Fluorinated cyclopropanes: Synthesis and chemistry of the aryl α,β,β-trifluorocyclopropane motif

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Contents
General information .............................................................................................................................. 1
General synthetic procedures and analytical data .................................................................................. 2
References ........................................................................................................................................... 13
NMR spectra of new compounds ........................................................................................................ 14
Figure S1: Comparison of $^1$H NMR of 25 in CDCl$_3$ and MeOD ......................................................... 46
Figure S2: Comparison of $^{19}$F NMR of 25 in CDCl$_3$ and MeOD ......................................................... 46
Scheme S1: Enolisation responsible for H/D exchange of 25 in MeOD .................................................... 47
DFP computations for 11a ...................................................................................................................... 48
Figure S3: Rotational profiles about the C(F)-C(=C) bond in 11a (B3LYP/6-311+G** level) .............. 48
Figure S4: Electrostatic potential of rotamer bis of 11a at the B3LYP/6-311+G** level ................. 48
Coordinates of the DFT-optimised structures for 11a .......................................................................... 49
DFT Computations for 19b through a truncated model 20 .............................................................. 50
Table S1: Computed properties of the model amide 20 (the truncated model of 19b) ....... 50
Coordinates of the DFT-optimised structures for amide 20 (the truncated model of 19b) ....... 50

General information
All reactions involving air- or moisture-sensitive reagents or intermediates were carried out in oven-dried glassware or PTFE flask under an atmosphere of argon. Styrenes 8c and 8d were prepared by Wittig olefination of benzaldehydes. THF, DCM, Et$_2$O and toluene were dried and deoxygenated using a MBraun SPS-800 solvent system. $^1$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra were recorded on a Bruker AV 300, Bruker AV 400, Bruker AVII 400, Bruker AVIII-HD 500 or Bruker AVIII 500 instrument. CDCl$_3$, MeOD, DMSO-d$_6$ or toluene-d$_8$ were used as solvents. Chemical shifts are reported in parts per million (ppm). Tetramethylsilane (δ 0 ppm) functioned as an external standard for $^1$H and $^{13}$C NMR experiments. CFCl$_3$ was used as an external standard for $^{19}$F NMR experiments. Where appropriate, solvent signals were used as internal standard for calibration. Coupling constants (J) are reported in Hertz (Hz). High resolution mass spectra were recorded on a Waters Micromass GCT time of flight mass spectrometer or on a Thermo Scientific Exactive orbitrap mass spectrometer by internal mass spectroscopy service or on a Waters Xevo G2-S by the EPSRC UK National Mass Spectrometry Facility at Swansea University, UK.
General Synthetic Procedures and Analytical Data

General procedure A for fluorobromination of styrenes 9a-9f

A flame-dried round-bottomed flask equipped with a magnetic stir bar was charged with NBS (1.50 equiv). The reaction vessel was sealed, then evacuated and backfilled with nitrogen. Anhydrous CH$_2$Cl$_2$ and the appropriate styrene (1.00 equiv) were added sequentially via syringe. The resulting suspension was cooled to 0 °C and stirred for 30 minutes, followed by addition of NEt$_3$,3HF via syringe. The reaction mixture was warmed to RT, and then stirred for 18 h. After completion, the reaction was quenched with a 28% aqueous solution of NH$_3$ and stirred for 10 minutes. The resulting solution was extracted with CH$_2$Cl$_2$ (3 x 50 mL) and the combined organic phases were washed sequentially with aqueous dilute HCl (0.1 M, 50 mL) and a saturated aqueous solution of NaHCO$_3$ (50 mL), followed by drying over Na$_2$SO$_4$. After filtration, solvent was removed in vacuo.

Purification by flash column chromatography (petroleum ether/CH$_2$Cl$_2$) afforded the appropriate (2-bromo-1-fluoroethyl)benzenes (9a-9f).

(2-Bromo-1-fluoroethyl)benzene (9a) was prepared following general procedure A, using styrene (8a) (5.00 g, 48.0 mmol, 1.0 equiv), N-bromosuccinimide (9.56 g, 52.8 mmol, 1.5 equiv), and NEt$_3$,HF (11.76 mL, 72.00 mmol, 1.5 equiv) in CH$_2$Cl$_2$ (80 mL). The product was obtained by flash column chromatography (silica gel, 100% petroleum ether) as a colourless oil (7.209 g, 74%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$H 7.45-7.36 (5H, m, Ar-CH), 5.64 (1H, ddd, $^2J_{HF} = 46.8$, $^3J_{HF} = 7.9$, 4.1 Hz, CHF), 3.74-3.57 (2H, m, CH$_2$Br); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$C 137.1 (d, $^1J_{CF} = 20.3$ Hz, Ar-CH), 129.3 (d, $^1J_{CF} = 1.4$ Hz, Ar-CH), 128.8 (2 x Ar-CH), 125.7 (d, $^1J_{CF} = 6.6$ Hz, 2 x Ar-CH), 92.8 (d, $J = 177.9$ Hz, CHF$_2$), 34.3 (d, $J = 28.4$ Hz, CH$_2$Br);$^{19}$F NMR (400 MHz, CDCl$_3$) $\delta$F -174.9 (ddd, $^2J_{HF} = 46.8$ Hz, $^3J_{HF} = 25.2$, 15.9 Hz, CHF).

1-Bromo-4-(2-bromo-1-fluoroethyl)benzene (9b) was prepared following general procedure A, using 1-bromo-4-vinylbenzene (8b) (6.00 g, 32.78 mmol, 1.00 equiv), N-bromosuccinimide (8.90 g, 49.17 mmol, 1.50 equiv), and NEt$_3$,HF (8.02 mL, 49.17 mmol, 1.50 equiv) in CH$_2$Cl$_2$ (40 mL). The product was obtained by flash column chromatography (silica gel, 95% petroleum ether/5% CH$_2$Cl$_2$) as a colourless oil (6.15 g, 67%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$H 7.89 (2H, d, $J = 8.4$ Hz, Ar-CH), 7.58 (2H, d, $J = 8.4$ Hz, Ar-CH), 5.93 (1H, ddd, $^2J_{HF} = 46.6$, $^3J_{HF} = 7.4$, 4.5 Hz, CHF), 4.03-3.89 (2H, m, CH$_2$Br);$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$C 131.92 (2 x Ar-CH), 123.6 (Ar-CH), 92.0 (d, $^1J_{CF} = 178.8$ Hz, CHF$_2$), 33.8 (d, $^1J_{CF} = 28.7$ Hz, CH$_2$Br);$^{19}$F NMR (471 MHz, CDCl$_3$) $\delta$F -174.1 (ddd, $^2J_{HF} = 46.6$ Hz, $^3J_{HF} = 24.1$, 16.5 Hz, CHF$_2$); HRMS (APPI) 281.8875 [M]$^+$, C$_{6}$H$_{7}$Br$_{2}$F requires 281.8878.

1-(2-Bromo-1-fluoroethyl)-4-fluorobenzene (9c) was prepared following general procedure A, using 1-fluoro-4-vinylbenzene (8c) (1.00 g, 8.19 mmol, 1.00 equiv), N-bromosuccinimide (2.22 g, 12.29 mmol, 1.50 equiv), and NEt$_3$,HF (2.00 mL, 12.29 mmol, 1.50 equiv) in CH$_2$Cl$_2$ (20 mL). The product was obtained by flash column chromatography (silica gel, 90% petroleum ether/10% CH$_2$Cl$_2$) as a colourless oil (1.279 g, 71%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$H 7.38 – 7.31 (2H, m, Ar-CH), 7.17 – 7.06 (2H, m, Ar-CH), 5.61 (1H, ddd, $^2J_{HF} = 46.4$, $^3J_{HF} = 7.6$, 4.4 Hz, CHF), 3.87 – 3.41 (2H, m, CH$_2$Br);$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$C
163.1 (d, $^1J_{CF} = 248.2$ Hz, Ar-$\text{CF}$), 133.0 (dd, $^3J_{CF} = 20.8$ Hz, $^2J_{CF} = 3.4$ Hz, Ar-$\text{CF}$), 127.8 (dd, $^3J_{CF} = 6.9$, 7.8 Hz, 2 x Ar-$\text{CF}$), 115.8 (d, $^2J_{CF} = 21.8$ Hz, 2 x Ar-$\text{CF}$), 92.1 (d, $^1J_{CF} = 178.0$ Hz, CH$_F$), 34.1 (d, $^2J_{CF} = 29.0$ Hz, CH$_{Br}$); $^{19}$F NMR (471 MHz, CDCl$_3$) $\delta_{F} = -111.9$ to $-111.9$ (m, Ar-$F$), $-171.6$ (dd, $^2J_{HF} = 46.4$ Hz, $^3J_{HF} = 24.5, 15.0$ Hz, CH$_F$).

