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Fluorosugars: An improved synthesis of the 2,3,4-trideoxy-2,3,4-trifluoro hexose analogue of D-glucose

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ABSTRACT

An improved synthetic route for the synthesis of the 2,3,4-trideoxy-2,3,4-trifluoro hexose analogue of D-glucose has been developed. The newly reported synthesis features improved fluorination reactions and simpler chromatographic separations.

1. Introduction

Selectively fluorinated carbohydrates play an important role in understanding and investigating the role of carbohydrate metabolism in enzymatic systems [1–7]. We have previously reported the synthesis [8–9] and X-ray crystal structure [9] of the 2,3,4-trideoxy-2,3,4-trifluoro hexose analogue of D-glucose (**1**) and investigated its efflux across erythrocyte cell membranes [9]. The synthesis, however, was inefficient and we sought to develop an improved synthesis in order to obtain more material for the study of new enzymatic systems. In the previously reported synthesis [8,9], introduction of the first and second fluorine atoms gave rise to multiple products and mixtures of diastereoisomers that required laborious silica gel chromatography to obtain the desired fluorinated product, generally in low yield. We now report an improved synthesis of fluorosugar **1**.

2. Results and discussion

2.1. Synthesis of trifluorosugar *1*

The synthesis of trifluorosugar **1** is shown in Scheme 1. Commercially available butynediol **2** was selectively mono-protected with TBDMS chloride to give alkyne **3** in 86% yield [10]. Reduction of **3** with Red-Al® gave *trans*-allylic alcohol **4** in 91% yield. Sharpless epoxidation [11] of allylic alcohol **4** provided epoxide (2*R*,3*R*)-**5** in 62% yield (derivitisation [12] with Moshers acid chloride followed by $\{^1H\}^{19}F$-NMR analysis indicated an 89%ee for epoxide **5**). Swern oxidation [13] of epoxide **5**, followed by reaction with triethylphosophonoacetate gave ester **6** in 52% yield over the two steps. Treatment of enone **6** with triethylamine trihydrofluoride provided both deprotection of the TBDMS group and opening of the epoxide to provide the first fluorinated intermediate **7**. The opening of the epoxide with fluoride proceeded in a satisfactory fashion to give the desired regioisomer **7** as the major product in a ratio of 10:1 (by ^{19}F NMR analysis) and as a single diastereoisomer. Protection of the diol as the acetonide allowed intermediate **8** to be purified as a single isomer after silica gel chromatography. Reduction of the ester with DIBAL-H gave alcohol **9** in 62% yield, with subsequent Sharpless epoxidation [11] giving epoxide **10** in 77% yield (*dr* 10:1). Benzyl protection of the free alcohol occurred in 81% yield (*dr* 10:1), followed by triethylamine trihydrofluoride opening of the epoxide to generate difluoro intermediate **12** in 46% yield. The difluoroalcohol **12** was isolated as a single diastereoisomer, which we assume to be >98%ee for the remainder of the synthesis. With common intermediate **12** in hand, the synthesis could be readily completed using the previously reported conditions [9] to give trifluorosugar **1**.

The first synthesis [8–9] was completed in 11 steps in an overall yield of 0.05%, the synthesis reported here was completed in 15 synthetic steps in an overall yield of 0.37%. The new synthesis has several advantages over the previously reported synthesis. First, the synthesis was designed so that only the desired diastereoisomer is generated from the fluorination reactions. This decreases the purification time for the reactions as the products can be

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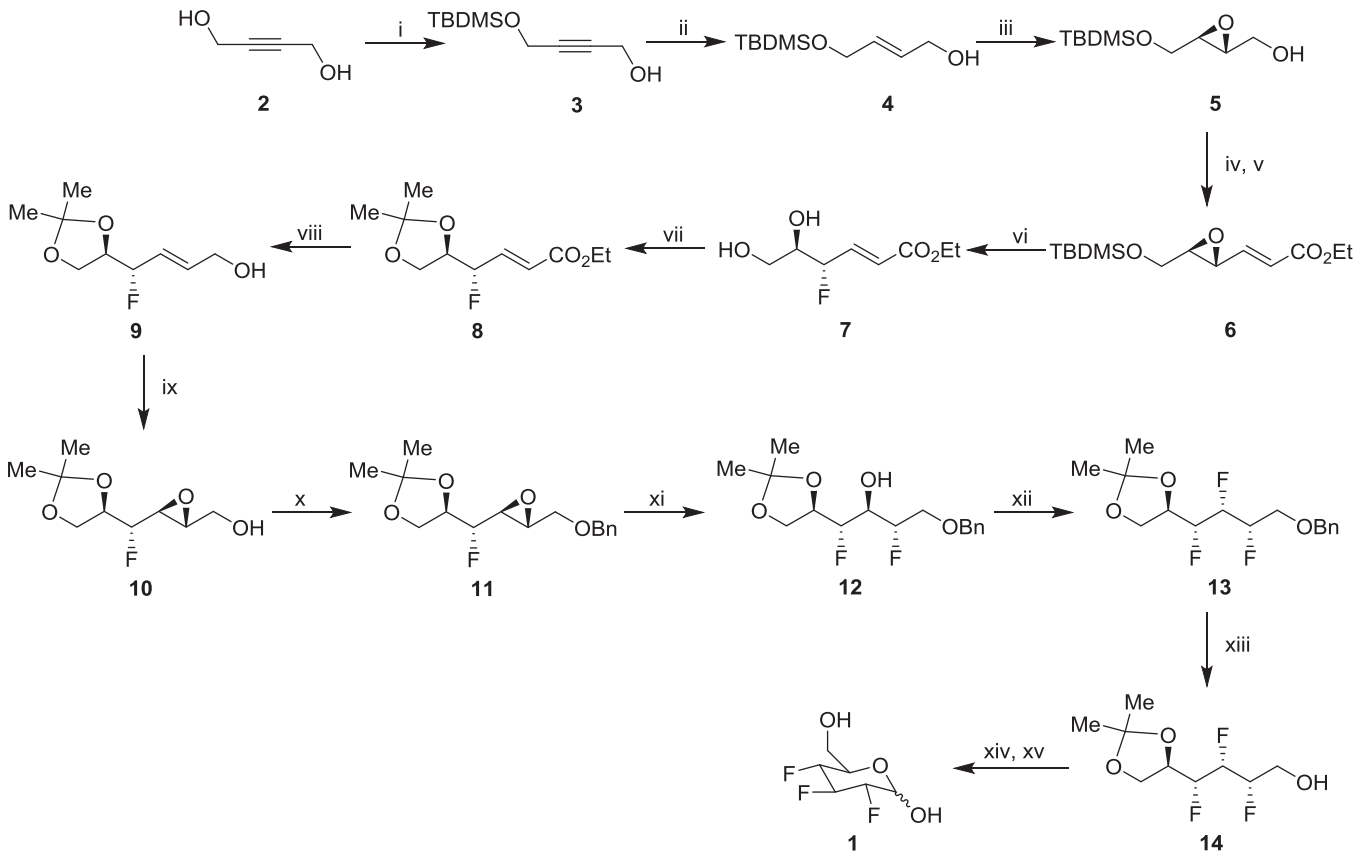


