C), 39.22 (t, $J$ = 21.9
Hz, 1C), 21.07; $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -101.28 (d, $^2J_{FF}$ = 270.8 Hz), -104.38 (d, $^2J_{FF}$ = 270.7 Hz, $^3J_{HF}$ = 17.2, 13.8 Hz).

1-(4-(Tert-butyl) phenyl)-3,3-difluoro-5-phenylpyrrolidin-2-one (3af). The title compound was prepared according to Representative Procedure I except that 2-bromo-N-(4-(tert-butyl) phenyl)-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-N-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 89%, 292.8 mg, white solid, m.p.164.5-165.4 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.27-7.13 (m, 9H), 5.23-5.19 (m, 1H), 3.03-2.96 (m, 1H), 2.46-2.41 (m, 1H), 1.15 (s, 9H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.26 (t, $^1C$, $J$ = 31.0 Hz, 1C), 149.62, 138.99, 133.86, 129.35 (2C), 128.64, 126.34 (2C), 126.01 (2C), 122.34 (2C), 117.55 (t, $J = 249.47$ Hz, 1C), 58.35(t, $J = 3.0$ Hz, 1C), 39.21 (t, $J = 21.9$ Hz, 1C), 34.56, 31.27 (3C); $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -100.83 (d, $^2J_{FF}$ = 270.6 Hz, $^3J_{HF}$ = 16.6, 13.3 Hz), -104.24 (d, $^2J_{FF}$ = 270.7 Hz, $^3J_{HF}$ = 17.2, 12.5 Hz)); HRMS (ESI), m/z [M+Na$^+$] calcd for C$_{20}$H$_{23}$F$_2$NO$, 352.1483$ found, 352.1487.

3,3-Difluoro-1-(4-methoxyphenyl)-5-phenylpyrrolidin-2-one (3ag).[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-N-(4-methoxyphenyl) acetamide was used instead of 2-bromo-2,2-difluoro-N-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 87%, 263.6 mg, white solid, m.p. 122.5-123.2 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.34-7.28 (m, 5H), 7.23 (d, $J = 6.7$ Hz, 1H), 6.80 (d, $J = 9.1$ Hz, 1H),5.25 (m, 1H), 3.72 (s, 3H), 3.18-3.05 (m, 1H), 2.61-2.48 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.13 (t, $J = 31.0$ Hz, 1C), 158.03, 138.64, 129.28 (2C), 129.21, 128.72, 126.57 (2C), 124.72 (2C),
117.63 (t, $J = 249.47$ Hz, 1C), 114.31 (2C), 58.74 (t, $J = 3.3$ Hz, 1C), 55.39, 39.04 (t, $J = 21.9$ Hz, 1C); $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -100.94 (d, $^2J_{FF} = 271.4$ Hz), -104.28 (d, $^2J_{FF} = 271.4$ Hz, $^3J_{HF} = 17.4$, 13.9 Hz).

3,3-Difluoro-5-phenyl-1-(m-tolyl) pyrrolidin-2-one (3ah).$^{[1]}$ The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-N-(m-tolyl) acetamide was used instead of 2-bromo-2,2-difluoro-N-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 90%, 258.3 mg, white solid, m.p. 96.4-97.3 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.20-7.11 (m, 6H), 7.03-7.02 (m, 2H), 6.84-6.82 (m, 1H), 5.22-5.18 (m, 1H), 3.02-2.92 (m, 1H), 2.46-2.34 (m, 1H), 2.15 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.18 (t, $^1J_{CF} = 31.1$ Hz, 1C), 138.98, 138.59, 136.15, 129.21 (2C), 128.75, 128.59, 127.53, 126.35 (2C), 123.74, 119.95, 117.55 (t, $J = 249.47$ Hz, 1C), 58.28 (t, $J = 3.4$ Hz, 1C), 38.99 (t, $J = 21.8$ Hz, 1C), 21.42; $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -101.01 (d, $^2J_{FF} = 270.4$ Hz, $^3J_{HF} = 16.0$, 12.3 Hz), -104.31 (d, $^2J_{FF} = 270.4$ Hz, $^3J_{HF} = 17.4$, 13.6 Hz).