4-(2-Bromo-1-fluoroethyl)-1,1'-biphenyl (9d) was prepared following general procedure A, using 1-vinyl-1,1'-biphenyl (8d) (1.00 g, 5.55 mmol, 1.00 equiv), N-bromosuccinimide (1.51 g, 8.32 mmol, 1.50 equiv), and NEt$_3$/HF (1.36 mL, 8.32 mmol, 1.50 equiv) in CH$_2$Cl$_2$ (10 mL). The product was obtained by flash column chromatography (silica gel, 95% petroleum ether/5% CH$_2$Cl$_2$ as a colourless solid (1.23 g, 80%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta_{H} = 7.64-7.37$ (9H, m, Ar-$\text{CH}$), 5.68 (1H, dd, $^2J_{HF} = 46.5$ Hz, $^3J_{HH} = 7.9$, 4.1 Hz, CH$_F$), 4.77-3.61 (2H, m, CH$_{Br}$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta_{C} = 142.2$ (Ar-$\text{C}$), 140.3 (Ar-$\text{C}$), 136.0 (Ar-$\text{C}$, d, $^2J_{CF} = 20.3$ Hz), 128.9 (2 x Ar-$\text{CH}$), 127.7 (Ar-$\text{CH}$), 127.5 (2 x Ar-$\text{CH}$), 127.1 (2 x Ar-$\text{CH}$), 126.2 (d, $^3J_{CF} = 6.5$ Hz, 2 x Ar-$\text{CH}$), 92.6 (d, $^1J_{CF} = 177.9$ Hz, CH$_F$), 34.2 (d, $^2J_{CF} = 28.6$ Hz, CH$_{Br}$); $^{19}$F NMR (471 MHz, CDCl$_3$) $\delta_{F} = -176.6$ (dd, $^2J_{HF} = 46.5$ Hz, $^3J_{HF} = 25.8, 15.3$ Hz, CH$_F$), HRMS (ASAP$^+$) 261.0102 [M-F]$^+$, C$_4$H$_{12}$Br requires 261.0102.

1-(2-Bromo-1-fluoroethyl)-4-nitrobenzene (9f) and 1-(1-bromo-2-fluoroethyl)-4-nitrobenzene (9f') were prepared following general procedure A (except for the use of HF-pyridine), using 1-nitro-4-vinylbenzene (8f) (0.25 g, 1.83 mmol, 1.00 equiv), N-bromosuccinimide (0.495 g, 2.78 mmol, 1.50 equiv), and HF-pyridine (0.050 mL, 2.78 mmol, 1.50 equiv) in CH$_2$Cl$_2$ (7 mL). The crude product was purified by flash column chromatography (silica gel, 70% petroleum ether/30% CH$_2$Cl$_2$) to afford the title compounds 9f and 9f' as a light yellow oil (0.483 g) and a light yellow oil (0.046 g), respectively (overall 39%).

9f: $^1$H NMR (400 MHz, CDCl$_3$) $\delta_{H} = 8.28$ (2H, d, $^3J_{HH} = 8.6$ Hz, Ar-$\text{CH}$), 7.56 (2H, d, $^3J_{HH} = 8.6$ Hz, Ar-$\text{CH}$), 5.76 (1H, dt, $^2J_{HF} = 46.6$ Hz, $^3J_{HH} = 5.6$ Hz, CH$_F$), 3.72-3.65 (2H, m, CH$_{Br}$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta_{C} = 148.3$ (Ar-$\text{C}$), 143.9 (d, $^2J_{CF} = 20.8$ Hz, Ar-$\text{C}$), 126.7 (d, $^1J_{CF} = 7.4$ Hz, 2 x Ar-$\text{CH}$), 124.0 (2 x Ar-$\text{CH}$), 91.2 (d, $^1J_{CF} = 180.9$ Hz, CH$_F$), 133.4 (d, $^2J_{CF} = 27.4$ Hz, CH$_{Br}$). $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta_{F} = -176.94$ (dt, $^2J_{HF} = 46.6$ Hz, $^3J_{HF} = 19.7$ Hz, CH$_F$). 9f': $^1$H NMR (400 MHz, CDCl$_3$) $\delta_{H} = 8.26-8.20$ (2H, m, Ar-$\text{CH}$), 7.62-7.59 (2H, m, Ar-$\text{CH}$), 5.07 (1H, m, CH$_{Br}$), 3.60-3.49 (2H, m, CH$_F$); $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta_{F} = -150.8$ to $-150.9$ (m, CH$_F$). HRMS (EI$^+$) 248.9624 [M]$^+$, C$_8$H$_{10}$NO$_2$Br requires 248.9624.

General Procedure B for Synthesis of Vinyl Fluorides 10a-10f.$^2$

A flame-dried round-bottomed flask equipped with a magnetic stir bar was charged with potassium tert-butoxide (1.15-3.00 equiv). The reaction vessel was sealed, then evacuated and backfilled with nitrogen. Anhydrous THF was added via syringe after cooling the resulting suspension to 0°C. After stirring at this temperature for 15 minutes, the appropriate fluorobromoethane 9a-9f (1.00 equiv) was added via syringe. The resulting suspension was allowed to warm to RT, and then stirred for 18 h. After completion, the reaction mixture was filtered and solvent removed in vacuo. Purification by flash column chromatography (petroleum ether/5% MeOH) afforded the products.
ether/CH$_2$Cl$_2$ afforded the appropriate vinyl fluoride.

**1-Fluorovinyl)benzene (10a)** was prepared following general procedure B, using (2-bromo-1-fluoroethyl)benzene (9a) (5.00 g, 24.60 mmol, 1.00 eq), potassium tert-butoxide (4.12 g, 36.19 mmol, 1.50 eq) and THF (30 ml). The product was obtained by flash column chromatography (silica gel, 100% petroleum ether) as a colourless oil (1.506 g, 59%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$H 7.61-6.54 (2H, m, Ar-CH), 7.41-7.34 (3H, m, Ar-CH), 5.04 (1H, dd, J$_{HF}$ = 49.8 Hz, J$_{HH}$ = 3.5 Hz, CH$_2$N transH$_{cis}$), 4.86 (1H, dd, $^3$J$_{HF(cis)}$ = 17.3 Hz, $^2$J$_{HH}$ = 3.5 Hz, CH$_2$N transH$_{cis}$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$C 162.9 (d, J$_{CF}$ = 250.5 Hz, CF), 132.0 (d, J$_{CF}$ = 29.2 Hz, Ar-C), 129.4 (Ar-CH), 128.5 (2 x Ar-CH), 124.6 (d, $^3$J$_{CF}$ = 7.1 Hz, 2 x Ar-CH), 89.6 (d, $^2$J$_{CF}$ = 22.6 Hz, CH$_2$); $^{19}$F NMR (471 MHz, CDCl$_3$) $\delta$F -107.9 (dd, $^3$J$_{HF(trans)}$ = 49.8 Hz, $^3$J$_{HF(cis)}$ = 17.3 Hz, CF).

**1-Bromo-4-(1-Fluorovinyl)benzene (10b)** was prepared following general procedure B, using 1-bromo-4-(2-bromo-1-fluoroethyl)benzene (9b) (2.70 g, 9.65 mmol, 1.00 equiv), potassium tert-butoxide (1.25 g, 11.10 mmol, 1.15 equiv) and THF (25 ml). The product was obtained by flash column chromatography (silica gel, 95% petroleum ether/5% CH$_2$Cl$_2$) as a colourless oil (0.459 g, 70%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$H 7.54-7.49 (2H, m, Ar-CH), 7.43-7.40 (2H, m, Ar-CH), 5.04 (1H, dd, $^3$J$_{HF(trans)}$ = 49.4 Hz, $^2$J$_{HH}$ = 3.7 Hz, CH$_2$N transH$_{trans}$), 4.88 (1H, dd, $^3$J$_{HF(cis)}$ = 17.7 Hz, $^2$J$_{HH}$ = 3.7 Hz, CH$_2$N transH$_{trans}$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$C 162.0 (d, J$_{CF}$ = 250.3 Hz, CF), 131.9 (Ar-C) 130.9 (Ar-C) 131.7 (2 x Ar-CH), 126.2 (d, $^3$J$_{CF}$ = 7.1 Hz, 2 x Ar-CH), 90.5 (d, $^2$J$_{CF}$ = 22.1 Hz, CH$_2$); $^{19}$F NMR (471 MHz, CDCl$_3$) $\delta$F -108.0 (dd, $^3$J$_{HF(trans)}$ = 49.4 Hz, $^3$J$_{HF(cis)}$ = 17.7 Hz, CF).

**Fluoro-4-(1-Fluorovinyl)benzene (10c)** was prepared following general procedure B, using 1-(2-bromo-1-fluoroethyl)-4-fluorobenzene (9c) (3.00 g, 13.59 mmol, 1.00 equiv), potassium tert-butoxide (1.91 g, 16.98 mmol, 1.25 equiv) and THF (50 ml). The product was obtained by flash column chromatography (silica gel, 90% petroleum ether/10% CH$_2$Cl$_2$) to afford the title compound (10c) as a colourless solid (1.408 g, 74%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$H 7.59-7.51 (2H, m, Ar-CH), 7.10-7.03 (2H, m, Ar-CH), 4.96 (1H, dd, $^3$J$_{HF(trans)}$ = 49.7 Hz, $^2$J$_{HH}$ = 3.6 Hz, CH$_2$N transH$_{trans}$), 5.10 (1H, dd, $^3$J$_{HF(cis)}$ = 17.9 Hz, $^2$J$_{HH}$ = 3.6 Hz, CH$_2$N transH$_{trans}$); $^{19}$F NMR (471 MHz, CDCl$_3$) $\delta$F -107.03 (dd, $^3$J$_{HF(trans)}$ = 49.7 Hz, $^3$J$_{HF(cis)}$ = 17.9 Hz, CF), -111.5 (m, Ar-$F$).