Scheme 1. *Reagents and conditions*: (i) TBDMSCl, NaH, THF, 0 °C-r.t., 18.5 h, 86%. (ii) Red-Al®, THF, 0 °C-r.t., 4 h, 91%. (iii) Ti(O*i*Pr)$_4$, (-)-DIPT, *t*BuOOH, DCM, 4 Å molecular sieves, −25 °C–(−20) °C, 19.5 h, 62%, 89%ee. (iv) Oxalyl chloride, DMSO, NEt$_3$, −78 °C–0 °C, 2 h. (v) Triethylphosphonoacetate, NaH, THF, 0 °C–(−78) °C, 2.5 h, 52% over two steps. (vi) 3HF.NEt$_3$, 90 °C, 24 h, 50% (regioisomer 10:1). (vii) 2,2-Dimethoxypropane, CSA, DMF, r.t., 18 h, 88%. (viii) DIBAL-H, THF, −78 °C-r.t., 3 h, 62%. (ix) Ti(O*i*Pr)$_4$, (-)-DIPT, *t*BuOOH, DCM, 4 Å molecular sieves, −25 °C–(−20) °C, 19.5 h, 77% (*dr* 10:1). (x) BnBr, NaH, DMF, 0 °C-r.t., 18.5 h, 81% (*dr* 10:1). (xi) 3HF.NEt$_3$, NEt$_3$, 100 °C, 3 days, 46%. (xii) Deoxofluor® (in THF), DCM, 0 °C-r.t., 19 h, 53%. (xiii) $NaBrO_3$, $Na_2S_2O_4$, H_2O, EtOAc, r.t., 1.5 h, 61%. (xiv) DMP, DCM, 0 °C-r.t., 1 h. (xv) $SnCl_2$, DCM, r.t., 1 h, 58% over 2 steps.

isolated after a single round of silica gel chromatography. In addition, the yields of the fluorination reactions for the introduction of the first and second fluorines are greatly improved; introduction of the first fluorine to give **7** and the second fluorine to give **12** occurred in 50% and 46% yield, respectively, compared to the previously reported fluorinations [8,9], which occurred in 13% and 16% yield, respectively. With an improved route for the synthesis of the 2,3,4-trideoxy-2,3,4-trifluoro hexose analogue of D-glucose (**1**) in hand, we examined the reactivity of **1** with glucose enzymes.

Trifluoroglucose **1** was assayed against glucose oxidase and glucose kinase, but showed no activity with either enzyme.

3. Conclusion

An improved route for the synthesis of the 2,3,4-trideoxy-2,3,4-trifluoro hexose analogue of D-glucose (**1**) is reported. Although the synthetic sequence contains an additional 4 steps to the previously reported route [8,9], it provides a significant increase in the overall yield of the route with improved fluorination reactions and more straight-forward chromatographic separations.

4. Experimental

4.1. General

All reagents were purchased from commercial suppliers and were used without further purification unless otherwise stated. Tetrahydrofuran, dichloromethane and diethyl ether were dried and deoxygenated with an MBraun SPS-800 solvent purification system and the moisture content of the solvents was analysed using a Karl Fischer coulometer (Metler Toledo DL32). Dry DMF was purchased from Merck and was used as purchased. Dry triethylamine was obtained by distilling triethylamine from potassium hydroxide onto potassium hydroxide under argon. Molecular sieves were activated by storing in an oven at 160 °C, then flame-drying under high vacuum immediately prior to use.

Infra-red spectra were recorded on a Perkin Elmer Spectrum GX FT-IR system. Proton NMR (^{1}H), carbon NMR (^{13}C) and fluorine NMR (^{19}F) were recorded on a Bruker Advance 500 (500 MHz), Bruker Avance II (400 MHz) or a Bruker Avance 300 (300 MHz) spectrometer. Fluorine NMR was proton decoupled (^{19}F{^{1}H}). Using a deptq sequence, the ^{13}C NMR signals were assigned to CH_3, CH_2, CH and C. The NMR experiments were carried out in deuterochloroform ($CDCl_3$). The chemical shifts (δ) are quoted in parts per million (ppm). Multiplicities are abbreviated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and b, broad for the ^{1}H NMR, ^{19}F NMR and ^{13}C NMR spectra. Coupling constants are reported in hertz (Hz).

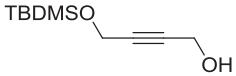
High and low resolution mass spectra were recorded at the EPSRC National Mass Spectrometry Service, Swansea or at the University of St Andrews on a Waters Micromass LCT time of flight mass spectrometer coupled to a Waters 2975 HPLC system. Optical rotation values were recorded on a Perkin-Elmer Model 341 Polarimeter using a Na/Hal lamp (589 nm) at 20 °C in a 1 dm polarimeter cell and are given in 10^{-1} deg cm^2 g^{-1}.

Flash chromatography was performed using silica gel 60 (200–400 mesh). Thin layer chromatography (TLC) was performed using aluminium sheets of silica gel 60 F254 and was visualised under a Mineralight model UVGL-58 lamp (254 nm). The plates were

developed with acidic methanolic vanillin solutions, ethanolic phosphomolybdic acid solutions or basic potassium permanganate solutions.

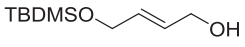
The IUPAC names of some compounds were obtained using ChemDraw Ultra version 12.0.

