sp^3 Carbon–Fluorine Bond Activation in 2,2-Difluorohomoallylic Alcohols via Nucleophilic 5-endo-trig Cyclisation: Synthesis of 3-Fluorinated Furan Derivatives

Takeshi Fujita, Ryutaro Morioka, Tomohiro Arita, and Junji Ichikawa*

Division of Chemistry, Faculty of Pure and Applied Sciences, University of Tsukuba
Tsukuba, Ibaraki 305-8571, Japan
junji@chem.tsukuba.ac.jp

Supporting Information

Table of Contents
1. General Statement .............................................................................................................. S2
2. Preparation of Bromodifluoromethyl Ketones 2 .............................................................. S2
3. Preparation of 3-Bromo-3,3-difluoropropenes 3 ............................................................. S3
4. Preparation of 2,2-Difluorohomoallylic Alcohols 1 ........................................................ S4
5. Synthesis of 3-Fluoro-2,5-dihydrofurans 4 .................................................................... S10
6. Synthesis of 4-Fluorofuranones 5 .................................................................................. S15
7. References ....................................................................................................................... S16
8. \(^1\text{H}, ^{13}\text{C}\) and \(^{19}\text{F}\) NMR charts .............................................................................. S17
1. General Statement

$^1$H NMR, $^{13}$C NMR, and $^{19}$F NMR spectra were recorded on a Bruker Avance 500 spectrometer. Chemical shift values are given in ppm relative to internal Me$_4$Si (for $^1$H NMR: δ = 0.00 ppm), CDCl$_3$ (for $^{13}$C NMR: δ = 77.0 ppm) and C$_6$F$_6$ (for $^{19}$F NMR: δ = 0.00 ppm; –164.9). IR spectra were recorded on a Horiba FT-300S spectrometer by the attenuated total reflectance (ATR) method. Mass spectra were measured on a JEOl JMS-T100GCV or a JEOl JMS-T100CS spectrometer. Elemental analyses were carried out at Elemental Analysis Laboratory, Division of Chemistry, Faculty of Pure and Applied Sciences, University of Tsukuba. Melting points were measured on a Yanaco micro melting point apparatus and were uncorrected.

Column chromatography was conducted on Florisil (Wako Pure Chemical Industries, Ltd., 75–150 µm) or silica gel (Silica Gel 60 N, Kanto Chemical Co., Inc., 63–210 µm). All the reactions were conducted under argon or nitrogen.

Tetrahydrofuran (THF) was purified by a solvent-purification system (GlassContour) equipped with columns of activated alumina and supported-copper catalyst (Q-5) before use. N,N-Dimethylformamide (DMF) was distilled from CaH$_2$, and stored over activated molecular sieves 4A. Potassium hydride was washed with dry hexane three times, dried under vacuum and stored in a glove box. Unless otherwise noted, materials were obtained from commercial sources and used directly without further purifications.

2. Preparation of Bromodifluoromethyl Ketones 2

2-Bromo-2,2-difluoro-1-phenylethan-1-one (2a)

To a THF (30 mL) solution of ethyl bromodifluoroacetate (6.1 g, 30 mmol) was added phenylmagnesium bromide, prepared from bromobenzene (5.0 g, 32 mmol), magnesium turnings (0.80 g, 33 mmol) and THF (30 mL), at –78 °C over 0.5 h. After stirring for 3 h at –78 °C, the reaction was quenched with an aqueous HCl solution (2 M, 30 mL). Organic materials were extracted with ether three times. The combined extracts were washed with brine and dried over Na$_2$SO$_4$. The solvent was removed under reduced pressure, and the residue was purified by passing through a short column of silica gel (hexane/ethyl acetate = 50/1) to give 2a (6.3 g, 90%) as a colourless liquid.

Spectral data for this compound showed good agreement with the literature data.¹

2-Bromo-2,2-difluoro-1-(4-methylphenyl)ethan-1-one (2b)
Bromodifluoromethyl ketone 2b was prepared by the method described for 2a using ethyl bromodifluoroacetate (6.1 g, 30 mmol), 4-bromotoluene (5.38 g, 31.5 mmol) and magnesium turnings (802 mg, 33.0 mmol). Passing through a short column of silica gel (hexane/ethyl acetate = 10/1) gave 2b (6.90 g, 93%) as a colourless liquid. Spectral data for this compound showed good agreement with the literature data.²

2-Bromo-1-(4-chlorophenyl)-2,2-difluoroethan-1-one (2c)

Bromodifluoromethyl ketone 2c was prepared by the method described for 2a using ethyl bromodifluoroacetate (3.05 g, 15.0 mmol), 1-bromo-4-chlorobenzene (3.03 g, 15.8 mmol) and magnesium turnings (401 mg, 16.5 mmol). Passing through a short column of silica gel (hexane/ethyl acetate = 10/1) gave 2c (1.84 g, 45%) as a colourless liquid. Spectral data for this compound showed good agreement with the literature data.³

3. Preparation of 3-Bromo-3,3-difluoropropenes 3
(3-Bromo-3,3-difluoroprop-1-en-2-yl)benzene (3a)

To a THF (60 mL) solution of methyltriphenylphosphonium bromide (5.0 g, 14 mmol) was added NaHMDS (1.9 M in THF, 7.5 mL, 14 mmol) at −78 °C over 0.5 h. After stirring −78 °C for 1 h, the mixture was warmed to 0 °C. After stirring at 0 °C for 1 h, bromodifluoromethyl ketone 2a (2.4 g, 10 mmol) was added to the reaction mixture. After stirring at room temperature for 2 h, the reaction was quenched with an aqueous HCl solution (2 M, 30 mL). Organic materials were extracted with ether three times. The combined extracts were washed with brine and dried over Na₂SO₄. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (hexane) to give 3a (1.5 g, 65%) as a colourless liquid. Spectral data for this compound showed good agreement with the literature data.⁴

1-(3-Bromo-3,3-difluoroprop-1-en-2-yl)-4-methylbenzene (3b)

3-Bromo-3,3-difluoropropene 3b was prepared by the method described for 3a using methyl triphenylphosphonium bromide (5.1 g, 14 mmol), NaHMDS (1.9 M in THF, 7.5 mL, 14 mmol) and
bromodifluoromethyl ketone 2b (2.5 g, 10 mmol). Purification by silica gel column chromatography (hexane) gave 3b (1.6 g, 65%) as a colourless liquid.

\[ ^1H \text{ NMR} (500 \text{ MHz, CDCl}_3): \delta 2.38 (s, 3H), 5.51 (s, 1H), 5.84 (s, 1H), 7.20 (d, \text{ J} = 7.6 \text{ Hz, 2H}), 7.38 (d, \text{ J} = 7.6 \text{ Hz, 2H}). \]

\[ ^{13}C \text{ NMR} (126 \text{ MHz, CDCl}_3): \delta 21.2, 117.7 (t, \text{ J}_{CF} = 7 \text{ Hz}), 118.3 (t, \text{ J}_{CF} = 303 \text{ Hz}), 128.1, 129.1, 131.2, 139.0, 145.5 (t, \text{ J}_{CF} = 22 \text{ Hz}). \]

\[ ^{19}F \text{ NMR} (470 \text{ MHz, CDCl}_3): \delta 115.7 (s). \]

IR (neat): ν 2923, 1504, 1151, 1070, 914, 821, 742, 571 cm\(^{-1}\). HRMS (EI): m/z Calcd for C\(_{16}\)H\(_9\)BrF\(_2\) [M]: 245.9856; Found: 245.9856.