**4-(1-Fluorovinyl)-1,1'-biphenyl (10d)** was prepared following general procedure B, using 4-(2-bromo-1-fluoroethyl)-1,1'-biphenyl (9d) (0.80 g, 2.87 mmol, 1.00 equiv), potassium tert-butoxide (0.371 g, 3.31 mmol, 1.15 equiv) and THF (10 ml). The product was obtained by flash column chromatography (silica gel, 95% petroleum ether/5% CH$_2$Cl$_2$) as a colourless solid (0.387 g, 68%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$H 7.67-7.62 (6H, m, Ar-CH), 7.46-7.50 (2H, m, Ar-CH), 7.38-7.41 (1H, m, Ar-CH), 5.08 (1H, dd, $^3$J$_{HF(trans)}$ = 49.7 Hz, $^2$J$_{HH}$ = 3.5 Hz, CH$_2$N transH$_{trans}$), 4.89 (1H, dd, $^3$J$_{HF(cis)}$ = 17.9 Hz, $^2$J$_{HH}$ = 3.5 Hz, CH$_2$N transH$_{trans}$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$C 162.8 (d, J$_{CF}$ = 250.0 Hz, CF), 142.1 (Ar-C), 140.3 (Ar-C), 130.9 (Ar-C), 128.9 (2 x Ar-CH), 127.7 (Ar-CH), 127.2 (2 x Ar-CH), 127.1 (2 x Ar-CH), 125.1 (d, J$_{CF}$ = 6.9 Hz, 2 x Ar-CH), 89.6
evaporation of solvent mixture was allowed to cool to RT and solvent was removed sequentially via syringe. The resulting suspension was stirred at 3 Ar = 48.3 Hz, NMR (400 MHz, CDCl₃) δ = 75.1-7.46 (2H, Ar-CH), 5.88 (1H, dd, J₆₋₅ = 50.2 Hz, J₅₋₆ = 3.2 Hz, CH₃Htrans), 4.86 (1H, dd, J₄₋₃ (cis) = 18.4 Hz, J₃₋₄ (trans) = 3.5 Hz, CH₂Htrans), 3.85 (3H, s, CH₃). ¹³C NMR (125 MHz, CDCl₃) δC = 162.9 (d, JCF = 248.9 Hz, CF), 160.5 (Ar-CH), 124.6 (d, JCF = 29.9 Hz, Ar-CH), 126.1 (d, JCF = 7.2 Hz, 2 x Ar-CH), 113.8 (2 x Ar-CH), 87.6 (d, JCF = 23.2 Hz, CH₂), 55.3 (CH₃). ¹⁹F NMR (471 MHz, CDCl₃) δF = -107.1 (dd, J₃₋₂ (trans) = 50.3 Hz, J₃₋₂ (cis) = 18.1 Hz, CF). ¹³C NMR (125 MHz, CDCl₃) δC = 162.9 (d, JCF = 248.9 Hz, CF), 160.5 (Ar-CH), 124.6 (d, JCF = 29.9 Hz, Ar-CH), 126.1 (d, JCF = 7.2 Hz, 2 x Ar-CH), 113.8 (2 x Ar-CH), 87.6 (d, JCF = 23.2 Hz, CH₂), 55.3 (CH₃). ¹⁹F NMR (471 MHz, CDCl₃) δF = -107.1 (dd, J₃₋₂ (trans) = 50.3 Hz, J₃₋₂ (cis) = 18.1 Hz, CF). ¹³C NMR (125 MHz, CDCl₃) δC = 162.9 (d, JCF = 248.9 Hz, CF), 160.5 (Ar-CH), 124.6 (d, JCF = 29.9 Hz, Ar-CH), 126.1 (d, JCF = 7.2 Hz, 2 x Ar-CH), 113.8 (2 x Ar-CH), 87.6 (d, JCF = 23.2 Hz, CH₂), 55.3 (CH₃). ¹⁹F NMR (471 MHz, CDCl₃) δF = -107.1 (dd, J₃₋₂ (trans) = 50.3 Hz, J₃₋₂ (cis) = 18.1 Hz, CF).

**General Procedure C for Cyclopropanation of Vinyl Fluorides 11a-11f.**

A flame-dried round-bottomed flask equipped with a magnetic stir bar was charged with NaI (2.50-5.00 equiv). The reaction vessel was sealed, then evacuated and backfilled with nitrogen. Anhydrous THF, the appropriate vinyl fluoride 10a-10f (1.00 equiv) and trifluoromethyltrimethylsilane (2.50-5.00 equiv) were added sequentially via syringe. The resulting suspension was stirred at 75 °C for 20 h. After completion, the reaction mixture was allowed to cool to RT and solvent was removed in vacuo. The crude residue was diluted with diethyl ether (50 mL) and washed with distilled water (50 mL). The phases were separated and the aqueous layer was extracted with diethyl ether (2 x 50 mL). The combined organic phases were washed sequentially with saturated aqueous solutions of Na₂SO₃ and NaHCO₃, followed by drying over Na₂SO₄, filtration and evaporation of solvent in vacuo. Purification by flash column chromatography (petroleum ether/CH₂Cl₂)
afforded the appropriate 1,2,2-trifluorocyclopropane.

(1,2,2-Trifluorocyclopropyl)benzene (11a) was prepared following general procedure C, using (1-fluorovinyl)benzene (10a) (2.00 g, 16.38 mmol, 1.00 equiv), trifluoromethyltrimethylsilane (6.05 mL, 40.94 mmol, 2.50 equiv), and NaI (6.14 g, 40.94 mmol, 2.50 equiv) in THF (60 mL). The product was obtained by flash column chromatography (silica gel, 100% petroleum ether) as a colourless oil (1.506 g, 53%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$H 7.44 (5H, s, Ar-CH$_3$), 2.21-2.01 (2H, m, CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$C 131.1 (d, $^2$JC = 21.0 Hz, Ar-CH$_3$), 129.5 (d, $^2$JC = 2.3 Hz, Ar-CH$_3$), 128.7 (2 x Ar-CH$_3$), 126.9 (d, $^3$JC = 5.0 Hz, 2 x Ar-CH$_3$), 109.3 (ddd, $^1$JC = 294.4, 294.1 Hz, $^2$JC = 12.0 Hz, CF$_3$), 78.8 (ddd, $^1$JC = 233.5 Hz, $^2$JC = 13.0, 10.2 Hz, CF), 22.2 (dt, $^3$JC = 12.9, 10.0 Hz, CH$_2$); $^{19}$F ($^1$H) NMR (376 MHz, CDCl$_3$) $\delta$F -136.8 (dd, $^3$JF = 167.3 Hz, $^3$JF = 9.6 Hz, CF$\,^3$F$^-^{-}$), -180.9 (dd, $^3$JF = 9.6 Hz, $^3$JF = 3.9 Hz, CF$\,^3$F$^-^{-}$). HRMS (APCI$^+$) 173.0583 [M+H]$^+$, C$_8$H$_6$F$_3$ requires 173.0578.

1-Bromo-4-(1,2,2-trifluorocyclopropyl)benzene (11b) was prepared following general procedure C, using 1-(1-fluorovinyl)-4-bromobenzene (10b) (0.500 g, 2.50 mmol, 1.00 equiv), trifluoromethyltrimethylsilane (0.924 mL, 6.25 mmol, 2.50 equiv), and NaI (0.957 g, 6.25 mmol, 2.50 equiv) in THF (25 mL). The product was obtained by flash column chromatography (silica gel, 90% petroleum ether/10% CH$_2$Cl$_2$) as a yellow oil (0.128 g, 66%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$H 7.58-7.56 (2H, d, $J$ = 8.4 Hz, Ar-CH$_3$), 7.31-7.28 (2H, d, $J$ = 8.4 Hz, Ar-CH$_3$), 2.22-1.98 (2H, m, CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$C 131.9 (2 x Ar-CH$_3$), 130.1 (d, $^2$JC = 19.9 Hz, Ar-CH$_3$), 128.4 (d, $^2$JC = 5.1 Hz, 2 x Ar-CH$_3$), 123.8 (Ar-C), 108.9 (ddd, $^1$JC = 294.8, 294.8 Hz, $^2$JC = 4.1 Hz, CF$_3$), 79.2 (ddd, $^1$JC = 235.6 Hz, $^2$JC = 10.6, 2.1 Hz, CF), 22.4 (dt, $^3$JC = 12.9, 10.0 Hz, CH$_2$); $^{19}$F NMR (471 MHz, CDCl$_3$) $\delta$F -136.9 (dd, $^3$JF = 167.8 Hz, $^3$JF = 8.3 Hz, $^3$JF = 15.2 Hz, $^3$JF$^-^{-}$ = 5.6 Hz, CCF$^-^{-}$), -141.9 (ddd, $^3$JF$^-^{-}$ = 167.8 Hz, $^3$JF$^-^{-}$ = 3.7 Hz, $^3$JF$^-^{-}$ = 7.1 Hz, $^3$JF$^-^{-}$ = 16.6 Hz, CCF$^-^{-}$), -181.5 -- -182.7 (m, CF). HRMS (APCI$^+$): 232.9596 [M-F]$^+$, C$_8$H$_6$F$_3$Br requires 232.9600.

