

Electronic Supplementary Information

Full synthesis and characterisation data for additional intermediates and products

6R*-(N,N-diethylcarbamoyloxy)-9,9-difluoro-7S*-methyl-2R*-phenylsulfanyl-4,8-dioxa-1S*-tricyclo[4.2.1.0^{3,7}]nonan-5-one 9b, and ethyl 2,2-difluoro-8S*-methyl-5-oxo-10R*-phenylsulfanyl-4,6,9-trioxa-tricyclo[5.2.1.0^{3,8}]-1S*-decane-3S*-carboxylate **10b** and ethyl 2S*-(N,N-diethylcarbamoyloxy)-3,3-difluoro-6S*-hydroxy-1S*-methyl-5R*-phenylsulfanyl-7-oxa-bicyclo[2.2.1]heptane-2-carboxylate **11b**

A solution of phenyl sulfenyl chloride (13.5 mL of a 2M solution in dichloromethane prepared *in situ*, 27 mmol) was added over 15 minutes to a solution of *endo/exo* mixture **7b** and **8b** (9 mmol, 3 g) in dry DCM (14 mL) at 0 °C under an atmosphere of nitrogen. The solution was warmed to room temperature and stirred for 72 hours. The solvent was removed *in vacuo* to afford an orange solid that was purified by column chromatography (20% to 40% diethyl ether, in light petroleum) to afford lactone **9b** (1.63 g, 44%) as colourless cubes; R_f (20% diethyl ether in light petroleum) 0.3; mp 106-108 °C; (Found: C, 55.10; H, 5.19; N, 3.46 C₁₉H₂₁F₂NO₅S requires: C, 55.20; H, 5.12; N 3.39 %); ν_{max} film/cm⁻¹ 1814s (C=O), 1720s (C=O), 1258m (C-O), 1213m (C-O), 1170s (C-O), 1152s (C-O), 739s (C-H), 690m (C-H); δ_H (300MHz, CDCl₃) 7.44-7.30 (5H, m, Ar), 4.52-4.48 (2H, m, CHCF₂, CHCHSPh), 3.81 (1H, s, CHSPh), 3.37-3.28 (4H, m, N(CH₂CH₃)₂), 1.68 (3H, s, CH₃), 1.22-1.13 (6H, m, N(CH₂CH₃)₂); δ_C(75MHz, CDCl₃) 165.5 (d, ³J_{C-F} 2.4), 151.9, 132.0, 131.1, 129.7, 128.1, 122.8 (dd, J_{C-F} 278.8, 269.3), 94.0 (d, ³J_{C-F} 6.0), 85.3, 82.4 (t, ²J_{C-F} 26.3), 81.2 (t, ²J_{C-F} 26.3), 51.7 (d, ³J_{C-F} 4.8), 42.6, 42.2, 14.9, 13.9, 13.2; δ_F (235MHz, CDCl₃), -112.1 (d, br, ²J_{F-F} 236.4), -116.5 (d, ²J_{F-F} 236.4); *m/z* (ES) 415 (32%, [M+H]⁺), 414 (100%); and carbonate **10b** (0.68 g, 11%) as colourless cubes; R_f (40% diethyl ether in light petroleum) 0.34; mp 138-139 °C; (Found: C, 53.01; H, 4.25; C₁₇H₁₆F₂O₆S requires: C, 52.85; H, 4.17 %); ν_{max} film/cm⁻¹ 1774 s (C=O), 1735 s (C=O), 1277 (C-O), 1220 s (C-O), 1195 s (C-O), 1166 s (C-O), 746 (C-H), 692 (C-H); δ_H (300MHz, CDCl₃) 7.50-7.32 (5H, m, Ar), 4.50 (1H, d, ³J_{H-F} 7.4, CHCF₂), 4.47 (1H, dd, J 2.1, ⁴J_{H-F} 1.0, CHSPh), 4.38 (2H, m, OCH₂CH₃), 3.80 (1H, s, CHOCO), 1.75 (3H, s, CH₃), 1.36 (3H, t, J 7.1, OCH₂CH₃); δ_C(63MHz, CDCl₃) 161.7 (d, ³J_{C-F} 2.3), 142.6, 132.3, 132.0, 130.2, 129.0, 121.4 (t, J_{C-F} 273.0), 88.9, 84.7 (dd, ²J_{C-F} 27.1, 20.0), 82.1 (dd, ²J_{C-F} 25.2, 25.0), 78.6, 63.8, 51.1 (d, ³J_{C-F} 3.2), 15.7, 14.4; δ_F (235MHz, CDCl₃) -108.6 (dd, ²J_{F-F} 236.1 ³J_{F-H} 7.4), -110.7 (d, ²J_{F-F} 236.1); *m/z* (ES) 387 (15%, [M+H]⁺), 325 (100); and alcohol **11b** (1.0 g, 27%) as colourless cubes; R_f (40% diethyl ether in light petroleum) 0.24; mp 119-121 °C; (Found: C, 54.98; H, 5.83; N, 3.15; C₂₁H₂₇F₂NO₆S requires: C, 54.89; H, 5.92; N 3.05 %); ν_{max} film/cm⁻¹ 3385m (OH), 1754s (C=O), 1684s (C=O), 1290m (C-O), 1238m (C-O), 1186s (C-O), 1054s (C-O), 739 (C-H), 691 (C-H); δ_H (300MHz, CDCl₃) 7.42-7.26 (5H, m, Ar), 4.38 (1H, d, J 6.4, CHOH), 4.28 (2H, q, J 7.1, OCH₂CH₃), 3.89 (1H, d, J 5.3, CHCF₂), 3.62 (1H, d, J 5.5, CHSPh), 3.39-3.23 (4H, m, N(CH₂CH₃)₂), 1.81 (3H, s, CH₃), 1.29 (3H, t, J 7.1, OCH₂CH₃), 1.22 (3H, t, J 7.1, NCH₂CH₃), 1.13 (3H, t, J 7.1, NCH₂CH₃); δ_C(75MHz, CD₃COCD₃) 164.2 (d, ³J_{C-F} 6.0), 153.3, 135.2, 129.8, 129.3, 126.9, 122.3 (dd, ³J_{C-F} 275.8, 262.7), 88.5, 86.3, 82.9 (t, ²J_{C-F} 24.5), 60.9, 49.1 (d, ³J_{C-F} 3.6), 41.8, 41.6, 17.6, 13.4, 13.3, 12.7 (one quaternary carbon signal is coincident with the signal at 82.9); δ_F (235MHz, CDCl₃) -104.2-(-109.8) (br. d, ²J 198.8) -114.3-(-121.2), (br); *m/z* (ES⁺) 461 (24 %, [M+H]⁺), 460 (100), 404 (23).

6R*-(N,N-diethylcarbamoyloxy)-9,9-difluoro-2R*-methyl-2R*-phenylsulfanyl-4,8-dioxa-1S*,7S*-tricyclo[4.2.1.0^{3,7}]-nonan-5-one 9c

Phenylsulfenyl chloride (1.5 mmol, 0.2 mL) was added slowly to a solution of *endo-7c* (0.5 mmol, 0.16 g) in CHCl₃ (3 mL) at room temperature. The orange-coloured solution was stirred at room temperature for 48 hours then concentrated. The orange oil was purified by chromatography to afford **9c** as colourless cubes (0.138g, 70 %), mp 110-111 °C; R_f (10 % ethyl acetate in hexane) 0.1; (Found: C, 55.25; H, 5.23; N, 3.47; C₁₉H₂₁F₂NO₅S requires: C, 55.20; H, 5.12; N 3.39 %); δ_H (300 MHz, CDCl₃) 7.58-7.55 (2H, m, Ar-H), 7.46-7.37 (3H, m, Ar-H), 5.84-5.82 (1H, m, HCOCHCF₂), 4.88 (1H, dd, *J* 5.4, 1.5, HCCHOCH), 4.21 (1H, dd, *J* 7.8, 1.5, HCOCHCF₂), 3.38-3.24 (4H, m, N(CH₂CH₃)₂), 1.44 (3H, d, ⁵J_{H-F} 3.6 CH₃), 1.20 (3H, t, *J* 7.05, NCH₂CH₃), 1.14 (3H, t, *J* 7.05, NCH₂CH₃); δ_C (75 MHz, CDCl₃) 166.2, 153.1, 137.7, 130.3, 129.4, 128.6, 122.6 (dd, ¹J_{C-F} 277.7, 271.8), 85.3, (d, ³J_{C-F} 7.2), 83.6 (t, ²J_{C-F} 24.4), 80.7 (dd, ²J_{C-F} 25.9, 14.9), 80.4, 57.4 (dd, ⁴J_{C-F} 4.8, 2.3), 42.4, 42.0, 16.9 (d, ⁴J_{C-F} 9.4), 13.7, 13.1; δ_F (282 MHz, CDCl₃) -106.5 (dd, ²J_{F-F} 239.8, 7.2), -117.8 (d, ²J_{F-F} 239.8); *m/z* (ES) 414 (100%, [M+H⁺]), 357 (3), 224 (2), 100 (23).

6*R(*N,N*-diethylcarbamoyloxy)-9,9-difluoro-3*S**,7*S**-dimethyl-2*R**-phenylsulfanyl-4,8-dioxo-1*S**-tricyclo-[4.2.1.0^{3,7}]nonan-5-one **9d** and ethyl 2*R**-(*N,N*-diethylcarbamoyloxy)-3,3-difluoro-1*S**-methyl-6-methylene-5*R**-phenylsulfanyl-7-oxa-bicyclo[2.2.1]-7*S**-heptane-2-carboxylate **12****

A solution of phenylsulfenyl chloride, prepared *in situ*,^{ref} (13.5 mL of a 2M solution, 27 mmol) was added over 15 minutes to a solution of a mixture of *endo 7d* and *exo 8d* (9 mmol of a 1:1.7 mixture, 3.1 g) in DCM (50 mL) at 0 °C under an atmosphere of nitrogen. The solution was warmed to room temperature and stirred for 72 hours. The solvent was removed *in vacuo* and the inseparable mixture was eluted through a short silica gel column (30% diethyl ether in hexane) which afforded an inseparable mixture of **9d** and **12** (1:1.5 by ¹H NMR) as a pale yellow solid (3.78 g); δ_H (300MHz, CDCl₃) 7.38-7.20 (10H, m, Ar), 5.39 (1H, d, ²J 1.8 C=CH_aH_b), 5.22 (1H, d, ²J 1.8 C=CH_aH_b), 4.39-4.34 (2H, m, 2 x CHCF₂), 4.25-4.17 [4H, q, *J* 7.1, OCH₂CH₃, (including 4.16, 2H, s, 2 x CHSPh)], 3.29-3.12 (8H, m, 2 x N(CH₂CH₃)₂), 1.72 (3H, s, CH₃), 1.57 (3H, s, CH₃), 1.45 (3H, s, CH₃), 1.22 (3H, t, *J* 7.1, OCH₂CH₃), 1.15-1.02 (12H, m, 2 x N(CH₂CH₃)₂); δ_F (282MHz, CDCl₃) (-106.0)-(-112.7) (br), -112.7 (d, ²J_{F-F}, 236.0), *m/z* (ES⁺) 456 (100%, [M+H]⁺, **12**), 428 (84, [M+H]⁺, **9d**). Allylic sulfide **12** was obtained as a pure compound by the subsequent procedure.

