Supporting Information
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Supplementary Material for:

Synthesis of Chroman-4-ones with gem-difluoroalkyl Side Chains in Position 2


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1. General procedure for the protection of hydroxyl group (2)

To a solution of salicylaldehyde (1 equiv) in THF, sodium hydride (5 equiv, 60% by weight, dispersed in oil) was added at 0°C under nitrogen atmosphere. After 5 min, chloromethyl methyl ether (MOMCl) (1.5 equiv) was added and the reaction mixture was stirred for 4 hours at room temperature. After this time, a 3M NaOH solution (20 mL) was added to the reaction mixture and the two phases were separated. Aqueous phase was extracted with ethyl acetate (100 mL), and organic phase was washed with NaOH solution (100 mL), dried over Na₂SO₄, and then concentrated in vacuo. The crude product was purified by chromatography on silica gel (pentane/ethyl acetate).

1.1 Synthesis of 2-methoxymethoxy-benzaldehyde (2a)

2-Hydroxybenzaldehyde (1 g, 8.19 mmol) was added to a solution of sodium hydride (0.98 g) and MOMCl (0.93 mL, 12.29 mmol) in THF (20 mL), according to the general procedure. After purification by chromatography on silica gel, the product 2a was obtained as a colorless oil (1.07 g, 79% yield). \( R_f = 0.45 \) (pentane/ethyl acetate 9/1). \(^1\)H NMR (CDCl₃, 300 MHz), \( \delta \) ppm: 10.51 (d, 1H, \( J_B = 0.7 \) Hz); 7.84 (dd, 1H, \( J_B = 7.7 \) Hz, \( J_B = 1.8 \) Hz); 7.53 (ddd, 1H, \( J_B = 8.5 \) Hz, \( J_B = 7.3 \) Hz, \( J_B = 1.9 \) Hz); 7.22 (ddd, 1H, \( J_B = 8.4 \) Hz, \( J_B = 0.7 \) Hz); 7.10 (tt, 1H, \( J_B = 7.4 \) Hz, \( J_B = 0.9 \) Hz); 5.31 (s, 2H); 3.53 (s, 3H). \(^{13}\)C NMR (CDCl₃, 75 MHz), \( \delta \) (ppm): 189.7; 159.7; 135.8; 128.4; 125.6; 121.9; 115.1; 94.7; 56.5. HRMS (ESI) calcd for C₉H₁₀O₃Na: [M +Na]⁺: m/z 189.0527. Found: m/z 189.0525 (1 ppm).

1.2 Synthesis of 5-Bromo-2-methoxymethoxy-benzaldehyde (2b)

5-Bromo-2-hydroxybenzaldehyde (2 g, 10 mmol) was added to a solution of sodium hydride (1.20 g) and MOMCl (1.12 mL, 15 mmol) in THF (30 mL), according to the general procedure. After purification by chromatography on silica gel, the product 2b was obtained as a yellow oil (2.02 g, 83% yield). \( R_f = 0.48 \) (pentane/ethyl acetate 9/1). \(^1\)H NMR (CDCl₃, 300 MHz), \( \delta \) (ppm): 10.42 (s, 1H); 7.94 (d, 1H, \( J_B = 2.6 \) Hz); 7.61 (dd, 1H, \( J_B = 8.9 \) Hz, \( J_B = 2.6 \) Hz); 7.22 (d, 1H, \( J_B = 8.9 \) Hz); 5.29 (s, 2H); 3.52 (s, 3H). \(^{13}\)C NMR (CDCl₃, 75 MHz), \( \delta \) (ppm): 188.2; 158.6; 138.2; 130.9; 126.8; 117.2; 114.3; 94.9; 56.6. HRMS (ESI) calcd for C₉H₈O₃⁷⁹BrNa: [M +Na]⁺: m/z 266.96328. Found: m/z 266.9633 (0 ppm).
1.3 Synthesis of 2-methoxymethoxy-5-methyl-benzaldehyde (2c)

2-Hydroxy-5-methyl-benzaldehyde (1 g, 7.35 mmol) was added to a solution of sodium hydride (0.88 g) and MOMCl (0.84 mL, 11.03 mmol) in THF (20 mL), according to the general procedure. After purification by chromatography on silica gel, the product 2c was obtained as a colorless oil (1.16 g, 88% yield). $R_f = 0.42$ (pentane/ethyl acetate 9/1). $^1$H NMR (CDCl$_3$, 300 MHz), δ (ppm): 10.47 (s, 1H); 7.62 (d, 1H, $J = 2.4$ Hz); 7.32 (ddq, 1H, $J = 8.5$ Hz, $J = 2.4$ Hz, $J = 0.6$ Hz); 7.22 (d, 1H, $J = 8.5$ Hz); 5.26 (s, 2H); 3.51 (s, 2H); 2.31 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz), δ (ppm): 189.9; 157.7; 136.5; 131.4; 128.2; 125.1; 115.1; 94.7; 56.4; 20.3. HRMS (ESI) calcd for C$_{10}$H$_{12}$O$_3$Na: [M +Na]$^+$: m/z 203.0684. Found: m/z 203.0685 (0 ppm).

1.4 Synthesis of 3-Bromo-2-methoxymethoxy-benzaldehyde (2d)

3-Bromo-2-hydroxybenzaldehyde (1 g, 5 mmol) was added to a solution of sodium hydride (0.6 g) and MOMCl (0.56 mL, 7.5 mmol) in THF (20 mL), according to the general procedure. After purification by chromatography on silica gel, the product 2d was obtained as yellow crystals (1.01 g, 82% yield). $R_f = 0.53$ (pentane/ethyl acetate 9/1). $M_p = 52^\circ$C. $^1$H NMR (CDCl$_3$, 300 MHz), δ (ppm): 10.32 (d, 1H, $J = 0.8$ Hz); 7.80 (dd, 1H, $J = 7.8$ Hz, $J = 1.7$ Hz); 7.78 (dd, 1H, $J = 7.8$ Hz, $J = 1.7$ Hz); 7.13 (td, 1H, $J = 7.8$ Hz, $J = 0.8$ Hz); 5.18 (s, 2H); 3.60 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz), δ (ppm): 189.9; 157.7; 136.5; 131.4; 128.2; 125.1; 115.1; 94.7; 56.4; 20.3. HRMS (ESI) calcd for C$_9$H$_9$O$_3$BrNa: [M +Na]$^+$: m/z 266.9633. Found: m/z 266.9633 (0 ppm).

1.5 Synthesis of 2-methoxymethoxy-3-methyl-benzaldehyde (2e)

2-Hydroxy-3-methyl-benzaldehyde (1 g, 7.35 mmol) was added to a solution of sodium hydride (0.88 g) and MOMCl (0.84 mL, 11.03 mmol) in THF (20 mL), according to the general procedure. After purification by chromatography on silica gel, the product 2e was obtained as a colorless oil (1.11 g, 84% yield). $R_f = 0.40$ (pentane/ethyl acetate 9/1). $^1$H NMR (CDCl$_3$, 300 MHz), δ (ppm): 10.30 (d, 1H, $J = 0.7$ Hz); 7.64 (ddd, 1H, $J = 7.6$ Hz, $J = 1.8$ Hz, $J = 0.7$ Hz); 7.44 (ddq, 1H, $J = 7.6$ Hz, $J = 1.8$ Hz, $J = 0.7$ Hz); 7.17 (t, 1H, $J = 7.6$ Hz); 5.08 (s, 2H); 3.60 (s, 3H); 2.35 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz), δ (ppm): 190.8; 158.9; 137.3;
132.3; 129.8, 126.8, 124.6; 100.9; 57.8, 16.3. HRMS (ESI) calcd for C_{10}H_{12}O_{3}BrNa [M + Na]^+ : m/z 203.06841. Found: m/z 203.0685 (0 ppm).

1.6 Synthesis of 3,5-Dibromo-2-methoxymethoxy-benzaldehyde (2f)

3,5-dibromo-2-hydroxybenzaldehyde (2 g, 7.19 mmol) was added to a solution of sodium hydride (0.86 g) and MOMCl (0.82 mL, 10.79 mmol) in THF (40 mL), according to the general procedure. After purification by chromatography on silica gel, the product 2f was obtained as white crystals (1.76 g, 76% yield). Rf = 0.47 (pentane/ethyl acetate 95/5). Mp = 79 °C. ^1H NMR (CDCl₃, 300 MHz), δ (ppm): 10.25 (s, 1H); 7.95 (d, 1H, J = 2.5 Hz); 7.91 (d, 1H, J = 2.5 Hz); 5.12 (s, 2H); 3.61 (s, 3H). ^13C NMR (CDCl₃, 75 MHz), δ (ppm): 188.3; 156.4; 141.1; 132.4; 130.4; 119.3; 118.5; 101.0; 58.4. HRMS (ESI) calcd for C₉H₆O₃Br₂Na: [M + Na]^+ : m/z 344.8737. Found: m/z 344.8743 (2 ppm).

1.7 Synthesis of 3-Bromo-5-chloro-2-methoxymethoxy-benzaldehyde (2g)

3-Bromo-5-chloro-2-hydroxybenzaldehyde (2 g, 8.55 mmol) was added to a solution of sodium hydride (1.03 g) and MOMCl (0.98 mL, 12.82 mmol) in THF (40 mL), according to the general procedure. After purification by chromatography on silica gel, the product 2g was obtained as white crystals (1.90 g, 80% yield). Rf = 0.49 (pentane/ethyl acetate 95/5). Mp = 85 °C. ^1H NMR (CDCl₃, 300 MHz), δ (ppm): 10.16 (s, 1H); 7.70 (d, 1H, J = 2.6 Hz); 7.66 (d, 1H, J = 2.6 Hz); 5.09 (s, 2H); 3.52 (s, 3H). ^13C NMR (CDCl₃, 75 MHz), δ (ppm): 188.2; 155.9; 138.2; 132.0; 131.1; 127.2; 118.9; 101.0; 58.3. HRMS (ESI) calcd for C₉H₆O₃Br²Na: [M + Na]^+ : m/z 300.92430. Found: m/z 300.9240 (1 ppm) (2 ppm).