1-(3-Bromo-3,3-difluoroprop-1-en-2-yl)-4-chlorobenzene (3c)

3-Bromo-3,3-difluoropropene 3c was prepared by the method described for 3a using methyl triphenylphosphonium bromide (3.38 g, 9.46 mmol), NaHMDS (1.9 M in THF, 5.0 mL, 9.5 mmol) and bromodifluoromethyl ketone 2e (1.84 g, 6.83 mmol). Purification by silica gel column chromatography (hexane) gave 3c (578 mg, 32%) as a colourless liquid.

\[ ^1H \text{ NMR} (500 \text{ MHz, CDCl}_3): \delta 5.51 (t, \text{ J}_{HF} = 1.8 \text{ Hz, 1H}), 5.87 (s, 1H), 7.33–7.40 (m, 4H). \]

\[ ^{13}C \text{ NMR} (126 \text{ MHz, CDCl}_3): \delta 117.7 (t, \text{ J}_{CF} = 306 \text{ Hz}), 118.7 (t, \text{ J}_{CF} = 7 \text{ Hz}), 128.6, 129.6, 133.0, 135.1, 144.6 (t, \text{ J}_{CF} = 21 \text{ Hz}). \]

\[ ^{19}F \text{ NMR} (470 \text{ MHz, CDCl}_3): \delta 116.4 (s). \]

IR (neat): ν 1491, 1155, 1093, 1072, 922, 833, 555 cm\(^{-1}\). HRMS (EI): m/z Calcd for C\(_9\)H\(_6\)BrClF\(_2\) [M]: 265.9309; Found: 265.9315.

4. Preparation of 2,2-Difluorohomoallylic Alcohols 1

3,3-Difluoro-2-methyl-4-phenylpent-4-en-2-ol (1a)

\[
\begin{align*}
\text{Ph} & \quad \text{CBrF}_2 \\
\text{O} & \\
\text{THF, 0 °C to rt, 5 h} & \quad \text{Zn (2.0 equiv)} \\
\text{3a} & \quad \text{acetone (2.5 mL, 5 mmol)} \\
\text{3.0 equiv} & \quad \text{acetone (2.5 mL, 5 mmol)} \\
\text{1a} & \quad \text{OH}
\end{align*}
\]

To the mixture of acetone (517 mg, 8.90 mmol) and zinc powder (activated with an aqueous HCl solution, 390 mg, 5.96 mmol) in THF (4.0 mL) was added a THF (4.0 mL) solution of 3-bromo-3,3-difluoropropene 3a (699 mg, 3.00 mmol) at 0 °C over 30 min. Then, the reaction mixture was warmed to room temperature, and stirred at room temperature for 5 h. The reaction was quenched with an aqueous HCl solution (2 M, 5 mL). Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine and dried over Na\(_2\)SO\(_4\). After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1) to give 1a (575 mg, 90%) as a colourless liquid.

\[ ^1H \text{ NMR} (500 \text{ MHz, CDCl}_3): \delta 1.20 (s, 6H), 5.53 (d, \text{ J} = 2.3 \text{ Hz, 1H}), 5.78 (d, \text{ J} = 2.3 \text{ Hz, 1H}), 7.30–7.34 (m, 3H), 7.40–7.43 (m, 2H). \]

\[ ^{13}C \text{ NMR} (126 \text{ MHz, CDCl}_3): \delta 24.1, 74.1 (t, \text{ J}_{CF} = 28 \text{ Hz}), \]

S4
122.0 (t, JCF = 9 Hz), 122.3 (t, JCF = 252 Hz), 128.0, 128.2, 128.6, 138.4, 142.9 (t, JCF = 22 Hz). 19F NMR (470 MHz, CDCl3): δ 52.7 (s). IR (neat): ν 3442, 2989, 1494, 1147, 1070, 775, 698, 590 cm⁻¹. HRMS (ESI+): m/z Calcd for C12H14F2NaO [M + Na⁺]: 235.0910; Found: 235.0914.

3-Ethyl-4,4-difluoro-5-phenylhex-5-en-3-ol (1b)

2,2-Difluorohomoallylic alcohol 1b was prepared by the method described for 1a using diethyl ketone (258 mg, 3.00 mmol), zinc powder (131 mg, 2.0 mmol) and 3-bromo-3,3-difluoropropene 3a (231 mg, 0.996 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave 1b (186 mg, 78%) as a colourless liquid.

1H NMR (500 MHz, CDCl3): δ 0.84 (t, J = 7.5 Hz, 6H), 1.28 (s, 1H), 1.55–1.66 (m, 4H), 5.49 (s, 1H), 5.77 (s, 1H), 7.30–7.32 (m, 3H), 7.40–7.42 (m, 2H). 13C NMR (126 MHz, CDCl3): δ 7.4, 25.6, 77.7 (t, JCF = 27 Hz), 121.5 (t, JCF = 9 Hz), 123.2 (t, JCF = 253 Hz), 127.8, 128.0, 128.5, 138.4, 143.4 (t, JCF = 21 Hz). 19F NMR (470 MHz, CDCl3): δ 58.0 (s). IR (neat): ν 3585, 3482, 2972, 2949, 2887, 1496, 1463, 1078, 1027, 935, 775, 700 cm⁻¹. HRMS (ESI+): m/z Calcd for C14H18F2NaO [M + Na⁺]: 262.1223; Found: 262.1224.

3,3-Difluoro-2,4-diphenylpent-4-en-2-ol (1c)

2,2-Difluorohomoallylic alcohol 1c was prepared by the method described for 1a using acetonitrile (132 mg, 1.1 mmol), zinc powder (126 mg, 1.9 mmol) and 3-bromo-3,3-difluoropropene 3a (235 mg, 1.01 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave 1c (148 mg, 53%) as a colourless liquid.