6*R(*N,N*-diethylcarbamoyloxy)-9,9-difluoro-1*S**,7*S**-dimethyl-2*R**-phenylsulfanyl-4,8-dioxatricyclo-[4.2.1.0^{3,7}]nonan-5-one **9e** and ethyl 2*S**-(*N,N*-diethylcarbamoyloxy)-3,3-difluoro-1*S**,7*S**-dimethyl-6*S**-hydroxy-5*R**-phenylsulfanyl-7-oxa-bicyclo[2.2.1]heptane-2-carboxylate **11e****

Phenylsulfenyl chloride (22 mmol, 2.7 mL) was added slowly to a solution of *endo-7e* and *exo-8e* (7.6 mmol, 2.62 g) in CHCl₃ (50 mL) at room temperature. The resulting orange coloured solution was stirred at room temperature for 48 hours before the solvent was removed and the resulting orange coloured oil was purified by chromatography, to afford **9e** (1.28 g, 40 %) as an oil, R_f (50 % diethyl ether in hexane) 0.23; δ_H (300 MHz, CDCl₃) 7.44-7.27 (5H, m, ArH), 4.59 (1H, s, HCCSPh), 3.81 (1H, s, HCSPH), 3.38-3.29 (4H, m, N(CH₂CH₃)₂), 1.62 (6H, s, 2 x CH₃), 1.20 (3H, t, *J* 6.0, N(CH₂CH₃)₂), 1.15 (3H, t, *J* 6.0, N(CH₂CH₃)₂); δ_C (75 MHz, CDCl₃) 165.9, 151.9, 136.6, 130.5, 129.6, 127.7, 123.2 (t, ¹J_{C-F} 276.0), 92.4, 87.8 (t, ²J_{C-F} 23.6), 87.5, 82.4 (t, ²J_{C-F} 21.0), 55.3, 42.6, 42.2, 14.9, 13.9, 13.2, 11.1; δ_F (282 MHz, CDCl₃) -116.9 (d, ²J_{F-F} 233.1), -118.7 (br, d, ²J_{F-F} 233.1); [HRMS Found: 428.1348. Calc. for C₂₀H₂₄F₂NO₅S 428.1343]; *m/z* (ES) 428 (100 %, [M+H]⁺), 287 (3), 231 (3), 100 (3): and **11e** (0.79 g, 22%) as cubes, R_f (50 % diethyl

ether in hexane) 0.12; mp 141-142 °C; (Found: C, 55.91; H, 6.25; N, 2.93; C₂₂H₂₉F₂NO₆S requires: C, 55.80; H, 6.17; N 2.96 %); δ_{H} (300 MHz, CDCl₃) 7.40 – 7.19 (5H, m, ArH), 4.28 (2H, q, J 7.0, OCH₂CH₃), 3.85 (1H, d, J 6.5, CHSPh), 3.72 (1H, d, J 6.6, CHOH), 3.41-3.25 (4H, m, N(CH₂CH₃)₂), 2.50 (1H, br s, OH), 1.80 (3H, s, CH₃), 1.49 (3H, s, CH₃), 1.29 (3H, t, J 7.2, OCH₂CH₃), 1.21 (3H, t, J 7.1, N(CH₂CH₃)₂), 1.12 (3H, t, J 7.1, N(CH₂CH₃)₂); δ_{F} (282 MHz, CDCl₃) -113.3 (br. d, $^2J_{\text{F-F}}$ 209.8), -119.2 (br. s); m/z (ES) 474 (100 %, [M+H]⁺), 436 (2), 428 (3), 357 (5) 100(22).

3,3-Difluoro-1S*,6S*-dimethyl-2R*-(hydroxymethyl)-5R*-phenylsulfanyl-7-oxabicyclo[2.2.1]heptane-2,6S*-diol 17d and 3,3-difluoro-2S*-(hydroxymethyl)-6-methylene-5R*-phenylsulfanyl-7-oxabicyclo[2.2.1]heptan-2-ol 19

Were prepared as for **17b** from a mixture of crude lactone **9d** (1.4 g, 3.3 mmol) and alkene **12** (2.38 g, 5.2 mmol) in THF (16 mL) and lithium aluminium hydride (48 mmol, 1.8 g) in THF (70 mL) at 0 °C under an atmosphere of nitrogen. The suspension was refluxed overnight; after cooling, the excess lithium aluminum hydride was destroyed carefully with water (10 mL) and dilute HCl (30 mL of a 1 M of a aqueous solution). The resulting solution was neutralised with aqueous sodium hydroxide (7.5 mL of a 0.5 M of a aqueous solution) and extracted with ethyl acetate (6 x 30 mL). The combined organic extracts were dried (MgSO₄) and concentrated *in vacuo* to afford a yellow solid which was purified by column chromatography (50% diethyl ether in hexane) to yield triol **17d** (0.7 g, 68 %); white powder mp 120-121 °C, R_f (30% ethyl acetate in light petroleum) 0.14; (Found: C, 54.44; H, 5.46; C₁₅H₁₈F₂O₄S requires: C, 54.21; H, 5.46 %); ν_{max} (film)/cm⁻¹ 3508w br (OH), 3372m br (OH), 1116s (CO), 1085s (CO), 741s (C-H def.), 687s (C-H def.); δ_{H} (300MHz, ((CD₃)₂SO) 7.38-7.33 (4H, m, Ar), 7.29-7.21 (1H, m, Ar), 5.75 (1H, s, OH), 5.22 (1H, d, J 1.7, OH), 4.58-4.56 (1H, m), 4.14 (1H, dd, J 9.1, CHCF₂), 4.02-3.95 (1H, m, CH_aH_bO), 3.69 (1H, s, CHSPh), 3.60-3.53 (1H, m, CH_aH_bO), 1.31 (3H, s, CH₃), 1.26 (3H, s, CH₃); δ_{C} (100MHz, CD₃COCD₃), 136.6, 129.6, 129.4, 126.7, 125.2 (dd, $^1J_{\text{C-F}}$ 266.3, 262.9), 94.4 (d, $^3J_{\text{C-F}}$ 6.0), 85.0 (t, $^2J_{\text{C-F}}$ 27.1), 82.2, 81.9 (t, $^2J_{\text{C-F}}$ 15.5), 62.1 (d, $^3J_{\text{C-F}}$ 7.3), 55.9 (d, $^3J_{\text{C-F}}$ 8.6), 23.9, 11.7; δ_{F} (376MHz, CD₃COCD₃), -112.5 (d, $J_{\text{F-F}}$ 226.7), 124.1 (d, $J_{\text{F-F}}$ 226.7); m/z (ES) (M-H⁺) 331 (14%), 329 (52), 223 (100):

and diol **19** (1.4 g, 76 %), white powder; mp 129-131 °C, R_f (30% ethyl acetate in light petroleum) 0.17; ν_{max} (film)/cm⁻¹ 3443s br (OH), 3059w (C-H), 1160s (C-O), 1091s (CO), 964s (C-H), 735s (C-H def.), 687s (C-H def.); δ_{H} (300MHz, CDCl₃) 7.50-7.19 (5H, m, Ar), 5.47 (1H, s, C=CH_aH_b), 5.23 (1H, s, C=CH_aH_b), 4.25 (1H, t, $^3J_{\text{H-F}}$ 3.9, CHCF₂), 4.17 (1H, s, CHSPh), 3.92 (1H, d, 2J 11.7, OCH_aH_b), 3.61 (1H, d, 2J 11.7, OCH_aH_b), 2.40 (2H, s, br, OH), 1.39 (3H, s, CH₃); δ_{C} (75MHz, CDCl₃), 147.1, 134.0, 136.6, 131.6, 129.3, 127.8, (t, $^1J_{\text{C-F}}$ 266.9), 113.6, 90.1 (t, $^3J_{\text{C-F}}$ 2.4), 82.2 (t, $^2J_{\text{C-F}}$ 26.3), 78.0 (t, $^2J_{\text{C-F}}$ 19.6), 62.1 (t, $^3J_{\text{C-F}}$ 6.0), 48.9 (d, $^3J_{\text{C-F}}$ 3.6), 14.0; δ_{F} (282MHz, CDCl₃) -114.3 (s); HRMS Found: 314.07882, Calc. For C₁₅H₁₆F₂O₃S 314.07879; m/z (EI) 314 (25%, M⁺), 218 (25), 110 (100). Satisfactory microanalysis could not be obtained for this compound.

The yields are quoted over two steps from the cycloadduct mixture and refer to the theoretical maximum from the amount of cycloadduct.

3,3-Difluoro-2S*-(hydroxymethyl)-5R*-phenylsulfanyl-7-oxabicyclo[2.2.1]-1S*,7S*-heptane-2,6S*-diol 18a

A solution of **11a** (3.2 mmol, 1.2 g) in THF (10 mL) was added dropwise to a suspension of lithium aluminium hydride (19 mmol, 0.7 g) in THF (10 mL) at 0°C. The suspension was warmed to reflux and stirred for 3 hours before

being cooled to 0 °C and quenched by the cautious addition of water (10 mL), then HCl (5mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (6 x 15mL), the combined extracts were dried (MgSO₄), filtered and concentrated to afford an oil which was purified by column chromatography (Biotage 25M, 80% ethyl acetate in hexane) to afford triol **18a** as a white solid (0.59 g, 67%); mp 148-149 °C; R_f (80 % ethyl acetate in hexane) 0.24; δ_H (300 MHz, CD₃COCD₃) 7.44-7.28 (5H, m, ArH), 5.51 (1H, d, *J* 4.5, OH), 4.78 (1H, s, OH), 4.33-4.30 (2H, m, CHOCHCF₂, CHOH), 4.27-4.24 (1H, m, CHOCHCF₂), 4.00 (3H, s, CHS, CH₂OH), 3.56-3.55 (1H, m, OH); δ_C (75 MHz, CD₃COCD₃) 135.6, 129.7, 129.4, 127.1, 124.9 (dd, ¹J_{C-F} 269.3, 264.7), 87.6, (d, ³J_{C-F} 6.0), 86.4 (t, ²J_{C-F} 27.1), 81.2 (dd, ¹J_{C-F} 23.8, 16.0), 77.8, 61.5 (d, ³J_{C-F} 7.5), 50.2 (dd, ³J_{C-F} 4.9, 2.6); δ_F (282MHz, (CD₃)₂CO) -112.5 (d, ²J_{F-F} 232.0), -125.7 (d, ²J_{F-F} 232.0); *m/z* (ES) 253 (3 %, [M-F]⁺), 223 (100), 195 (3), 109 (45). The product was taken on directly without further purification or characterization.