2. General procedure for the synthesis of difluoro-propargylic alcohols (3)

To a solution of 3,3-difluoro-dodec-1-yne (1 equiv) in anhydrous THF (2 mL per mmol) cooled at -78°C, was added under nitrogen, a solution of n-butyllithium in hexane (1.2 equiv). The mixture was stirred for 1 h at t ≤ -40°C. Then, aldehyde 2 (1.2 equiv) in anhydrous THF (1 mL per mmol) was added at -78°C and allowed to warm to room temperature for 2 h. The mixture was then treated with a saturated ammonium chloride solution, extracted by ether. The combined organic phases were washed with water, dried over MgSO₄ and concentrated in
vacuo. The crude product was purified by chromatography on silica gel, using as eluent mixture of pentane/ether.

2.1 Synthesis of 4,4-difluoro-1-(2-methoxymethoxy-phenyl)-tridec-2-yn-1-ol (3a)

The reaction was performed with 3,3-difluoro-dodec-1-yne (0.48 g, 2.37 mmol) and 2-methoxymethoxy-benzaldehyde 2a (0.47 g, 2.85 mmol), according to the general procedure. After purification by chromatography on silica gel, propargylic alcohol 3a was obtained as a yellow oil (0.80 g, 92% yield). Rf = 0.41 (pentane/ether 9/1). 1H NMR (CDCl3, 300 MHz), δ (ppm): 7.46 (dd, 1H, J = 7.6 Hz, J = 1.7 Hz); 7.32 (ddd, 1H, J = 8.3 Hz, J = 1.0 Hz); 7.05 (td, 1H, J = 7.5 Hz, J = 1.1 Hz); 5.7 (bs, 1H); 5.27 (s, 2H); 3.52 (s, 3H); 2.10-1.95 (m, 2H); 1.56-1.51 (m, 2H); 1.33-1.26 (m, 12H); 0.88 (t, 3H, J = 6.5 Hz). 13C NMR (CDCl3, 75 MHz), δ (ppm): 154.5; 130.2; 128.2; 127.9; 122.2; 114.9 (t, 1JCF = 232.5 Hz); 114.6; 94.6; 86.4 (t, 3JCF = 6.8 Hz); 78.5 (t, 2JCF = 41.0 Hz); 61.0; 56.4; 39.2 (t, 3JCF = 25.9 Hz); 31.8; 29.4; 29.3; 29.2; 28.9; 22.7 (t, 3JCF = 3.6 Hz); 22.6; 14.1. 19F NMR (CDCl3, 282 MHz), δ (ppm): -82.89 (td, 2F, 2JFH = 14.9 Hz, 3JFH = 4.1 Hz). HRMS (ESI) calcd for C21H30O3F2Na: [M+Na]+: m/z 391.2067. Found: m/z 391.2056 (1 ppm).

2.2 Synthesis of 1-(5-Bromo-2-methoxymethoxy-phenyl)-4,4-difluoro-tridec-2-yn-1-ol (3b)

The reaction was performed with 3,3-difluoro-dodec-1-yne (0.41 g, 2.02 mmol) and 5-Bromo-2-methoxymethoxy-benzaldehyde 2b (0.59 g, 2.43 mmol), according to the general procedure. After purification by chromatography on silica gel, propargylic alcohol 3b was obtained as a yellow oil (0.67 g, 74% yield). Rf = 0.44 (pentane/ether 9/1). 1H NMR (CDCl3, 300 MHz), δ (ppm): 7.59 (d, 1H, J = 2.5 Hz); 7.41 (dd, 1H, J = 8.8 Hz, J = 2.5 Hz); 7.04 (d, 1H, J = 8.8 Hz); 5.66 (t, 1H, 5JHF = 4.0 Hz); 5.24 (s, 2H); 3.50 (s, 3H); 2.10-1.95 (m, 2H); 1.58-1.48 (m, 2H); 1.30-1.26 (m, 12H); 0.88 (t, 3H, J = 6.6 Hz). 13C NMR (CDCl3, 75 MHz), δ (ppm): 153.5; 132.7; 130.6; 130.2; 116.4; 114.8 (t, 1JCF = 232.9 Hz); 114.5; 94.8; 85.7 (t, 3JCF = 6.6 Hz); 78.9 (t, 2JCF = 41.3 Hz); 60.3; 56.4; 39.1 (t, 2JCF = 25.8 Hz); 31.8; 29.4; 29.3; 29.2; 28.9; 22.7 (t, 3JCF = 3.7 Hz); 22.6; 14.1. 19F NMR (CDCl3, 282 MHz), δ (ppm): -83.07 (td, 2F, 2JFH = 15.0 Hz, 3JFH = 3.9 Hz). HRMS (ESI) calcd for C21H30O3F2BrNa: [M+Na]+: m/z 469.11658. Found: m/z 469.1161 (1 ppm).
2.3 Synthesis of 4,4-difluoro-1-(2-methoxymethoxy-5-methyl-phenyl)-tridec-2-yn-1-ol (3c)

The reaction was performed with 3,3-difluoro-dodec-1-yne (0.45 g, 2.02 mmol) and methoxymethoxy-5-methyl-benzaldehyde \(2c\) (0.48 g, 2.67 mmol), according to the general procedure. After purification by chromatography on silica gel, propargylic alcohol \(3c\) was obtained as a yellow oil (0.65 g, 76% yield). \(R_f = 0.48\) (pentane/ether 8/2). \(^1\)H NMR (CDCl\(_3\), 300 MHz), \(\delta\) (ppm): 7.25 (d, 1H, \(J = 0.8\) Hz); 7.11 (dd, 1H, \(J = 8.4\) Hz, \(J = 1.8\) Hz); 7.03 (d, 1H, \(J = 8.4\) Hz); 5.66 (t, 1H, \(^5J_{HF} = 4.1\) Hz); 5.23 (s, 2H); 3.50 (s, 3H); 2.31 (s, 3H); 2.10-1.95 (m, 2H); 1.55-1.49 (m, 2H); 1.35-1.26 (m, 12H); 0.88 (t, 3H, \(J = 6.6\) Hz). \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) (ppm): 152.4; 131.7; 130.5; 128.5; 128.0; 114.9 (t, \(J_{CF} = 232.5\) Hz); 114.8; 94.9; 86.5 (t, \(^3J_{CF} = 6.8\) Hz); 78.5 (t, \(^2J_{CF} = 41.0\) Hz); 61.2 (t, \(^4J_{CF} = 1.8\) Hz); 56.3; 39.2 (t, \(^2J_{CF} = 25.9\) Hz); 31.8; 29.4; 29.3; 29.2; 28.9; 22.7 (t, \(^3J_{CF} = 3.5\) Hz); 22.6; 20.6; 14.1. \(^{19}\)F NMR (CDCl\(_3\), 282 MHz), \(\delta\) (ppm): -83.07 (td, 2F, \(^2J_{FH} = 15.0\) Hz, \(^3J_{FH} = 4.0\) Hz). HRMS (ESI) calcd for C\(_{22}\)H\(_{32}\)O\(_3\)F\(_2\)Na: [M +Na\(^+\)] : \(m/z = 405.22172\). Found: \(m/z = 405.2213\) (1 ppm).

2.4 Synthesis of 1-(3-Bromo-2-methoxymethoxy-phenyl)-4,4-difluoro-tridec-2-yn-1-ol (3d)

The reaction was performed with 3,3-difluoro-dodec-1-yne (0.51 g, 2.52 mmol) and 3-Bromo-2-methoxymethoxy-benzaldehyde \(2d\) (0.75 g, 3.03 mmol), according to the general procedure. After purification by chromatography on silica gel, propargylic alcohol \(3d\) was obtained as a yellow oil (0.84 g, 74 % yield). \(R_f = 0.40\) (pentane/ether 9/1). \(^1\)H NMR (CDCl\(_3\), 300 MHz), \(\delta\) ppm: 7.59 (dd, 1H, \(J = 7.8\) Hz, \(J = 1.6\) Hz); 7.58 (dd, 1H, \(J = 7.8\) Hz, \(J = 1.6\) Hz); 7.09 (t, 1H, \(J = 7.9\) Hz); 5.79 (dt, 1H, \(^5J_{HF} = 4.2\) Hz); 5.20 (d, 1H, \(J = 6.3\) Hz); 5.11 (d, 1H, \(J = 6.3\) Hz); 3.67 (s, 3H); 2.13-1.98 (m, 2H); 1.61-1.54 (m, 2H); 1.33-1.24 (m, 12H); 0.88 (t, 3H, \(J = 6.7\) Hz). \(^{13}\)C NMR (CDCl\(_3\), 75 MHz), \(\delta\) (ppm): 152.9; 135.6; 134.2; 128.0; 126.4; 117.4; 114.9 (t, \(J_{CF} = 232.8\) Hz); 100.1; 85.7 (t, \(^3J_{CF} = 6.8\) Hz); 79.4 (t, \(^2J_{CF} = 41.1\) Hz); 60.1; 58.0; 39.2 (t, \(^2J_{CF} = 25.8\) Hz); 31.8; 29.4; 29.3; 29.2; 29.0; 22.7 (t, \(^3J_{CF} = 3.3\) Hz); 22.6; 14.1. \(^{19}\)F NMR (CDCl\(_3\), 282 MHz), \(\delta\) (ppm): -83.06 (td, 2F, \(^2J_{FH} = 14.7\) Hz, \(^3J_{FH} = 3.9\) Hz). HRMS (ESI) calcd for C\(_{21}\)H\(_{29}\)O\(_3\)F\(_2\)\(^{79}\)BrNa: [M +Na\(^+\)] : \(m/z = 469.11657\). Found: \(m/z = 469.1160\) (1 ppm).
2.5 Synthesis of 4,4-difluoro-1-(2-methoxymethoxy-3-methyl-phenyl)-tridec-2-yn-1-ol (3e)