1H NMR (500 MHz, CDCl3): δ 1.67 (s, 3H), 2.05 (s, 1H), 5.31 (d, J = 0.8 Hz, 1H), 5.37 (d, J = 0.8 Hz, 1H), 7.21–7.28 (m, 8H), 7.43–7.45 (m, 2H). 13C NMR (126 MHz, CDCl3): δ 24.6 (dd, JCF = 2, 2 Hz), 77.6 (dd, JCF = 27, 27 Hz), 121.6 (dd, JCF = 254, 254 Hz), 122.5 (dd, JCF = 9, 9 Hz), 126.4, 127.6, 127.7, 127.9, 128.6, 138.2, 140.6, 142.6 (dd, JCF = 24, 24 Hz). 19F NMR (470 MHz, CDCl3): δ 56.3 (d, JFF = 248 Hz, 1F), 58.6 (d, JFF = 248 Hz, 1F). IR (neat): ν 3566, 3483, 3059, 2993, 2941, 1495, 1448, 1070, 1028, 933, 760, 698 cm⁻¹. HRMS (ESI+): m/z Calcd for C17H17F2O [M + H⁺]: 275.1247; Found: 275.1239.

3,3-Difluoro-2-(4-methoxyphenyl)-4-phenylpent-4-en-2-ol (1d)
2,2-Difluorohomoallylic alcohol 1d was prepared by the method described for 1a using 4'-methoxyacetophenone (331 mg, 2.20 mmol), zinc powder (261 mg, 3.99 mmol) and 3-bromo-3,3-difluoropropene 3a (466 mg, 2.00 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave 1d (275 mg, 45%) as a colourless oil.

\[ \text{IR (neat): } \nu = 2931, 2999, 2839, 1612, 1514, 1252, 1028, 775, 700 \text{ cm}^{-1}. \]

HRMS (ESI+): m/z Calcd for C_{12}H_{18}F_{2}NaO [M + Na]^+; 327.1173; Found: 327.1166.

2-(4-Chlorophenyl)-3,3-difluoro-4-phenylpent-4-en-2-ol (1e)

2,2-Difluorohomoallylic alcohol 1e was prepared by the method described for 1a using 4'-chlooroacetophenone (340 mg, 2.20 mmol), zinc powder (261 mg, 3.99 mmol) and 3-bromo-3,3-difluoropropene 3a (467 mg, 2.00 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave 1e (293 mg, 47%) as a colourless oil.

\[ \text{IR (neat): } \nu = 3581, 1495, 1095, 1012, 941, 798, 700, 548 \text{ cm}^{-1}. \]

HRMS (ESI+): m/z Calcd for C_{13}H_{15}ClF_{2}NaO [M + Na]^+; 331.0677; Found: 331.0678.

1,1,3,3-Pentafluoro-2,4-diphenylpent-4-en-2-ol (1f)

2,2-Difluorohomoallylic alcohol 1f was prepared by the method described for 1a using 2,2,2-trifluoroacetophenone (96 mg, 0.55 mmol), zinc powder (65 mg, 0.99 mmol) and 3-bromo-3,3-difluoropropene 3a (116 mg, 0.50 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave 1f (106 mg, 65%) as a colourless liquid.

\[ \text{IR (neat): } \nu = 2839, 1612, 1514, 1252, 1028, 775, 700 \text{ cm}^{-1}. \]

HRMS (ESI+): m/z Calcd for C_{17}H_{13}F_{4}NaO [M + Na]^+; 331.0677; Found: 331.0678.
(470 MHz, CDCl$_3$): $\delta$ 57.9 (dq, $J_{FF} = 249$ Hz, $J_{FF} = 12$ Hz, 2F), 58.9 (dq, $J_{FF} = 249$ Hz, $J_{FF} = 12$ Hz, 2F), 89.5 (dd, $J_{FF} = 12$, 12 Hz). IR (neat): $\nu$ 3589, 3548, 1259, 1205, 1173, 1074, 916, 901, 729, 698 cm$^{-1}$. Elem. Anal. Calcd for C$_{17}$H$_{13}$F$_5$O: C, 62.20; H, 3.99. Found: C, 62.2; H, 4.20.

1-(1,1-Difluoro-2-phenylallyl)cyclopentan-1-ol (1g)

![Diagram of 1g](image)

2,2-Difluorohomoallylic alcohol 1g was prepared by the method described for 1a using cyclopentanone (190 mg, 2.3 mmol), zinc powder (266 mg, 4.07 mmol) and 3-bromo-3,3-difluoropropene 3a (468 mg, 2.01 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave 1g (245 mg, 51%) as a colourless liquid.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.42–1.48 (m, 2H), 1.57–1.63 (m, 2H), 1.70–1.79 (m, 2H), 1.84–1.89 (s, 2H), 5.51 (s, 1H), 5.81 (s, 1H), 7.32–7.33 (m, 3H), 7.33–7.41 (m, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 24.0, 35.6, 85.1 (t, $J_{CF} = 29$ Hz), 121.5 (t, $J_{CF} = 9$ Hz), 121.9 (t, $J_{CF} = 287$ Hz), 128.0, 128.1, 128.7, 138.3, 143.5 (t, $J_{CF} = 22$ Hz).

$^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 55.9 (s). IR (neat): $\nu$ 3593, 3464, 2958, 2875, 1153, 1030, 1016, 937, 775, 698 cm$^{-1}$. HRMS (ESI+): $m/z$ Calcd for C$_{14}$H$_{16}$F$_2$NaO [M + Na]$^+$: 261.1067; Found: 261.1073.

2,2-Difluorohomoallylic alcohol 1h was prepared by the method described for 1a using cyclohexanone (389 mg, 3.96 mmol), zinc powder (240 mg, 3.67 mmol) and 3-bromo-3,3-difluoropropene 3a (471 mg, 2.02 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave 1h (424 mg, 83%) as a colourless liquid.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.14 (s, 1H), 1.36–1.56 (m, 10H), 5.45 (s, 1H), 5.66 (s, 1H), 7.24–7.25 (m, 3H), 7.34–7.35 (m, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 20.6, 25.2, 30.6, 74.8 (t, $J_{CF} = 27$ Hz), 121.8 (t, $J_{CF} = 10$ Hz), 122.3 (t, $J_{CF} = 254$ Hz), 127.8, 128.1, 128.5, 138.5, 142.8 (t, $J_{CF} = 24$ Hz). $^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 52.4 (s). IR (neat): $\nu$ 3575, 3482, 2937, 2862, 1446, 1263, 1139, 1041, 987, 775, 698, 590 cm$^{-1}$. Elem. Anal. Calcd for C$_{15}$H$_{18}$F$_2$O: C, 71.41; H, 7.19. Found: C, 71.46; H, 7.28.