3,3-Difluoro-2R*-(hydroxymethyl)-5R*-phenylsulfanyl-7-oxabicyclo[2.2.1]-1S*,7S*-heptane-2,6S*-diol 18b

A solution of alcohol **11b** (0.8 mmol, 0.37 g) in THF (2 mL) was added to a suspension of lithium aluminium hydride (4.8 mmol, 0.2 g) in THF (8 mL) at 0 °C under an atmosphere of nitrogen. The suspension was refluxed overnight; after cooling, the excess lithium aluminum hydride was destroyed carefully with water and dilute HCl (3 mL of a 1M aqueous solution). The resulting solution was neutralised with aqueous sodium hydroxide (0.5 M) and extracted with ethyl acetate (6 x 20 mL). The combined organic extracts were dried (MgSO₄) and concentrated *in vacuo* to afford a yellow solid which was triturated with hexane to yield triol **18b** (0.2 g, 79 %) as colourless cubes; mp 125-127 °C, R_f (40% ethyl acetate in light petroleum) 0.39; (Found: C, 52.92; H, 5.06; C₁₄H₁₆F₂O₄S requires: C, 52.82; H, 5.07 %); ν_{max} (film)/cm⁻¹ 3570m br (O-H), 3345m br (O-H), 1144m (C-O), 1087s (C-O) 748s (C-H def.), 694s (C-H def.); δ_H (300MHz, CDCl₃) 7.45-7.25 (5H, m, Ar), 4.33-4.28 (2H, m, 2 x OH), 4.20 (1H, d, ³J_{H-F} 9.5, CHCF₂), 4.00 (1H, d, ²J 11.7, OCH_aH_b), 3.88-3.83 (1H, m, CHOH), 3.74-3.65 (2H, m, OCH_aH_b, CHSPh), 1.94 (1H, s, br, OH), 1.49 (3H, s, CH₃); δ_C(75MHz, CD₃COCD₃) 135.1, 129.9, 129.3, 126.9, 123.3 (dd, J_{C-F} 266.3, 263.9), 87.4, 84.6 (t, ³J_{C-F} 2.4, 2.3), 83.7 (dd, ²J_{C-F} 27.5, 25.1) 81.3 (dd, ²J_{C-F} 20.3, 17.9), 61.4 (d, ³J_{C-F} 13.2), 50.9 (d, ³J_{C-F} 4.8), 15.2; δ_F (300MHz, CD₃COCD₃), -116.4 (dd, ²J_{F-F} 232.2, ³J_{F-H} 9.5), -118.0 (d, ²J_{F-F} 232.2); *m/z* (ES) 317 (100%, [M-H]⁺).

3,3-Difluoro-2R*-(hydroxymethyl)-1S*-methyl-5R*-phenylsulfanyl-7-oxabicyclo[2.2.1]-7S*-heptane-2,6S*-diol acetone acetal 20b

A solution of triol **17b** (4 mmol, 1.24 g) in acetone (40 mL) was added to a mixture of dry CuSO₄ (12 mmol, 2.0 g) and catalytic *p*-toluenesulfonic acid monohydrate (5 mol%, 0.6 mmol, 0.114 g) at room temperature under an atmosphere of nitrogen. The reaction was stirred for 5 hours at room temperature, then quenched with NH₄Cl (20 mL of a saturated aqueous solution). The mixture was extracted with ethyl acetate (3 x 20 mL) and the combined organic extracts were then washed with NaHCO₃ (3 x 20 mL) of a saturated aqueous solution, before being dried (MgSO₄) and concentrated *in vacuo*. The brown solid product was washed with hexane to afford acetone **20b** (1.36 g, 95 %) as colourless cubes; R_f (40% diethyl ether in light petroleum) 0.37; mp 116-117 °C; (Found: C, 57.05; H, 5.56 C₁₇H₂₀F₂O₄S requires: C, 56.97; H, 5.62 %); ν_{max} (film)/cm⁻¹ 3526w br (OH), 2991w (C-H), 1485m (C-C), 1264w (C-O), 1167m (C-O), 1134w (C-O), 1091s (C-O), 748s (C-H def.), 692s (C-H def.); δ_H (300MHz, CDCl₃) 7.40-7.23 (5H, m, Ar), 4.41 (1H, d, ²J 10.6, CH_aH_bO), 4.23 (1H, d, ³J_{H-F} 8.1, CHCF₂), 3.95-3.93 (1H, m, CHOH), 3.90 (1H, dt, ²J

10.6, $^4J_{\text{H-F}}$ 3.3, $\text{CH}_a\text{H}_b\text{O}$) 3.56 (1H, br. s, *CHSPh*), 2.39 (1H, br, *OH*), 1.51 (6H, s, CH_3), 1.39 (3H, s, CH_3); δ_{C} (75MHz, CDCl_3) 134.2, 130.5, 129.4, 127.4, 123.5 (t, $^1J_{\text{C-F}}$ 267.6), 109.9, 89.0 (d, $^3J_{\text{C-F}}$ 6.0), 86.8 (dd, $^2J_{\text{C-F}}$ 25.6, 16.0), 83.2, 83.1 (dd, $^2J_{\text{C-F}}$ 28.8, 25.6), 64.8 (d, $^3J_{\text{C-F}}$ 7.2), 51.1 (d, $^4J_{\text{C-F}}$ 2.4), 26.1, 25.2, 14.7; δ_{F} (235 MHz, CDCl_3) -109.7 (dd, $^2J_{\text{F-F}}$ 228.4, $^3J_{\text{F-H}}$ 8.1), -119.8 (d, $^2J_{\text{F-F}}$ 228.4); m/z (ES) 359 (15%, $[\text{M}+\text{H}]^+$), 317 (44), 301 (40), 90 (100).

3,3-Difluoro-1*S**,6*S**-dimethyl-2*R**-(hydroxymethyl)-5*R**-phenylsulfanyl-7-oxabicyclo[2.2.1]heptane-2,6*S**-diol acetone acetal **20d**

Was prepared as for **20b** from a solution of triol **17d** (2.4 mmol, 0.82 g) in acetone (25 mL), dry CuSO_4 (7.2 mmol, 1.1 g) and *p*-toluenesulfonic acid monohydrate (0.12 mmol, 0.21 g) at room temperature under an atmosphere of nitrogen. The reaction was stirred for 18 hours at room temperature, then quenched with NH_4Cl (15 mL of a saturated aqueous solution). The mixture was extracted with ethyl acetate (3 x 20 mL), then washed with NaHCO_3 (3 x 20 mL of a saturated aqueous solution), and dried (MgSO_4). The solution was concentrated *in vacuo* to yield a brown solid that was washed with hexane to afford acetonide **20d** (0.79 g, 89 %) as colourless cubes; mp 134-136 °C; R_f (30% diethyl ether in light petroleum) 0.12; (Found: C, 57.89; H, 5.63; $\text{C}_{18}\text{H}_{22}\text{F}_2\text{O}_4\text{S}$ requires: C, 58.05; H, 5.95 %); ν_{max} (film)/ cm^{-1} 3443w br (*OH*), 2988w (*C-H*), 1483m (*C-C*), 1231w (*C-O*), 1176s (*C-O*), 1113m (*C-O*), 1081s (*C-O*), 729s (*C-H* def.), 684m (*C-H* def.); δ_{H} (300MHz, CDCl_3) 7.37-7.19 (5H, m, Ar), 4.59 (1H, dt, 2J 10.8, $^4J_{\text{H-F}}$ 1.3 $\text{CH}_a\text{H}_b\text{O}$), 4.26 (1H, dd, $^3J_{\text{H-F}}$ 8.8, 1.8 CHCF_2), 3.91 (1H, dt, 2J 10.8, $^4J_{\text{H-F}}$ 3.5 $\text{CH}_a\text{H}_b\text{O}$), 3.82-3.81 (1H, m, *CHSPh*), 1.94 (1H, s, *OH*), 1.51 (3H, s, CH_3), 1.50 (3H, s, CH_3), 1.41 (1H, s, CH_3), 1.39 (1H, s, CH_3); δ_{C} (75MHz, CDCl_3) 135.3, 129.4, 129.2, 126.7, 123.3 (dd, $^1J_{\text{C-F}}$ 268.7, 265.1), 109.8, 91.8, 88.0 (dd, $^2J_{\text{C-F}}$ 26.4, 15.5), 84.1 (dd, $^2J_{\text{C-F}}$ 28.7, 26.3), 81.9, 65.5 (d, $^3J_{\text{C-F}}$ 7.5), 55.7 (dd, $^3J_{\text{C-F}}$ 6.0, 2.4), 26.3, 25.1, 24.1, 11.6; δ_{F} (376MHz, CDCl_3) -109.3 (dd, $^2J_{\text{F-F}}$ 225.6, $^3J_{\text{F-H}}$ 8.8) -119.8 (d, $^2J_{\text{F-F}}$ 225.6); m/z (ES) 373 (23%, $[\text{M}+\text{H}]^+$), 315 (100).

3,3-Difluoro-2*S**-(hydroxymethyl)-5*R**-phenylsulfanyl-7-oxabicyclo[2.2.1]-1*S**,7*S**-heptane-2,6*S**-diol acetone acetal **21a**

Was prepared as for **20b** from a suspension of triol **18a** (0.4 mmol, 0.13g), CuSO_4 (1.3 mmol, 0.2 g) and *p*-toluene sulfonic acid monohydrate (0.1 mmol, 0.02 g) in acetone (5 mL) after stirring overnight at room temperature the reaction was quenched with saturated aqueous ammonium chloride (5 mL), then extracted with ethyl acetate (3 x 10 mL), the combined extracts were washed with saturated aqueous sodium bicarbonate (3 x 5 mL), dried (MgSO_4) filtered and concentrated to afford acetonide **21a** as a white solid (0.137 g, est. 100%) which was used without further purification. mp 114-115 °C; R_f (50 % diethyl ether in hexane) 0.27; δ_{H} (300MHz, CDCl_3) 7.38-7.22 (5H, m, Ar), 4.44-4.41 (2H, m, [includes 4.43 (1H, d, J 10.8, $\text{CH}_a\text{H}_b\text{O}$)], *CHOCH*), 4.33-4.27 (2H, m, *CHOH*, CHCF_2), 4.11 (1H, dt, J 10.8, $^3J_{\text{H-F}}$ 3.2, $\text{CH}_a\text{H}_b\text{O}$), 3.49 (1H, s, *PhSCH*), 3.19 (1H, d, J 3.3, *OH*), 1.48 (3H, s, CH_3), 1.39 (3H, s, CH_3); δ_{C} (75 MHz, CDCl_3) 134.2, 130.2, 129.4, 127.3, 123.1 (dd $^1J_{\text{C-F}}$ 271.4, 266.9), 110.1, 86.2 (dd $^2J_{\text{C-F}}$ 26.3, 16.8), 85.6, (d $^3J_{\text{C-F}}$ 4.9), 84.8 (dd $^2J_{\text{C-F}}$ 28.3, 26.7), 77.1, 64.4, (d $^3J_{\text{C-F}}$ 7.6), 50.5 (d $^4J_{\text{C-F}}$ 2.3), 25.6, 25.3; δ_{F} (282MHz, CDCl_3) -108.8-108.9 (m), -109.6-109.8 (m) [comprise apparent doublet $^2J_{\text{F-F}}$ 230.1), -120.7 (d, $^2J_{\text{F-F}}$ 230.1); m/z (ES) 344 (100%, M^+), 321 (3), 303 (7), 287 (17), 269 (5), 174 (3), 125 (11). The product was taken on directly without further purification or characterization.