1-Fluoro-(1,2,2-trifluorocyclopropyl)benzene (11c) was prepared following general procedure C, using 1-(1-fluorovinyl)-4-fluorobenzene (10c) (0.300 g, 1.76 mmol, 1.00 equiv), trifluoromethyltrimethylsilane (0.792 mL, 5.36 mmol, 2.50 equiv), and NaI (0.804 g, 5.36 mmol, 2.50 equiv) in THF (20 mL. The product was obtained by flash column chromatography (silica gel, 90% petroleum ether/10% CH$_2$Cl$_2$) as a colourless oil (0.224 g, 67%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$H 7.52-7.37 (2H, br s, Ar-CH$_3$), 7.17-7.06 (2H, m, Ar-CH$_3$), 2.21-1.96 (2H, m, CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$C 163.4 (d, $^2$JC = 249.8 Hz, Ar-C), 129.4 (ddd, $^1$JC = 8.8, 4.6 Hz, 2 x Ar-CH$_3$), 126.9 (d, $^3$JC = 20.4 Hz, Ar-C), 115.9 (d, $^2$JC = 21.9 Hz, 2 x Ar-CH$_3$), 108.7 (ddd, $^1$JC = 295.0, 297.1 Hz, $^2$JC = 12.6 Hz, CF$_3$), 78.7 (ddd, $^1$JC = 233.3 Hz, $^2$JC = 9.8, 2.2 Hz, CF), 22.3 (dt, $^3$JC = 14.0, 10.2 Hz, CH$_2$); $^{19}$F NMR (471 MHz, CDCl$_3$) $\delta$F -111.1 -- -111.2 (m, Ar-F), -136.3 (ddd, $^3$JF$^-^{-}$ = 167.4 Hz, $^3$JF$^-^{-}$ = 9.3 Hz, $^3$JF$^-{-}$ = 15.2 Hz, $^3$JF$^-{-}$ = 5.5 Hz, CCF$^-{-}$), -142.31 (ddd, $^3$JF$^-{-}$ = 167.4 Hz, $^3$JF$^-{-}$ = 3.8 Hz, $^3$JF$^-{-}$ = 6.7 Hz, $^3$JF$^-{-}$ = 16.2 Hz, CCF$^-{-}$), -178.5 to -178.6 (m, CF). HRMS (APCI$^+$): 189.0326 [M-H]$^+$, C$_9$H$_7$F$_4$ requires 189.0327.
4-(1,2,2-Trifluorocyclopropyl)-1,1'-biphenyl (11d) was prepared following general procedure C, using 4-(1-fluoro vinyl)-1,1'-biphenyl (10d) (0.180 g, 0.908 mmol, 1.00 equiv), trifluoromethyltrimethylsilane (0.335 mL, 2.27 mmol, 2.50 equiv), and NaI (0.340 g, 2.27 mmol, 2.50 equiv) in THF (10 mL). The product was obtained by flash column chromatography (silica gel, 95% petroleum ether/5% CH₂Cl₂) as a pale yellow solid (0.209 g, 93%). ¹H NMR (500 MHz, CDCl₃) δH 7.67-7.59 (4H, m, Ar-CH), 7.51-7.44 (4H, m, Ar-CH), 7.40-7.36 (1H, m, Ar-CH), 2.24-2.05 (2H, m, CH₂); ¹³C NMR (101 MHz, CDCl₃) δC 130.0 (d, ²JC = 19.7 Hz, Ar-Ç), 128.9 (2 x Ar-Ç), 127.8 (Ar-Ç), 127.4 (2 x Ar-Ç), 127.3 (2 x Ar-Ç), 127.2 (2 x Ar-Ç), 126.9 (Ar-Ç), 126.5 (Ar-Ç), 108.9 (ddd, ³JC = 294.5, 294.5 Hz, ²JC = 2.5 Hz, CF₃), 80.0-77.4 (m, CF), 22.4 (dt, ²JC = 13.5, 10.1 Hz, CH₃); ¹⁹F NMR (377 MHz, CDCl₃) δF -136.6 (ddd, ²JI = 166.0 Hz, ³JI = 8.3 Hz, ³JS = 14.9 Hz, ³JHF = 5.9 Hz, CF₂), -141.7 (ddd, ²JI = 166.0 Hz, ³JII = 4.0 Hz, ³JHF = 7.8 Hz, ³JFF = 15.6 Hz, CF₂), -180.8 – -181.0 (m, CF). HRMS (ASAP⁺) 248.0809 [M⁺], C₁₅H₁₁F₃ requires 248.0813.

1-Methoxy-4-(1,2,2-trifluorocyclopropyl)benzene (11e) was prepared following general procedure C, using 1-(1-fluoro vinyl)-4-methoxybenzene (10e) (0.150 g, 0.990 mmol, 1.00 equiv), trifluoromethyltrimethylsilane (0.365 mL, 2.47 mmol, 2.50 equiv), and NaI (0.369 g, 2.47 mmol, 2.50 equiv) in THF (8 mL). The product was obtained by flash column chromatography (silica gel, 80% petroleum ether/20% CH₂Cl₂) as a light yellow oil (0.128 g, 64%). ¹H NMR (500 MHz, CDCl₃) δH 7.42-7.38 (2H, m, Ar-CH), 6.97-6.92 (2H, m, Ar-CH), 3.84 (3H, s, CH₃), 2.16-1.91 (2H, m, CH₂); ¹³C NMR (125 MHz, CDCl₃) δC 160.7 (Ar-Ç), 129.5 (d, ³JC = 3.7 Hz, 2 x Ar-CH), 122.8 (d, ²JC = 20.0 Hz, Ar-Ç), 114.1 (2 x Ar-CH), 109.5 (ddd, ³JC = 295.3, 293.9 Hz, ²JC = 13.4 Hz, CF₃), 78.6 (ddd, ³JC = 233.5 Hz, ²JC = 12.8, 9.9 Hz, CF); 55.4 (CH₃), 22.2 (dt, ²JC = 14.4, 10.1 Hz, CH₃); ¹⁹F NMR (471 MHz, CDCl₃) δF -135.7 (ddd, ²JI = 166.4 Hz, ³JI = 9.7 Hz, ³JS = 15.6 Hz, ³JHF = 5.5 Hz, CF₂), -142.5 (ddd, ²JI = 166.4 Hz, ³JII = 5.2 Hz, ³JHF = 7.1 Hz, ³JFF = 16.7 Hz, CF₂), -175.0 – -175.2 (m, CF). HRMS (ASAP⁺) 183.0625 [M-F⁺], C₁₅H₁₀F₂O requires 183.0621.

1-Nitro-4-(1,2,2-trifluorocyclopropyl)benzene (11f) was prepared following general procedure C, using 1-(1-fluoro vinyl)-4-nitrobenzene (10f) (0.500 g, 2.994 mmol, 1.0 equiv), trifluoromethyltrimethylsilane (2.21 mL, 14.97 mmol, 5.00 equiv), and NaI (2.24 g, 14.97 mmol, 5.00 equiv) in THF (10 mL). The product was obtained by flash column chromatography (silica gel, 80% petroleum ether/20% CH₂Cl₂) as a pale yellow oil (0.480 g, 74%). ¹H NMR (500 MHz, CDCl₃) δH 8.29 (2H, d, J = 9.0 Hz, Ar-CH), 7.55 (2H, d, J = 9.0 Hz, Ar-CH), 2.40-2.11 (2H, m, CH₂); ¹³C NMR (125 MHz, CDCl₃) δC 148.1 (Ar-Ç), 138.5 (d, J = 19.3 Hz, Ar-Ç), 126.6 (d, J = 5.1 Hz, 2 x Ar-CH), 123.8 (2 x Ar-CH), 108.7 (ddd, ²JC = 299.0, 294.5 Hz, ³JC = 11.0 Hz, CF₂), 77.4 (ddd, ³JC = 234.5 Hz, ²JC = 12.6, 2.2 Hz, CF), 23.5 (dt, ²JC = 13.4, 9.7 Hz, CH₃); ¹⁹F NMR (471 MHz, CDCl₃) δF -137.8 (ddd, ²JI = 167.8 Hz, ³JI = 8.5 Hz, ³JS = 15.3 Hz, ³JHF = 6.8 Hz, CF₂), -140.4 (ddd, ²JI = 167.8 Hz, ³JI = 2.9 Hz, ³JHF = 6.9 Hz, ³JFF = 16.3 Hz, CF₂), -187.3 – -187.4 (m, CF); HRMS (ASAP⁺) 218.0431 [M+H⁺], C₁₅H₁₀F₂NO₂ requires 218.0429.
Nitration of 11a. A flame-dried round-bottomed flask equipped with a magnetic stir bar was charged with ammonium nitrate (0.174 g, 2.56 mmol, 1.10 equiv). The reaction vessel was sealed, then evacuated and backfilled with nitrogen. 11a (0.400 g, 2.32 mmol, 1.00 equiv), acetonitrile (25 mL) and trifluoroacetic anhydride (1.147 mL, 8.12 mmol, 3.50 equiv) were added via syringe. The resulting solution was stirred at 60°C for 24 h before quenching with 1M aqueous HCl solution and washing sequentially with saturated aqueous solution of NaHCO₃ (25 mL) and brine (25 mL). The combined organic layers were dried over Na₂SO₄, filtered and evaporated to dryness in vacuo. Purification of the crude residue by flash column chromatography (silica gel, 70% petroleum ether/30% CH₂Cl₂) afforded the meta-isomer 11f (0.087 g) as a pure material and the para- and ortho-isomers 11f and 11f″ as a 3.85:1.00 mixture (0.172 g) (overall 48%).