4.2. 4-((Tert-butyldimethylsilyl)oxy)but-2-yn-1-ol **3** [10]



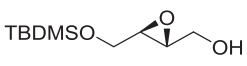
A solution of 2-butyne-1,4-diol **2** (100 g, 1162 mmol, 3.0 eq) in dry THF (250 mL) was added to a suspension of sodium hydride (60% in oil, 19.5 g, 813 mmol, 2.1 eq) in dry THF (250 mL) at 0 °C under argon. The reaction mixture was stirred at 0 °C for 30 min, then *tert*-butyldimethylchlorosilane (58.1 g, 387 mmol, 1.0 eq) was added. The reaction mixture was allowed to warmed to r.t. and stirred for 18 h. The reaction mixture was quenched with sat. NH_4Cl solution (500 mL). The organic layer was separated and the aqueous layer was re-extracted with diethyl ether (3 × 250 mL). The combined organic layers were washed with brine (500 mL), dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 1:4) gave 4-((*tert*-butyldimethylsilyl)oxy)but-2-yn-1-ol **3** (67.0 g, 86%) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.13 (6H, s, CH_3), 0.92 (9H, s, CH_3), 4.31–4.32 (2H, m, CH_2), 4.36–4.37 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ = −5.0 (CH_3), 18.6 (C), 26.0 (CH_3), 51.5 (CH_2), 51.9 (CH_2), 83.1 (C), 84.7 (C); IR (thin film) $\nu^{\sim}$ = 3345, 2956, 2930, 2859, 1718, 1473, 1464, 1362, 1256, 1134, 1085, 1010, 838, 779; MS (ESI) 255 (20), 223 (50) $[M+Na]^+$, 201 (100) $[M+H]^+$; HRMS: *m*/*z* calcd for $C_{10}H_{20}Na_1O_2Si_1$ $[M+Na]^+$: 223.1130; found: 223.1130.

4.3. (E)-4-((tert-butyldimethylsilyl)oxy)but-2-en-1-ol **4**



Red-Al® solution (65 wt% in toluene, 60 mL, 200 mmol, 2.0 eq) was added dropwise to a solution of 4-((*tert*-butyldimethylsilyl)oxy)but-2-yn-1-ol **3** (20 g, 100 mmol, 1.0 eq) in dry THF (500 mL) at 0 °C under argon. The reaction mixture was stirred at 0 °C for 1 h, then warmed to r.t. and stirred for 3 h. The reaction mixture was quenched with sat. Rochelle's salt solution (500 mL). The organic layer was separated and the aqueous layer was re-extracted with diethyl ether (2 × 200 mL). The combined organic layers were washed with brine (500 mL), dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo* to give (*E*)-4-((*tert*-butyldimethylsilyl)oxy)but-2-en-1-ol **4** (18.4 g, 91%) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.09 (6H, s, CH_3), 0.92 (9H, s, CH_3), 4.16–4.21 (4H, m, CH_2), 5.77–5.93 (2H, m, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = −5.0 (CH_3), 18.6 (C), 26.2 (CH_3), 63.3 (CH_2), 63.4 (CH_2), 129.1 (CH), 131.3 (CH); IR (thin film) $\nu^{\sim}$ = 3310, 2956, 2929, 2885, 2858, 1473, 1463, 1379, 1362, 1256, 1132, 1096, 1062, 1005, 984, 836, 777; MS (ESI) 225 (40) $[M+Na]^+$, 185 (100), 147 (85), 133 (65); HRMS: *m*/*z* calcd for $C_{10}H_{22}Na_1O_2Si_1$ $[M+Na]^+$: 225.1287; found: 225.1279.

4.4. ((2R,3R)-3-(((tert-butyldimethylsilyl)oxy)methyl)oxiran-2-yl)methanol **5**



Freshly distilled titanium (IV) isopropoxide (3.7 mL, 1.3 mmol, 0.2 eq) was added to a solution of (-)-DIPT (3.2 mL, 1.5 mmol, 0.24 eq) and activated 4 Å molecular sieves in dry DCM (300 mL) at −25 °C under argon and stirred at −25 °C for 30 min. *tert*-Butyl hydroperoxide (5.5 M in decane, stored over activated 4 Å molecular sieves, 23 mL, 126 mmol, 2.0 eq) was then added dropwise and the reaction mixture was stirred at −25 °C for 30 min. A solution of (*E*)-4-((*tert*-butyldimethylsilyl)oxy)but-2-en-1-ol **4** (stored over activated 4 Å molecular sieves, 12.7 g, 63 mmol, 1.0 eq) in dry DCM (20 mL) was then added over 30 min *via* cannula. The reaction mixture was warmed to −20 °C and stirred for 18 h. The reaction mixture was then warmed to 0 °C and a solution of iron (II) sulfate hexahydrate (40 g) and tartaric acid (15 g) in water (300 mL) was added, and the reaction mixture was stirred vigorously for 15 min. The organic layer was separated and the aqueous layer was re-extracted with DCM (2 × 200 mL). The combined organic layers were washed with water (300 mL) and brine (300 mL), dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 1:4) gave ((2*R*,3*R*)-3-(((*tert*-butyldimethylsilyl)oxy)methyl)oxiran-2-yl)methanol **5** (8.6 g, 62%, 89%ee) as a colourless oil; $[\alpha]_D$ + 19.8° (*c* 1.04, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.08 (3H, s, CH_3), 0.09 (3H, s, CH_3), 0.91 (9H, s, CH_3), 1.65 (1H, bs, OH), 3.12–3.16 (2H, m, CH), 3.64–3.68 (1H, m, CH_2), 3.73 (1H, dd, *J*(H,H) = 12.2, 4.2 Hz, CH_AH_B), 3.91 (1H, dd, *J*(H,H) = 12.2, 2.6 Hz, CH_AH_B), 3.96–3.99 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ = −5.1 (CH_3), 18.6 (C), 26.1 (CH_3), 55.8 (CH), 56.1 (CH), 61.4 (CH_2), 62.8 (CH_2); MS (ESI) 459 (40) $[2M+Na]^+$, 315 (30), 301 (50), 257 (100) $[M+K]^+$, 241 (40) $[M+Na]^+$; HRMS: *m*/*z* calcd for $C_{10}H_{22}Na_1O_3Si_1$ $[M+Na]^+$: 241.1236; found: 241.1227.

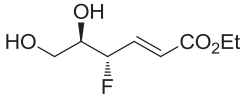
4.5. (E)-ethyl 3-((2R,3R)-3-(((tert-butyldimethylsilyl)oxy)methyl)oxiran-2-yl)acrylate **6**

A solution of DMSO (9.4 mL, 132 mmol, 3.0 eq) in dry DCM (20 mL) was added to a solution of oxalyl chloride (7.8 mL, 92 mmol, 2.1 eq) in dry DCM (230 mL) at −78 °C under argon. The reaction mixture was stirred at −78 °C for 30 min, then a solution of ((2*R*,3*R*)-3-(((*tert*-butyldimethylsilyl)oxy)methyl)oxiran-2-yl)methanol **5** (9.6 g, 44 mmol, 1.0 eq) in dry DCM (50 mL) was added. The reaction mixture was stirred at −78 °C for 1 h, then triethylamine (61 mL, 440 mmol, 10.0 eq) was added and the reaction mixture was warmed to 0 °C and stirred for 30 min. The reaction mixture was warmed to r.t. and diluted with water (500 mL). The organic layer was separated and re-extracted with DCM (2 × 200 mL). The combined organic layers were washed with brine (500 mL), dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo* to give the intermediate aldehyde, which was used without further purification.