3,3-difluoro-2S*-(hydroxymethyl)-6-methylene-5R*-phenylsulfanyl-7-oxabicyclo[2.2.1]heptan-2-ol acetone acetal 22

Phenyl sulfenyl chloride (3.6 mL of a 2M solution, 7.2 mmol) was added dropwise to a solution of acetone **28**¹⁸ (2.4 mmol, 0.6 g) in DCM (4 mL) at 0 °C under an atmosphere of nitrogen. The solution was warmed to room temperature and stirred for 72 hours. The solvent was removed *in vacuo* afforded an orange solid which was purified through a short column of silica gel (30 % diethyl ether in light petroleum) to yield sulfide **22** (0.18 g, 21%) as a pale yellow powder; R_f (30% diethyl ether in light petroleum) 0.45; mp 95-97 °C; (Found: C, 60.81; H, 5.76; C₁₈H₂₀F₂O₃S requires: C, 61.00; H, 5.69 %) v_{max} (film)/cm⁻¹ 2981w (C-H), 1375w (C-C), 1105m (C-O), 1044m (C-O), 744m (C-H def.), 670m (C-H def.); δ_H (300MHz, CDCl₃) 7.44-7.26 (5H, m, Ar), 5.50 (1H, d, ²J 1.8 CH_aH_b), 5.24 (1H, d, ²J 1.8 CH_aH_b), 4.32-4.25 [3H, m, CHCF₂, CHSPh, including 4.26 (1H, d, ²J 10.2, CH_aCH_bO)], 4.11 (1H, d, ²J 10.2, CH_aCH_bO), 1.50 (3H, s, CH₃), 1.46 (3H, s, CH₃), 1.38 (3H, s, CH₃); δ_C (300MHz, CDCl₃) 146.6, 134.3, 131.4, 129.3, 127.6, 122.1 (dd, ¹J_{C-F} 268.1, 265.7), 113.3, 111.4, 89.1 (d, ³J_{C-F} 2.4), 84.9 (dd, ²J_{C-F} 22.7, 16.7), 82.3 (dd, ²J_{C-F} 28.1, 24.5), 65.3 (d, ³J_{C-F} 15.5), 49.0 (d, ³J_{C-F} 6.0), 26.6, 24.4, 13.7; δ_F (282MHz, CDCl₃) -110.3 (dd, ²J_{F-F} 234.2, ³J_{H-F} 8.6), -114.0 (d, ²J_{F-F} 234.2); [HRMS (Found: 354.11018, Calc. For C₁₈H₂₀ F₂O₃S 354.11012]; m/z (EI) 354 (18%, M⁺), 245 (M-SPh) (100): and diol **19**^{*} (0.39 g, 52%) as a colourless powder.

6S*-Benzyloxy-3,3-difluoro-2R*-(hydroxymethyl)-1S*-methyl-5R*-phenylsulfanyl-7-oxabicyclo[2.2.1]-7S*-heptan-2-ol acetone acetal 23b

A solution of alcohol **20b** (5.8 mmol, 2.0 g), in THF (16 mL), was added slowly to a suspension of sodium hydride (11.6 mmol, 0.28 g of 60% dispersion from which the mineral oil had been removed by washing with hexane) in THF (10 mL) at 0 °C under an atmosphere of nitrogen. The resulting white suspension was stirred at 0 °C for one hour before TBAI (5 mol%, 0.58 mmol, 0.214 g) and benzyl bromide (11.6 mmol, 1.4 mL) were each added in one portion. The mixture was allowed to warm to room temperature and stirred for 4 hours before being quenched cautiously with water (10 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic extracts were dried (MgSO₄) and concentrated *in vacuo* to leave a yellow semi solid which was triturated with hexane to afford acetone **23b** (2.4 g, 86 %) as colourless cubes; R_f (30% diethyl ether in light petroleum) 0.52; mp 94-95 °C; (Found: C, 64.31; H, 5.71; C₂₄H₂₆F₂O₄S requires: C, 64.27; H, 5.84 %); v_{max} (film)/cm⁻¹ 2991w (C-H), 1258m (C-O), 1171m (C-O), 1098s (C-O), 743s (C-H def.), 697s (C-H def.); δ_H (250 MHz, CDCl₃) 7.38-7.22 (10H, m, Ar), 4.56 (1H, d, ²J 12.0, PhCH_aH_b), 4.44-4.34 (2H, m, CH_aH_bO and PhCH_aH_b [including 4.41 (1H, d, ²J 12.0, PhCH_aH_b)]), 4.28 (1H, d, ³J_{H-F} 8.2 CHCF₂), 3.88 (1H, dt, ²J 10.8, ⁴J_{H-F} 3.3, CH_aH_bO), 3.66 (1H, d, J 3.2, CHOBn), 3.59-3.57 (1H, m, CHSPh), 1.48 (3H, s, CH₃), 1.45 (3H, s, CH₃), 1.36 (3H, s, CH₃); δ_C (63 MHz, CDCl₃) 137.2, 134.6, 131.2, 129.8, 129.0, 128.6, 128.1, 128.0, 123.9 (dd, ¹J_{C-F} 270.1, 265.5), 110.4, 89.2, 89.0 (d, ³J_{C-F} 5.1), 87.5 (dd, ²J_{C-F} 26.4, 16.3), 84.0 (dd, ²J_{C-F} 28.0, 26.0), 74.0, 65.4 (d, ³J_{C-F} 7.1), 49.6 (d, ³J_{C-F} 2.5), 26.6, 25.6, 15.4; δ_F (235 MHz, CDCl₃) -109.4 (dd, ²J_{F-F} 228.7, ³J_{F-H} 8.2) -118.7 (d, ²J_{F-F} 228.7); m/z (ES) 449 (20%, [M+H]⁺), 391 (100), 392 (47).

6S*-Benzyloxy-3,3-difluoro-1S*,6-dimethyl-2R*-(hydroxymethyl)-5R*-phenylsulfanyl-7-oxabicyclo[2.2.1]heptane-2-ol acetone acetal 23d

A solution of alcohol **20d** (1 mmol, 0.4 g) in DMF (5.2 mL), was added slowly to a suspension of sodium hydride (1.1 mmol, 0.06 g of 60% dispersion from which the mineral oil had been removed by washing with hexane) in THF at 0 °C under an atmosphere of nitrogen. The resulting white suspension was stirred at 0 °C for one hour before benzyl bromide (4 mmol, 0.5 mL) was added in one portion. The mixture was allowed to warm to room temperature and stirred for 18 hours before being quenched cautiously with water (2 mL), and extracted with ethyl acetate (3 x 5 mL). The combined organic extracts were dried over MgSO₄ and concentrated *in vacuo* to leave a pale yellow powder which was triturated with hexane to afford acetonide **23d** (0.43 g, 93 %) as a white powder; R_f (20% diethyl ether in light petroleum) 0.43; mp 85-87 °C; (Found: C, 65.13; H, 5.93; C₂₅H₂₈F₂O₄S requires: C, 64.92; H, 6.10 %); ν_{max} (film)/cm⁻¹ 2986 (C-H), 1262m (C-O), 1107s (C-O), 1056s (C-O), 738s (C-H def.), 691s (C-H def.); δ_H (300MHz, CDCl₃), 7.35-7.14 (5H, m, Ar), 4.41 (1H, d, ²J 10.8, PhCH_aH_b), 4.24-4.18 (2H, m, PhCH_aH_b, CHCF₂), 4.12 (d, ²J 10.8, CH_aH_bO) 3.83 (1H, s, CHSPh), 3.63 (1H, d, ²J 10.8, CH_aH_bO), 1.49 (1H, s, CH₃), 1.39 (1H, s, CH₃), 1.37 (1H, s, CH₃), 1.26 (1H, s, CH₃); δ_C (75MHz, CDCl₃) 137.1, 134.6, 130.6, 129.5, 128.6, 128.1, 128.0, 127.4, 123.3 (dd, ¹J_{C-F} 269.2, 264.5), 109.6, 93.0 (d, ³J_{C-F} 4.8), 88.1 (dd, ²J_{C-F} 26.3, 15.5), 86.9, 84.6 (dd, ²J_{C-F} 28.7, 25.1), 67.9, 65.7 (d, ³J_{C-F} 7.2), 53.0 (d, ³J_{C-F} 6.0), 26.3, 25.1, 19.1, 12.0; δ_F (282MHz, CDCl₃) -108.3 (dd, ²J_{F-F} 226.5, ³J_{F-H} 8.0), -118.1 (d, ²J_{F-F} 226.5); *m/z* (FAB) 463 (18%, [M+H]⁺), 405 (100).

6S*-Benzyloxy-3,3-difluoro-2S*-(hydroxymethyl)-5R*-phenylsulfanyl-7-oxabicyclo[2.2.1]-1S*,7S*-heptan-2-ol acetone acetal 24a

Was prepared as for **23d** from acetonide **21a** (0.4 mmol, 0.137 g), in THF (1 mL) and NaH (0.44 mmol, 0.02 g) in THF (2 mL) at 0 °C, after stirring for 1 hour benzyl bromide (0.44 mmol, 0.05 mL), and tetra n-butyl ammonium iodide (10 mol%, 0.015g) were added and the resulting mixture stirred for 48 hours at room temperature. The reaction was quenched with water (5 mL) and extracted with ethyl acetate (3 x 10 mL) the combined extracts were dried (MgSO₄), filtered, and concentrated to afford benzyl ether **24a** as a white solid (0.174g) which was used without further purification or characterization; R_f (50 % diethyl ether in hexane) 0.49; *m/z* (ES) 435 (3 %, [M+H]⁺), 377 (5), 243 (52), 242 (100), 186 (14), 142 (19).