4,4-Difluoro-2,2-dimethyl-5-phenylhex-5-en-3-ol (1i)

![Diagram of 1i](image)

2,2-Difluorohomoallylic alcohol 1i was prepared by the method described for 1a using
2,2-dimethylpropanal (95 mg, 1.1 mmol), zinc powder (133 mg, 2.0 mmol) and 3-bromo-3,3-difluoropropene 3a (230 mg, 0.987 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave 1i (106 mg, 45%) as a colourless liquid.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.05 (s, 9H), 1.74 (s, 1H), 3.43 (dd, $J_{HF} = 22.0$, 5.3 Hz, 1H), 5.53 (d, $J = 3.3$ Hz, 1H), 5.81 (d, $J = 3.3$ Hz, 1H), 7.34–7.35 (m, 3H), 7.43–7.44 (m, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 26.9 (dd, $J_{CF} = 3$, 3 Hz), 34.9, 77.2 (dd, $J_{CF} = 26$, 26 Hz), 119.2 (dd, $J_{CF} = 11$, 8 Hz), 122.6 (dd, $J_{CF} = 254$, 249 Hz), 128.1, 128.2, 128.4, 137.0 (d, $J_{CF} = 4$ Hz), 144.6 (dd, $J_{CF} = 21$, 21 Hz). $^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 50.4 (dd, $J_{FF} = 248$ Hz, $J_{FH} = 22$ Hz, 1F), 66.4 (d, $J_{FF} = 248$ Hz, 1F). IR ( neat): $\nu$ 3600, 3496, 2960, 2912, 2877, 1496, 1369, 1180, 1049, 1016, 935, 779, 698 cm$^{-1}$. HRMS (ESI+): m/z Calcd for C$_{14}$H$_{18}$F$_2$NaO [M + Na]$^+$: 263.1223; Found: 263.1222.

3-Ethyl-4,4-difluoro-5-(4-methylphenyl)hex-5-en-3-ol (1j)

2,2-Difluorohomoallylic alcohol 1j was prepared by the method described for 1a using diethyl ketone (277 mg, 3.22 mmol), zinc powder (388 mg, 5.93 mmol) and 3-bromo-3,3-difluoropropene 3b (744 mg, 3.01 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave 1j (598 mg, 78%) as a colourless liquid.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.85 (t, $J = 7.6$ Hz, 6H), 1.53–1.68 (m, 4H), 2.34 (s, 3H), 5.48 (d, $J = 2.4$ Hz 1H), 5.74 (d, $J = 2.4$ Hz 1H), 7.13 (d, $J = 7.9$ Hz, 2H), 7.32 (d, $J = 7.9$ Hz, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 7.5, 21.1, 25.8, 77.8 (t, $J_{CF} = 2$ Hz), 121.0 (t, $J_{CF} = 9$ Hz), 123.3 (t, $J_{CF} = 252$ Hz), 128.5, 128.9, 135.6, 137.8, 143.3 (t, $J_{CF} = 23$ Hz). $^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 56.9 (s). IR ( neat): $\nu$ 3597, 2974, 2887, 1084, 912, 742 cm$^{-1}$. HRMS (ESI+): m/z Calcd for C$_{15}$H$_{20}$F$_2$NaO [M + Na]$^+$: 277.1380; Found: 277.1382.

5-(4-Chlorophenyl)-3-ethyl-4,4-difluorohex-5-en-3-ol (1k)

2,2-Difluorohomoallylic alcohol 1k was prepared by the method described for 1a using diethyl ketone (261 mg, 3.03 mmol), zinc powder (131 mg, 2.0 mmol) and 3-bromo-3,3-difluoropropene 3c (267 mg, 0.998 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave 1k (93 mg, 34%) as a colourless oil.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.86 (t, $J = 7.6$ Hz, 6H), 1.57–1.65 (m, 4H), 5.50 (s, 1H), 5.78 (s, 1H), 7.28–7.32 (m, 2H), 7.36 (d, $J = 8.5$ Hz, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 7.4, 25.6, 77.7 (t, $J_{CF} = 26$ Hz), 122.0 (t, $J_{CF} = 9$ Hz), 122.0 (t, $J_{CF} = 254$ Hz), 128.2, 130.0, 133.9, 137.0, 142.6 (t, $J_{CF}$
= 24 Hz). $^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 58.1 (s). IR (neat): $\nu$ 3587, 3469, 2974, 2887, 1493, 1092, 835 cm$^{-1}$. HRMS (ESI+): $m/z$ Calcd for C$_{14}$H$_{17}$ClF$_2$NaO [M + H]$^+$: 275.1014; Found: 275.1009.

3,3-Difluoro-2-methyl-4,5-diphenylpent-4-en-2-ol (1I)

![Chemical structure diagram]

To the mixture of acetone (870 mg, 15.0 mmol) and zinc powder (activated with an aqueous HCl solution, 645 mg, 9.87 mmol) in THF (5.0 mL) was added a THF (5.0 mL) solution of bromodifluorodifluoromethyl ketone 2a (1.17 g, 4.98 mmol) at 0 °C over 30 min. Then, the reaction mixture was warmed to room temperature and stirred at room temperature for 2 h. The reaction was quenched with aqueous HCl solution (2 M, 5 mL). Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine and dried over Na$_2$SO$_4$. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1) to give 2,2-difluoro-3-hydroxy-3-methyl-phenylbutan-1-one (423 mg, 40%) as a colourless liquid.

Spectral data for this compound showed good agreement with the literature data.$^5$

To the mixture of 2,2-difluoro-3-hydroxy-3-methyl-phenylbutan-1-one (513 mg, 2.39 mmol) and 3,4-dihydro-2H-pyran (546 mg, 6.49 mmol) was added AlCl$_3$.6H$_2$O (12 mg, 0.050 mmol) at room temperature. After stirring at 40 °C for 72 h, the reaction was quenched with water. Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine and dried over Na$_2$SO$_4$. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1) to give 2,2-difluoro-3-methyl-1-phenyl-3-[(tetrahydro-2H-pyran-2-yl)oxy]butan-1-one (687 mg, 96%) as a colourless liquid.

2,2-Difluoro-3-methyl-1-phenyl-3-[(tetrahydro-2H-pyran-2-yl)oxy]butan-1-one: $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.26–1.57 (m, 12H), 3.39–3.43 (m, 1H), 3.68–3.73 (m, 1H), 4.91 (dd, $J = 3.4$, 3.4 Hz, 1H), 7.44 (dd, $J = 8.1$, 7.5 Hz, 2H), 7.56 (t, $J = 7.5$ Hz, 1H), 8.13 (d, $J = 8.1$ Hz, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 18.82, 18.85, 21.9 (dd, $J_{CF} = 3$, 3 Hz), 25.0, 30.9, 61.7, 78.8 (dd, $J_{CF} = 26$, 26 Hz), 93.2, 118.5 (dd, $J_{CF} = 260$, 260 Hz), 127.9, 130.5, 133.5, 134.6, 191.8 (dd, $J_{CF} = 28$, 28 Hz). $^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 50.9 (d, $J_{EF} = 253$ Hz, 1F), 51.5 (d, $J_{EF} = 253$ Hz, 1F). IR (neat): $\nu$
To a THF (5.0 mL) solution of benzyltriphenylphosphonium bromide (603 mg, 1.39 mmol) was added NaHMDS (1.9 M in THF, 0.750 mL, 1.4 mmol) at –78 °C over 0.5 h. After stirring at –78 °C for 1 h, the reaction mixture was warmed to 0 °C. After stirring at 0 °C for 1 h, a THF (1.0 mL) solution of 2,2-difluoro-3-methyl-1-phenyl-3-[(tetrahydro-2H-pyran-2-yl)oxy]butan-1-one (305 mg, 1.02 mmol) was added to the reaction mixture at 0 °C over 0.5 h. After stirring at room temperature for 1 h, the reaction was quenched with an aqueous HCl solution (2 M, 5 mL). Organic materials were extracted with ether and were washed with brine and dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was purified by silica gel column gel chromatography (hexane/ethyl acetate = 1/1) to give 11 (230 mg, 78%, E/Z = 99/1) as white solid.