The reaction was performed with 3,3-difluoro-dodec-1-yne (0.45 g, 2.02 mmol) and methoxymethoxy-3-methyl-benzaldehyde 2e (0.48 g, 2.67 mmol), according to the general procedure. After purification by chromatography on silica gel, propargylic alcohol 3e was obtained as a yellow oil (0.61 g, 72% yield). Rf = 0.46 (pentane/ether 8/2). $^1$H NMR (CDCl$_3$, 300 MHz), δ (ppm): 7.44 (dd, 1H, $J = 7.6$ Hz, $J = 1.6$ Hz); 7.22 (ddd, 1H, $J = 7.6$ Hz, $J = 1.8$ Hz, $J = 0.7$ Hz); 7.11 (t, 1H, $J = 7.5$ Hz); 5.79 (t, 1H, $^5J_{HF} = 4.2$ Hz); 5.07 (d, 1H, $J = 6.1$ Hz); 4.98 (d, 1H, $J = 6.1$ Hz); 3.65 (s, 3H); 2.29 (s, 3H); 2.10-1.97 (m, 2H); 1.62-1.52 (m, 2H); 1.32-1.16 (m, 12H); 0.88 (t, 3H, $J = 6.5$ Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz), δ (ppm): 154.3; 133.3; 132.3; 131.2; 126.4; 125.1; 114.9 (t, $^1J_{CF} = 232.6$ Hz), 99.6; 86.4 (t, $^3J_{CF} = 6.8$ Hz); 78.9 (t, $^2J_{CF} = 40.5$ Hz); 60.1; 57.6; 39.2 (t, $^2J_{CF} = 25.8$ Hz); 31.8; 29.4; 29.3; 28.9; 22.7 (t, $^3J_{CF} = 3.5$ Hz); 22.6; 16.8; 14.1. $^{19}$F NMR (CDCl$_3$, 282 MHz), δ (ppm): -82.90 (td, 2F, $^2J_{FH} = 15.0$ Hz, $^3J_{FH} = 4.1$ Hz). HRMS (ESI) calcd for C$_{22}$H$_{32}$F$_2$O$_3$: [M+Na]$^+$: m/z: 405.22172. Found: m/z: 405.2218 (0 ppm).

2.6 Synthesis of 1-(3,5-Dibromo-2-methoxymethoxy-phenyl)-4,4-difluoro-tridec-2-yn-1-ol (3f)

The reaction was performed with 3,3-difluoro-dodec-1-yne (0.40 g, 1.98 mmol) and 3,5-Dibromo-2-methoxymethoxy-benzaldehyde 2f (0.76 g, 2.37 mmol), according to the general procedure. After purification by chromatography on silica gel, propargylic alcohol 3f was obtained as a yellow oil (0.74 g, 71% yield). Rf = 0.39 (pentane/ether 9/1). $^1$H NMR (CDCl$_3$, 300 MHz), δ (ppm): 7.73 (d, 1H, $J = 2.4$ Hz); 7.69 (d, 1H, $J = 2.4$ Hz); 5.76 (bs 1H); 5.17 (d, 1H, $J = 6.3$ Hz); 4.00 (bs, 1H, OH); 5.08 (d, 1H, $J = 6.3$ Hz); 3.66 (s, 3H); 2.13-1.98 (m, 2H); 1.61-1.53 (m, 2H); 1.37-1.26 (m, 12H); 0.88 (t, 3H, $J = 6.7$ Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz) δ (ppm): 152.1; 136.9; 136.3; 131.0; 118.36; 118.34; 114.8 (t, $^1J_{CF} = 233.0$ Hz), 100.1; 84.9 (t, $^3J_{CF} = 6.7$ Hz); 79.7 (t, $^2J_{CF} = 41.3$ Hz); 59.6 (t, $^4J_{CF} = 1.8$ Hz); 58.1; 39.1 (t, $^2J_{CF} = 25.6$ Hz); 31.8; 29.4; 29.3; 29.2; 28.9; 22.7 (t, $^3J_{CF} = 3.5$ Hz); 22.6; 14.1. $^{19}$F NMR (CDCl$_3$, 282 MHz), δ (ppm): -83.22 (td, 2F, $^2J_{FH} = 14.9$ Hz, $^3J_{FH} = 3.8$ Hz). HRMS (ESI) calcd for C$_{21}$H$_{28}$O$_3$F$_2$Br$_2$Na: [M+Na]$^+$: m/z: 547.02709. Found: m/z 547.0277 (1 ppm).
2.7 Synthesis of 1-(3-Bromo-5-chloro-2-methoxymethoxy-phenyl)-4,4-difluoro-tridec-2-yn-1-ol (3g)

The reaction was performed with 3,3-difluoro-dodec-1-yne (0.40 g, 1.98 mmol) and 3-bromo-5-dichloromethoxybenzaldehyde 2g (0.66 g, 2.38 mmol), according to the general procedure. After purification by chromatography on silica gel, propargylic alcohol 3g was obtained as a yellow oil (0.70 g, 74% yield). \( R_f = 0.36 \) (pentane/ether 9/1). \(^1\)H NMR (CDCl\(_3\), 300 MHz), \( \delta \) (ppm): 7.57 (d, 1H, \( J = 2.5 \) Hz); 7.54 (d, 1H, \( J = 2.5 \) Hz); 5.77 (t, 1H, \( J_{HF} = 4.1 \) Hz); 5.17 (d, 1H, \( J = 6.3 \) Hz); 5.08 (d, 1H, \( J = 6.3 \) Hz); 3.66 (s, 3H); 2.13-1.98 (m, 2H); 1.61-1.51 (m, 2H); 1.31-1.26 (m, 12H); 0.88 (t, 3H, \( J = 6.7 \) Hz). \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \( \delta \) (ppm): 151.6; 136.5; 133.6; 131.0; 128.0; 118.0; 114.8 (t, \( J_{CF} = 233.0 \) Hz); 100.2; 84.9 (t, \( J_{CF} = 6.7 \) Hz); 79.7 (t, \( J_{CF} = 41.3 \) Hz); 59.7 (t, \( J_{CF} = 1.7 \) Hz); 58.1; 39.1 (t, \( J_{CF} = 25.6 \) Hz); 31.8; 29.4; 29.3; 29.2; 28.9; 22.7 (t, \( J_{CF} = 3.5 \) Hz); 22.6; 14.1. \(^{19}\)F NMR (CDCl\(_3\), 282 MHz), \( \delta \) (ppm): -83.23 (td, 2F, \( J_{FH} = 15.0 \) Hz, \( J_{FH} = 3.9 \) Hz). HRMS (ESI) calcd for C\(_{21}\)H\(_{28}\)O\(_3\)F\(_2\)\(_{35}\)Cl\(_7\)BrNa: \([\text{M+Na}]^+\): \( m/\ell = 503.07761 \). Found: \( m/\ell = 503.0779 \) (1 ppm).

3. General procedure for the synthesis of gem-difluoroenones (4)

The gem-difluoropropargylic alcohol (1 equiv) was dissolved in THF (2 mL per mmol), then DBU (1.5 equiv) was added, and stirred (3.1: stirred at 35 °C; 3.2: stirred under reflux) for the appropriate time (monitored by \(^{19}\)F NMR). After completion of the reaction, the mixture was neutralized by addition of a saturated NH\(_4\)Cl solution. After extraction with diethyl ether, the organic phases were washed with water, dried over MgSO\(_4\) and concentrated in vacuo. The crude product was purified by chromatography on silica gel, using pentane/ether as eluent.

3.1 Synthesis of 4,4-Difluoro-1-(2-methoxymethoxy-phenyl)-tridec-2-en-1-one (4a)

The reaction was performed with 3a (0.65 mg, 1.77 mmol) according to general procedure 3.1. After 8 h, \(^{19}\)F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the enone 4a was isolated as a yellow oil (0.42 g, 65%). \( R_f = 0.52 \) (pentane/ether 9/1). \(^1\)H NMR (CDCl\(_3\), 300 MHz), \( \delta \) (ppm): 7.63 (dd, 1H, \( J = 7.8 \) Hz, \( J = 1.8 \) Hz); 7.47 (ddd, 1H, \( J = 8.1 \) Hz, \( J = 7.2 \) Hz, \( J = 1.8 \) Hz); 7.19 (dd, 1H, \( J = 7.8 \) Hz, \( J = 0.8 \) Hz); 7.18 (dt, 1H, \( J = 15.7 \) Hz, \( J_{HF} = 2.1 \) Hz); 7.08 (dt, 1H, \( J = 7.5 \) Hz, \( J = 0.8 \) Hz); 6.67 (dt,
1H, J = 15.7 Hz, 3JHF = 11.6 Hz); 5.25 (s, 2H); 3.50 (s, 3H); 2.04-1.88 (m, 2H); 1.50-1.42 (m, 2H); 1.36-1.26 (m, 12H); 0.88 (t, 3H, J = 6.7 Hz). 13C NMR (CDCl3, 75 MHz) δ (ppm): 191.5; 156.2; 136.5 (t, 2JCF = 27.5 Hz); 133.8; 132.1 (t, 3JCF = 7.8 Hz); 130.5; 128.7; 122.0; 121.4 (t, 1JCF = 239.4 Hz); 114.9; 94.6; 56.5; 37.3 (t, 2JCF = 25.8 Hz); 31.8; 29.4; 29.3; 29.26; 28.23; 22.6; 22.2 (t, 3JCF = 4.1 Hz); 14.1. 19F NMR (CDCl3, 282 MHz), δ (ppm): -98.05 (tdd, 2F, 2JFH = 16.0 Hz, 3JFH = 11.6 Hz, 4JFH = 2.1 Hz). HRMS (ESI) calcd for C21H30O3F2Na: [M +Na]+: m/z 391.20607. Found: m/z 391.2063 (1 ppm).