6S*-Benzyloxy-3,3-difluoro-2R*-(hydroxymethyl)-1S*-methyl-5R*-phenylsulfonyl-7-oxabicyclo[2.2.1]-7S*-heptan-2-ol acetone acetal 25b

Was prepared as for **25a** from a solution of sulfide **23b** (4.5 mmol, 2.0 g) in DCM (9 mL), *m*CPBA (9.5 mmol, 1.6 g) and sodium dihydrogen phosphate (9.5 mmol, 1.1 g) in DCM (36 mL). The colourless solution was stirred a room temperature for 2 hours, during which time a white precipitate formed. The mixture was quenched with saturated aqueous sodium bicarbonate (30 mL) and diluted with ethyl acetate (60 mL). The phases were separated and the organic layer was washed with aqueous sodium bicarbonate (6 x 30 mL) before being dried (MgSO₄) and concentrated *in vacuo* to afford sulfone **25b** (2.04 g, 94%) as white cubes; R_f (30% diethyl ether in light petroleum) 0.20; mp 100-102 °C; (Found: C, 60.12; H, 5.33; C₂₄H₂₆F₂O₆S requires: C, 59.99; H, 5.45 %); ν_{max} (film)/cm⁻¹ 2990w (C-H), 1306 m (C-O), 1152s (C-O), 1135s (C-O), 1053s (C-O), 735s (C-H def.), 695s (C-H def.); δ_H (250MHz, CDCl₃) 8.10 (2H, d, *J* 7.8 Ar), 7.93-7.76 (3H, env. Ar), 7.62-7.47 (5H, env. Ar), 4.92 (1H, d, ²J 11.9, PhCH_aCH_b), 4.78 (2H, m, PhCH_aCH_b, CHCF₂), 4.52 (1H, d, ²J 10.8, CH_aCH_bO), 4.39 (1H, d, *J* 3.4, CHOBn), 4.05 (1H, dt, ²J 10.8, ⁴J_{H-F} 3.2, CH_aCH_bO),

3.87 (1H, br s, PhSO₂CH), 1.65 (3H, s, CH₃), 1.54 (3H, s, CH₃), 1.49 (3H, s, CH₃); δ_C (63 MHz, CDCl₃) 137.6, 136.8, 134.9, 129.9, 129.3, 129.0, 128.7, 128.5, 123.5 (dd, ¹J_{C-F} 269.8, 268.0), 110.5, 89.1 (d, ³J_{C-F} 5.1), 87.5 (dd, ²J_{C-F}, 27.1, 16.3), 83.0, 80.3 (dd, ²J_{C-F} 32.1, 26.2), 73.9, 69.2 (dd, ³J_{C-F} 5.7, 2.4), 65.2 (d, ³J_{C-F} 7.1), 26.4, 25.5, 14.8; δ_F (235MHz, CDCl₃) -110.49 (dd, ²J_{F-F} 228.2, ³J_{F-H} 7.3), -116.87 (d, ²J_{F-F} 228.2); *m/z* (ES) 481 (20%, [M+H]⁺), 423 (100), 424 (8).

6S*-Benzyloxy-3,3-difluoro-1S*,6-dimethyl-2R*-(hydroxymethyl)-5R*-phenylsulfonyl-7-oxabicyclo[2.2.1]heptane-2-ol acetone acetal 25d

Was prepared as for **25a** from a solution of sulfide **23d** (0.2 mmol, 0.09 g) in DCM (0.5 mL), *m*CPBA (0.6 mmol, 0.1 g) and sodium dihydrogen phosphate (0.6 mmol, 0.07 g) in DCM (2 mL). The resulting colourless solution was stirred at room temperature for 2 hours, during which time a white precipitate formed. The mixture was quenched with saturated aqueous sodium bicarbonate (1 mL) and diluted with ethyl acetate (3 x 2 mL). The phases were separated and the organic layer was washed with aqueous sodium bicarbonate (6 x 2 mL) before being dried (MgSO₄) and concentrated *in vacuo* to afford sulfone **25d** (0.09 g, 91 %) as a white powder; R_f (20% diethyl ether in light petroleum) 0.18; mp 185-187 °C; (Found: C, 60.43; H, 5.67; C₂₅H₂₈F₂O₆S requires: C, 60.72; H, 5.71 %); ν_{max} (film)/cm⁻¹ 2938w (C-H), 1316m (C-O), 1229s (C-O), 1147s (C-O), 1053s (C-O), 748s (C-H def.), 696s (C-H def.); δ_H (400MHz, CDCl₃) 7.98-7.96 (2H, m, Ar), 7.77-7.65 (3H, m, Ar), 7.43-7.33 (5H, m, Ar), 4.78 (1H, d, ²J 11.2, PhCH_aH_b), 4.69 (1H, d, ²J 11.2 PhCH_aH_b), 4.37 (1H, dd, ³J_{H-F} 7.5, 1.5, CHCF₂), 4.12 (1H, d, ²J 11.2, CH_aH_bO), 3.76 (1H, s, CHSO₂Ph), 3.73 (1H, dt, ²J 11.2, ⁴J_{H-F} 3.3 CH_aH_bO), 1.93 (3H, s, CH₃), 1.48 (3H, s, CH₃), 1.43 (3H, s, CH₃), 1.34 (3H, s, CH₃); δ_C(100MHz, CDCl₃) 138.8, 136.8, 134.4, 129.8, 128.7, 128.3, 128.2, 128.1, 122.9 (dd, ¹J_{C-F} 270.0, 265.2), 109.8, 93.6 (d, ³J_{C-F} 4.8), 88.2, 87.9 (dd, ²J_{C-F} 26.4, 15.2), 80.0 (dd, ²J_{C-F} 31.9, 25.6), 69.6 (d, ³J_{C-F} 3.2), 68.8, 65.6 (d, ³J_{C-F} 6.4), 26.2, 25.0, 18.3, 11.7; δ_F (282MHz, CDCl₃) -109.3 (dd, ²J_{F-F} 224.2, ³J_{F-H} 7.5), -118.4 (d, ²J_{F-F} 224.2); *m/z* (FAB) 495 (18%, [M+H]⁺), 479 (33, [M-CH₃]⁺), 307 (100).

6S*-Benzyloxy-3,3-difluoro-2S*-(hydroxymethyl)-5R*-phenylsulfonyl-7-oxabicyclo[2.2.1]-1S*,7S*-heptan-2-ol acetone acetal 26a

Was prepared as for **25a** from sulfide **24a** (0.4 mmol, 0.174g) in CH₂Cl₂ (1 mL), *m*CPBA (0.84 mmol, 0.15 g) and sodium dihydrogen phosphate (0.1 g) in DCM (3 mL), at room temperature. After stirring for 30 minutes the reaction was quenched by the addition of saturated aqueous sodium bicarbonate (5 mL), the layers were separated and the aqueous layers extracted with ethyl acetate (3 x 10 mL), the combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate (6 x 5 mL), dried (MgSO₄), filtered and concentrated to afford a white solid. Purification by trituration with hexane afforded sulfone **26a** as a white solid (0.103 g, 54 %). Mp 138-139 °C; R_f (50 % diethyl ether in hexane) 0.20; (Found: C, 59.00; H, 4.98; C₂₃H₂₄F₂O₆S requires: C, 59.22; H, 5.19 %); δ_H (300MHz, CDCl₃) 7.91-7.88 (2H, m, Ar), 7.74-7.68 (1H, m, Ar), 7.62-5.57 (2H, m, Ar), 7.44-7.25 (5H, m, Ar), 4.71 (1H, d, *J* 8.4, CHCF₂), 4.64 (1H, d, ²*J* 11.7, OCH_aH_bPh), 4.53-4.48 (2H, m, [includes 4.50 (1H, d, ²*J* 11.7, OCH_aH_bPh)], CHOBn), 4.38-4.36 (1H, m, CHCOCH), 4.29 (1H, d, ²*J* 10.7, OCH_aH_bC(CH₃)₂), 3.99, (1H, dt ²*J* 10.7, ⁴J_{H-F} 3.2, OCH_aH_bC(CH₃)₂), 3.60 (1H, d, *J* 3.0, CHSPh), 1.44 (3H, s, CH₃), 1.33 (3H, s, CH₃); δ_C (75 MHz, CDCl₃) 137.2, 136.3, 134.6, 129.7, 128.9, 128.7, 128.4, 128.0, 122.8 (t, ¹J_{C-F} 270.3), 110.4, 86.3 (dd ²J_{C-F} 27.2, 16.6), 84.3 (d ³J_{C-F} 4.5), 81.1 (dd ²J_{C-F} 32.1, 26.8), 78.1, 73.7, 67.8, 64.4 (d ³J_{C-F} 6.8), 25.9, 25.3; δ_F (282MHz, CDCl₃) (-110.1) – (-110.2)

(m), (-110.9) – (-111.0) (m) [comprise apparent doublet $^2J_{F-F}$ 228.7), -118.5 (d, $^2J_{F-F}$ 228.7); m/z (ES) 467 (20 %, $[M+H]^+$), 428 (6), 242 (100).

3,3-Difluoro-2S*-(hydroxymethyl)-6-methylene-5R*-phenylsulfonyl-7-oxabicyclo[2.2.1]heptan-2-ol acetone acetal 27

A solution of sulfide **22** (0.1 mmol, 0.035 g) in DCM (0.5 mL) was added to a solution of *m*CPBA (0.3 mmol, 0.05 g) and sodium dihydrogen phosphate (0.3 mmol, 0.036 g) in DCM (1 mL). The colourless solution was stirred at room temperature for 2 hours, during this time a white precipitate had formed. The mixture was quenched with saturated aqueous sodium bicarbonate (1 mL) and diluted with ethyl acetate (1 mL). The phases were separated and the organic layer was washed with aqueous sodium bicarbonate (6 x 2 mL) before being dried ($MgSO_4$) and concentrated *in vacuo* then columned in 30% diethyl ether to afford sulfone **27** (0.03 g, 78%) as a white powder; R_f (30% diethyl ether in light petroleum) 0.20; mp 115-118 °C; (Found: C, 55.82; H, 5.34; $C_{18}H_{20}F_2O_5S$ requires: C, 55.95; H, 5.22 %) ν_{max} (film)/ cm^{-1} 2988w (C-H), 1329w (C-C), 1156m (C-O), 1044m (C-O), 739m (C-H def.), 687m (C-H def.); δ_H (300MHz, $CDCl_3$) 7.77-7.74 (2H, m, Ar), 7.62-7.56 (1H, m, Ar), 7.49-7.44 (2H, m, Ar), 5.78 (1H, d, 2J 1.9, = CH_aH_b) 5.23 (1H, d, 2J 1.9, = CH_aH_b), 4.79 (1H, d, $^3J_{H-F}$ 5.8, $CHCF_2$), 4.20 (1H, br s, $CHSO_2Ph$), 4.11 (1H, d, 2J 10.3, OCH_aH_b), 3.87 (1H, d, 2J 10.3, OCH_aH_b), 1.34 (3H, s, CH_3), 1.27 (3H, s, CH_3), 1.05 (3H, s, CH_3); δ_C (400MHz, $CDCl_3$) 139.6, 137.1, 134.2, 130.0, 128.7, 121.6 (t, $^1J_{C-F}$ 270.0), 116.3, 111.6, 89.1, 84.9 (t, $^2J_{C-F}$ 16.0), 79.7 (dd, $^2J_{C-F}$ 30.3, 27.7), 67.8 (d, $^3J_{C-F}$ 4.8), 65.1 (d, $^3J_{C-F}$ 14.4), 26.3, 24.3, 13.1; δ_F (235MHz, $CDCl_3$) -112.4 (d, $^3J_{F-H}$ 5.8), -112.5; [HRMS (+FAB) Found: 387.10770. Calc. For $C_{18}H_{21}F_2O_5S$ 387.10778]; m/z (ES) 387 (3%, $[M+H]^+$), 176 (100).