\[(E)\text{-11i}: \text{mp } 76.5–77.2 \degree C. \text{ }^1\text{H NMR (500 MHz, CDCl}_3\text{): }\delta 1.31 (s, 6H), 2.17 (s, 1H), 6.89 (m, 2H), 7.06–7.13 (m, 4H), 7.30–7.33 (m, 5H). \text{ }^{13}\text{C NMR (126 MHz, CDCl}_3\text{): }\delta 24.2, 74.8 (t, J_{CF} = 29 \text{ Hz}), 122.2 (t, J_{CF} = 253 \text{ Hz}), 127.5 (t, J_{CF} = 64 \text{ Hz}), 127.8, 127.9, 128.5, 129.8, 130.5, 133.3 (t, J_{CF} = 10 \text{ Hz}), 134.6 (t, J_{CF} = 23 \text{ Hz}), 134.9, 135.9. \text{ }^{19}\text{F NMR (470 MHz, CDCl}_3\text{): }\delta 55.2 (s). \text{ IR (neat): } \nu 3560, 3477, 3059, 2987, 1448, 1225, 1151, 1066, 943, 719, 696 \text{ cm}^{-1}. \text{ HRMS (ESI+): } m/z \text{ Calcd for C}_{18}\text{H}_{19}\text{F}_2\text{O }[\text{M} + \text{H}]^+: 289.1404; \text{ Found: 289.1399.}

### 5. Synthesis of 3-Fluoro-2,5-dihydrofurans 4

#### 3-Fluoro-2,2-dimethyl-4-phenyl-2,5-dihydrofuran (4a)

![Chemical Structure](image)

To the suspension of potassium hydride (9.1 mg, 0.23 mmol) in DMF (2 mL) was slowly added 2,2-difluorohomoallylic alcohol 1a (32 mg, 0.15 mmol) at 0 °C. Then, the reaction mixture was warmed to room temperature and stirred at 0 °C for 5 h. Organic materials were extracted with ether three times. The combined extracts were washed with brine and dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was purified by silica gel column gel chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) to give 4a (24 mg, 85%) as a colourless oil.

\[\text{^1H NMR (500 MHz, CDCl}_3\text{): }\delta 1.45 (s, 6H), 4.92 (d, J_{HF} = 4.9 \text{ Hz}, 2H), 7.26–7.29 (m, 1H), 7.35–7.39 (m, 4H). \text{ }^{13}\text{C NMR (126 MHz, CDCl}_3\text{): }\delta 25.6, 69.9 (d, J_{CF} = 10 \text{ Hz}), 82.0 (d, J_{CF} = 25 \text{ Hz}), 107.9 (d, J_{CF} = 4 \text{ Hz}), 126.3 (d, J_{CF} = 6 \text{ Hz}), 127.6 (d, J_{CF} = 1 \text{ Hz}), 128.6, 130.2 (d, J_{CF} = 5 \text{ Hz}), 157.7 (d, J_{CF} = 286 \text{ Hz}). \text{ }^{19}\text{F NMR (470 MHz, CDCl}_3\text{): }\delta 24.1 (t, J_{HF} = 5 \text{ Hz}). \text{ IR (neat): } \nu 2966, 2947, 1695, 1138, 1024, 897, 715 \text{ cm}^{-1}. \text{ HRMS (EI): } m/z \text{ Calcd for C}_{12}\text{H}_{13}\text{FO }[\text{M}^+]^+: 192.0950; \text{ Found: 192.0960.} \]
2,2-Diethyl-3-fluoro-4-phenyl-2,5-dihydrofuran (4b)

3-Fluoro-2,5-dihydrofurans 4b was synthesised by the method described for 4a using potassium hydride (18 mg, 0.45 mmol) and 2,2-difluorohomoallylic alcohol 1b (72 mg, 0.30 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4b (56 mg, 86%) as a colourless oil.

1H NMR (500 MHz, CDCl3): δ 0.95 (t, J = 7.4 Hz, 6H), 1.65–1.77 (m, 4H), 4.94 (d, J_{HF} = 4.8 Hz, 2H), 7.25–7.30 (m, 1H), 7.35–7.41 (m, 4H). ^13C NMR (126 MHz, CDCl3): δ 7.8, 30.7 (d, J_{CF} = 3 Hz), 72.0 (d, J_{CF} = 10 Hz), 88.4 (d, J_{CF} = 23 Hz), 110.5 (d, J_{CF} = 4 Hz), 126.3 (d, J_{CF} = 6 Hz), 127.5 (d, J_{CF} = 2 Hz), 128.6, 130.2 (d, J_{CF} = 6 Hz), 154.4 (d, J_{CF} = 285 Hz). ^19F NMR (470 MHz, CDCl3): δ 25.6 (t, J_{FH} = 5 Hz). IR (neat): ν 2970, 2854, 1704, 1498, 1446, 1072, 1022, 762, 692 cm⁻¹. HRMS (EI): m/z Calcd for C_{14}H_{13}FO [M]⁺: 220.1263; Found: 220.1268.

3-Fluoro-2-methyl-2,4-diphenyl-2,5-dihydrofuran (4c)

3-Fluoro-2,5-dihydrofurans 4c was synthesised by the method described for 4a using potassium hydride (9.1 mg, 0.23 mmol) and 2,2-difluorohomoallylic alcohol 1c (41 mg, 0.15 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4c (28 mg, 74%) as a colourless oil.

1H NMR (500 MHz, CDCl3): δ 1.81 (s, 3H), 5.05 (d, J = 10.8 Hz, J_{HF} = 4.9 Hz, 1H), 5.08 (d, J = 10.8 Hz, J_{HF} = 5.0 Hz, 1H), 7.24–7.31 (m, 2H), 7.33–7.40 (m, 6H), 7.51–7.53 (m, 2H). ^13C NMR (126 MHz, CDCl3): δ 25.4 (d, J_{CF} = 3 Hz), 70.6 (d, J_{CF} = 10 Hz), 84.8 (d, J_{CF} = 24 Hz), 108.8 (d, J_{CF} = 4 Hz), 124.9, 126.4 (d, J_{CF} = 6 Hz), 127.6, 127.7 (d, J_{CF} = 1 Hz), 128.4, 128.6, 129.9 (d, J_{CF} = 5 Hz), 143.2 (d, J_{CF} = 4 Hz), 156.1 (d, J_{CF} = 289 Hz). ^19F NMR (470 MHz, CDCl3): δ 27.5 (dd, J_{FH} = 5, 5 Hz). IR (neat): ν 3089, 3060, 3030, 2935, 2979, 2852, 1699, 1498, 1446, 1072, 1022, 762, 692 cm⁻¹. HRMS (EI): m/z Calcd for C_{17}H_{15}FO [M]⁺: 254.1107; Found: 254.1112.