3,3-Difluoro-1-(3-methoxyphenyl)-5-phenylpyrrolidin-2-one (3ai).$^{[1]}$ The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-N-(3-methoxyphenyl) acetamide was used instead of 2-bromo-2,2-difluoro-N-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 83%, 251.4 mg, white solid, m.p. 107-108 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.21-7.11 (m, 5H), 7.06-7.00 (m, 2H), 6.84 (d, $J = 8.0$ Hz, 1H), 6.56 (d, $J = 8.0$, 1H), 5.22-5.18 (m, 1H), 3.58 (s, 3H), 3.05-2.92 (m, 1H), 2.47-2.34 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.20 (t, $J = 31.3$ Hz, 1C), 159.87, 138.60, 137.41, 129.68, 129.26 (2C), 128.62,
126.24 (2C), 117.48 (t, J = 250.48 Hz, 1C), 114.85, 112.24, 108.85, 58.28 (t, J = 3.4 Hz, 1C), 55.27, 38.93 (t, J = 21.8 Hz, 1C); \(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -100.99 (d, \(^{2}J_{F\text{F}} = 270.5\) Hz, \(^{3}J_{HF} = 16.2, 12.7\) Hz), -104.25 (d, \(^{2}J_{F\text{F}} = 270.5\) Hz, \(^{3}J_{HF} = 17.4, 13.9\) Hz).

![](image)

3,3-Difluoro-5-phenyl-1-(o-tolyl) pyrrolidin-2-one (3aj).\(^{[1]}\) The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-N-(o-tolyl) acetamide was used instead of 2-bromo-2,2-difluoro-N-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 88\%, 252.6 mg, white solid, m.p. 103.6-104.6 °C. \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.15-7.09 (m, 5H), 7.02-6.98 (m, 2H), 6.93-6.89 (m, 1H), 6.79 (m, 1H), 4.95 (s, 1H), 3.07-2.95 (m, 1H), 2.66-2.52 (m, 1H), 2.04 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 162.61 (t, J = 30.7 Hz, 1C), 137.24, 135.43, 134.20, 131.19, 128.97, 128.87 (2C), 128.46, 127.46 (2C), 126.49, 117.58 (t, J = 249.5 Hz, 1C), 59.72 (t, J = 3.3 Hz, 1C), 38.21 (t, J = 22.3 Hz, 1C), 17.92; \(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -101.28 (d, \(^{2}J_{F\text{F}} = 270.8\) Hz), -104.38 (d, \(^{2}J_{F\text{F}} = 270.7\) Hz).

![](image)

1-[(1,1'-Biphenyl)-2-yl]-3,3-difluoro-5-phenylpyrrolidin-2-one (3ak).\(^{[1]}\) The title compound was prepared according to Representative Procedure I except that N-[(1,1'-biphenyl)-2-yl]-2-bromo-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-N-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 90\%, 314.1 mg, white solid, m.p. 144.4-145.6 °C. \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.36-7.31 (m, 3H), 7.19-6.98 (m, 9H), 6.81 (d, J = 7.1 Hz, 2H), 3.98 (s, 1H), 2.57-2.44 (m, 1H),
2.34-2.21 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 164.26 (t, $J = 30.9$ Hz, 1C), 139.08, 138.38, 136.99, 132.74, 130.73, 129.73, 128.85 (2C), 128.77 (2C), 128.74, 128.37 (2C), 128.17, 128.15, 127.18 (2C), 117.53 (t, $J = 249.47$ Hz, 1C), 117.53 (t, $J = 249.47$ Hz, 1C), 58.47, 38.84 (t, $J = 22.1$ Hz, 1C); $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -102.29 (d, $^2J_{FF} = 270.5$ Hz, $^3J_{HF} = 16.0, 9.4$ Hz), -105.03 (d, $^2J_{FF} = 270.6$ Hz).

1-(2,4-Difluorophenyl)-3,3-difluoro-5-phenylpyrrolidin-2-one (3a).$^{[1]}$ The title compound was prepared according to Representative Procedure I except that 2-bromo-$N$-(2,4-difluorophenyl)-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-$N$-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 79%, 244.1 mg, white solid, m.p. 118.0-118.9 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.22-7.04 (m, 6H), 6.72-6.66 (m, 2H), 5.15-5.11 (m, 1H), 3.13-3.01 (m, 1H), 2.60-2.46 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.25 (t, $J = 29.8$ Hz, 1C), 162.09 (dd, $J = 256.1, 6.2$ Hz, 1C), 157.46 (dd, $J = 254.1, 12.6$ Hz, 1C), 137.16, 129.54 (dd, $J = 10.1, 2.7$ Hz, 1C), 129.28 (2C), 127.10 (2C), 119.56 (dd, $J = 12.4, 3.8$ Hz, 1C), 117.20 (t, $J = 249.6$ Hz, 1C), 117.18 , 111.96 (dd, $J = 22.5, 3.7$ Hz, 1C), 105.17 (dd, $J = 26.4, 23.7$ Hz, 1C), 59.37-59.28 (m, 1C), 39.27 (t, $J = 21.2$ Hz); $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -103.00 (d, $^2J_{FF} = 271.4$ Hz, $^3J_{HF} = 16.0, 8.0$ Hz), -104.96 (d, $^2J_{FF} = 271.4$ Hz), -108.29, -114.45.