3S*-Benzyloxy-6,6-difluoro-1S*-(hydroxymethyl)-2S*-methyl-4-phenylsulfonyl-cyclohex-4-en-1,2-diol acetone acetal 29b

n-Butyllithium (1.5 mmol, 0.6 mL of a 2.4 M solution in hexane) was added slowly to a solution of sulfone **25b** (1 mmol, 0.48 g), in THF (10 mL) at -78 °C under an atmosphere of nitrogen. The reaction was stirred at -78 °C for 1 hour, then warmed from -78 °C to -30 °C and quenched cautiously with water (10 mL). The mixture was allowed to warm to room temperature before being extracted with ethyl acetate (6 x 10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to afford a yellow solid, which was triturated with hexane to yield alcohol **29b** (0.42 g, 87%) as a white powder. R_f (30% ethyl acetate in light petroleum) 0.15; mp 164-166 °C, (Found: C, 60.13; H, 5.38; $C_{24}H_{26}F_2O_6S$ requires: C, 59.99; H, 5.45 %) ν_{max} (film)/ cm^{-1} 3501w br (O-H), 2987w (C-H), 1455w (C-C), 1112s (C-O), 1057s (C-O), 751m (C-H def.), 698m (C-H def.); δ_H (250MHz, $CDCl_3$) 7.76-7.72 (2H, m, Ar), 7.58-7.51 (1H, m, Ar), 7.39-7.22 (7H, m, Ar), 7.03 (1H, dt, 4J 7.0, $^3J_{H-F}$ 2.3, C=CH), 5.03 (1H, d, 2J 10.8, $PhCH_aH_b$), 4.91 (1H, d, 2J 10.8, $PhCH_aH_b$), 4.74 (1H, dt, 4J 7.0, $^5J_{H-F}$ 2.2, $CHOBn$), 4.45 (1H, dd, 2J 10.0, $^4J_{H-F}$ 1.4, CH_aH_bO), 4.30 (1H, dd, 2J 10.0, $^4J_{H-F}$ 1.0, CH_aH_bO), 2.27 (1H, br, s, OH), 1.58 (6H, s, CH_3), 1.15 (3H, d, $^5J_{H-F}$ 4.4, CH_3); δ_C (75MHz, $CDCl_3$) 148.8 (dd, $^3J_{C-F}$ 12.6, 10.2), 140.0, 137.4, 133.2, 130.4 (dd, $^2J_{C-F}$ 35.9, 27.5), 128.7, 128.2, 127.9, 127.7, 127.6, 119.2, 115.9 (dd, $^1J_{C-F}$ 251.3, 240.5), 112.8, 86.2 (dd, $^2J_{C-F}$ 27.5, 17.9), 79.4 (d, $^3J_{C-F}$ 2.4), 76.1, 64.5 (d, $^3J_{C-F}$ 4.8), 26.6, 25.5 (d, $^5J_{C-F}$ 3.6), 17.8 (d, $^4J_{C-F}$ 6.0); δ_F (235MHz, $CDCl_3$), -93.0 (d, $^2J_{F-F}$ 299.9), -105.2 (d, $^2J_{F-F}$ 299.9); m/z (ES) 479 (49%, $[M-H]^-$), 403 (36), 351 (100).

Attempted ring opening of **35** under Lewis acid conditions

Magnesium bromide diethyletherate (0.27 mmol, 0.1 mL) was added to a solution of epoxide **35** (0.15 mmol, 0.07 g) in THF (1 mL) under an atmosphere of nitrogen at room temperature. The resulting mixture was stirred at this temperature for 16 hours before being quenched with water (5 mL) and extracted with diethyl ether (3 x 10 mL), the combined organic extracts were dried (MgSO₄), filtered and concentrated. The crude ¹⁹F NMR spectrum showed the presence of starting material alone.

Attempted ring opening of **35** under metal hydride conditions

Diisobutyl aluminium hydride (0.5 mmol, 0.5 mL of a 1M solution in toluene) was added slowly to a solution of epoxide **35** (0.5 mmol, 0.24 g) in THF (5 mL) under an atmosphere of nitrogen at room temperature, the resulting solution was stirred at this temperature for 24 hours before being quenched by the cautious addition of 5M HCl (5 mL). The organic layer was separated and the aqueous layer extracted with diethyl ether (3 x 10 mL), then the combined organic extracts were dried (MgSO₄), filtered and concentrated. The crude ¹⁹F NMR spectrum showed the presence of starting material alone.

Attempted dihydroxylation of **29a**; *in situ* ruthenium tetroxide method

To a solution of **29a** (0.7 mmol, 0.33 g) in a mixture of carbon tetrachloride (2 mL), acetonitrile (2 mL) and water (3 mL) was added RuO₂ (0.02 mmol, 0.003 g) and sodium periodate (1.4 mmol, 0.3 g). The resulting mixture was stirred at room temperature for 48 hours. TLC showed no consumption of starting material. The reaction was quenched with water (5 mL), and the aqueous phase extracted with ethyl acetate (3 x 10 mL) the combined organic layers were dried (MgSO₄) filtered and concentrated to afford an oil. ¹⁹F NMR showed only unreacted starting material.

Attempted dihydroxylation of **29a**; osmium tetroxide method

Osmium tetroxide (0.4 mL of a 2.5% sol in ^tBuOH) was added to a solution of **29a** (0.5 mmol 0.23 g) in acetone/water (3 mL, 4:1, v/v) at 0 °C, followed by the addition of NMO (0.2 g). The yellow solution was stirred for 2 days at room temperature (TLC suggested no reaction) then Na₂SO₃ (1.0 mmol, 0.13 g) was added to destroy any excess OsO₄ and the mixture was stirred for a further 30 minutes. The resulting solution was extracted with ethyl acetate (5 x 15 mL), dried over MgSO₄ and concentrated *in vacuo* ¹⁹F NMR showed only unreacted starting material.

3S*-Benzyloxy-6,6-difluoro-1S*-(hydroxymethyl)-2S*-methyl-cyclohex-4-en-1,2-diol acetone acetal **46b**

Magnesium powder (5 mmol, 0.12 g) was heated under vacuum (130 °C, 0.15 mmHg) for 4 hours, then allowed to cool. Mercuric chloride (0.25 mmol, 0.075 g) was added and the mixture was cooled to 0 °C, then dry EtOH (2.5 mL) and a solution of sulfone **25b** (0.5 mmol, 0.24 g) in THF (2.5 mL) were added. The reaction was stirred at 0 °C for 3 hours then quenched with water (5 mL), extracted with ethyl acetate (3 x 20 mL) and concentrated *in vacuo* to afford alcohol **46b** (0.12 g, 70 %) as a white powder; R_f (40% diethyl ether in light petroleum) 0.35; mp 68-70 °C; (Found: C, 63.44; H, 6.44; C₁₈H₂₂F₂O₄ requires: C, 63.52; H, 6.52 %); ν_{max} (film)/cm⁻¹ 3501 br, (OH), 2987w (C-H), 1379m (C-C), 1113s (C-O), 1053s (C-O), 752s (C-H def.), 698s (C-H def.); δ_H (400 MHz, CDCl₃) 7.42-7.30 (5H, m, Ar), 6.13 (1H, dq, *J* 9.8, *J* 1.8, ⁴J_{H-F} 1.8, CH=CH), 5.77 (1H, ddt, *J* 9.8, ³J_{H-F} 6.6, ³J_{H-F} 2.5, HC=CHCF₂), 4.87 (1H, d, ²*J* 11.8,

PhCH_aCH_b), 4.76 (1H, d, ²J 11.8, PhCH_aCH_b), 4.41 (1H, dd, ²J 9.3, ⁴J_{H-F} 1.4, CH_aCH_bO) 4.31 (1H, dd, ²J 9.3, ⁴J_{H-F} 1.4, CH_aCH_bO), 4.27-4.23 (1H, m, CHOBn), 2.17 (1H, s, OH), 1.50 (3H, s, CH₃), 1.49 (3H, s, CH₃), 1.24 (3H, s, CH₃); δ_C(100 MHz, CDCl₃) 138.5, 137.2 (dd, ³J_{C-F} 12.3, 9.9), 129.0, 128.3, 128.2, 122.4 (dd, ²J_{C-F} 32.1, 26.3), 117.6 (dd, J_{C-F} 245.0, 236.2), 112.8, 87.0 (dd, ²J_{C-F} 29.2, 18.7), 80.3, 76.3 (d, ³J_{C-F} 4.7), 74.1, 64.8 (d, ³J_{C-F} 5.8), 27.0, 25.9 (d, ⁵J_{C-F} 4.7), 18.0 (d, ⁵J_{C-F} 4.7); δ_F (235 MHz, CDCl₃) -91.1 (d, br, ²J_{F-F} 287.9), -105.6 (d, br, ²J_{F-F} 287.9); *m/z* (ES) 339 (30%, [M-H]⁺), 319 (72).

3S*-Benzyloxy-6,6-difluoro-2S*,3-methyl-1S*-(hydroxymethyl)-cyclohex-4-en-1,2-diol acetone acetal 46d

Was prepared as for **46b** from magnesium powder (1.25 mmol, 0.03 g), mercuric chloride (0.07 mmol, 0.02 g), dry EtOH (0.6 mL) and a solution of sulfone **25d** (0.12 mmol, 0.06 g) in THF (0.6 mL). The reaction was stirred at 0 °C for 3 hours then quenched with water (0.6 mL), extracted with ethyl acetate (3 x 0.5 mL), dried over MgSO₄ and concentrated *in vacuo* to afford alcohol **46d** (0.026 g, 61 %) as a white powder; R_f (30% diethyl ether in light petroleum) 0.3; mp 82-83 °C; ν_{max} (film)/cm⁻¹ 3406 br, (OH), 2975w (C-H), 1367m (C-C), 1127s (C-O), 1064s (C-O), 738s (C-H def.), 675s (C-H def.); δ_H (300MHz, CDCl₃) 7.30-7.19 (5H, m, Ar), 6.06 (1H, d, *J* 10.5, CH=CHCF₂), 5.83 (1H, dt, *J* 10.5, ³J_{H-F} 5.5 CH=CHCF₂)*, 4.54 (1H, d, ²J 10.9, PhCH_aCH_b), 4.40 (1H, d, ²J 10.9, PhCH_aCH_b), 4.08 (1H, d, ²J 10.0, OCH_aCH_b), 4.03 (1H, dt, ²J 10.0, ⁴J_{H-F} 2.1, OCH_aCH_b), 1.46 (3H, s, CH₃), 1.45 (3H, s, CH₃), 1.39 (3H, s, CH₃), 1.33 (3H, s, CH₃); δ_C(100MHz, CDCl₃) 138.8, 138.6, 138.5, 138.4, 128.4, 127.6, 127.3, 123.4 (t, ²J_{C-F} 29.5), 117.3 (t, ¹J_{C-F} 242.0), 111.3, 85.7 (t, ²J_{C-F} 19.2), 67.9, 65.0, 26.3, 26.2, 19.0, 18.5; δ_F (376MHz, C₇D₈, 213 K, major:minor 5.3:1) -85.4 (br d, ²J_{F-F} 285.1, minor conformer), -90.5 (d, ²J_{F-F} 280.5, major conformer), -103.2 (br d, ²J_{F-F} 285.1, minor conformer), -108.0 (d, br, ²J_{F-F} 280.5, major conformer); δ_F (376MHz, d⁸-PhMe, 373 K) -95.6 (d, ²J_{F-F} 287.3), -97.1 (d, ²J_{F-F} 287.3); [HRMS (EI) Found: 354.16426 Calc. For C₁₉H₂₄O₄F₂ 354.16427]; *m/z* (ES) 355 (13%, [M+H]⁺), 307 (47), 97 (100).