Triethylphosphonoacetate (12.4 mL, 61.6 mmol, 1.4 eq) was added to a suspension of sodium hydride (60% in oil, 2.3 g, 57.2 mmol, 1.3 eq) in dry THF (250 mL) at 0 °C under argon and stirred at 0 °C for 30 min. The reaction mixture was cooled to −78 °C and a solution of the intermediate aldehyde in dry THF (50 mL) was added. The reaction mixture was stirred at −78 °C for 2 h. The reaction mixture was diluted with ethyl acetate (250 mL) and warmed to r.t. The organic layer was washed with half-saturated brine solution (2 × 250 mL). The organic layer was separated and the aqueous layer was re-extracted with ethyl acetate (200 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 1:4) gave (*E*)-ethyl 3-((2*R*,3*R*)-3-(((*tert*-butyldimethylsilyl)oxy)methyl)oxiran-2-yl)-acrylate **6** (6.6 g, 52% over 2 steps) as a colourless oil; $[\alpha]_D$ + 13.8° (*c* 1.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.08 (3H, s, CH_3), 0.08 (3H, s, CH_3), 0.90 (9H, s, CH_3), 1.29 (3H, t, *J*(H,H) = 7.1 Hz, CH_3), 3.05–3.08 (1H, m, CH), 3.43 (1H, dd, *J*(H,H) = 7.2, 1.8 Hz, CH), 3.78 (1H, dd, *J*(H,H) = 12.1, 4.0 Hz, CH_AH_B), 3.89 (1H, dd, *J*(H,H) = 12.1, 3.0 Hz, CH_AH_B), 4.20 (2H, q, *J*(H,H) = 7.1 Hz, CH_2), 6.15 (1H, dd, *J*(H,H) = 15.7, 0.7 Hz, CH), 6.70

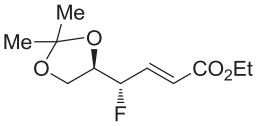
(1H, dd, J(H,H) = 15.7, 7.2 Hz, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = −5.1 (CH_3), 14.4 (CH_3), 18.6 (C), 26.0 (CH_3), 53.8 (CH), 60.8 (CH_2), 61.3 (CH), 62.4 (CH_2), 124.3 (CH), 144.3 (CH), 165.8 (CO); IR (thin film) $\nu^{\sim}$ = 2956, 2929, 2858, 1724, 1659, 1473, 1464, 1390, 1367, 1303, 1257, 1185, 1139, 1106, 1040, 977, 890, 838, 779; MS (ESI) 309 (100) $[M+Na]^+$, 257 (80); HRMS: m/z calcd for $C_{14}H_{26}Na_1O_4Si_1$ $[M+Na]^+$: 309.1498; found: 309.1488.

4.6. (4S,5R,E)-ethyl 4-fluoro-5,6-dihydroxyhex-2-enoate 7



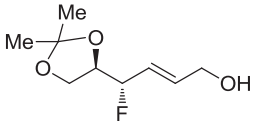
Two batches of a solution of (*E*)-ethyl 3-((2*R*,3*R*)-3-(((*tert*-butyldimethylsilyl)oxy)-methyl)oxiran-2-yl)acrylate **6** (3.8 g, 13.2 mmol, 1.0 eq) in triethylamine trihydrofluoride (12.9 mL, 79.3 mmol, 6.0 eq) were heated at 90 °C under argon for 24 h. The reaction mixture was cooled to r.t. and quenched with sat. $NaHCO_3$ solution (150 mL). The two batches were combined and the solvent was removed *in vacuo*. The residue was stirred in DCM (300 mL) for 18 h. The suspension was filtered, the filtrate collected and the solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 2:3) gave (4*S*,5*R*,*E*)-ethyl 4-fluoro-5,6-dihydroxyhex-2-enoate **7** (3.8 g, 50%) as an orange oil, as a 10:1 mixture of regioisomers. Data for major regioisomer; $[\alpha]_D$ −18.6° (*c* 1.43, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.30 (3H, t, J(H,H) = 7.2 Hz, CH_3), 3.30 (2H, bs, OH), 3.70–3.80 (2H, m, CH_2), 3.81–3.89 (1H, m, CH), 4.21 (2H, q, J(H,H) = 7.2 Hz, CH_2), 5.11 (1H, dddd, J(H,F) = 47.3 Hz, J(H,H) = 6.0, 4.2, 1.9 Hz, CHF), 6.15 (1H, ddd, J(H,H) = 16.2, 1.7, 1.3, CH), 7.02 (1H, dddd, J(H,F) = 20.0 Hz, J(H,H) = 15.9, 4.2, 1.7 Hz, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.3 (CH_3), 61.2 (CH_2), 62.5 (d, J(C,F) = 4.8 Hz, CH_2), 72.9 (d, J(C,F) = 23.3 Hz, CH), 91.0 (d, J(C,F) = 177.1 Hz, CHF), 122.9 (d, J(C,F) = 11.5 Hz, CH), 142.1 (d, J(C,F) = 17.7 Hz, CH), 166.3 (CO); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = −195.4 (1F, s); IR (thin film) $\nu^{\sim}$ = 3423, 3306, 2981, 2933, 1717, 1664, 1467, 1448, 1372, 1310, 1273, 1185, 1086, 1037, 980, 867; MS (ESI) 231 (35), 215 (100) $[M+Na]^+$, 193 (50) $[M+H]^+$; HRMS: m/z calcd for $C_8H_{13}F_1Na_1O_4$ $[M+H]^+$: 215.0696; found: 215.0688.