1-Nitro-3-(1,2,2-trifluorocyclopropyl) benzene (11f) 1H NMR (300 MHz, CDCl₃) δₓ 8.25-8.14 (1H, m, Ar-CH), 7.81 – 7.66 (3H, m, Ar-CH), 2.12-1.93 (2H, m, CH₂); 19F¹{¹H} NMR (282 MHz, CDCl₃) δₓ 111.9 Hz, Jₓₓ = 7.1 Hz, Jₓₓ = 1.46 Hz, (dd, Jₓₓ = 171.9 Hz, Jₓₓ = 141.4 Hz, (dd, Jₓₓ = 2.6 Hz, CHF) F, Jₓₓ = 187.4 Hz, Jₓₓ = 7.2 Hz, Jₓₓ = 2.6 Hz, CF); HRMS (EI⁺) 217.0340 [M⁺], C₇H₆F₂NO₂ requires 217.0345.

11f and 1-nitro-2-(1,2,2-trifluorocyclopropyl)benzene (11f″) (approx. 4:1 isolated). ¹H NMR (300 MHz, CDCl₃) δₓ 8.31 (2H, d, J = 8.8 Hz, 11f Ar-CH), 7.83 – 7.62 (1H, m, 11f″ Ar-CH), 7.58 (2H, d, J = 8.8 Hz, 11f Ar-CH), 2.48-2.12 (2.5 H, m, 11f and 11f″ CH₂); ¹H NMR (300 MHz, CDCl₃) δₓ 111.9 Hz, Jₓₓ = 7.1 Hz, Jₓₓ = 1.46 Hz, (dd, Jₓₓ = 171.9 Hz, Jₓₓ = 141.4 Hz, (dd, Jₓₓ = 2.6 Hz, CHF) F, Jₓₓ = 187.4 Hz, Jₓₓ = 7.2 Hz, Jₓₓ = 2.6 Hz, CF); HRMS (APCI⁺) 218.0423 [M+H⁺], C₇H₆F₂NO₂ requires 218.0429.

1-Propyl-4-(4-(1,2,2trifluorocyclopropyl)-phenylethynyl)- benzene (13). ¹H flame-dried round-bottomed flask equipped with a magnetic stir bar was charged with PPh₃ (0.058 g, 0.220 mmol, 0.825 equiv), Cul (0.010 g, 0.058 mmol, 0.21 equiv) and Pd(PPh₃)Cl₂ (0.010 g, 0.014 mmol, 0.05 equiv). The reaction vessel was sealed, then evacuated and backfilled with nitrogen. Anhydrous DMF (5.4 mL), Et₃N (5.4 mL), 1-ethyl-4-propylbenzene (0.078 g, 0.540 mmol, 0.825 equiv) and 11a (0.070 g, 0.270 mmol, 1.00 equiv) were added via syringe. The resulting suspension was stirred at 80°C for 24 h before quenching with EtOAc and washing sequentially with an aqueous 1M solution of HCl (25 mL), a saturated aqueous solution of NaHCO₃ (25 mL) and brine (25 mL). The combined organic layers were dried over Na₂SO₄, filtered and evaporated to dryness in vacuo. The titled compound was obtained by flash column chromatography (silica gel, 75% petroleum ether/25% CH₂Cl₂) as a light yellow oil (0.064 g, 76%). ¹H NMR (400 MHz, CDCl₃) δₓ 7.61 – 7.55 (2H, m, Ar-CH), 7.49 – 7.42 (2H, m, Ar-CH), 7.39 (2H, m, Ar-CH), 7.20 – 7.14 (2H, m, Ar-CH), 2.60 (2H, t, J = 7.2 Hz, CH₂), 2.28 – 1.97 (2H, m, CF₂–CF₂), 1.74 – 1.57 (2H, m, CH₂–CH₂), 0.94 (3H, t, J = 7.3 Hz, CH₃); ¹³C NMR (126 MHz, CDCl₃) δₓ 143.6 (Ar-C), 131.7 (2 x Ar-CH), 131.6 (2 x Ar-CH), 130.7 (d, Jₓₓ = 19.8 Hz, Ar-CH), 128.6 (2 x Ar-CH), 124.7 (Ar-CH), 124.0 (Ar-CH), 109.1 (d, Jₓₓ = 295.1, 291.2 Hz, Jₓₓ = 11.3 Hz, CF₂), 91.0 (CCH), 87.9 (CCH), 74.9-77.4 (m, CF), 38.0 (CH₂), 24.4 (CH₃), 23.5
(126 MHz, CDCl₃) δₖ -136.9 (ddd, ²Jₖ = 166.9 Hz, ³Jₖ = 15.2 Hz, ⁴Jₖ = 8.8 Hz, ⁵Jₖ = 5.7 Hz, CEF), -141.5 (ddd, ²Jₖ = 167.1 Hz, ³Jₖ = 16.2 Hz, ⁴Jₖ = 6.6 Hz, ⁵Jₖ = 3.8 Hz, CFF), -182.5 – -185.7 (m, CF); HRMS (ASAP) 315.136 [M+H]^+ C₂₀H₁₈F₃ requires 315.1361.

4-(4-(1,2,2-trifluorocyclopropyl)phenyl)-morpohline (14). A flame-dried round-bottomed flask equipped with a magnetic stir bar was charged with BINAP (0.037 g, 0.060 mmol, 0.15 equiv), Cs₂CO₃ (0.267 g, 0.637 mmol, 1.60 equiv) and Pd₃dba (0.018 g, 0.020 mmol, 0.05 equiv). The reaction vessel was sealed, then evacuated and backfilled with nitrogen. Anhydrous toluene (6.0 mL), morpholine (0.055 g, 0.637 mmol, 1.60 equiv) and 11a (0.100 g, 0.398 mmol, 1.00 equiv) were added via syringe. The resulting suspension was stirred at 70°C for 24 h before quenching with EtOAc and washing sequentially with an aqueous 1 M solution of HCl (25 mL), a saturated aqueous solution of NaHCO₃ (25 mL) and brine (25 mL). The combined organic layers were dried over Na₂SO₄, filtered and evaporated to dryness in vacuo. Purification of the crude residue by flash column chromatography (70% petroleum ether/30% CH₂Cl₂) afforded the title compound as a light yellow oil (0.095 g, 93%). ¹H NMR (400 MHz, CDCl₃) δₙ 7.44 – 7.32 (2H, m, Ar-CH), 6.99 – 6.87 (2H, m, Ar-CH), 3.96 – 3.80 (4H, m, 2xCH₂), 3.31 – 3.12 (4H, m, 2xCH₂), 2.13 – 1.89 (2H, m, CF-CH₂-CF₂); ¹³C NMR (126 MHz, CDCl₃) δₚ 152.2 (Ar-C), 129.1 (2xAr-CH), 121.3 (d, ²Jₚ = 20.0, Ar-C), 115.0 (2xAr-CH), 108.6 (ddd, ²Jₚ = 294.7, ²Jₚ = 10.8 Hz, CₘG), 79.1-77.9 (m, Cₘ), 66.8 (2xOCH₂), 48.5 (2xNCH₂), 22.0 (dt, ²Jₚ = 14.8, 10.3 Hz, CH₂); ¹⁹F NMR (471 MHz, CDCl₃) δₖ -135.7 (ddd, ²Jₖ = 166.3 Hz, ³Jₖ = 14.5 Hz, ⁴Jₖ = 8.7 Hz, ⁵Jₖ = 5.3 Hz, CFF), -142.6 (ddd, ²Jₖ = 166.4 Hz, ³Jₖ = 16.2 Hz, ⁴Jₖ = 11.4, 6.2 Hz, CFF), -178.5 – -178.6 (m, CF); HRMS (ESI′) 258.1100 [M+H]^+ C₁₃H₁₅F₃NO requires 258.1100.

4-(2,2-Difluoro-1-hydroxycyclopropyl)phenol (17). A flame-dried round-bottomed flask equipped with a magnetic stir bar was sealed, then evacuated and backfilled with nitrogen. 11e (0.100 g, 0.546 mmol, 1.00 equiv) and CH₂Cl₂ (18 mL) were added and the solution cooled to 0°C. Boron tribromide (0.520 mL, 5.46 mmol, 10.00 equiv) was added dropwise over 5 minutes and the reaction mixture was stirred at 0°C for 1 h. After completion, the reaction mixture was warmed to RT, quenched with H₂O (20 mL) and extracted with CH₂Cl₂ (3 x 30 mL). The combined organic layers were dried over Na₂SO₄, filtered and evaporated to dryness in vacuo to afford the title compound as colourless oil (0.091 g, 90%). ³¹H NMR (500 MHz, CDCl₃) δₙ 7.35 (2H, d, J = 8.6 Hz, Ar-CH), 6.83 (2H, d, J = 8.6 Hz, Ar-CH), 2.19 (1H, ddd, ³Jₙ = 4.7, 13.7 Hz, ⁴Jₙ = 9.4 Hz, CH₃H), 2.05 (1H, ddd, 1H, ddd, ³Jₙ = 4.7, 13.7 Hz, ⁴Jₙ = 9.3 Hz, CH₃H); ¹³C NMR (126 MHz, CDCl₃) δₚ 156.3 (Ar-C), 131.0 (2xAr-CH), 128.4 (Ar-C), 115.8 (2xAr-CH), 109.6 (t, ²Jₚ = 290.8 Hz, CₘG), 27.3 (t, ²Jₚ = 10.5 Hz, CₘG); ¹⁹F NMR (471 MHz, CDCl₃) δₖ -126.9 (ddd, ²Jₖ = 149.2 Hz, ³Jₖ = 11.5 Hz, ⁴Jₖ = 4.8 Hz, CFF), -132.3 (ddd, ²Jₖ = 148.5 Hz, ³Jₖ = 13.1 Hz, ⁴Jₖ = 4.7 Hz, CFF); HRMS (ESI′) 186.0484 [M]^+ C₁₀H₈F₂O₂ requires 186.0492.