*The ³J_{H-F} coupling (5.5 Hz) from the ¹H NMR spectrum could not be resolved in any of the VT ¹⁹F NMR spectra.

3S*-Benzyloxy-6,6-difluoro-1R*-(hydroxymethyl)-cyclohex-4-en-1,2S*-diol acetone acetal 47a

A solution of sulfone **26a** (0.2 mmol, 0.1g), in THF (1 mL) was added to a suspension of magnesium (2.9 mmol, 0.07g), and HgCl₂ (0.07 mmol, 0.02g) in ethanol (1 mL), at 0 °C after 24 hours a further portion of HgCl₂ was added (0.07 mmol, 0.02g). After 5 days at 5 °C, the mixture was warmed to room temperature and stirred for a further 2 days, then sonicated for 1 day. The reaction was quenched with water (5 mL) and extracted with ethyl acetate (6 x 10 mL) the combined extracts were dried (MgSO₄), filtered and concentrated to afford an oil (0.035g) which was purified by column chromatography (Biotage 12 S, 30% diethyl ether in hexane) to afford an oil which solidified upon trituration with hexane to afford **47a** as a white solid (0.024g, 37 %); mp 84-85 °C; R_f (50 % diethyl ether in hexane) 0.26; (Found C, 62.54; H, 6.19; C₁₇H₂₀F₂O₄ requires: C, 62.57; H, 6.19 %); δ_H (400MHz, CDCl₃) 7.40-7.30 (5H, m, Ar), 6.20 (1H, dq, *J* 10.4, 2.0, HC=CHCF₂), 5.82 (1H, dtd, *J* 10.4, ³J_{H-F} 7.2, ⁴J 2.0, HC=CHCF₂), 4.77 (1H, d, ²J 11.6, OCH_aH_bPh), 4.72 (1H, d, ²J 11.6, OCH_aH_bPh), 4.37 (1H, dd, *J* 9.2, ⁴J_{H-F} 1.2 CH_aH_bOC), 4.32 (1H, d, *J* 9.2, CH_aH_bOC), 4.26 (1H, ddq, *J* 7.6, 2.0, ⁵J_{H-F} 9.4, CHOBn), 3.95-3.87 (1H, m, CHOH)*, 2.35 (1H, s, OH), 1.51 (3H, s, CCH₃), 1.46 (3H, s, CCH₃); δ_C (100 MHz, CDCl₃) 137.7, 135.4 (t, ²J_{C-F} 46.3), 128.6, 128.1, 127.9, 122.8 (dd, ³J_{C-F} 33.7, 24.7), 117.2 (dd, ¹J_{C-F} 248.5, 235.0), 112.3, 84.0 (dd, ²J_{C-F} 30.2, 19.2), 77.8, 72.4, 72.4, 65.4 (d, ³J_{C-F} 4.0), 26.5,

25.4; δ_F (376MHz, $CDCl_3$) -90.7 (dd, $^2J_{F-F}$ 282.3, $^3J_{F-H}$ 9.4), -112.3 (dd, $^2J_{F-F}$ 282.3, $^3J_{F-H}$ 7.2); [HRMS (CI, $M^+ + NH_4$) Found 344.1671, Calc. For $C_{17}H_{24}F_2NO_4$ 344.1668; m/z (ES) 325 (80 %, $[M-H]^-$), 219 (95), 199 (24), 107 (100).

*This signal simplified to 3.90 (1H, d, J 7.6) in the $\{^{19}F\}^1H$ NMR spectrum.

3,3-Difluoro-2*R(hydroxymethyl)-1*S**-methyl-5*R**-phenylsulfonyl-7-oxabicyclo[2.2.1]-7*S**-heptane-2,6*S**-diol acetone acetal **54****

A solution of sulfide **20b** (0.04 mmol, 0.013 g) in DCM (0.1 mL) was added to a solution of *m*CPBA (0.12 mmol, 0.02 g) and sodium dihydrogen phosphate (0.12 mmol, 0.014 g) in DCM (0.4 mL). The colourless solution was stirred at room temperature for 3 hours, during this time a white precipitate had formed. The mixture was quenched with saturated aqueous sodium bicarbonate (0.5 mL) and diluted with ethyl acetate (1 mL). The phases were separated and the organic layer was washed with aqueous sodium bicarbonate (6 x 1 mL) before being dried ($MgSO_4$) and concentrated *in vacuo* to afford a white powder which was purified by column chromatography (50% diethyl ether in light petroleum) to yield sulfone **54** (0.014 g, 90 %) ; R_f (50% diethyl ether in light petroleum) 0.19; mp 137-139 °C; ν_{max} (film)/ cm^{-1} 3496w br (OH), 2993w (C-H), 1258m (C-O), 1143w (C-O), 1126w (C-O), 1085s (C-O), 732s (C-H def.), 685s (C-H def.); δ_H (300 MHz, $CDCl_3$) 7.89-7.86 (2H, m, Ar), 7.69-7.63 (1H, m, Ar), 7.59-7.54 (2H, m, Ar), 4.48 (1H, t, J 4.5, $CHSO_2Ph$), 4.43 (1H, d, $^3J_{H-F}$ 8.3, $CHCF_2$), 4.26 (1H, d, 2J 10.9, OCH_aH_b), 3.84 (1H, dt, 2J 10.9, $^4J_{H-F}$ 3.4, OCH_aH_b), 3.50 (1H, d, J 4.4, $CHOH$) 3.09 (1H, d, J 5.0, OH), 1.40 (6H, s, 2 x CH_3), 1.29 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 137.1, 134.7, 129.8, 128.7, 123.1 (dd, $^1J_{C-F}$ 270.0, 266.8), 110.1, 88.7 (d, $^3J_{C-F}$ 4.8), 86.7 (dd, $^2J_{C-F}$ 25.6, 16.0), 79.1 (dd, $^2J_{C-F}$ 30.3, 25.6), 76.8, 69.6 (t, $^3J_{C-F}$ 4.8), 64.7 (d, $^3J_{C-F}$ 8.0), 26.1, 25.1, 14.3; δ_F (282 MHz, $CDCl_3$) -110.6 (dd, $^2J_{F-F}$ 226.5, $^3J_{F-H}$ 8.3), -118.7 (d, $^2J_{F-F}$ 226.5); HRMS Found 390.09489, Calc. for $C_{17}H_{20}F_2O_6S$ 390.09487; m/z (ES) 391 (100%, $[M+H]^+$), 333 (59).

Attempted ring opening by reductive desulfonation of **27; 3,3-difluoro-2*R**(hydroxymethyl)-1*S**-dimethyl-6-methylene -7-oxabicyclo[2.2.1]-4*S**-hept-5-en-2-ol acetone acetal **55** and 3,3-difluoro-1*S**,6-dimethyl-2*R**(hydroxymethyl)-7-oxabicyclo[2.2.1]-4*S**-heptan-2-ol acetone acetal **56****

Magnesium powder (1.8 mmol, 0.04 g) was heated at 130 °C under high vacuum (0.15 mmHg) for 4 hours, then allowed to cool to room temperature. Mercuric chloride (0.09 mmol, 0.02 g) was added and the mixture was cooled to 0 °C then dry EtOH (1 mL) and a solution of sulfone **27** (0.18 mmol, 0.07 g) in THF (1 mL) was added. The reaction was stirred at 0 °C for 3 hours then quenched with water (1 mL), extracted with ethyl acetate (3 x 1 mL), dried ($MgSO_4$) and concentrated *in vacuo* to afford a mixture of alkenes **55** and **56** (5:1) which were separated by column chromatography to afford **55** (0.033g, 75%), R_f (10% diethyl ether in light petroleum) 0.32; mp 68-69 °C; (Found C, 58.42; H 6.69; $C_{12}H_{16}F_2O_3$ requires C, 58.53; H 6.55 %); ν_{max} (film)/ cm^{-1} 2990w (C-H), 1375w (C-C), 1195m (C-O), 1098m (C-O) 1076m (C-O); δ_H (300MHz, $CDCl_3$) 5.09-5.08 (1H, m, $CH_aH_b=C$), 4.93-4.91 (1H, m, $CH_aH_b=C$), 4.38-4.33 (1H, m, $CHCF_2$), 4.20 (1H, d, 2J 10.2, OCH_aH_b), 4.05 (1H, d, 2J 10.2, OCH_aH_b), 2.65 (1H, br d, 2J 16.4, CH_aH_b), 2.54-2.44 (1H, m, CH_aH_b), 1.41 (3H, s, CH_3), 1.39 (3H, s, CH_3), 1.32 (3H, s, CH_3); δ_C (75MHz, $CDCl_3$) 145.7, 122.7 (dd, $^1J_{C-F}$ 268.1, 263.3), 111.2, 108.8, 88.7 (d, $^3J_{C-F}$ 2.4), 85.3 (dd, $^2J_{C-F}$ 21.5, 17.9), 78.4 (dd, $^2J_{C-F}$ 28.7, 25.1), 65.3 (d, $^3J_{C-F}$ 15.5), 32.6 (dd, $^3J_{C-F}$ 6.0, 3.6), 26.6, 24.4, 13.5; δ_F (282MHz, $CDCl_3$) -111.8 (dd, $^2J_{F-F}$ 230.7, $^3J_{H-F}$ 9.5), -113.8 (d,

$^2J_{F-F}$ 230.7); [HRMS (Found 246.10675, Calc. For C₁₂H₁₆F₂O₃ 246.10673]; m/z (EI) 246 (7 %, M⁺), 231 (35), 188 (100), 146 (94), 131 (77), 111 (71), 103 (23), 95 (66); and known **56** (7mg, 15%).

Attempt to ring open 54

Magnesium powder (1 mmol, 0.024 g) was heated under vacuum (130 °C, 0.15 mmHg) for 4 hours, then allowed to cool under nitrogen. Mercuric chloride (0.05 mmol, 0.013 g) was added and the mixture was cooled to 0 °C, then dry EtOH (0.5 mL) and a solution of sulfone **54** (0.1 mmol, 0.04 g) in THF (0.5 mL) were added. The reaction was stirred at 0 °C for 2 days then quenched with water (1 mL), extracted with ethyl acetate (3 x 1 mL) and concentrated *in vacuo* to afford only starting material **54**.