4.7. (S,E)-ethyl 4-(R)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-fluorobut-2-enoate 8



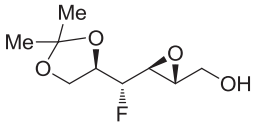
d-Camphor-10-sulfinic acid (0.42 g, 1.8 mmol, 0.1 eq) was added to a solution of (4*S*,5*R*,*E*)-ethyl 4-fluoro-5,6-dihydroxyhex-2-enoate **7** (3.5 g, 18.0 mmol, 1.0 eq) and 2,2-dimethoxypropane (4.4 mL, 36.0 mmol, 2.0 eq) in dry DMF (100 mL) under argon at r.t. The reaction mixture was stirred at r.t. for 18 h. The reaction mixture was quenched with sat. $NaHCO_3$ solution (200 mL) and extracted with ethyl acetate (500 mL). The organic layer was washed with water (3 × 200 mL), brine (500 mL), dried over anhydrous Na_2SO_4 and the solvent removed *in vacuo* to give (*S*,*E*)-ethyl 4-(*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-fluorobut-2-enoate **8** (3.7 g, 88%) as a colourless oil; $[\alpha]_D$ −45.9° (*c* 0.61, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.31 (3H, t, J(H,H) = 7.2 Hz, CH_3), 1.36 (3H, s, CH_3), 1.45 (3H, s, CH_3), 4.02 (1H, ddd, J(H,H) = 8.3, 4.7, 1.6 Hz, CH_AH$_B$), 4.07–4.19 (2H, m, CH$_A$H$_B$, CH), 4.22 (2H, q, J(H,H) = 7.2 Hz, CH_2), 5.00 (1H, dddd, J(H,F) = 47.6 Hz, J(H,H) = 6.3, 3.9, 1.9 Hz, CHF), 6.15 (1H, ddd, J(H,H) = 15.9, 1.8, 1.2, CH), 6.96 (1H, dddd, J(H,F) = 19.8 Hz, J(H,H) = 15.9, 3.9, 1.9 Hz, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.4 (CH_3), 25.3 (CH_3), 26.7 (CH_3), 60.9 (CH_2), 65.8 (d, J(C,F) = 3.6 Hz, CH_2), 76.3 (d, J(C,F) = 26.5 Hz, CH), 90.5 (d, J(C,F) = 179.8 Hz, CHF), 110.6 (C), 123.0 (d, J(C,F) = 11.2 Hz, CH), 141.6 (d, J(C,F) = 17.6 Hz, CH), 165.8 (CO); ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ = −195.0 (1F, s); IR (thin film) $\nu^{\sim}$ = 3435, 2958, 2932, 2855, 1729, 1665, 1461, 1373, 1306, 1263, 1179, 1074, 1040, 980, 846, 796; MS (ESI) 255 (100) $[M+Na]^+$, 233 (40) $[M+H]^+$; HRMS: m/z calcd for $C_{11}H_{17}F_1Na_1O_4$ $[M+Na]^+$: 255.1009; found: 255.0997.

4.8. (S,E)-4-((R)-4-2,2-dimethyl-1,3-dioxolan-4-yl)-4-fluorobut-2-en-1-ol 9



DIBAL-H solution (1.0 M in hexanes, 25.8 mL, 25.8 mmol, 3.0 eq) was added to a solution of (*S*,*E*)-ethyl 4-(*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-fluorobut-2-enoate **8** (2.0 g, 8.6 mmol, 1.0 eq) in dry THF (200 mL) at −78 °C under argon. The reaction mixture was stirred at −78 °C for 1 h, then warmed to r.t. and stirred for a further 2 h. The reaction mixture was diluted with ethyl acetate (200 mL) and quenched with HCl solution (5%, 100 mL). The organic layer was separated and washed with sat. $NaHCO_3$ solution (200 mL), brine (200 mL), dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 1:1) gave (*S*,*E*)-4-((*R*)-4-2,2-dimethyl-1,3-dioxolan-4-yl)-4-fluorobut-2-en-1-ol **9** (1.02 g, 62%) as a colourless oil; $[\alpha]_D$ −14.8° (*c* 1.04, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.37 (3H, s, CH_3). 1.45 (3H, s, CH_3), 4.00 (1H, dd, J(H,H) = 8.5, 5.2 Hz, CH_AH$_B$), 4.08–4.11 (1H, m, CH$_A$H$_B$), 4.12–4.19 (1H, m, CH), 4.23–4.25 (2H, m, CH_2), 4.87 (1H, ddd, J(H,F) = 47.9 Hz, J(H,H) = 6.0, 6.0 Hz, CHF), 5.84 (1H, ddd, J(H,F) = 15.4 Hz, J(H,H) = 15.1, 5.8 Hz, CH), 6.03–6.08 (1H, m, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 25.4 (CH_3), 26.7 (CH_3), 62.8 (CH_2), 65.8 (d, J(C,F) = 3.7 Hz, CH_2), 76.7 (CH), 91.8 (d, J(C,F) = 173.4 Hz, CHF), 110.2 (C), 125.4 (d, J(C,F) = 18.4 Hz, CH), 134.6 (d, J(C,F) = 11.0 Hz, CH); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = −187.3 (1F, s); IR (thin film) $\nu^{\sim}$ = 3422, 2989, 2936, 2893, 1679, 1457, 1383, 1373, 1259, 1217, 1155, 1071, 974, 847, 794; MS (ESI) 257 (15), 241 (25), 213 (100) $[M+Na]^+$; HRMS: m/z calcd for $C_9H_{15}F_1Na_1O_4$ $[M+Na]^+$: 213.0903; found: 213.0893.

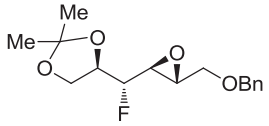
4.9. (2R,3S)-3-((R)-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)fluoromethyl)oxiran-2-yl)methanol 10



Freshly distilled titanium (IV) isopropoxide (0.31 mL, 1.1 mmol, 0.2 eq) was added to a solution of (-)-DIPT (0.26 mL, 1.3 mL, 0.24 eq) and activated 4 Å molecular sieves in dry DCM (20 mL) at −25 °C under argon and stirred at −25 °C for 30 min. *tert*-Butyl hydroperoxide (5.5 M in decane, stored over activated 4 Å molecular sieves, 1.9 mL, 10.6 mmol, 2.0 eq) was then added dropwise and the reaction mixture was stirred at −25 °C for 30 min. A solution of (*S*,*E*)-4-((*R*)-4-2,2-dimethyl-1,3-dioxolan-4-yl)-4-fluorobut-2-en-1-ol **9** (stored over activated 4 Å molecular sieves, 1.0 g, 5.3 mmol, 1.0 eq) in dry DCM (5 mL) was then added over 30 min *via* cannula. The reaction mixture was warmed to −20 °C and stirred for 18 h. The reaction mixture was then warmed to 0 °C and a solution of iron (II) sulfate hexahydrate (2 g) and tartaric acid (1 g) in water (30 mL) was added, and the reaction mixture was stirred vigorously for 15 min. The organic layer was separated and the aqueous layer was re-extracted with DCM (2 × 100 mL). The combined organic layers were washed with