3-Fluoro-2-(4-methoxyphenyl)-2-methyl-4-phenyl-2,5-dihydrofuran (4d)

3-Fluoro-2,5-dihydrofurans 4d was synthesised by the method described for 4a using potassium hydride (9.1 mg, 0.23 mmol) and 2,2-difluorohomoallylic alcohol 1d (46 mg, 0.15 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4d (40 mg, 93%) as a colourless oil.
$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.78 (s, 3H), 3.79 (s, 3H), 5.03 (dd, $J = 10.6$ Hz, $J_{HF} = 4.9$ Hz, 1H), 5.06 (dd, $J = 10.6$ Hz, $J_{HF} = 4.9$ Hz, 1H), 6.89–6.90 (m, 2H), 7.24–7.27 (m, 1H), 7.33–7.42 (m, 4H), 7.42–7.44 (m, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 25.2 (d, $J_{CF} = 3$ Hz), 55.2, 70.5 (d, $J_{CF} = 10$ Hz), 84.6 (d, $J_{CF} = 24$ Hz), 108.6 (d, $J_{CF} = 4$ Hz), 113.7, 126.36 (d, $J_{CF} = 3$ Hz), 126.42, 127.7, 128.6, 130.0 (d, $J_{CF} = 5$ Hz), 135.4 (d, $J_{CF} = 4$ Hz), 156.4 (d, $J_{CF} = 289$ Hz), 159.1. $^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 27.7 (dd, $J_{FG} = 5, 5$ Hz). IR (neat): $\nu$ 2979, 2836, 1699, 1610, 1508, 1250, 1024, 829, 762, 692 cm$^{-1}$. HRMS (EI): $m/z$ Calcd for C$_{18}$H$_{17}$FO [M$^+$]: 284.1213; Found: 284.1204.

2-(4-Chlorophenyl)-3-fluoro-2-methyl-4-phenyl-2,5-dihydrofuran (4e)

3-Fluoro-2,5-dihydrofurans 4e was synthesised by the method described for 4a using potassium hydride (9.2 mg, 0.23 mmol) and 2,2-difluorohomoallylic alcohol 1e (46 mg, 0.15 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4e (30 mg, 69%) as a colourless oil.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.76 (s, 3H), 5.02 (dd, $J = 10.8$ Hz, $J_{HF} = 4.9$ Hz, 1H), 5.06 (dd, $J = 10.8$ Hz, $J_{HF} = 4.9$ Hz, 1H), 7.24–7.35 (m, 7H), 7.43–7.44 (m, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 25.5 (d, $J_{CF} = 3$ Hz), 70.7 (d, $J_{CF} = 10$ Hz), 84.5 (d, $J_{CF} = 24$ Hz), 109.1 (d, $J_{CF} = 4$ Hz), 126.4, 126.5, 127.9 (d, $J_{CF} = 1$ Hz), 128.6, 128.7, 129.7 (d, $J_{CF} = 5$ Hz), 133.5, 141.9 (d, $J_{CF} = 3$ Hz), 155.6 (d, $J_{CF} = 289$ Hz). $^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 27.0 (br s). IR (neat): $\nu$ 2981, 2854, 1701, 1489, 1092, 1012, 829, 762, 692 cm$^{-1}$. HRMS (EI): $m/z$ Calcd for C$_{17}$H$_{14}$ClFO [M$^+$]: 288.0717; Found: 288.0722.

3-Fluoro-2,4-diphenyl-2-(trifluoromethyl)-2,5-dihydrofuran (4f)

3-Fluoro-2,5-dihydrofurans 4f was synthesised by the method described for 4a using potassium hydride (17 mg, 0.42 mmol) and 2,2-difluorohomoallylic alcohol 1f (90 mg, 0.27 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4f (51 mg, 60%) as a colourless oil.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 5.11 (dd, $J = 11.0$ Hz, $J_{HF} = 5.4$ Hz, 1H), 5.24 (dd, $J = 11.0$ Hz, $J_{HF} = 5.3$ Hz, 1H), 7.32–7.46 (m, 8H), 7.72 (d, $J = 7.4$ Hz, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 72.3 (d, $J_{CF} = 9$ Hz), 114.9, 124.0 (qd, $J_{CF} = 288$, 4 Hz), 125.9, 126.8 (d, $J_{CF} = 6$ Hz), 127.9 (q, $J_{CF} = 12$ Hz), 128.5, 128.6 (q, $J_{CF} = 15$ Hz), 128.77, 128.81 (d, $J_{CF} = 2$ Hz), 129.2, 134.1 (d, $J_{CF} = 4$ Hz), 148.2 (d, $J_{CF} = 289$ Hz). $^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 27.7 (s, 1F), 85.4 (s, 3F). IR (neat): $\nu$ 3066, 2877, 2852, 1701, 1263, 1172, 912, 733, 690 cm$^{-1}$. HRMS (EI): $m/z$ Calcd for C$_{17}$H$_{12}$F$_4$O [M$^+$]: 308.0824; Found: 308.0827.
4-Fluoro-3-phenyl-1-oxaspiro[4.4]non-3-ene (4g)

3-Fluoro-2,5-dihydrofurans 4g was synthesised by the method described for 4a using potassium hydride (12 mg, 0.30 mmol) and 2,2-difluorohomoallylic alcohol 1g (48 mg, 0.20 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4g (23 mg, 52%) as a colourless oil.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.65–1.75 (m, 2H), 1.78–1.96 (m, 6H), 4.87 (d, $J_{HF} = 5.0$ Hz, 2H), 7.23–7.27 (m, 1H), 7.33–7.38 (m, 4H). $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 24.7, 36.6 (d, $J_{CF} = 3$ Hz), 70.1 (d, $J_{CF} = 1$ Hz), 92.1 (d, $J_{CF} = 25$ Hz), 108.7 (d, $J_{CF} = 4$ Hz), 126.2 (d, $J_{CF} = 6$ Hz), 127.4 (d, $J_{CF} = 1$ Hz), 128.5, 130.2 (d, $J_{CF} = 6$ Hz), 155.4 (d, $J_{CF} = 285$ Hz). $^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 25.2 (s). IR (neat): $\nu$ 2960, 2871, 2850, 1700, 1362, 1078, 993, 761, 692 cm$^{-1}$. HRMS (EI): $m/z$ Calcd for C$_{14}$H$_{15}$FO [M]+: 218.1107; Found: 218.1111.