3.2 Synthesis of 1-(5-Bromo-2-methoxymethoxy-phenyl)-4,4-difluoro-tridec-2-en-1-one (4b)

The reaction was performed with 3b (0.61 g, 1.37 mmol) according to general procedure 3.1. After 3 h, 19F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the enone 4b was isolated as a yellow oil (0.40 g, 66%). Rf = 0.62 (pentane/ether 9/1). 1H NMR (CDCl3, 300 MHz), δ (ppm): 7.73 (d, 1H, J = 2.6 Hz); 7.55 (dd, 1H, J = 8.9 Hz, J = 2.6 Hz); 7.13 (dt, 1H, J = 15.7 Hz, 4JHF = 2.2 Hz); 7.10 (d, 1H, J = 7.9 Hz); 6.67 (dt, 1H, J = 15.7 Hz, 3JHF = 11.5 Hz); 5.22 (s, 2H); 3.48 (s, 3H); 2.04-1.88 (m, 2H); 1.51-1.41 (m, 12H); 0.88 (t, 3H, J = 6.7 Hz). 13C NMR (CDCl3, 75 MHz) δ (ppm): 190.1; 155.2; 137.3 (t, 2JCF = 27.5 Hz); 136.3; 133.0; 131.5 (t, 3JCF = 7.8 Hz); 130.2; 121.3 (t, 1JCF = 239.5 Hz); 116.9; 114.5; 94.8; 56.6; 37.2 (t, 2JCF = 25.7 Hz); 31.8; 29.7; 29.4; 29.3; 29.2; 22.7; 22.2 (t, 3JCF = 4.2 Hz); 14.1. 19F NMR (CDCl3, 282 MHz), δ (ppm): -98.24 (td, 2F, 2JFH = 15.9 Hz, 4JFH = 1.6 Hz). HRMS (ESI) calcd for C21H30O3F279BrNa: [M+Na]+: m/z 469.11658. Found: m/z 469.1172 (1 ppm).

3.3 Synthesis of 4,4-Difluoro-1-(2-methoxymethoxy-5-methyl-phenyl)-tridec-2-en-1-one (4c)

The reaction was performed with 3c (0.58 g, 1.52 mmol) according to general procedure 3.1. After 18 h, 19F NMR showed 100% conversion with two stereoisomeric enones (cis / trans: 2/100). After purification by flash chromatography on silica gel, the enone 4c was isolated as a yellow oil (0.38 g, 66%). Rf = 0.49 (pentane/ether 9/1). 1H NMR (CDCl3, 300 MHz), δ (ppm): 7.43 (d, 1H, J = 2.2 Hz); 7.27 (dd, 1H, J = 8.5 Hz, J = 2.3 Hz, J = 0.8 Hz); 7.19 (dt, 1H, J = 15.7 Hz, 4JHF = 2.3 Hz); 7.07 (d, 1H, J = 8.5 Hz); 6.68 (dt, 1H, J = 15.7 Hz, 3JHF = 11.6 Hz); 5.20 (s, 2H); 3.48 (s, 3H); 2.32 (s, 3H); 2.08-1.88 (m, 2H); 1.52-1.42 (m, 12H); 0.88 (t, 3H, J = 6.7 Hz). 13C NMR (CDCl3, 75 MHz) δ (ppm): 191.6;
154.2; 136.4 (t, \(^2J_{CF} = 27.3\) Hz); 134.4; 132.2 (t, \(^3J_{CF} = 7.8\) Hz); 131.6; 130.7; 128.5; 121.4 (t, \(^1J_{CF} = 239.0\) Hz); 115.1; 94.8; 56.5; 37.3 (t, \(^2J_{CF} = 25.8\) Hz); 31.8; 29.4; 29.3; 29.27; 29.24; 22.65; 22.2 (t, \(^3J_{CF} = 3.9\) Hz); 22.7; 14.1. 19F NMR (CDCl\(_3\), 282 MHz), \(\delta\) (ppm): -97.97 (tdd, \(2J_{FH} = 15.6\) Hz, \(3J_{FH} = 11.6\) Hz, \(4J_{FH} = 1.8\) Hz). HRMS (ESI) calcd for C\(_{22}\)H\(_{32}\)O\(_3\)F\(_2\)Na: \([M + Na]^+\): m/z 405.2217. Found: m/z 405.2213 (1 ppm).

3.4 Synthesis of 1-(3-Bromo-2-methoxymethoxy-phenyl)-4,4-difluorotridec-2-en-1-one (4d)

The reaction was performed with 3d (0.72 mg, 1.61 mmol) according to general procedure 3.1. After 4 h, 19F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the enone 4d was isolated as a yellow oil (0.49 mg, 68%). \(R_f = 0.31\) (pentane/ether 95/1). 1H NMR (CDCl\(_3\), 300 MHz), \(\delta\) (ppm): 7.74 (dd, 1H, \(J = 7.9\) Hz, \(J = 1.7\) Hz); 7.49 (dd, 1H, \(J = 7.7\) Hz, \(J = 1.6\) Hz); 7.11 (t, 1H, \(J = 7.8\) Hz); 7.08 (dt, 1H, \(J = 15.8\) Hz, \(4J_{HF} = 2.2\) Hz); 6.73 (dt, 1H, \(J = 15.8\) Hz, \(3J_{HF} = 11.4\) Hz); 5.03 (s, 2H); 3.48 (s, 3H); 2.04-1.88 (m, 2H); 1.51-1.41 (m, 2H); 1.31-1.26 (m, 12H); 0.88 (t, 3H, \(J = 6.7\) Hz). 13C NMR (CDCl\(_3\), 75 MHz) \(\delta\) (ppm): 190.9; 153.0; 138.6 (t, \(2J_{CF} = 27.8\) Hz); 137.0; 135.5; 131.2 (t, \(3J_{CF} = 7.7\) Hz); 129.1; 125.8; 121.1 (t, \(1J_{CF} = 239.7\) Hz); 118.4; 100.9; 58.3; 37.2 (t, \(2J_{CF} = 25.7\) Hz); 31.8; 29.37; 29.30; 29.2 (2C); 22.6; 22.1 (t, \(3J_{CF} = 4.1\) Hz); 14.1. 19F NMR (CDCl\(_3\), 282 MHz), \(\delta\) (ppm): -98.06 (tdd, 2F, \(2J_{FH} = 15.6\) Hz, \(3J_{FH} = 11.3\) Hz, \(4J_{FH} = 1.8\) Hz). HRMS (ESI) calcd for C\(_{21}\)H\(_{29}\)O\(_3\)F\(_2\)BrNa: \([M + Na]^+\): m/z 469.1165. Found: m/z 469.1159 (1 ppm).

3.5 Synthesis of 4,4-Difluoro-1-(2-methoxymethoxy-3-methyl-phenyl)-tridec-2-en-1-one (4e)

The reaction was performed with 3e (0.55 g, 1.44 mmol) according to general procedure 3.1. After 16 h, 19F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the enone 4e was isolated as a yellow oil (0.35 g, 64%). \(R_f = 0.48\) (pentane/ether 9/1). 1H NMR (CDCl\(_3\), 300 MHz), \(\delta\) (ppm): 7.41-7.37 (m, 2H); 7.12 (t, 1H, \(J = 7.6\) Hz); 7.08 (dt, 1H, \(J = 15.8\) Hz, \(4J_{HF} = 2.2\) Hz); 6.71 (dt, 1H, \(J = 15.8\) Hz, \(3J_{HF} = 11.5\) Hz); 4.90 (s, 2H); 3.47 (s, 3H); 2.36 (s, 3H); 2.04-1.88 (m, 2H); 1.51-1.40 (m, 2H); 1.34-1.26 (m, 12H); 0.88 (t, 3H, \(J = 6.7\) Hz). 13C NMR (CDCl\(_3\), 75 MHz) \(\delta\) (ppm): 192.2; 154.9; 137.9 (t, \(2J_{CF} = 27.5\) Hz); 135.1; 133.1; 132.6; 131.6 (t, \(3J_{CF} = 7.7\) Hz); 127.7; 124.4; 121.3 (t, \(1J_{CF} = 239.3\) Hz); 100.8; 57.8; 37.2 (t, \(2J_{CF} = 25.7\) Hz); 31.8; 29.4; 29.3; 29.2 (2C); 22.6; 22.1 (t, \(3J_{CF} = 3.9\) Hz); 16.6; 14.1. 19F NMR (CDCl\(_3\), 282 MHz), \(\delta\) (ppm): -97.94 (tdd, 2F, \(2J_{FH} = 16.0\) Hz,
\[ J_{HF} = 11.5 \text{ Hz}, \quad J_{HF} = 1.9 \text{ Hz} \]. HRMS (ESI) calcd for C_{22}H_{32}O_{3}F_{2}Na: [M+Na]^+: m/z 405.22172. Found: m/z 405.2214 (1 ppm).