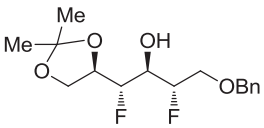
water (200 mL) and brine (200 mL), dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 2:3) gave (2*R*,3*S*)-3-((*R*)-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)fluoromethyl)-oxiran-2-yl)methanol **10** (0.48 g, 77%) as a colourless oil (*dr* 10:1); $[\alpha]_D$ +4.4° (*c* 1.09, $CHCl_3$). Data for major diastereoisomer; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.37 (3H, s, CH_3), 1.45 (3H, s, CH_3), 3.31–3.38 (2H, m, CH), 3.68–3.73 (1H, m, CH_2), 3.97–4.15 (3H, m, CH_2, CH_2), 4.20–4.28 (1H, m, CH), 4.51 (1H, ddd, *J*(H,F) = 47.8 Hz, *J*(H,H) = 6.4, 3.2 Hz, CHF); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 25.3 (CH_3), 26.7 (CH_3), 53.4 (d, *J*(C,F) = 25.9 Hz, CH), 55.3 (d, *J*(C,F) = 6.5 Hz, CH), 60.9 (CH_2), 65.9 (d, *J*(C,F) = 4.5 Hz, CH_2), 74.3 (d, *J*(C,F) = 25.9 Hz, CH), 90.2 (d, *J*(C,F) = 178.7 Hz, CHF), 110.4 (C); ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ = −199.6 (1F, s); IR (thin film) $\tilde{\nu}$ = 3461, 2989, 2937, 1457, 1383, 1374, 1260, 1222, 1157, 1071, 976, 917, 845; MS (ESI) 229 (100) [M+Na]$^+$; HRMS: *m*/*z* calcd for $C_9H_{15}F_1Na_1O_4$ [M+Na]$^+$: 229.0852; found: 229.0840.

4.10. (R)-4-((R)-((2S,3R)-3-((benzyloxy)methyl)oxiran-2-yl)fluoromethyl)-2-2dimethyl-1,3-dioxolane **11**



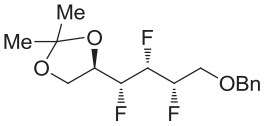
Sodium hydride (60% in oil, 0.233 g, 5.8 mmol, 1.5 eq) was added to a solution of (2*R*,3*S*)-3-((*R*)-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)fluoromethyl)oxiran-2-yl)methan-ol **10** (0.8 g, 3.9 mmol, 1.0 eq) in dry DMF (25 mL) at 0 °C under argon and stirred at 0 °C for 30 min. Benzyl bromide (0.7 mL, 5.8 mmol, 1.5 eq) was added and the reaction mixture was stirred at 0 °C for 1 h, then warmed to r.t. and stirred for 18 h. The reaction mixture was quenched with water (100 mL) and extracted with ethyl acetate (250 mL). The organic layer was separated and washed with water (2 × 200 mL), brine (250 mL), dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 1:9) gave (*R*)-4-((*R*)-((2*S*,3*R*)-3-((benzyloxy)methyl)oxiran-2-yl)fluoro-methyl)-2-2dimethyl-1,3-dioxolane **11** (0.93 g, 81%) as a colourless oil (*dr* 10:1); $[\alpha]_D$ −0.4° (c 1.04, $CHCl_3$). Data for major diastereoisomer; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.37 (3H, s, CH_3), 1.45 (1H, s, CH_3), 3.23 (1H, ddd, *J*(H,F) = 13.9 Hz, *J*(H,H) = 3.4, 2.4 Hz, CH), 3.35 (1H, dt, *J*(H,H) = 5.3, 2.5 Hz, CH), 3.52 (1H, dd, *J*(H,H) = 11.6, 5.4 Hz, CH_AH_B), 3.82 (1H, dd, *J*(H,H) = 11.6, 2.7 Hz, CH_AH_B), 4.03 (1H, ddd, *J*(H,H) = 8.7, 5.4, 1.2 Hz, CH_AH_B), 4.09–4.15 (1H, m, CH_AH_B), 4.18–4.27 (1H, m, CH), 4.49 (1H, ddd, *J*(H,F) = 48.1 Hz, *J*(H,H) = 6.1, 3.2 Hz, CHF), 4.57 (1H, d, *J*(H,H) = 12.1 Hz, CH_AH_B), 4.61 (1H, d, *J*(H,H) = 12.1 Hz, CH_AH_B), 7.29–7.39 (5H, m, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 25.3 (CH_3), 26.7 (CH_3), 53.6 (d, *J*(C,F) = 25.7 Hz, CH), 54.1 (d, *J*(C,F) = 6.8 Hz, CH), 65.8 (d, *J*(C,F) = 4.7 Hz, CH_2), 69.4 (CH_2), 73.5 (CH_2), 74.4 (d, *J*(C,F) = 26.0 Hz, CH), 90.2 (d, *J*(C,F) = 179.1 Hz, CHF), 110.4 (C), 128.0 (CH), 128.0 (CH), 128.7 (CH), 137.9 (C); ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ = −199.6 (1F, s); IR (thin film) $\tilde{\nu}$ = 2988, 2936, 2892, 1497, 1455, 1382, 1373, 1258, 1216, 1156, 1104, 1072, 1001, 845, 740, 699; MS (ESI) 655 (65) [2M+Na]$^+$, 339 (100) [M+Na]$^+$, 317 (35) [M+H]$^+$, 277 (25); HRMS: *m*/*z* calcd for $C_{16}H_{21}F_1Na_1O_4$ [M+Na]$^+$: 319.1322; found: 319.1311.