1-(2,4-Dimethylphenyl)-3,3-difluoro-5-phenylpyrrolidin-2-one (3am).$^{[1]}$ The title compound was prepared according to Representative Procedure I except that 2-bromo-$N$-(2,4-dimethylphenyl)-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-$N$-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 85%, 255.8 mg.
white solid, m.p. 105-106.2 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.20-7.12 (m, 5H), 6.86 (s, 1H), 6.75 (d, $J = 7.6$ Hz, 1H), 6.66 (s, 1H), 4.93 (s, 1H), 3.10-2.97 (m, 1H), 2.69-2.56 (m, 1H), 2.11 (s, 3H), 2.03 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 162.87 (t, $J = 29.8$ Hz), 138.48, 137.53, 135.11, 132.02, 129.07, 129.00, 127.59, 127.34, 117.61 (t, $J = 249.6$ Hz), 59.89 (t, $J = 3.3$ Hz), 38.45 (t, $J = 22.3$ Hz), 21.01, 17.94. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -101.29 (d, $^2J_{FF} = 271.4$ Hz), -104.53 (d, $^2J_{FF} = 271.4$ Hz).

**(E)-2,2-Difluoro-N-hexyl-4-phenylbut-3-enamide.** The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-N-hexylacetamide was used instead of 2-bromo-2,2-difluoro-N-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 63%, 177 mg, yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.44 (d, $J = 6.6$ Hz, 1H), 7.34 (t, $J = 8.8$ Hz, 1H), 7.06 (d, $J = 16.2$ Hz, 1H), 6.57-6.24 (m, 2H), 3.34 (q, $J = 6.6$ Hz, 2H), 1.59-1.53 (m, 2H), 1.31 (s, 4H), 0.87 (d, $J = 6.1$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.94 (t, $J = 29.9$ Hz), 136.52 (t, $J = 9.6$ Hz), 134.40, 129.62, 128.91 (2C), 127.55 (2C), 119.33 (t, $J = 25.2$ Hz), 114.53 (t, $J = 249.5$ Hz), 39.80, 31.48, 29.31, 26.55, 22.62, 14.09; $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -102.50 (d, $^2J_{FF} = 11.4$ Hz).

**2,2-Difluoro-N-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)acetamide.** To a mixture of 2-bromo-2,2-difluoro-N-phenylacetamide 2a (125 mg, 0.5 mmol), CuI (10.0 mg, 0.05 mmol) and 2,2,6,6-Tetramethyl-1-piperidinyloxy (156.2 mg, 1.0 mmol) in CH$_3$CN (1.0 mL) were added N,N,N',N''-Pentamethyldiethylenetriamine (156 µL, 0.75 mmol) and styrene 1a (115 µL, 1.0 mmol) successively. The resultant mixture was stirred at 80 °C for 10 h and monitored by TLC. The reaction was quenched with water, and then extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over anhydrous Na$_2$SO$_4$. After filtration, the filtrate was concentrated in vacuum and the residue was purified by silica gel column
chromatography (petroleum ether/EtOAc = 5/1) to give the TEMPO-adduct (19.5 mg) in 12% yield as white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.01 (s, 1H), 7.58 (t, $J$ = 8.5, 2H), 7.38 (t, $J$ = 8.0 Hz, 2H), 7.20 (t, $J$ = 7.4 Hz, 1H), 1.71-1.47 (m, 6H), 1.41-1.03 (m, 12H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 158.33 (t, $J$ = 38.2 Hz), 136.13, 129.36 (2C), 125.67, 120.22 (2C), 115.75 (t, $J$ = 274.4 Hz), 61.62, 40.42, 33.68, 21.01, 17.00; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -73.88.

References

3ka

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S35
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3aj