### 3.6 Synthesis of 1-(3,5-Dibromo-2-methoxymethoxy-phenyl)-4,4-difluorotridec-2-en-1-one (4f)

The reaction was performed with 3f (0.63 g, 1.20 mmol) according to general procedure 3.2. After 1 h, \(^1^9\)F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the enone 4f was isolated as a yellow oil (0.41 g, 65%). \( R_t = 0.39 \) (pentane/ether 95/5). \(^1\)H NMR (CDCl\(_3\), 300 MHz), \( \delta \) (ppm): 7.88 (d, 1H, \( J = 2.4 \) Hz); 7.60 (d, 1H, \( J = 2.4 \) Hz); 7.03 (dt, 1H, \( J = 15.8 \) Hz, \( J_{HF} = 2.2 \) Hz); 6.74 (dt, 1H, \( J = 15.8 \) Hz, \( J_{HF} = 11.3 \) Hz); 5.00 (s, 2H); 3.46 (s, 3H); 2.04-1.88 (m, 2H); 1.50-1.41 (m, 2H); 1.37-1.26 (m, 12H); 0.88 (t, 3H, \( J = 6.7 \) Hz). \(^1^3\)C NMR (CDCl\(_3\), 75 MHz), \( \delta \) (ppm): 189.4; 152.2; 139.2 (t, \( J_{CF} = 27.8 \) Hz); 139.0; 136.4; 131.8; 130.7 (t, \( J_{CF} = 7.7 \) Hz); 121.0 (t, \( J_{CF} = 239.9 \) Hz); 119.4; 118.0; 101.0; 58.4; 37.2 (t, \( J_{CF} = 25.7 \) Hz); 31.8; 29.4; 29.3; 29.2(2C); 22.6; 22.1 (t, \( J_{CF} = 4.0 \) Hz); 14.1. \(^1^9\)F NMR (CDCl\(_3\), 282 MHz), \( \delta \) (ppm): -98.20 (ddt, \( J_{HF} = 16.2 \) Hz, \( J_{HF} = 11.3 \) Hz, \( J_{HF} = 1.7 \) Hz). HRMS (ESI) calcd for C_{21}H_{28}O_{3}F_{2}79Br_{2}Na: [M+Na]^+: m/z 547.02709. Found: m/z 547.0273 (0 ppm).

### 3.7 Synthesis of 1-(3-Bromo-5-chloro-2-methoxymethoxy-phenyl)-4,4-difluorotridec-2-en-1-one (4g)

The reaction was performed with 3g (0.58 g, 1.20 mmol) according to general procedure 3.2. After 1 h, \(^1^9\)F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the enone 4g was isolated as a yellow oil (0.41 g, 65%). \( R_t = 0.39 \) (pentane/ether 95/5). \(^1\)H NMR (CDCl\(_3\), 300 MHz), \( \delta \) (ppm): 7.74 (d, 1H, \( J = 2.6 \) Hz); 7.47 (t, 1H, \( J = 2.6 \) Hz); 7.04 (dt, 1H, \( J = 15.8 \) Hz, \( J_{HF} = 2.2 \) Hz); 6.74 (dt, 1H, \( J = 15.8 \) Hz, \( J_{HF} = 11.3 \) Hz); 5.00 (s, 2H); 3.47 (s, 3H); 2.04-1.88 (m, 2H); 1.50-1.41 (m, 2H); 1.34-1.26 (m, 12H); 0.88 (t, 3H, \( J = 6.7 \) Hz). \(^1^3\)C NMR (CDCl\(_3\), 75 MHz), \( \delta \) (ppm): 189.6; 151.7; 139.2 (t, \( J_{CF} = 27.8 \) Hz); 136.3; 136.0; 130.8; 130.7 (t, \( J_{CF} = 7.9 \) Hz); 128.9; 121.0 (t, \( J_{CF} = 239.9 \) Hz); 119.1; 101.0; 58.4; 37.2 (t, \( J_{CF} = 25.6 \) Hz); 31.8; 29.4; 29.3; 29.2(2C); 22.6; 22.1 (t, \( J_{CF} = 4.0 \) Hz); 14.1. \(^1^9\)F NMR (CDCl\(_3\), 282 MHz), \( \delta \) (ppm): -98.22 (ddt, \( J_{HF} = 16.2 \) Hz, \( J_{HF} = 11.3 \) Hz, \( J_{HF} = 1.7 \) Hz). HRMS (ESI) calcd for C_{21}H_{28}O_{3}F_{3}79Br_{2}Na: [M+Na]^+: m/z 503.07759. Found: m/z 503.0778 (1 ppm).
4.1 General procedure for the deprotection of hydroxyl group (5)

Gem-difluoroenone 4 was diluted in THF and then APTS (4 equiv) was added. The mixture was then, stirred under reflux for appropriate time (monitored by $^1$H NMR). After completion of the reaction, water was added and the two phases were separated. Aqueous phase was extracted with diethyl ether, and the combined organic phases were washed with water, dried over Na$_2$SO$_4$, and then concentrated in vacuo. The product was then purified by chromatography on silica gel (pentane/ether).

4.1 Synthesis of 4,4-Difluoro-1-(2-hydroxy-phenyl)-tridec-2-en-1-one (5a)

The reaction was performed with 4a (0.38 g, 1.03 mmol) according to general procedure. After 16 h, $^{19}$F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the product 5a was isolated as yellow oil (0.27 g, 80%). Rf = 0.59 (pentane/ether 9/1). $^1$H NMR (CDCl$_3$, 300 MHz), $\delta$ (ppm): 12.34 (s, 1H); 7.81 (dd, 1H, $J = 8.0$ Hz, $J = 1.6$ Hz); 7.53 (ddd, 1H, $J = 8.7$ Hz, $J = 7.4$ Hz, $J = 1.6$ Hz); 7.43 (dt, 1H, $J = 15.4$ Hz, $^4$J$_{HF}$ = 2.3 Hz); 7.03 (dd, 1H, $J = 8.4$ Hz, $J = 0.9$ Hz); 7.00-6.88 (m, 2H); 2.08-1.92 (m, 2H); 1.54-1.44 (m, 2H); 1.30-1.26 (m, 12H); 0.88 (t, 3H, $J = 6.7$ Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ (ppm): 193.1; 163.6; 139.5 (t, $^2$J$_{CF}$ = 27.3 Hz); 137.3; 130.1; 126.1 (t, $^3$J$_{CF}$ = 7.8 Hz); 121.2 (t, $^1$J$_{CF}$ = 240.0 Hz); 119.4; 119.2; 118.7; 37.2 (t, $^2$J$_{CF}$ = 25.8 Hz); 31.8; 29.4; 29.3; 29.2 (2C); 22.6; 22.1 (t, $^3$J$_{CF}$ = 4.1 Hz); 14.1. $^{19}$F NMR (CDCl$_3$, 282 MHz), $\delta$ (ppm): -98.57 (tdd, 2F, $^2$J$_{FH}$ = 16.1 Hz, $^3$J$_{FH}$ = 11.6 Hz, $^4$J$_{FH}$ = 2.0 Hz). HRMS (ESI) calcd for C$_{19}$H$_{26}$O$_2$F$_2$Na: [M+Na]$^+$: m/z 347.17986. Found: m/z 347.1798 (0 ppm)

4.2 Synthesis of 1-(5-Bromo-2-hydroxy-phenyl)-4,4-difluoro-tridec-2-en-1-one (5b)

The reaction was performed with 4b (0.36 g, 0.81 mmol) according to general procedure. After 18 h, $^{19}$F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the product 5b was isolated as a yellow oil (0.30 g, 93%). Rf = 0.39 (pentane/ether 95/5). $^1$H NMR (CDCl$_3$, 300 MHz), $\delta$ (ppm): 12.17 (s, 1H); 7.82 (d, 1H, $J = 2.4$ Hz); 7.53 (dd, 1H, $J = 8.9$ Hz, $J = 2.4$ Hz); 7.27 (dt, 1H, $J = 15.3$ Hz, $^4$J$_{HF}$ = 2.2 Hz); 6.89 (dt, 1H, $J = 15.3$ Hz, $^3$J$_{HF}$ = 11.5 Hz); 6.87 (d, 1H, $J = 8.9$ Hz); 2.01-1.86 (m, 2H); 1.48-1.37 (m, 2H); 1.31-1.16 (m, 12H); 0.81 (t, 3H, $J = 6.7$ Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ (ppm): 192.2; 162.5; 140.6 (t, $^2$J$_{CF}$ = 27.4 Hz); 139.9; 132.2; 125.5 (t, $^3$J$_{CF}$ = 7.7 Hz); 121.0 (t, $^1$J$_{CF}$ = 240.1 Hz); 120.7; 120.6; 110.8; 37.2 (t, $^2$J$_{CF}$ = 25.6 Hz); 31.8; 29.4; 29.3; 29.2 (2C); 22.6; 22.1 (t, $^3$J$_{CF}$ = 4.1 Hz); 14.1.
$^{19}$F NMR (CDCl$_3$, 282 MHz), $\delta$ (ppm): -98.70 (tdd, 2F, $^2$$J_{FH} = 16.2$ Hz, $^3$$J_{FH} = 11.5$ Hz, $^4$$J_{FH} = 1.7$ Hz). HRMS (ESI) calcd for C$_{19}$H$_{25}$O$_2$F$_2$Na$^+$: m/z 425.09037. Found: m/z 425.0909 (1 ppm).