4.11. (1S,2S,3S)-4-(benzyloxy)-1-((R)-2,2,-dimethyl-1,3-dioxolan-4-yl)-1,3-difluorobutan-2-ol **12** [9]



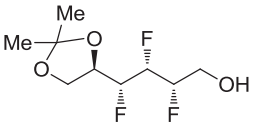
A solution of (*R*)-4-((*R*)-((2*S*,3*R*)-3-((benzyloxy)methyl) oxiran-2-yl)fluoromethyl)-2-2dimethyl-1,3-dioxolane **16** (0.529 g, 1.8 mmol, 1.0 eq) in triethylamine trihydrofluoride (5.3 mL, 32.1 mmol, 18.0 eq) and triethylamine (2.3 mL, 16.2 mmol, 9.0 eq) was heated at 100 °C under argon for 3 days. The reaction mixture was cooled to r.t. and quenched with sat. $NaHCO_3$ solution (150 mL) and extracted with DCM (2 × 150 mL). The combined organic layers were washed with brine (200 mL), dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 1:9) gave (1*S*,2*S*,3*S*)-4-(benzyloxy)-1-((*R*)-2,2,-dimethyl-1,3-dioxolan-4-yl)-1,3-difluorobutan-2-ol **12** (0.259, 46%) as a colourless oil, as a single diastereoisomer; $[\alpha]_D$ −6.6° (c 0.80, $CHCl_3$), lit [9]. $[\alpha]_D$ −6.23° (*c* 1.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.37 (3H, s, CH_3), 1.45 (3H, s, CH_3), 2.80 (1H, d, *J*(H,H) = 5.3 Hz, OH), 3.84 (1H, dd, *J*(H,H) = 3.6, 0.7 Hz, CH_AH_B), 3.89–3.91 (1H, m, CH_AH_B), 4.07 (1H, ddd, *J*(H,H) = 9.0, 5.2, 1.8 Hz, CH_AH_B), 4.13 (1H, ddd, *J*(H,H) = 9.0, 6.3, 1.4 Hz, CH_AH_B), 4.20–4.31 (1H, m, CH), 4.39–4.46 (1H, m, CH), 4.53–4.67 (3H, m, CH_2, CHF), 4.84 (1H, dm, *J*(H,F) = 46.1 Hz, CHF), 7.30–7.40 (5H, m, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 25.4 (CH_3), 26.7 (CH_3), 66.2 (d, *J*(C,F) = 4.0 Hz, CH_2), 69.4 (d, *J*(C,F) = 21.8 Hz, CH_2), 71.0 (dd, *J*(C,F) = 24.8, 21.8 Hz, CH), 73.9 (d, *J*(C,F) = 29.2 Hz, CH), 74.0 (CH_2), 90.7 (dd, *J*(C,F) = 175.1, 6.3 Hz, CHF), 91.8 (dd, *J*(C,F) = 176.4, 3.6 Hz, CHF), 110.2 (C), 128.0 (CH), 128.2 (CH), 128.8 (CH), 137.6 (C); ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ = −196.6 (1F, s), −200.7 (1F, s); MS (ESI) 655 (65) [2M+Na]$^+$, 339 (100) [M+Na]$^+$, 317 (35) [M+H]$^+$, 277 (25); HRMS: *m*/*z* calcd for $C_{16}H_{22}F_2Na_1O_4$ [M+Na]$^+$: 339.1384; found: 339.1372.

4.12. (R)-4-((1R,2R,3S)-4-(benzyloxy)-1,2,3-trifluorobutyl)-2,2-dimethyl-1,3-dioxolane **13** [9]



Deoxofluor® solution (50% in THF, 0.65 mL, 1.5 mmol, 3.0 eq) was added to a solution of (1*S*,2*S*,3*S*)-4-(benzyloxy)-1-((*R*)-2,2,-dimethyl-1,3-dioxolan-4-yl)-1,3-difluorobutan-2-ol **12** (0.16 g, 0.5 mmol, 1.0 eq) in dry DCM (30 mL) under argon at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, then warmed to r.t. and stirred for 18 h. The solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 1:9) gave (*R*)-4-((1*R*,2*R*,3*S*)-4-(benzyloxy)-1,2,3-trifluorobutyl)-2,2-dimethyl-1,3-dioxolane **13** (0.085 g, 53%) as a colourless oil; $[\alpha]_D$ −16.9° (*c* 0.95, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.37 (3H, s, CH_3), 1.37 (3H, s, CH_3), 3.73–3.92 (2H, m, CH_2), 4.06 (1H, ddd, *J*(H,H) = 9.1, 4.0, 2.0 Hz, CH_AH_B), 4.11–4.15 (1H, m, CH_AH_B), 4.11–4.15 (1H, m, CH), 4.33–4.40 (1H, m, CH), 4.43–4.64 (3H, m, CH_2, CHF), 4.81–5.14 (2H, m, CHF), 7.31–7.39 (5H, m, ArH); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = −198.3 (1F, d, *J*(F,F) = 14.3 Hz), −209.4 (1F, d, *J*(F,F) = 9.8 Hz), −214.2 (1F, dd, *J*(F,F) = 14.3, 9.8 Hz); MS (ESI) 341 (100) [M+Na]$^+$, 319 (20) [M+H]$^+$, 91 (45); HRMS: *m*/*z* calcd for $C_{16}H_{21}F_3Na_1O_3$ [M+Na]$^+$: 341.1340; found: 341.1329. Data were in agreement with the previously reported compound [9].

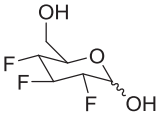
4.13. (2S,3R,4R)-4-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,3,4-trifluorobutan-1-ol **14** [9]



A solution of sodium bromate (142 mg, 0.9 mmol, 3.0 eq) in water (3 mL) was added to a solution of (*R*)-4-((1*R*,2*R*,3*S*)-4-(benzyloxy)-1,2,3-trifluorobutyl)-2,2-dimethyl-1,3-dioxolane

13 (100 mg, 0.3 mmol, 1.0 eq) in ethyl acetate (4.2 mL) and stirred at r.t. for 10 min. A solution of sodium dithionite (85% technical grade, 161 mg, 0.8 mmol, 2.5 eq) in water (6 mL) was added dropwise over 15 min. The reaction mixture was stirred at r.t. for 1 h, then diluted with ethyl acetate (30 mL). The reaction mixture was washed with sat. sodium thiosulfate solution (30 mL). The organic layer was separated and the aqueous layer was re-extracted with ethyl acetate (30 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 3:7) gave (2*S*,3*R*,4*R*)-4-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,3,4-trifluorobutan-1-ol **14** (44 mg, 61%) as a colourless oil; $[\alpha]_D$ −15.8° (*c* 0.72, $CHCl_3$), lit [9]. $[\alpha]_D$ −20.1° (*c* 0.57, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.37 (3H, s, CH_3), 1.44 (3H, s, CH_3), 3.83–4.18 (4H, m, CH_2), 4.35–4.43 (1H, m, CH), 4.50–5.16 (3H, m, CHF); ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ = −202.0 (1F, d, *J*(F,F) = 14.4 Hz), −209.4 (1F, d, *J*(F,F) = 9.6 Hz), −215.0 (1F, dd, *J*(F,F) = 14.4, 9.6 Hz); MS (ESI) 323 (55), 229 (65) $[M+H]^+$, 183 (50), 147 (100), 115 (45), 102 (65); HRMS: *m*/*z* calcd for $C_9H_{16}F_3O_3$ $[M+H]^+$: 229.1052; found: 229.1045. Data were in agreement with the previously reported compound [9].