4-Fluoro-3-phenyl-1-oxaspiro[4.5]dec-3-ene (4h)

3-Fluoro-2,5-dihydrofurans 4h was synthesised by the method described for 4a using potassium hydride (15 mg, 0.37 mmol) and 2,2-difluorohomoallylic alcohol 1h (63 mg, 0.25 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 25/1/1) gave 4h (40 mg, 70%) as a white solid.

mp 58.6–59.2 °C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.21–1.31 (m, 1H), 1.63–1.77 (m, 9H), 4.90 (d, $J_{HF} = 4.9$ Hz, 2H), 7.24–7.28 (m, 1H), 7.33–7.39 (m, 4H). $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 21.9, 24.9, 34.0 (d, $J_{CF} = 3$ Hz), 69.8 (d, $J_{CF} = 10$ Hz), 83.1 (d, $J_{CF} = 23$ Hz), 108.1 (d, $J_{CF} = 4$ Hz), 126.3 (d, $J_{CF} = 6$ Hz), 127.4 (d, $J_{CF} = 1$ Hz), 128.6, 130.4 (d, $J_{CF} = 5$ Hz), 158.3 (d, $J_{CF} = 286$ Hz). $^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 25.4 (s). IR (neat): $\nu$ 3060, 2933, 2852, 1703, 1078, 906, 731, 692 cm$^{-1}$. HRMS (EI): $m/z$ Calcd for C$_{15}$H$_{17}$FO [M]$^+$: 232.1263; Found: 232.1261.

<1 mmol scale>

3-Fluoro-2,5-dihydrofurans 4h was synthesised by the method described for 4a using potassium hydride (61 mg, 1.5 mmol) and 2,2-difluorohomoallylic alcohol 1h (252 mg, 0.999 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4h (117 mg, 50%) as a white solid.

S13
2-(tert-Butyl)-3-fluoro-4-phenyl-2,5-dihydrofuran (4i)

3-Fluoro-2,5-dihydrofurans 4i was synthesised by the method described for 4a using potassium hydride (9.1 mg, 0.23 mmol) and 2,2-difluorohomoallylic alcohol 1i (37 mg, 0.15 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4i (26 mg, 77%) as a colourless oil.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.01 (s, 9H), 4.47 (ddd, $J_{HF}$ = 4.6 Hz, $J$ = 4.6, 4.6 Hz 1H), 4.92 (dd, $J$ = 10.8 Hz, $J_{HF}$ = 4.2 Hz, 1H), 4.95 (dd, $J$ = 10.8 Hz, $J_{HF}$ = 4.6 Hz, 1H), 7.25–7.30 (m, 1H), 7.35–7.40 (m, 4H).

$^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 25.2 (d, $J_{CF}$ = 2 Hz), 35.8 (d, $J_{CF}$ = 4 Hz), 72.3 (d, $J_{CF}$ = 10 Hz), 87.8 (d, $J_{CF}$ = 22 Hz), 111.5 (d, $J_{CF}$ = 4 Hz), 126.3 (d, $J_{CF}$ = 6 Hz), 127.6 (d, $J_{CF}$ = 2 Hz), 128.6, 130.0 (d, $J_{CF}$ = 5 Hz), 154.2 (d, $J_{CF}$ = 287 Hz).

$^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 33.9 (s).

IR (neat): $\nu$ 2956, 2850, 1697, 1498, 1363, 1078, 760, 692 cm$^{-1}$.

HRMS (EI): $m/z$ Calcd for C$_{14}$H$_{17}$FO [M]$^+$: 220.1263; Found: 220.1258.

2,2-Diethyl-3-fluoro-4-(4-methylphenyl)-2,5-dihydrofuran (4j)

3-Fluoro-2,5-dihydrofurans 4j was synthesised by the method described for 4a using potassium hydride (46 mg, 1.1 mmol) and 2,2-difluorohomoallylic alcohol 1j (190 mg, 0.75 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4j (126 mg, 72%) as a colourless oil.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.94 (t, $J$ = 7.4 Hz, 6H), 1.64–1.76 (m, 4H), 2.35 (s, 3H), 4.94 (d, $J_{HF}$ = 4.8 Hz, 2H), 7.18 (d, $J$ = 8.2 Hz, 2H), 7.28 (d, $J$ = 8.2 Hz, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 8.0, 21.2, 30.8 (d, $J_{CF}$ = 3 Hz), 72.1 (d, $J_{CF}$ = 11 Hz), 88.4 (d, $J_{CF}$ = 24 Hz), 110.4 (d, $J_{CF}$ = 4 Hz), 126.18, 126.23, 129.3, 137.4, 153.8 (d, $J_{CF}$ = 284 Hz).

$^{19}$F NMR (470 MHz, CDCl$_3$): $\delta$ 24.4 (t, $J_{FH}$ = 5 Hz). IR (neat): $\nu$ 2970, 2850, 1704, 912, 733, 650 cm$^{-1}$.

HRMS (EI): $m/z$ Calcd for C$_{15}$H$_{19}$FO [M]$^+$: 234.1420; Found: 234.1428.

4-(4-Chlorophenyl)-2,2-diethyl-3-fluoro-2,5-dihydrofuran (4k)

3-Fluoro-2,5-dihydrofurans 4k was synthesised by the method described for 4a using potassium hydride (9.2 mg, 0.23 mmol) and 2,2-difluorohomoallylic alcohol 1k (42 mg, 0.15 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4k (28 mg, 71%) as a colourless oil.
was purified by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1). After removal of the solvent under reduced pressure, the residue was synthesised by the method described for 4a using potassium hydride (18 mg, 0.45 mmol) and 2,2-difluorohomoallylic alcohol 11 (E/Z = 99/1, 86 mg, 0.30 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4l (42 mg, 52%) as a colourless oil.

3-Fluoro-2,2-dimethyl-4,5-diphenyl-2,5-dihydrofuran (4l)

3-Fluoro-2,5-dihydrofurans 4l was synthesised by the method described for 4a using potassium hydride (18 mg, 0.45 mmol) and 2,2-difluorohomoallylic alcohol 11 (E/Z = 99/1, 86 mg, 0.30 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 4l (42 mg, 52%) as a colourless oil.