4.3 Synthesis of 4,4-Difluoro-1-(2-hydroxy-5-methyl-phenyl)-tridec-2-en-1-one (5c)

The reaction was performed with 4c (0.57 g, 1.49 mmol) according to general procedure. After 20 h, $^{19}$F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the product 5c was isolated as a yellow oil (0.43 g, 86%). Rf = 0.58 (pentane/ether 9/1). $^1$H NMR (CDCl$_3$, 300 MHz), $\delta$ (ppm): 12.18 (s, 1H); 7.56 (d, 1H, $J = 1.4$ Hz); 7.42 (dt, 1H, $J = 15.4$ Hz, $^4$$J_{HF} = 2.3$ Hz); 7.34 (dd, 1H, $J = 8.5$ Hz, $J = 2.2$ Hz); 6.94 (d, 1H, $J = 8.6$ Hz); 6.92 (dt, 1H, $J = 15.4$, $J = 11.6$ Hz); 2.34 (s, 3H); 2.09-1.93 (m, 2H); 1.57-1.45 (m, 2H); 1.29-1.24 (m, 12H); 0.88 (t, 3H, $J = 6.7$ Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ (ppm): 192.9; 161.6; 139.3 (t, $^2$$J_{CF} = 27.3$ Hz); 138.4; 129.7; 128.3; 126.3 (t, $^3$$J_{CF} = 7.8$ Hz); 121.2 (t, $^1$$J_{CF} = 239.9$ Hz); 119.1; 118.5; 37.3 (t, $^2$$J_{CF} = 25.6$ Hz); 31.8; 29.4; 29.3; 29.23; 29.21; 22.6; 22.2 (t, $^3$$J_{CF} = 4.1$ Hz); 20.5; 14.1. $^{19}$F NMR (CDCl$_3$, 282 MHz), $\delta$ (ppm): -98.50 (ddt, $^2$$J_{FH} = 15.9$ Hz, $^3$$J_{FH} = 11.6$ Hz, $^4$$J_{FH} = 1.9$ Hz). HRMS (ESI) calcd for C$_{20}$H$_{28}$O$_2$F$_2$Na$^+$: m/z 361.19551. Found: m/z 361.1955 (0 ppm).

4.4 Synthesis of 1-(3-Bromo-2-hydroxy-phenyl)-4,4-difluoro-tridec-2-en-1-one (5d)

The reaction was performed with 4d (0.38 mg, 0.85 mmol) according to general procedure. After 20 h, $^{19}$F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the enone 5d was isolated as yellow crystals (0.29 mg, 84%). Rf = 0.40 (pentane/ether 95/5). Mp = 46 °C. $^1$H NMR (CDCl$_3$, 300 MHz), $\delta$ (ppm): 13.04 (s, 1H); 7.79 (d, 2H, $J = 8.0$ Hz); 7.41 (dt, 1H, $J = 15.3$ Hz, $^4$$J_{HF} = 2.3$ Hz); 6.97 (dt, 1H, $J = 15.3$ Hz, $^3$$J_{HF} = 11.5$ Hz); 6.87 (t, 1H, $J = 7.9$ Hz); 2.08-1.92 (m, 2H); 1.51-1.43 (m, 2H); 1.33-1.26 (m, 12H); 0.88 (t, 3H, $J = 6.7$ Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ (ppm): 192.9; 160.1; 140.5 (t, $^2$$J_{CF} = 27.4$ Hz); 140.3; 129.3; 125.7 (t, $^3$$J_{CF} = 7.7$ Hz); 121.0 (t, $^1$$J_{CF} = 240.1$ Hz); 120.2; 119.9; 112.4; 37.2 (t, $^2$$J_{CF} = 25.5$ Hz); 31.8; 29.4; 29.3; 29.2 (2C); 22.6; 22.1 (t, $^3$$J_{CF} = 4.2$ Hz); 14.1. $^{19}$F NMR (CDCl$_3$, 282 MHz), $\delta$ (ppm): -98.76 (tdd, 2F, $^2$$J_{FH} = 16.2$ Hz, $^3$$J_{FH} = 11.3$ Hz, $^4$$J_{FH} = 1.7$ Hz). HRMS (ESI) calcd for C$_{19}$H$_{25}$O$_2$F$_2$Br$^+$: m/z 425.09037 Found: m/z 425.0907 (1 ppm).
4.5 Synthesis of 4,4-Difluoro-1-(2-hydroxy-3-methyl-phenyl)-tridec-2-en-1-one (5e)

The reaction was performed with 4e (0.31 g, 0.81 mmol) according to general procedure. After 18 h, $^{19}$F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the product 5e was isolated as yellow crystals (0.23 g, 83%). $R_f = 0.56$ (pentane/ether 9/1). $M_p = 66 \, ^\circ C$. $^1$H NMR (CDCl$_3$, 300 MHz), $\delta$ (ppm): 12.66 (s, 1H); 7.65 (dd, 1H, $J = 8.1$ Hz, $J = 1.5$ Hz); 6.46-6.38 (m, 2H); 6.93 (dt, 1H, $J = 15.4$ Hz, $^3J_{HF} = 11.6$ Hz); 6.85 (dd, 1H, $J = 7.9$ Hz, $J = 7.5$ Hz); 2.28 (s, 3H); 2.08-1.92 (m, 2H); 1.54-1.44 (m, 2H); 1.36-1.26 (m, 12H); 0.88 (t, 3H, $J = 6.7$ Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ (ppm): 193.2; 162.2; 139.2 (t, $^2J_{CF} = 27.2$ Hz); 138.0; 127.8; 127.7; 126.4 (t, $^3J_{CF} = 7.7$ Hz); 121.2 (t, $^1J_{CF} = 239.9$ Hz); 118.7, 118.5; 37.3 (t, $^2J_{CF} = 25.6$ Hz); 31.8; 29.4; 29.3; 29.2 (2C); 22.6; 22.1 (t, $^3J_{CF} = 4.1$ Hz); 15.5; 14.1. $^{19}$F NMR (CDCl$_3$, 282 MHz), $\delta$ (ppm): -98.50 (ddt, 2F, $^2J_{FH} = 16.1$ Hz, $^3J_{FH} = 11.6$ Hz, $^4J_{FH} = 1.9$ Hz). HRMS (ESI) calcd for C$_{20}$H$_{28}$O$_2$F$_2$Na: [M +Na]$^+$: $m/z$ 361.19551. Found: $m/z$ 361.1958 (1 ppm).

4.6 Synthesis of 1-(3,5-Dibromo-2-hydroxy-phenyl)-4,4-difluoro-tridec-2-en-1-one (5f)

The reaction was performed with 4f (0.28 g, 0.53 mmol) according to general procedure. After 20 h, $^{19}$F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the product 5f was isolated as yellow crystals (0.23 g, 89%). $R_f = 0.48$ (pentane/ether 95/5). $M_p = 77 \, ^\circ C$. $^1$H NMR (CDCl$_3$, 300 MHz), $\delta$ (ppm): 12.93; 7.91 (d, 1H, $J = 2.3$ Hz); 7.33 (dt, 1H, $J = 15.3$ Hz, $^4J_{HF} = 2.2$ Hz); 7.33 (dt, 1H, $J = 15.3$ Hz, $^3J_{HF} = 11.4$ Hz); 2.09-1.92 (m, 2H); 1.52-1.43 (m, 2H); 1.37-1.23 (m, 12H); 0.88 (t, 3H, $J = 6.7$ Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ (ppm): 192.0; 159.2; 142.2; 141.8 (t, $^2J_{CF} = 27.4$ Hz); 131.5; 125.1 (t, $^3J_{CF} = 7.7$ Hz); 120.9 (t, $^1J_{CF} = 240.3$ Hz); 120.8; 113.6; 110.7; 37.2 (t, $^2J_{CF} = 25.6$ Hz); 31.8; 29.4; 29.3; 29.2 (2C); 22.6; 22.1 (t, $^3J_{CF} = 3.9$ Hz); 14.1. $^{19}$F NMR (CDCl$_3$, 282 MHz), $\delta$ (ppm): -98.85 (ddt, 2F, $^2J_{FH} = 16.1$ Hz, $^3J_{FH} = 11.4$ Hz, $^4J_{FH} = 1.7$ Hz). HRMS (ESI) calcd for C$_{19}$H$_{24}$O$_2$F$_2$Br$_2$Na: [M +Na]$^+$: $m/z$ 503.00088. Found: $m/z$ 503.0007 (0 ppm).
4.7 Synthesis of 1-(3-Bromo-5-chloro-2-hydroxy-phenyl)-4,4-difluoro-tridec-2-en-1-one (5g)

The reaction was performed with 4g (0.34 g, 0.71 mmol) according to general procedure. After 22 h, $^{19}$F NMR showed 100% conversion. After purification by flash chromatography on silica gel, the product 5g was isolated as yellow crystals (0.28 g, 92%). $R_f = 0.46$ (pentane/ether 95/5). $M_p = 74 \degree C$. $^1$H NMR (CDCl$_3$, 300 MHz), $\delta$ (ppm): 12.91 (s, 1H); 7.79 (d, 1H, $J = 2.5$ Hz); 7.75 (d, 1H, $J = 2.5$ Hz); 7.33 (dt, 1H, $J = 15.3$ Hz, $^4J_{HF} = 2.2$ Hz); 7.00 (dt, 1H, $J = 15.3$ Hz, $^3J_{HF} = 11.4$ Hz); 2.09-1.92 (m, 2H); 1.52-1.33 (m, 2H); 1.32-1.26 (m, 12H); 0.88 (t, 3H, $J = 6.7$ Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ (ppm): 192.1; 158.8; 142.5 (t, $^2J_{CF} = 27.4$ Hz); 139.7; 128.5; 125.1 (t, $^3J_{CF} = 7.7$ Hz); 124.2; 120.9 (t, $^1J_{CF} = 240.3$ Hz); 120.1; 113.2; 37.1 (t, $^2J_{CF} = 25.5$ Hz); 31.8; 29.4; 29.3; 29.21; 29.19; 22.6; 22.1 (t, $^3J_{CF} = 4.1$ Hz); 14.1. $^{19}$F NMR (CDCl$_3$, 282 MHz), $\delta$ (ppm): -98.87 (ddt, 2F, $^2J_{FH} = 16.2$ Hz, $^3J_{FH} = 11.4$ Hz, $^4J_{FH} = 1.7$ Hz). HRMS (ESI) calcd for C$_{19}$H$_{24}$F$_2$O$_2$35Cl 7 9BrNa: [M +Na]$^+$ : $m/z$ 437.7465 Found: $m/z$ 437.7464 (1ppm).