1,2,2-Trifluorocyclopropane-1-carboxylic acid (18). Ruthenium chloride (0.4 g, 0.73 mmol, 0.1 equiv) and sodium periodate (12.5 g, 58.4 mmol, 7.9 equiv) were added to a solution of 11a (1.25 g, 7.3 mmol, 1.0 equiv) in mixed solvents of carbon tetrachloride/acetonitrile/water (70
mL, v/v/v 2/2/3). The mixture was stirred at 90°C for 3 days until all starting material is consumed as monitored by 19F NMR. The reaction mixture was diluted with water (100 mL). The organic layer was isolated. The aqueous layer was extracted with ethyl acetate (6 x 50 mL). The combined extracts were dried (Na2SO4) and the solvent was removed under vacuum to give a brown gum which gradually solidified into colourless needle crystals (0.6 g, 60%). 1H NMR (500 MHz, MeOD) δH 2.56-2.44 (1H, m, CH(H), 2.34-2.20(1H, m, CH(H)); 13C NMR (125 MHz, MeOD) δC 165.6 (d, 2JCF 23.1 Hz, C=O), 108.6 (ddd, 1JCF 298.4, 288.0, 2JCF 9.6 Hz, CF2), 74.6 (ddd, 1JCS 245.5 Hz, 2JCF 10.5, 13.2 Hz, CF), 22.2-21.9 (m, CH3); 19F(1H) NMR (470 MHz, CDCl3) δF -137.0 (dd, 2JFF = 163.8 Hz, 3JFF = 11.2 Hz, CFF), -139.0 (d, 2JFF = 163.8 Hz, CFF), -202.6 (d, 3JFF = 11.2 Hz, CF); HRMS (ESI') 139.0007 [M-H]-, C6H2F3O2 requires 139.0007.

1,2,2-Trifluoro-N-phenylcyclopropane-1-carboxamide (19a). HOBt (153 mg, 1.13 mmol, 2 equiv), EDC (218 mg, 1.13 mmol, 2 equiv) were added to a solution of 1,2,2-trifluoro-N-carboxylic acid (18) (80 mg, 0.57 mmol, 1 equiv), aniline (105 mg, 1.13 mmol, 2 equiv) and triethylamine (0.3 mL, 2.15 mmol, 3.8 equiv) in dichloromethane (10 mL) at 0°C. The mixture was stirred at this temperature for 1 h and then at rt overnight. After solvent removal, the residue was separated by flash column chromatography (80% petroleum ether/20% EtOAc) to afford the titled compound as light brown solid (98 mg, 86%). 1H NMR (400 MHz, CDCl3) δH 8.09 (br s, 1H, NH), 7.61-7.54 (2H, m, Ar-CH), 7.41-7.36 (2H, m, Ar-CH), 7.21 (1H, tt, J = 7.4, 1.1 Hz, Ar-H), 2.76-2.64 (1H, m, CHH), 2.22-2.07 (m, 1H, CHH); 13C NMR (125 MHz, CDCl3) δC 160.5 (d, 2JCS = 17.2 Hz, CO), 136.4 (Ar-C), 129.2 (2 x Ar-CH), 125.4 (Ar-CH), 120.4 (2 x Ar-CH), 107.6 (td, 2JCS = 291.7 Hz, 2JCS = 9.4 Hz, CF2), 77.7 (dt, 1JCS = 256.3 Hz, 2JCS = 11.1 Hz, CF), 22.9 (q, 1JCS = 11.1 Hz, CH2); 19F(1H) NMR (470 MHz, CDCl3) δF -138.7 (dd, 2JFF = 3.2, 2JFF = 164.1 Hz, CFF), -139.2 (dd, 3JFF = 11.1 Hz, 2JFF = 164.1 Hz, CFF), -200.5 (d, 3JFF = 11.2, 2.5 Hz, CF); HRMS (ESI') 216.0628 [M+H]+, C10H9F3NO requires 216.0636.

1,2,2-Trifluoro-N-benzylcyclopropane-1-carboxamide (19b). HOBt (52 mg, 0.38 mmol, 2 equiv), EDC (84 mg, 0.38 mmol, 2 equiv) and triethylamine (0.1 ml, 0.72 mmol, 3.8 equiv) was added to a solution of 1,2,2-trifluorocyclopropane-1-carboxylic acid (27 mg, 0.19 mmol, 1 equiv) and benzylamine (41 mg, 0.38 mmol, 2 equiv) in DCM (5 mL). The mixture was stirred at rt overnight. After solvent removal, the residue was purified by column chromatography (silica gel, 80% petroleum ether/20% EtOAc) to give the product as colourless solid (36 mg, 82%). 1H NMR (400 MHz, CDCl3) δH 7.43-7.33 (m, 5H, Ar-H), 6.68 (br s, 1H, NH), 4.62-4.53 (2H, m, CH2NH), 2.71-2.59 (1H, m, CHH), 2.06 (1H, m, CHH); 13C NMR (125 MHz, CDCl3) δC 162.5 (d, 2JCS = 18.8 Hz, CO), 137.0 (Ar-C), 128.9 (2 x Ar-CH), 120.0 (3 x Ar-CH), 107.0 (dt, 2JCS = 9.1, 3JCS 295.6 Hz, CF2), 77.8 (dt, 1JCF = 255.0 Hz, 2JCF = 11.0 Hz, CF), 43.8 (CH2), 22.9 (dt, 2JCS = 10.1 Hz); 19F(1H) NMR (470 MHz, CDCl3) δF -139.2 (m, CF2), -202.2 (dd, 3JFF = 5.8, 8.1Hz, CF); HRMS (ESI') 230.0788 [M+H]+, C11H11F3NO requires 230.0793.
3-(4-Bromophenoxy)-N-phenylcyclopropane-1,2,2-difluoro-1-carboxamide (22). 4-Bromophenol (32 mg, 0.185 mmol, 5 equiv) and potassium carbonate (26 mg, 0.188 mmol, 5 equiv) were added to a solution of 1,2,2-trifluoro-N-phenylcyclopropane-1-carboxamide 19a (8.0 mg, 0.037 mmol, 1 equiv) in acetonitrile (2 mL). The mixture was heated at 60°C for 3 days. The solvent was removed under reduced pressure. The residue was purified by preparative TLC (to give the product as white solid (4.3 mg, 32%). δH 7.55 (2H, d, J = 7.4 Hz, 2 x Ar-CH), 7.46 (2H, d, J = 8.9 Hz, 2 x Ar-CH), 7.40 (2H, J = 7.4 Hz, 2 x Ar-CH), 7.37 (s, 1H, NH), 7.20 (1H, t, J = 7.4 Hz, Ar-CH), 6.95 (2H, d, J = 8.9 Hz, 2 x Ar-CH), 4.79 (1H, ddd, 3JH H = 1.0, 9.9 Hz, 3JHH = 4.7 Hz, CHCO), 2.64 (ddd, 1H, 3JH H = 1.0, 15.8 Hz, 3JHH = 4.7 Hz, CHO); 13C NMR (125 MHz, CDCl3) δC 160.4 (C=O), 155.9 (Ar-CH), 137.0 (Ar-CH), 132.8 (2 x Ar-CH), 129.2 (2 x Ar-CH), 125.3 (Ar-CH), 120.0 (2 x Ar-CH), 116.7 (2 x Ar-CH), 115.2 (Ar-CH), 108.9 (t, 1JCf = 296.2 Hz, CF2), 58.1 (dd, 2JCf = 15.6, 7.7 Hz, C-3), 35.5 (dd, 2JCf = 12.3, 9.4 Hz, C-1); 19F NMR (470 MHz, CDCl3) δF -131.8 (1H, δF = 10.2 Hz, 2JFF 165.0 Hz, CFF), -133.7 (dd, 2JFF = 13.0, 1.5 Hz, 2JFF = 165.0 Hz, CFF); HRMS (ESI+) 368.0087 [M+H]+, C10H13BrF3NO2 requires 389.0992.

2,2-Difluoro-3-(naphthalen-2-ylthio)-N-phenylcyclopropane-1-carboxamide (23a). Sodium hydride (6 mg, 60% in mineral oil, 0.15 mmol, 3 equiv) was added to a solution of 1,2,2-trifluoro-N-phenylcyclopropane-1-carboxamide (11 mg, 0.05 mmol) 19a and naphthalene-2-thiol (18.9 mg, 0.1 mmol, 2 equiv) in THF (1 mL) at °C. The mixture was stirred at this temperature until the starting material was completely consumed (ca 4h). The solvent was removed under reduced pressure and the residue was purified by preparative TLC (silica gel, 80% petroleum ether/20% EtOAc) to give the product as brownish solid (12 mg, 72%). 1H NMR (400 MHz, CDCl3) δH 7.83-7.77 (4H, m, 4 x Ar-CH), 7.53-7.48 (4H, m, 4 x Ar-CH), 7.47-7.43 (1H, m, Ar-CH), 7.42 (br s, 1H, NH), 7.38-7.34 (2H, m, 2 x Ar-CH), 7.12 (1H, t, J = 7.5 Hz, Ar-CH), 3.89 (dd, 1H, 3JH H = 6.8 Hz, 3JHH = 13.3 Hz, CHCO), 2.54 (dd, 1H, 3JH H = 6.8 Hz, 3JHH = 12.5 Hz, CHS); 13C NMR (125 MHz, CDCl3) δC 161.0 (CO), 137.1 (Ar-C), 133.7 (Ar-C), 132.0 (Ar-C), 131.4 (Ar-C), 129.2 (2 x Ar-CH), 129.0 (Ar-CH), 127.8 (Ar-CH), 127.3 (Ar-CH), 126.9 (Ar-CH), 126.7 (Ar-CH), 126.2 (Ar-CH), 126.1 (Ar-CH), 125.1 (Ar-CH), 120.1 (2 x Ar-CH), 111.1 (t, 1JCf = 294.7 Hz, CF2), 36.7 (t, 2JCf 10.1 Hz, CH), 28.4 (t, 2JCf = 11.5 Hz, CH); 19F NMR (470 MHz, CDCl3) δF -130.5 (dd, 3JH F = 2.1 Hz, 2JFF = 150.5 Hz, CFF), -132.8 (dd, 3JH F = 13.2 Hz, 2JFF = 150.5 Hz, CFF); HRMS (ESI+) 378.0726 [M+Na]+, C20H15F3NOSNa requires 378.0740.