Attempted ring opening of 57: Ethyl 2-endo-(N,N-diethylcarbamoyloxy)-3,3-difluoro-1,6-dimethyl-7-oxabicyclo[2.2.1]hept-5-enyl-2-exo-carboxylate 8d and ethyl 2-endo-(N,N-diethylcarbamoyloxy)-3,3-difluoro-1-methyl-6-methylene-7-oxabicyclo[2.2.1]heptane-2-carboxylate 58

Magnesium powder (0.5 mmol, 0.012 g) was heated under vacuum (130 °C, 0.15 mmHg) for 4 hours, then allowed to cool to room temperature. Mercuric chloride (0.025 mmol, 0.007 g) was added and the mixture was cooled to 0 °C then dry EtOH (0.5 mL) and a solution of sulfone **57** (0.05 mmol, 0.025 g) in THF (0.5 mL) was added. The reaction was stirred at 0 °C for 3 hours then quenched with water (1 mL), extracted with ethyl acetate (3 x 1 mL), dried (MgSO₄) and concentrated *in vacuo* to afford a crude mixture of *exo* cycloadduct¹⁸ **8d** and alkene **58** (ratio 1:2 respectively, 0.015 g, 86 %). The data for the former were identical with those reported previously while the latter compound was identified by synthesis on a larger scale.

Geometry optimisations for products of reductive desulfonative ring opening 46a, 47a

Conformational searching in MacSpartan Pro (MMFF94)
Geometry optimisation at AM1, then 3-21G(*), then 6-31G*.

46a, conformer 1

Run type: Geometry optimization

Model: RHF/6-31G*

Number of shells: 132

63 S shells

46 SP shells

23 6D shells

Number of basis functions: 385

Number of electrons: 172

Number of heavy atoms: 23

Number of hydrogens: 20

Use of molecular symmetry disabled

Molecular charge: 0

Spin multiplicity: 1

Memory model: direct 43.4 Mb

Point Group = C1 Order = 1 Nsymop = 1

This system has 123 degrees of freedom

Hessian from 3-21G calculation used.

Max. Max. Neg.

Atom Label		Cartesian Coordinates (Angstroms)		
		X	Y	Z
H	H1	2.1340673	-0.5145652	-3.1090590
C	C1	1.3795368	-0.3922819	-2.3529697
C	C2	1.5024180	-0.9245319	-1.1549913
H	H2	2.3860252	-1.4835470	-0.9024990
C	C4	0.4766073	-0.8099308	-0.0592503
H	H4	0.2078881	-1.8095836	0.2633133
C	C5	-0.8209660	-0.1272297	-0.5144611
O	O2	-1.6538822	-1.1344329	-1.0057348
H	H7	-2.3387498	-0.7376339	-1.5303017
C	C6	-0.5974539	0.9625100	-1.5726204
C	C3	0.1779191	0.3981895	-2.7627990
F	F1	-0.6340909	-0.3562818	-3.5243762
F	F2	0.5769240	1.4072484	-3.5730561
O	O3	-1.8561618	1.4032831	-2.0160588
C	C15	-2.0802580	2.7491724	-1.6336350
O	O4	-1.0946146	3.0201369	-0.6826933
C	C14	0.0294216	2.2329583	-0.9686361
H	H12	0.6870278	2.7311395	-1.6671599
H	H15	0.5600132	2.0450608	-0.0505428
C	C16	-3.4401500	2.8623006	-0.9729806
H	H11	-3.4878741	2.2013736	-0.1166211
H	H16	-4.2219669	2.5912613	-1.6726664
H	H17	-3.6084880	3.8791649	-0.6384109
C	C17	-1.9455157	3.6501375	-2.8532578
H	H18	-0.9724148	3.5311497	-3.3111672
H	H19	-2.0744724	4.6871432	-2.5647291
H	H20	-2.6975162	3.3936678	-3.5905115
H	H10	-1.2782941	0.3561777	0.3446051
O	O1	1.0838851	-0.1097326	1.0012349
C	C7	0.6971549	-0.4963368	2.2960774
C	C8	1.3292872	-1.8000527	2.7363852
C	C9	0.5701728	-2.7997962	3.3238677
C	C10	1.1628407	-3.9781501	3.7565873
C	C11	2.5228550	-4.1672012	3.5974114
C	C12	3.2904628	-3.1732667	3.0055002
C	C13	2.6981535	-1.9991336	2.5800706
H	H3	3.2946344	-1.2304851	2.1219802
H	H8	4.3491458	-3.3151927	2.8797024
H	H9	2.9843896	-5.0802588	3.9282808
H	H13	0.5597326	-4.7448712	4.2090403

Supplementary Material for Organic & Biomolecular Chemistry
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H	H14	-0.4909341	-2.6646313	3.4441552
H	H5	-0.3844365	-0.5639062	2.3704499
H	H6	1.0176773	0.3109586	2.9425272

E(HF) = -1153.7053690 a.u.

Supplementary Material for Organic & Biomolecular Chemistry
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46a, conformer 2 (lowest energy)

Run type: Geometry optimization

Model: RHF/6-31G*

Number of shells: 132

63 S shells

46 SP shells

23 6D shells

Number of basis functions: 385

Number of electrons: 172

Number of heavy atoms: 23

Number of hydrogens: 20

Use of molecular symmetry disabled

Molecular charge: 0

Spin multiplicity: 1

Memory model: direct 43.4 Mb

Point Group = C1 Order = 1 Nsymop = 1

This system has 123 degrees of freedom

Hessian from 3-21G calculation used.

Max. Max. Neg.

Cartesian Coordinates (Angstroms)

Atom Label	X	Y	Z
H H1	2.8503502	2.4194561	1.3294307
C C1	1.9834935	1.8074325	1.1578543
C C2	1.8639229	1.0401990	0.0952695
H H2	2.6458210	1.0049414	-0.6418199
C C4	0.6715978	0.1638064	-0.1892679
H H4	0.0661545	0.6405894	-0.9583005
C C5	-0.1896918	-0.0373165	1.0626473
O O2	-1.4045572	-0.6581397	0.7630680
H H7	-1.9661819	-0.0417697	0.3123117
C C6	-0.4208856	1.2945629	1.7910920
C C3	0.9349685	1.8520783	2.2199676
F F1	0.8038253	3.1121350	2.6734282
F F2	1.3450257	1.1259228	3.2922990
O O3	-1.0548358	2.1825664	0.9040525
C C15	-2.2779135	2.6527217	1.4485692
O O4	-2.6005895	1.7225722	2.4360399
C C14	-1.4153486	1.1938721	2.9646632
H H12	-1.0818982	1.7668199	3.8203220
H H15	-1.6010366	0.1761331	3.2671953
C C16	-3.3431726	2.6166080	0.3683711
H H11	-3.4667427	1.6088839	-0.0090889
H H16	-3.0693474	3.2685266	-0.4526155
H H17	-4.2932177	2.9437817	0.7729812
C C17	-2.1114177	4.0521384	2.0248636
H H18	-1.3886556	4.0636342	2.8272177
H H19	-3.0628170	4.4007494	2.4099426
H H20	-1.7740760	4.7345943	1.2533333
H H10	0.3384982	-0.7144302	1.7204037
O O1	1.1777717	-1.0495352	-0.6706265
C C7	0.3554574	-1.8135798	-1.5112271
C C8	1.1744608	-2.8686761	-2.2228961
C C9	2.5596616	-2.8361897	-2.2547670
C C10	3.2681491	-3.8104137	-2.9431542
C C11	2.6022113	-4.8226865	-3.6098963
C C12	1.2166832	-4.8609733	-3.5814032
C C13	0.5116597	-3.8932492	-2.8894602
H H3	-0.5643449	-3.9366774	-2.8656655
H H8	0.6876806	-5.6460595	-4.0917730
H H9	3.1538675	-5.5764814	-4.1426828
H H13	4.3432018	-3.7757712	-2.9552867
H H14	3.0829482	-2.0581635	-1.7347246
H H5	-0.1137896	-1.1622419	-2.2488157
H H6	-0.4368919	-2.2823713	-0.9418518

E(HF) = -1153.7063155 a.u.

47a

Run type: Geometry optimization
Model: RHF/6-31G*
Number of shells: 132
63 S shells
46 SP shells
23 6D shells
Number of basis functions: 385
Number of electrons: 172
Number of heavy atoms: 23
Number of hydrogens: 20
Use of molecular symmetry disabled
Molecular charge: 0
Spin multiplicity: 1
Memory model: direct 43.4 Mb

Atom Label		Cartesian Coordinates (Angstroms)		
		X	Y	Z
H	H1	-1.6310362	-3.6227990	-0.4241603
C	C1	-1.2287532	-2.6623001	-0.1569715
C	C2	-0.2303862	-2.1162410	-0.8215181
H	H2	0.2084229	-2.6261669	-1.6601726
C	C4	0.3759655	-0.7719033	-0.5012252
H	H4	1.3420038	-0.9225085	-0.0209882
C	C5	-0.5271226	0.0159623	0.4432587
O	O2	0.1827141	1.1110869	0.9416898
H	H7	-0.4160291	1.6468062	1.4462652
C	C6	-1.0379340	-0.8622889	1.5944684
C	C3	-1.8968063	-1.9757207	0.9953397
F	F1	-2.2054986	-2.8907463	1.9368315
F	F2	-3.0738909	-1.4598038	0.5909788
C	C14	0.0531191	-1.4000445	2.5306530
H	H11	0.3391151	-2.4208019	2.3294315
O	O4	-0.5502935	-1.3481951	3.7902619
C	C15	-1.4888482	-0.3131973	3.8106224
O	O3	-1.7998006	-0.0573991	2.4496694
C	C16	-0.8917453	0.9468603	4.4207619
H	H12	0.0164246	1.2261381	3.8990091
H	H15	-0.6481945	0.7766426	5.4627947
H	H17	-1.5972449	1.7680207	4.3581664
C	C17	-2.7308678	-0.7860419	4.5410541
H	H18	-3.4873010	-0.0095263	4.5365258
H	H19	-2.4860099	-1.0304327	5.5683818
H	H20	-3.1241905	-1.6670915	4.0538878
H	H16	0.9304462	-0.7661668	2.4947085
H	H10	-1.3847245	0.3530208	-0.1291151
O	O1	0.5608656	-0.1138566	-1.7204054
C	C7	1.6115618	0.8125307	-1.8019801
C	C8	1.8148968	1.2428093	-3.2383489
C	C9	2.8011482	2.1837302	-3.5175873
C	C10	3.0303249	2.6058205	-4.8135871
C	C11	2.2710409	2.0931330	-5.8554987
C	C12	1.2874085	1.1603905	-5.5842717
C	C13	1.0589299	0.7350819	-4.2827154
H	H3	0.2923811	0.0131043	-4.0802174
H	H8	0.6920600	0.7586848	-6.3854697
H	H9	2.4460256	2.4203311	-6.8649254
H	H13	3.7975531	3.3331681	-5.0115200
H	H14	3.3949836	2.5890448	-2.7148519
H	H5	2.5268418	0.3564563	-1.4277088
H	H6	1.4024216	1.6744086	-1.1815211

E(HF) = -1153.7061003 a.u.