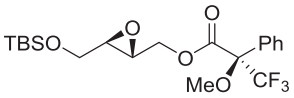
4.14. 2,3,4-Trideoxy-2,3,4-trifluoroglucose **1** [9]



Dess-Martin periodinane (123 mg, 0.3 mmol, 1.5 eq) was added to a solution of (2*S*,3*R*,4*R*)-4-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,3,4-trifluorobutan-1-ol **14** in dry DCM (2 mL) at r.t. under argon and stirred for 1 h. The reaction mixture was then diluted with ethyl acetate/pet. ether (1:9, 10 mL) and filtered through a short plug of silica (2.5 cm^3). The solvent was removed *in vacuo* to give the crude aldehyde intermediate that was used without further purification.

Anhydrous tin (II) chloride (60 mg, 0.3 mmol, 1.5 eq) was added to a solution of the intermediate aldehyde from the previous step in dry DCM (2 mL) under argon at r.t. The reaction mixture was stirred for 1 h at r.t., then the undissolved tin was removed by filtration. The filtrate was collected and the solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 4:1) gave 2,3,4-trideoxy-2,3,4-trifluoroglucose **1** (21 mg, 58% over 2 steps, mixture of α- and β-anomers) as a colourless oil. The ratio of the anomeric mixture was α/β: 1.00/0.34 by ^{19}F NMR ($CDCl_3$); $[\alpha]_D$ +131.6° (*c* 0.30, $CDCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.78 (1H, dd, *J*(H,H) = 7.3, 5.2 Hz, OH), 1.91 (1H, dd, *J*(H,H) = 6.6, 6.3 Hz, OH), 3.48 (1H, d, *J*(H,H) = 5.8 Hz, OH), 3.59–4.15 (6H, m), 4.27–4.79 (4H, m), 4.80–5.52 (4H, m); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = −195.8 (1F, dd, *J*(F,F) = 13.1, 12.8 Hz, β-anomer), −200.0 (1F, dd, *J*(F,F) = 12.7, 1.9 Hz, α-anomer), −200.5 (1F, dd, *J*(F,F) = 13.1, 2.7 Hz, β-anomer), −201.3 (1F, dd, *J*(F,F) = 12.8, 2.7 Hz, β-anomer), −201.7 (1F, dd, *J*(F,F) = 13.2, 12.7 Hz, α-anomer), −202.1 (1F, dd, *J*(F,F) = 13.2, 1.9 Hz, α-anomer). Data were in agreement with the previously reported compound [9].

4.15. ((2R,3R)-3-((tert-butyldimethylsilyl)oxy)methyl)oxiran-2-yl)methyl (2R)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate



Following a modified version of the reported procedure [12], (*R*)-(+)-α-methoxy-α-trifluoromethylphenylacetyl chloride (17 μL, 91 μmol, 2.0 eq) was added to a solution of ((2*R*,3*R*)-3-(((*tert*-butyldimethylsilyl)oxy)methyl)oxiran-2-yl)methanol (10 mg, 46 μmol, 1.0 eq), 4-DMAP (22 mg, 183 μmol, 4.0 eq) and triethylamine (10 μL, 69 μmol, 1.5 eq) in dry DCM (1.0 mL) at r.t. under argon and stirred at r.t. for 18 h. The solvent was removed *in vacuo*. Purification by column chromatography using silica gel (ethyl acetate/pet. ether 1:9) gave ((2*R*,3*R*)-3-((*tert*-butyldimethylsilyl)oxy)methyl)oxiran-2-yl)methyl (2*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (13.3 mg, 67%) as a colourless oil. ^{19}F{^{1}H} NMR showed two peaks at −71.73 and −71.74 ppm. Deconvolution by NMR software showed the diastereoisomers to be in a ratio of 94.5:5.5, giving 89%ee for the epoxide. The racemic epoxide was synthesised and derivitised using the same procedure for comparison.

Acknowledgements

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfluchem.2013.06.003.

References

[1] L.L. Lairson, B. Henrissat, G.J. Davies, S.G. Withers, Annu. Rev. Biochem. 77 (2008) 521–555.
[2] S.A. Allman, H.H. Jensen, B. Vijayakrishnan, J.A. Garnett, E. Leon, Y. Liu, D.C. Anthony, N.R. Sibson, T. Feizi, S. Matthews, B.G. Davies, ChemBioChem 10 (2009) 2522–2529.
[3] O. Boutureira, F. D'Hooge, M. Fernández-González, G.J.L. Bernardes, M. Sánchez-Navarro, J.R. Koeppe, B.G. Davis, Chem. Commun. 46 (2010) 8142–8144.
[4] F.-L. Qing, F. Zheng, Synlett 8 (2011) 1052–1072.
[5] Y. Yang, F. Zheng, M. Bols, L.G. Marinsescu, F.-L. Qing, J. Fluorine Chem. 132 (2011) 838–845.
[6] S. André, F.J. Cañada, T.C. Shiao, L. Largartera, T. Diercks, M. Bergeron-Brlek, K. el Biara, A. Papadopoulos, J.P. Ribeiro, M. Touaibia, D. Solís, M. Menéndez, J. Jiménez-Barbero, R. Roy, H.-J. Gabius, Eur. J. Org. Chem. 23 (2012) 4354–4364.
[7] C.B. Brown, M.S. Rusek, L.L. Kiessling, J. Am. Chem. Soc. 134 (2012) 6552–6555.
[8] S. Bresciani, A.M.Z. Slawin, D. O'Hagan, J. Fluorine Chem. 130 (2009) 537–543.
[9] S. Bresciani, T. Lebl, A.M.Z. Slawin, D. O'Hagan, Chem. Commun. 46 (2010) 5434–5436.
[10] H. Toshima, H. Aramaki, A. Ichihara, Tetrahedron Lett. 40 (1999) 3587–3590.
[11] T. Katsuki, K.B. Sharpless, J. Am. Chem. Soc. 102 (1980) 5974–5976.
[12] I. Ohtani, T. Kusumi, Y. Kashman, H. Kakisawa, J. Am. Chem. Soc. 113 (1991) 4092–4096.
[13] K. Omura, D. Swern, Tetrahedron 34 (1978) 1651–1660.