3-((4-Bromophenyl)thio)-2,2-difluoro-N-phenylcyclopropane-1-carboxamide (23b). Sodium hydride (4.5 mg, 60% in mineral oil, 0.11 mmol, 3 equiv) was added to a solution of 1,2,2-trifluoro-N-phenylcyclopropane-1-carboxamide 19a (7.8 mg, 0.036 mmol, 1 equiv) and 4-bromothiophenol (13.6 mg, 0.072 mmol, 2 equiv) in THF (1 mL) at °C under argon atmosphere. The mixture was stirred at this temperature until the starting material was completely consumed (ca 4h). The solvent was removed under reduced pressure and the residue was purified by preparative TLC (silica gel, 80% petroleum ether/20% EtOAc) to give the product as white solid (9.0 mg, 65%). 1H NMR (400 MHz, CDCl3) δH 7.53 (2H, d, J = 7.7 Hz, 2 x Ar-
SC

NMR (400 MHz, solid (bicarbonate and brine). After dryness (MgSO₄), the residue was purified by preparative TLC to give the product as white solid (8.1 mg, 71%).

1H NMR (400 MHz, CDCl₃) δH 7.53 (2H, d, J = 7.9 Hz, 2 x Ar-CH), 7.38 (1H, s, NH), 7.35 (2H, t, J = 7.9 Hz, 2 x Ar-CH), 7.17 (1H, t, J = 7.3 Hz, Ar-CH), 3.43 (ddd, 1H, 3JHH = 6.6 Hz, 3JHF = 1.9, 11.5 Hz, CH(=O)), 2.42 (ddd, 1H, 3JHH = 6.6 Hz, 3JHF = 1.7, 10.5 Hz, CHS), 2.29 (s, 3H, SMe); 13C NMR (125 MHz, CDCl₃) δC 161.4 (C=O), 137.2 (ArC), 129.2 (2 x Ar-CH), 125.0 (Ar-CH), 119.9 (2 x Ar-CH), 111.6 (dd, 1JCF = 288.3, 292.8 Hz, CF₂), 36.6 (t, 2JCF = 10.3 Hz, CHCO), 29.4 (t, 2JCF = 11.3 Hz, CHS), 16.1 (s, SCH₂); 19F NMR (470 MHz, CDCl₃) δF -132.6 (d, 2JFF = 151.2 Hz, CFF), -133.2 (d, 2JFF = 151.2 Hz, CFF); HRMS (ESI⁺) 405.9679 [M+Na]+, C₁₄H₁₂F₂NOBrSnA requires 405.9683.

2,2-difluoro-3-(methylthio)-N-phenylcyclopropane-1-carboxamide (23c). Sodium thiomethoxide (15.6 mg, 0.22 mmol, 4.8 eq) was added to a solution of 1,2,2-trifluoro-N-phenylcyclopropane-1-carboxamide (19a) (10.0 mg, 0.046 mmol, 1 eq) in acetonitrile (3 mL). The mixture was stirred at rt overnight. The solvent was removed under reduced pressure. The residue was purified by preparative TLC to give the product as white solid (8.1 mg, 71%).

1H NMR (400 MHz, CDCl₃) δH 7.53 (2H, d, J = 7.9 Hz, 2 x Ar-CH), 7.38 (1H, s, NH), 7.35 (2H, t, J = 7.9 Hz, 2 x Ar-CH), 7.17 (1H, t, J = 7.3 Hz, Ar-CH), 3.43 (ddd, 1H, 3JHH = 6.6 Hz, 3JHF = 1.9, 11.5 Hz, CH(=O)), 2.42 (ddd, 1H, 3JHH = 6.6 Hz, 3JHF = 1.7, 10.5 Hz, CHS), 2.29 (s, 3H, SMe); 13C NMR (125 MHz, CDCl₃) δC 161.4 (C=O), 137.2 (ArC), 129.2 (2 x Ar-CH), 125.0 (Ar-CH), 119.9 (2 x Ar-CH), 111.6 (dd, 1JCF = 288.3, 292.8 Hz, CF₂), 36.6 (t, 2JCF = 10.3 Hz, CHCO), 29.4 (t, 2JCF = 11.3 Hz, CHS), 16.1 (s, SCH₂); 19F NMR (470 MHz, CDCl₃) δF -132.6 (d, 2JFF = 151.2 Hz, CFF), -133.2 (d, 2JFF = 151.2 Hz, CFF); HRMS (ESI⁺) 266.0416 [M+Na]+, C₁₄H₁₂F₂NOBrSnA requires 266.0422.

2,2-Difluoro-3-(methylsulfonyl)-N-phenylcyclopropane-1-carboxamide (25). meta-Chloroperoxybenzoic acid (48.6 mg (70%), 197 µmol, 4.0 equiv) was added to a solution of 23c (12.1 mg, 49 µmol, 1.0 equiv) in DCM (5 mL). The mixture was stirred at rt for 4 hours before being quenched with saturated sodium metabisulfite. The mixture was diluted with DCM (5 mL) and the layers were isolated. The organic layer was washed with water, aqueous sodium bicarbonate and brine. After dryness (MgSO₄), the solvent was removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 70% petroleum ether/30% EtOAc), to give the product as white solid (10.9 mg, 81%).

1H NMR (400 MHz, CDCl₃) δH 7.60 (br s, 1H, NH), 7.53 (2H, d, J = 7.7 Hz, 2 x Ar-H), 7.38 (2H, t, J = 7.7 Hz, 2 x Ar-H), 7.21 (1H, t, J = 7.7 Hz, Ar-H), 3.98 (ddd, 1H, 3JHH = 7.0 Hz, 3JHF = 1.5, 11.5 Hz, CHCO), 3.41 (ddd, 1H, 3JHH = 7.0 Hz, 3JHF = 1.2, 13.1 Hz, CHS), 3.18 (s, 3H, SCH₃); 1H NMR (400 MHz, DMSO-d₆) δH 10.69 (s, 1H, NH), 7.58 (d, 2H, J = 7.8 Hz, 2 x Ar-CH), 7.38 (t, 1H, J = 7.8 Hz, Ar-CH), 7.12 (t, J = 7.4 Hz, Ar-CH), 4.45 (d, 1H, 3JHH = 7.9 Hz, 3JHF = 12.7 Hz, CHCO), 3.64 (dd, 1H, 3JHH = 7.9 Hz, 3JHF = 14.5 Hz, CHS), 3.31 (3H, s, SCH₃); 1H NMR (400 MHz, MeOD) δH 7.60-7.57 (2H, m, 2 x Ar-CH), 7.37-7.32 (2H, m, 2 x Ar-CH), 7.14 (1H, tt, J = 7.4, 1.1 Hz, Ar-CH), (CHCO at around 3.98 in CDCl₃ was not observed as it was exchanged to CDCO), 3.59 (1H, d, 3JHH = 14.0 Hz, CHS, over weekend, this signal disappeared as it was exchanged by deuterated MeOD), 3.22 (3H, s, SCH₃); 13C NMR (125 MHz, MeOD) δC 159.6 (C=O), 138.0 (Ar-C), 128.6 (2 x Ar-CH), 124.3 (Ar-CH), 119.6 (2 x Ar-
\( \text{CH} \), 107.2 (t, \( J_{CF} = 291.0 \text{ Hz}, \text{CF}_2 \)), signals for \( \text{CDCO} \) and \( \text{CDCS} \) too weak to be observed. 13\(^C\) NMR (125 MHz, DMSO-d\(_6\)) \( \delta_c \) 159.7 (\( \text{C} = \text{O} \)), 138.8 (Ar-\( \text{C} \)), 129.5 (2 x Ar-\( \text{CH} \)), 124.6 (Ar-\( \text{CH}_2 \)), 119.6 (2 x Ar-\( \text{CH}_2 \)), 108.0 (t, \( J_{CF} = 291.0 \text{ Hz}, \text{CF}_2 \)), 42.8 (S\( \text{CH}_{3} \)), 42.6 (t, \( J_{CF} = 9.6 \text{ Hz}, \text{CHCO} \)), 32.2 (t, \( J_{CF} = 9.0 \text{ Hz}, \text{CHS} \)); \( ^{19}\text{F}(^{1}\text{H}) \) NMR (470 MHz, CDCl\(_3\)) \( \delta_f \) -131.8 (d, \( J_{HF} 160.1 \text{ Hz}, \text{CFF} \)), -133.7 (d, \( J_{CF} = 160.1 \text{ Hz}, \text{CFF} \)); \( ^{19}\text{F} \) NMR (470 MHz, CDCl\(_3\)) \( \delta_f \) -131.8 (ddd, \( J_{HF} 11.0, 1.0 \text{ Hz}, J_{CF} 160.1 \text{ Hz,CFF} \)), -133.7 (ddd, \( J_{HF} 13.0, 1.5 \text{ Hz}, J_{CF} = 160.1 \text{ Hz,CFF} \)); \( ^{19}\text{F}(^{1}\text{H}) \) NMR (470 MHz, DMSO-d\(_6\)) \( \delta_t \) -131.2 (d, \( J_{HF} 157.1 \text{ Hz}, \text{CFF} \)), -133.8 (d, \( J_{CF} = 157.1 \text{ Hz}, \text{CFF} \)); \( ^{19}\text{F} \) NMR (470 MHz, DMSO-d\(_6\)) \( \delta_t \) -131.2 (dd, \( J_{HF} 12.8 \text{ Hz}, J_{CF} 157.1 \text{ Hz,CF}, \text{CF} \)), -133.8 (dd, \( J_{HF} 14.7 \text{ Hz}, J_{CF} = 160.1 \text{ Hz,CF,C} \)); HRMS (ESI\(^+\)) 276.0496 [M+H]\(^+\), \( \text{C}_{11}\text{H}_{13}\text{F}_{2}\text{NO}_{2}\text{S} \) requires 276.0500, for the deuterated version HRMS (ESI\(^+\)) 3010503 [M+Na]\(^+\), \( \text{C}_{11}\text{H}_{15}\text{D}_{2}\text{F}_{2}\text{NO}_{2}\text{S} \)Na requires 301.0514.