5. General procedure for the synthesis of chromanones with gem-difluorinated side chain (6)

To a solution of enone 5 in THF, potassium carbonate (powder, 4 equiv) was added, and the mixture was stirred at 35$\degree$C for appropriate time (monitored by $^{19}$F NMR). After completion of the reaction, water was added and the two phases were separated. The aqueous phase was extracted with ether, and the combined organic phase was washed with water, dried over Na$_2$SO$_4$, concentrated under vacuo. The product was then purified by chromatography on silica gel (pentane/ether).

5.1 Synthesis of 2-(1,1-Difluoro-decyl)-chroman-4-one (6a)

The reaction was performed with enone 5a (0.12 g, 0.37 mmol) in THF (7 mL) according to the general procedure. After 18 h, $^{19}$F NMR shows 100% conversion. After purification by chromatography on silica gel, the product was obtained as white crystals (0.09 g, 76%). $R_f = 0.35$ (pentane/ether 95/5). $M_p = 62 \degree C$. $^1$H NMR (CDCl$_3$, 400 MHz), $\delta$ (ppm): 7.90 (dd, 1H, $J = 7.8$ Hz, $J = 1.5$ Hz); 7.51 (ddd, 1H, $J = 8.4$ Hz, $J = 7.2$ Hz $J = 1.8$ Hz ); 7.07 (ddd, 1H, $J = 8.2$ Hz, $J = 7.2$ Hz $J = 1.0$ Hz); 7.03 (dd, 1H, $J = 8.4$ Hz, $J = 1.0$ Hz); 4.62-4.53 (m, 1H), 2.99 (dd, 1H, $J = 16.9$ Hz, $J = 12.8$ Hz); 2.85 (ddd, 1H, $J = 16.9$ Hz, $J = 3.4$ Hz, $^4J_{HF} = 0.7$ Hz);
2.16-2.02 (m, 2H), 1.61-1.53 (m, 2H); 1.39-1.26 (m, 12H); 0.89 (t, 3H, J = 6.8 Hz). 13C NMR (CDCl3, 125 MHz) δ (ppm): 190.5; 160.1; 136.3; 127.0; 122.2; 121.8 (dd, 1JCF = 247.4 Hz, 1JCF = 241.4 Hz), 120.9; 117.8; 77.3 (dd, 2JCF = 36.5 Hz, 2JCF = 29.3 Hz), 36.1 (t, 3JCF = 2.5 Hz), 33.0 (t, 2JCF = 23.7 Hz); 31.8; 29.4; 29.3 (2C); 29.2; 22.7; 21.4 (dd, 3JCF = 5.4 Hz, 3JCF = 3.2 Hz); 14.1. 19F NMR (CDCl3, 282 MHz), δ (ppm): -110.88 (AB system, 2F, 2JFF = 254.8 Hz). HRMS (ESI) calcd for C19H26O2F2Na: [M+Na]+: m/z 347.17986. Found: m/z 347.1802 (1 ppm).

5.2 Synthesis of 6-Bromo-2-(1,1-difluoro-decyl)-chroman-4-one (6b)

The reaction was performed with enone 5b (0.10 g, 0.24 mmol) in 6 mL of THF according to the general procedure. After 4 h, 19F NMR shows 100% conversion. After purification by chromatography on silica gel, the product was obtained as white crystals (0.09 g, 93%). Rf = 0.29 (pentane/ether 95/5). Mp = 78 °C. 1H NMR (CDCl3, 400 MHz), δ (ppm): 8.00 (d, 1H, J = 2.5 Hz); 7.59 (dd, 1H, J = 8.8 Hz, J = 2.5 Hz); 6.94 (d, 1H, J = 8.8 Hz), 4.60-5.51 (m, 1H), 2.97 (dd, 1H, J = 17.0 Hz, J = 12.4 Hz); 2.86 (ddd, 1H, J = 17.0 Hz, J = 3.6 Hz, JHF = 0.6 Hz), 2.14-2.00 (m, 2H), 1.60-1.52 (m, 2H); 1.35-1.25 (m, 12H), 0.89 (t, 3H, J = 6.9 Hz). 13C NMR (CDCl3, 125 MHz) δ (ppm): 189.2; 158.9; 138.9; 129.5; 122.1; 121.6 (dd, 1JCF = 248.0 Hz, 1JCF = 241.8 Hz), 119.8; 114.9; 77.1 (dd, 2JCF = 36.7 Hz, 2JCF = 29.2 Hz), 35.7 (t, 3JCF = 2.6 Hz); 33.0 (t, 2JCF = 23.7 Hz), 31.8; 29.4; 29.31; 29.28; 29.24; 22.6; 21.3 (dd, 3JCF = 5.0 Hz, 3JCF = 3.0 Hz); 14.1. 19F NMR (CDCl3, 282 MHz) δ (ppm): -110.74 (AB system, 2F, JFF = 255.4 Hz). HRMS (ESI) calcd for C19H25O2F279BrNa: [M+Na]+: m/z 425.09037. Found: m/z 425.0906 (0 ppm).

5.3 Synthesis of 2-(1,1-Difluoro-decyl)-6-methyl-chroman-4-one (6c)

The reaction was performed with enone 5c (0.14 g, 0.41 mmol) in THF (8 mL) according to the general procedure. After 24 h, 19F NMR shows 100% conversion. After purification by chromatography on silica gel, the product was obtained as white crystals (0.11 g, 82%). Rf = 0.34 (pentane/ether 95/5). Mp = 82 °C. 1H NMR (CDCl3, 400 MHz), δ (ppm): 7.68 (d, 1H, J = 2.3 Hz); 7.32 (ddd, 1H, J = 8.4 Hz, J = 2.3 Hz, J = 0.5 Hz), 6.92 (d, 1H, J = 8.4 Hz), 4.59-5.46 (m, 1H), 2.96 (dd, 1H, J = 17.0 Hz, J = 12.6 Hz), 2.81 (ddd, 1H, J = 17.0 Hz, J = 3.5 Hz, JHF = 0.7 Hz), 2.32 (s, 3H), 2.17-1.98 (m, 2H); 1.61-1.51 (m, 2H); 1.37-1.25 (m, 12H), 0.88 (t, 3H, J = 6.7 Hz). 13C NMR (CDCl3, 125 MHz) δ (ppm): 190.7; 158.2; 137.3; 131.7; 126.6; 121.9
(dd, $^1J_{CF} = 247.9$ Hz, $^1J_{CF} = 241.7$ Hz); 120.5; 117.6; 77.1 (t, $^2J_{CF} = 26.2$ Hz); 36.1 (t, $^3J_{CF} = 2.1$ Hz); 33.0 (t, $^2J_{CF} = 23.7$ Hz); 31.9; 29.4; 29.3 (2C); 29.2; 22.7; 21.4 (dd, $^3J_{CF} = 5.0$ Hz, $^3J_{CF} = 3.2$ Hz); 20.4; 14.1. $^{19}$F NMR (CDCl$_3$, 282 MHz), δ (ppm): -110.85 (AB system, 2F, $^2J_{FF} = 254.4$ Hz). HRMS (ESI) calcd for C$_{20}$H$_{28}$O$_2$F$_2$Na: [M +Na]$^+$ : m/z 361.19551. Found: m/z 361.1953 (1 ppm).

5.4 Synthesis of 8-Bromo-2-(1,1-difluoro-decyl)-chroman-4-one (6d)

The reaction was performed with enone 5d (0.18 g, 0.45 mmol) in THF (8 mL) according to the general procedure. After 5 h, $^{19}$F NMR shows 100% conversion. After purification by chromatography on silica gel, the product was obtained as white crystals (0.15 g, 81%). R$_f$ = 0.31 (pentane/ether 95/5). Mp = 73 °C. $^1$H NMR (CDCl$_3$, 300 MHz), δ (ppm): 7.85 (dd, 1H, $^1J = 7.8$ Hz, $^1J = 1.6$ Hz); 7.75 (dd, 1H, $^1J = 7.8$ Hz, $^1J = 1.6$ Hz); 6.97 (t, 1H, $^1J = 7.8$ Hz); 2.89 (dd, 1H, $^1J = 17.1$ Hz, $^1J = 3.7$ Hz); 2.26-2.08 (m, 2H); 1.63-1.53 (m, 2H); 1.40-1.27 (m, 12H); 0.88 (t, 3H, $^1J = 6.8$ Hz). $^{13}$C NMR (CDCl$_3$, 125 MHz) δ (ppm): 189.7; 156.5; 139.4; 126.3; 122.9; 122.1; 121.1 (dd, $^1J_{CF} = 246.0$ Hz, $^1J_{CF} = 243.7$ Hz); 111.7; 77.1 (t, $^2J_{CF} = 35.2$ Hz, $^2J_{CF} = 32.3$ Hz); 35.5 (t, $^3J_{CF} = 2.7$ Hz); 33.4 (t, $^2J_{CF} = 23.4$ Hz); 14.1. $^{19}$F NMR (CDCl$_3$, 282 MHz), δ (ppm): -110.47 (AB system, 2F, $^2J_{FF} = 254.7$ Hz). HRMS (ESI) calcd for C$_{19}$H$_{25}$O$_2$F$_2$Na$^{79}$Br Na: [M +Na]$^+$ : m/z 425.09037. Found: m/z 425.0908 (1 ppm).