6. Synthesis of 4-Fluorofuranones 5

5,5-Diethyl-4-fluoro-3-phenylfuran-2(5H)-one (5b)

To the suspension of CrO₃ (60 mg, 0.60 mmol) in dichloromethane (0.5 mL) was added 3,5-dimethylpyrazole (59 mg, 0.61 mmol) at −20 °C. After stirring at −20 °C for 15 min, 3-fluoro-2,5-dihydrofurans 4b (11 mg, 0.050 mmol) was added. After stirring at −20 °C for 1 h, an aqueous NaOH solution (5.0 M, 0.25 mL, 1.3 mmol) was added to the reaction mixture. Stirring at 0 °C for 1 h, the reaction was quenched with an aqueous HCl solution (2 M, 0.5 mL). Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine and dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (hexane/ethyl acetate/Et₃N = 20/2/1) to give 5b
(7.4 mg, 63%) as a colourless liquid.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 0.94 (t, \(J = 7.4\) Hz, 6H), 1.88–2.05 (m, 4H), 7.38 (t, \(J = 7.4\) Hz, 1H), 7.44 (dd, \(J = 7.4, 7.2\) Hz, 2H), 7.90 (d, \(J = 7.2\) Hz, 2H). 13\(^\circ\)C NMR (126 MHz, CDCl\(_3\)): \(\delta\) 7.3, 28.4 (d, \(J_{\text{CF}} = 3\) Hz), 84.8 (d, \(J_{\text{CF}} = 21\) Hz), 108.1, 126.4 (d, \(J_{\text{CF}} = 4\) Hz), 127.7 (d, \(J_{\text{CF}} = 5\) Hz), 128.6, 129.0, 169.1 (d, \(J_{\text{CF}} = 23\) Hz), 176.2 (d, \(J_{\text{CF}} = 304\) Hz).

19\(^\circ\)F NMR (470 MHz, CDCl\(_3\)): \(\delta\) 55.0 (s). IR (neat): \(\nu\) 2978, 1755, 1689, 1703, 1198, 904, 727, 650 cm\(^{-1}\). HRMS (EI): \(m/z\) Calcd for C\(_{14}\)H\(_{15}\)FO\(_2\) [M\(^+\)]: 234.1056; Found: 234.1045.

4-Fluoro-3-phenyl-1-oxaspiro[4.5]dec-3-ene-2-one (5h)

![Diagram](image)

4-Fluorofuranone 5h was synthesised by the method described for 5b using CrO\(_3\) (60 mg, 0.60 mmol), 3,5-dimethylpyrazole (59 mg, 0.62 mmol), 3-fluoro-2,5-dihydrofurans 4h (13 mg, 0.056 mmol) and an aqueous NaOH solution (5.0 M, 0.25 mL, 1.3 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave 5h (10 mg, 76%) as a colourless oil.

mp 112.4–113.2 \(^\circ\)C. 1\(^\circ\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 1.23–1.30 (m, 2H), 1.77–1.79 (m, 6H), 1.87–1.91 (m, 2H), 7.35–7.37 (m, 1H), 7.40–7.43 (m, 2H), 7.86–7.88 (m, 2H). 13\(^\circ\)C NMR (126 MHz, CDCl\(_3\)): \(\delta\) 21.5, 24.2, 32.6 (d, \(J_{\text{CF}} = 2\) Hz), 80.7 (d, \(J_{\text{CF}} = 21\) Hz), 105.7, 126.6 (d, \(J_{\text{CF}} = 5\) Hz), 127.7 (d, \(J_{\text{CF}} = 5\) Hz), 128.5, 128.9, 168.7 (d, \(J_{\text{CF}} = 21\) Hz), 179.1, (d, \(J_{\text{CF}} = 305\) Hz). 19\(^\circ\)F NMR (470 MHz, CDCl\(_3\)): \(\delta\) 55.4 (s). IR (neat): \(\nu\) 2941, 2858, 1757, 1699, 1362, 1192, 1126, 958, 787, 694 cm\(^{-1}\). HRMS (EI): \(m/z\) Calcd for C\(_{15}\)H\(_{15}\)FO\(_2\) [M\(^+\)]: 246.1056; Found: 246.1061.

7. References


8. $^1$H, $^{13}$C and $^{19}$F NMR charts
1-(3-Bromo-3,3-difluoroprop-1-en-2-yl)-4-methylbenzene (3b)
1-(3-Bromo-3,3-difluoroprop-1-en-2-yl)-4-chlorobenzene (3c)
3,3-Difluoro-2-methyl-4-phenylpent-4-en-2-ol (1a)
3-Ethyl-4,4-difluoro-5-phenylhex-5-en-3-ol (1b)
3,3-Difluoro-2,4-diphenylpent-4-en-2-ol (1c)
3,3-Difluoro-2-(4-methoxyphenyl)-4-phenylpent-4-en-2-ol (1d)
2-(4-Chlorophenyl)-3,3-difluoro-4-phenylpent-4-en-2-ol (1e)
1,1,1,3,3-Pentafluoro-2,4-diphenylpent-4-en-2-ol (1f)
1-(1,1-Difluoro-2-phenylallyl)cyclopentan-1-ol (1g)
1-(1,1-Difluoro-2-phenylallyl)cyclohexan-1-ol (1h)
4,4-Difluoro-2,2-dimethyl-5-phenylhex-5-en-3-ol (1i)
3-Ethyl-4,4-difluoro-5-(4-methylphenyl)hex-5-en-3-ol (1j)
5-(4-Chlorophenyl)-3-ethyl-4,4-difluorohex-5-en-3-ol (1k)
2,2-Difluoro-3-methyl-1-phenyl-3-[(tetrahydro-2H-pyran-2-yl)oxy]butan-1-one
3,3-Difluoro-2-methyl-4,5-diphenylpent-4-en-2-ol (1l)
3-Fluoro-2,2-dimethyl-4-phenyl-2,5-dihydrofuran (4a)
2,2-Diethyl-3-fluoro-4-phenyl-2,5-dihydrofuran (4b)
3-Fluoro-2-methyl-2,4-diphenyl-2,5-dihydrofuran (4c)
3-Fluoro-2-(4-methoxyphenyl)-2-methyl-4-phenyl-2,5-dihydrofuran (4d)
2-(4-Chlorophenyl)-3-fluoro-2-methyl-4-phenyl-2,5-dihydrofuran (4e)
3-Fluoro-2,4-diphenyl-2-(trifluoromethyl)-2,5-dihydrofuran (4f)
4-Fluoro-3-phenyl-1-oxaspiro[4.4]non-3-ene (4g)
4-Fluoro-3-phenyl-1-oxaspiro[4.5]dec-3-ene (4h)
2-(tert-Butyl)-3-fluoro-4-phenyl-2,5-dihydrofuran (4i)
2,2-Diethyl-3-fluoro-4-(4-methylphenyl)-2,5-dihydrofuran (4j)
4-(4-Chlorophenyl)-2,2-diethyl-3-fluoro-2,5-dihydrofuran (4k)
3-Fluoro-2,2-dimethyl-4,5-diphenyl-2,5-dihydrofuran (4l)
5,5-Diethyl-4-fluoro-3-phenylfuran-2(5H)-one (5b)
4-Fluoro-3-phenyl-1-oxaspiro[4.5]dec-3-ene-2-one (5h)