References

in MeOD
in CDCl₃
in CDCl$_3$
in CDCl₃
Figure S1. $^1$H NMR of 25 in MeOD. a) in several minutes, the NH was exchanged; b) in 3 h, the CH alpha to amide exchanged; c) in 3 days, the CH adjacent to sulfonyl group also exchanged.

Figure S2. $^{19}$F NMR of 25 in MeOD: a) in several minutes the NH was exchanged; b) in 3 h the CH alpha to amide exchanged, both F signals up-shifted slightly; c) in 3 days, the CH adjacent to sulfonyl group also exchanged, both F signals slightly further up-shifted.
Scheme S1. Enolisation responsible for proton exchange of 25 in MeOD.
**DFT Computations for 11a**

A conformational analysis was performed for (1,2,2-trifluorocyclopropyl)benzene **11a** by scanning an F-C-C=C dihedral angle (B2LYP/6-311+G** level of density functional theory, Figure S3). Due to the symmetry of the Ph substituent, only a rotation of 180° has to be considered. The rotational profile is very flat, with a maximum barrier of little more than 2 kcal mol⁻¹. Two minima are found in gas phase, one with the Ph ring approximately bisected with respect to the adjacent CF bond (bis, dihedral -77°), and one where both are eclipsed (ecl, dihedral -91°). After full optimization, rotamer bis is more stable than ecl by 0.3 Kcal mol⁻¹. Rotamer bis has the slightly higher dipole moment (3.0 D, as opposed to 2.7 D for ecl). In the plarsible continuum the higher lying minimum disappears, leaving bis as the sole stable minimum.

**Figure S3**: Rotational profiles about the C(F)-C(=C) bond in **11a** (B3LYP/6-311+G** level), energies given in kcal mol⁻¹ relative to the most stable conformer (bis); full circles: gas phase, open circles: in a polarizable continuum (CPCM). The electrostatic potential (ESP) for bis is shown in Figure 2 and Figure S4. Rather than a facial polarity characteristic for all-cis fluorinated rings, an "in-plane polarity" is obtained, pointing from the CH₂ group with positive ESP to the C₂F₃ moiety with negative ESP. The direction of the overall dipole moment vector, however, is rather dominated by the Ph ring with its notably positive ESP.

**Figure S4**: Electrostatic potential of rotamer bis of **11a** at the B3LYP/6-311+G** level, plotted on a colour scale from -0.003 a.u. (red) to +0.003 a.u. (blue) and mapped onto an isodensity surface (= 4 10⁻⁴ a.u.).
Coordinates of the DFT-optimised structures for 11a
Cartesian coordinates in Å, B3LYP/6-311+G** optimised (xyz format)

11a minimum bis

\[ \begin{align*}
F_0, & -2.5835629041, 0.2484324986, -0.6317291223 \\
F_0, & -0.2880882679, 1.6446698128, -0.1459826912 \\
F_0, & 0.1.6186436169, -1.6903853101, -0.1897502404 \\
C_0, & -1.3114659487, 0.1023813171, 1.4599971748 \\
H_0, & -1.064976162, -0.642021169, 2.2071664781 \\
H_0, & 1.8542649868, 0.9755208819, 1.8026595156 \\
C_0, & -0.3170256263, 0.3369594555, 0.3165567232 \\
C_0, & -1.6148390825, -0.3631046887, 0.0810068336 \\
C_0, & 1.0096832728, -0.3376907313, 0.232482776 \\
C_0, & 1.8176176292, -0.4682283372, 1.3640260062 \\
C_0, & -0.7969347276, 0.0036565161 \\
C_0, & 0.079984873, -1.0534500424, 1.2641230638 \\
H_0, & 1.4615230899, -0.1079879186, 2.322817639 \\
C_0, & 0.7355443265, -0.3797128947, -1.1039313142 \\
H_0, & -0.850287042, -0.6971909584, 1.883737676 \\
C_0, & 0.537339451, -0.5098141629, 0.0300557769 \\
H_0, & 0.6998461843, -1.1511792643, 2.1465647455 \\
H_0, & 0.3090083231, -1.7363830644, -0.2040319154 \\
H_0, & 0.5170654328, -1.9673647858, -0.0484344368 \\
\end{align*} \]

11a minimum ecl

\[ \begin{align*}
F_0, & -2.493338562, 0.5546605005, -0.681351615 \\
F_0, & -0.2287574157, 1.7244886739, 0.2363750316 \\
F_0, & 1.6241218745, -1.4729256437, -0.5834070117 \\
C_0, & -1.3880845554, -0.0674677519, 1.4127635658 \\
H_0, & -1.2055706882, -0.9495964329, 2.0146812103 \\
H_0, & -1.919249844, 0.7459249554, -1.8928339569 \\
C_0, & -0.2986806266, 0.3586595517, -0.4141903416 \\
C_0, & -1.6030449783, -0.2315808518, 0.0445966988 \\
C_0, & 1.0265708767, 0.3160320379, 0.2876305912 \\
C_0, & 2.1239536947, 0.4187319425, -0.1748231989 \\
C_0, & -1.2016725833, -1.6657769787, 0.616226468 \\
C_0, & 3.3727371207, -0.1862385721, -0.3004459882 \\
H_0, & 1.9995246321, 1.4632091053, -0.427682097 \\
\end{align*} \]
DFT Computations for 19b through a truncated model 20

The same conformational analysis was performed for a model amide at the same level as in our previous study on related tetrafluorocyclohexyl amides (B3LYP/6-311+G** level of density functional theory). Starting from the X-ray derived coordinates for the N-benzyl derivative 19b, a truncated model 20 was built by replacing the benzyl substituent with a methyl group. After initial optimisation to the minimum A, a full rotational profile was constructed through a relaxed scan of the F-C-C=O dihedral angle (θ). To model a polar environment, the same procedure was repeated using a simple solvent model, namely the polarizable conductor variant of the polarizable continuum model (CPCM), employing the parameters of water and the default options in Gaussian 09. The resulting profiles are displayed in Figure 5. In both environments, the conformation observed in the solid state of benzyl amide 19b with a 1,5-NH...F interaction is the lowest minimum (denoted A). Two higher lying minima are apparent, namely rotamers B with a 1,6-NH...F interaction and C with a more bisected orientation of amide and cyclopropane moieties. These structures were subjected to full energy minimisation; relative energies and salient geometrical parameters of all minima are collected in Table S1. Because minima B and C have the adjacent CO and CF bonds in syn orientation, these forms are characterized by higher dipole moments than the global minimum A, where these groups are oriented in an anti fashion. Conformers minima B and C are therefore somewhat stabilized in a polar environment, but not to an extent that would make them competitive with the global minima A, which remains at least 3 kcal mol⁻¹ more stable.

Table S1: Computed properties (energies ΔE_rel relative to A, dipole moments µ, selected angles and distances) of model amide compound 20 (truncated version of 19b) at the B3LYP/6-311+G** level (gas phase values, unless otherwise noted)

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<th>C</th>
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<td>6.5</td>
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<tr>
<td>ΔE_rel [kcal mol⁻¹] in water</td>
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<td>(3.4)</td>
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<tr>
<td>θ_{F-C-C=O} calc [°]</td>
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<td>µ [D]</td>
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<td>4.2</td>
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</table>

aCPCM method. bN-benzyl derivative 19b, this work. cDistance between NH proton and nearest F atom.

Coordinates of the DFT-optimised structures for amide 20 (the truncated model of 19b)
Cartesian coordinates in Å, B3LYP/6-311+G** optimised (xyz format)

20 (the truncated amide model of 19b) minimum A

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$^{20}$ (the truncated amide model of $^{19b}$) minimum C

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