5.5 Synthesis of 2-(1,1-Difluoro-decyl)-8-methyl-chroman-4-one (6e)

The reaction was performed with enone 5e (0.130 g, 0.38 mmol) in THF (8 mL) according to the general procedure. After 24 h, $^{19}$F NMR shows 100% conversion. After purification by chromatography on silica gel, the product was obtained as white crystals (0.10 g, 78%). R$_f$ = 0.32 (pentane/ether 95/5). Mp = 66 °C. $^1$H NMR (CDCl$_3$, 400 MHz), δ (ppm): 7.75 (ddd, 1H, $^1J = 7.9$ Hz, $^1J = 1.7$ Hz, $^1J = 0.5$ Hz); 7.37 (ddd, 1H, $^1J = 7.9$ Hz, $^1J = 7.3$ Hz, $^1J = 0.5$ Hz); 6.97 (t, 1H, $^1J = 7.9$ Hz); 4.60-4.51 (m, 1H); 2.98 (dd, 1H, $^1J = 16.9$ Hz, $^1J = 13.0$ Hz); 2.83 (ddd, 1H, $^1J = 16.9$ Hz, $^1J = 3.2$ Hz, $^4J_{HF} = 0.7$ Hz); 2.26 (s, 3H); 2.18-2.05 (m, 2H); 1.60-1.53 (m, 2H); 1.38-1.27 (m, 12H); 0.88 (t, 3H, $^1J = 6.8$ Hz). $^{13}$C NMR (CDCl$_3$, 125 MHz) δ (ppm): 190.6; 158.3; 137.1; 127.0; 124.6; 121.9 (dd, $^1J_{CF} = 247.5$ Hz, $^1J_{CF} = 241.5$ Hz); 121.6; 120.6; 76.8 (dd, $^2J_{CF} = 36.4$ Hz, $^2J_{CF} = 29.6$ Hz); 35.9 (t, $^3J_{CF} = 2.3$ Hz), 33.0 (t, $^2J_{CF} = 23.7$ Hz).
Hz); 31.8; 29.4 (2C); 29.3; 29.2; 22.7; 21.6 (dd, $^3\text{J}_{\text{CF}} = 5.3$ Hz, $^3\text{J}_{\text{CF}} = 3.2$ Hz); 15.5; 14.1. $^{19}$F NMR (CDCl$_3$, 282 MHz), $\delta$ (ppm): -110.75 (AB system, 2F, $^2\text{J}_{\text{FF}} = 254.3$ Hz). HRMS (ESI) calcd for C$_{20}$H$_{28}$O$_2$F$_2$ Na: [M + Na]$^+$ : m/z 361.19551. Found: m/z 361.1954 (0 ppm).

5.6 Synthesis of 6,8-Dibromo-2-(1,1-difluoro-decyl)-chroman-4-one (6f)

The reaction was performed with enone 5f (0.17 g, 0.35 mmol) in THF (9 mL) according to the general procedure. After 3 h, $^{19}$F NMR shows 100% conversion. After purification by chromatography on silica gel, the product was obtained as white crystals (0.15 g, 86%). $R_f = 0.38$ (pentane/ether 95/5). $\text{Mp} = 76^\circ \text{C}$. $^1$H NMR (C$_6$D$_6$, 300 MHz), $\delta$ (ppm): 7.97 (d, 1H, $J = 2.4$ Hz); 7.40 (d, 1H, $J = 2.4$ Hz); 3.76-3.64 (m, 1H); 2.49 (dd, 1H, $J = 17.0$ Hz, $J = 11.2$ Hz); 2.40 (ddd, 1H, $J = 17.0$ Hz, $J = 5.3$ Hz, $^3\text{J}_{\text{HF}} = 0.5$ Hz); 2.05-1.78 (m, 2H); 1.49-1.36 (m, 2H); 1.34-1.24 (m, 12H); 0.92 (t, 3H, $J = 6.7$ Hz). $^{13}$C NMR (C$_6$D$_6$, 75 MHz) $\delta$ (ppm): 187.1; 155.5; 140.8; 129.0; 123.2; 121.9 (dd, $^1\text{J}_{\text{CF}} = 248.0$ Hz, $^1\text{J}_{\text{CF}} = 242.0$ Hz); 114.9; 112.9; 77.4 (dd, $^2\text{J}_{\text{CF}} = 37.4$ Hz, $^2\text{J}_{\text{CF}} = 29.9$ Hz); 35.0; 33.5 (t, $^3\text{J}_{\text{CF}} = 23.5$ Hz); 32.2; 29.8; 29.7 (2C); 23.1 (dd, $^3\text{J}_{\text{CF}} = 5.3$ Hz, $^3\text{J}_{\text{CF}} = 3.0$ Hz); $^{13}$C NMR (d$_6$ acetone, 75 MHz) $\delta$ (ppm): 189.7; 157.7; 142.5; 130.2; 125.2; 124.2 (dd, $^1\text{J}_{\text{CF}} = 248.4$ Hz, $^1\text{J}_{\text{CF}} = 243.9$ Hz); 115.8; 114.5; 79.2 (dd, $^2\text{J}_{\text{CF}} = 33.6$ Hz, $^2\text{J}_{\text{CF}} = 31.9$ Hz); 36.8 (t, $^3\text{J}_{\text{CF}} = 2.7$ Hz); 35.0 (t, $^2\text{J}_{\text{CF}} = 23.5$ Hz); 33.6; 31.1; 31.0 (2C); 30.9; 24.3; 23.3 (dd, $^3\text{J}_{\text{CF}} = 5.3$ Hz, $^3\text{J}_{\text{CF}} = 3.0$ Hz); 15.3. $^{19}$F NMR (C$_6$D$_6$, 282 MHz) $\delta$ (ppm): -110.42 (AB system, 2F, $^2\text{J}_{\text{FF}} = 255.2$ Hz). HRMS (ESI) calcd for C$_{19}$H$_{24}$O$_2$F$_2$Br$_2$Na: [M + Na]$^+$ : m/z 503.00088. Found: m/z 503.0009 (0 ppm).

5.7 Synthesis of 8-Bromo-6-chloro-2-(1,1-difluoro-decyl)-chroman-4-one (6g)

The reaction was performed with enone 5g (0.12 g, 0.27 mmol) in THF (7 mL) according to the general procedure. After 6 h, $^{19}$F NMR shows 100% conversion. After purification by chromatography on silica gel, the product was obtained as white crystals (0.10 g, 83%). $R_f = 0.35$ (pentane/ether 95/5). $\text{Mp} = 77^\circ \text{C}$. $^1$H NMR (C$_6$D$_6$, 300 MHz), $\delta$ (ppm): 7.81 (d, 1H, $J = 2.5$ Hz); 7.24 (d, 1H, $J = 2.5$ Hz); 3.77-3.64 (m, 1H); 2.49 (dd, 1H, $J = 17.0$ Hz, $J = 11.2$ Hz); 2.41 (ddd, 1H, $J = 17.0$ Hz, $J = 5.3$ Hz, $^4\text{J}_{\text{HF}} = 0.3$ Hz); 2.03-1.83 (m, 2H); 1.49-1.40 (m, 2H); 1.34-1.21 (m, 12H); 0.92 (t, 3H, $J = 6.7$ Hz). $^{13}$C NMR (C$_6$D$_6$, 75 MHz) $\delta$ (ppm): 187.2; 155.1; 138.2; 125.9; 122.7; 121.9 (dd, $^1\text{J}_{\text{CF}} = 247.4$ Hz, $^1\text{J}_{\text{CF}} = 242.4$ Hz); 112.6; 77.4 (dd, $^2\text{J}_{\text{CF}} = 36.8$ Hz, $^2\text{J}_{\text{CF}} = 30.4$ Hz); 35.1 (t, $^3\text{J}_{\text{CF}} = 2.4$ Hz); 33.5 (t, $^2\text{J}_{\text{CF}} = 23.5$ Hz); 32.3; 29.8; 29.7 (2C); 23.1; 21.9 (dd, $^3\text{J}_{\text{CF}} = 5.3$ Hz, $^3\text{J}_{\text{CF}} = 3.7$ Hz); 14.3. $^{13}$C NMR (d$_6$ acetone, 75 MHz) $\delta$ (ppm):
189.8; 157.3; 139.9; 129.0; 127.0; 124.7; 124.2 (t, $^1\text{J}_{CF} = 244.2$ Hz); 114.2; 79.2 (dd, $^2\text{J}_{CF} = 33.4$ Hz, $^3\text{J}_{CF} = 32.3$ Hz); 36.7 (t, $^3\text{J}_{CF} = 2.4$ Hz); 34.9 (t, $^2\text{J}_{CF} = 23.4$ Hz); 33.6; 31.1; 24.3; 23.3 (t, $^3\text{J}_{CF} = 4.6$ Hz); 15.3. $^{19}$F NMR (CDCl$_3$, 282 MHz) $\delta$ (ppm): -110.42 (AB system, 2F, $^2\text{J}_{FF} = 255.1$ Hz). HRMS (ESI) calcd for C$_{19}$H$_{24}$O$_2$F$_2$Cl$_{79}$Br Na: [M + Na]$^+$ $m/z$ 437.7465. Found: $m/z$ 437.7464 (0 ppm).