Supplementary Information

Enantioselective synthesis of tetrafluorinated ribose and fructose

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1) Determination of the enantioselectivity of the SAD reaction

a) Conversion to (2R)-1,2-dibenzoyloxy-4-bromo-3,3,4,4-tetrafluoro-butane-1,2-diol

To a solution of 9 (0.30 g, 1.25 mmol, 1 equiv) in pyridine (3.00 mL), BzCl (0.58 mL, 4.98 mmol, 4 equiv) was added. The reaction was stirred at RT for 2.5 h. To the reaction was added water (5 mL) and the aqueous phase was extracted with CH2Cl2 (3 x 8 mL). The combined organic phase was washed with saturated aqueous NaHCO3 (2 x 10 mL), 1N aqueous HCl (2 x 10 mL), brine (2 x 10 mL) and dried over MgSO4, filtered, concentrated in vacuo to give the crude as a transparent gel. Column chromatography (Petroleum ether/EtOAc: 90/10) gave the product the title compound as a transparent gel (0.4772 g, 1.06 mmol, 85% yield). Rf 0.36 (Petroleum ether/EtOAc: 90/10).

IR (Neat): 1728 (s), 1602 (m), 1452 (m), 1274 (s), 1244 (s) cm⁻¹. 1H NMR (CDCl3, 400 MHz): δ 8.08–7.98 (4H, m), 7.63–7.54 (2H, m), 7.49–7.40 (4H, m), 6.21 (1H, dtd, J = 16.3, 6.8, 3.5 Hz), 4.91 (1H, ddd, J = 12.2, 3.4, 1.5 Hz), 4.69 ppm (1H, dd, J = 12.3, 7.0 Hz) ppm. 13C NMR (CDCl3, 100 MHz): δ 165.91 (C), 164.50 (C), 134.09(C), 133.53 (C) 130.24 (2 x C, CH), 129.91 (2 x C), 129.25 (CH), 128.76 (2 x C, CH), 128.60 (2 x C, CH), 128.39 (CH), 116.69 (tt, J = 310.6, 38.6 Hz), 113.63 (ddt, J = 262.7, 255.0, 31.9Hz), 67.43 (dd, J = 30.5, 22.7 Hz, CH), 60.94 (CH3) ppm. 19F NMR (CDCl3, 282 MHz): δ -119.64 (1F, app dd, J = 174.7, 16.0 Hz), -113.47 (1F, d, J = 174.7 Hz), -64.29 (2F, s) ppm. LR MS (ES⁺) m/z (%): 471 and 473 ((M + Na)⁺, 1:1 ratio, 100). HR MS (ES⁺): for C18H13F9BrF4O4Na (M + Na)⁺: calcd: 470.9826, found 470.9824.

b) Conversion to (2R)-1,2-diacetoxy-4-bromo-3,3,4,4-tetrafluoro-butane-1,2-diol

9 (0.1 g, 0.41mmol) was dissolved in CH2Cl2 (3 mL) and Et3N (0.14 mL, 1.0 mmol) and DMAP (0.005g, 0.04 mmol) were added. Acetyl chloride (0.071 mL, 1.0 mmol) was added dropwise and the reaction stirred at RT for 2 h. The reaction was quenched by the addition of HCl (0.5M, aq, 10 mL). The layers were separated and the aqueous phase extracted with CH2Cl2 (2 x 5 mL), the organic phases were combined, dried over MgSO4, filtered and
concentrated *in vacuo*. Column chromatography (pentane / Et₂O, 80:20) gave the title compound as a colourless oil (0.111 g, 83%).

**IR** (neat): 1752 (s), 1372 (m), 1203 (s), 1143 (s), 1085 (s). **¹H NMR** (400 MHz, CDCl₃): δ 5.77 (1H, dtd, J = 16.4, 7.1, 3.3 Hz, CHOAc), 4.60 (1H, ddd, J = 12.3, 3.3, 1.7 Hz, CHHCH), 4.24 (1H, dd, J = 12.2, 7.4 Hz, CHHCH), 2.15 (3H, s, CH₃), 2.07 (3H, s, CH₃) ppm. **¹³C NMR** (100 MHz, CDCl₃): δ 170.2 (CO), 168.7 (CO), 66.70 (1C, dd, J = 30.1, 22.4 Hz, CHCF₂), 60.1 (CH₂), 20.5 (CH₃), 20.3 (CH₃) ppm. The CF₂CF₂ carbons were not observed. **¹⁹F NMR** (282 MHz, CDCl₃): δ -64.70 (2F, s, CF₂Br), -114.25 (1F, d, J = 272.9 Hz, CHCFF), -120.21 (1F, ddt, J = 272.9, 17.2, 4.3 Hz, CHCF₂) ppm. **CIMS**: m/z (%): 344 and 342 (M+NH₄⁺) (6, 1:1 ratio) **HRMS** (ES⁺) for C₈H₉₇⁹BF₄O₄Na: calcd: 346.9613, found; 346.9513.

Analysis of (2S)-1,2-dibenzoyloxy-4-bromo-3,3,4,4-tetrafluoro-butane-1,2-diol by reverse HPLC (OJ column, IPA/hexane eluent) showed a 83% ee when (DHQD)₂PYR was used in the AD of 8 (Figure 1).
Analysis of the \( (2R)\)-1,2-diacetoxy-4-bromo-3,3,4,4-tetrafluoro-butane-1,2-diol by chiral GC (Chiradex G9511-16 column, ) showed a 78% ee when (DHQ)\(_2\)PYR was used in the AD (Figure 2).

![Area Percent Report Table](image)

**Figure 2**
2) Confirmation of the ee of 11 and 20

i) Alkylation under basic conditions.

The ee values of 11 were obtained on chiral HPLC with an OJ column. The eluent used for the resolution of 11 was 12% IPA in hexane and the concentration of the samples was 2 mg/mL. The injection volume was 10 μL and the flow 1 mL/min. The retention times were 5.8 min for (S)-11 and 6.7 min for (R)-11 (Figure 3).

**Figure 3:** Chiral HPLC trace (OJ column) of racemic 11.
Chiral HPLC chromatogram of a sample of 11 synthesised by treatment of 9 with Na$_2$CO$_3$ and BnBr. When compared to the 83% ee observed by a similar method in section 1 the sample shows no evidence of epimerisation (Figure 4).

![Chiral HPLC Chromatogram](image)

**Figure 4**

ii) Alkylation *via* the stannylene acetal methodology.

NMR analysis of the Mosher’s ester of 20 showed an *ee* of 77% i.e. no reduction in *ee* after alkylation *via* a stannylene acetal (Figure 5).

![NMR Analysis](image)

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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3) Crystal structure of 22

Thermal ellipsoids drawn at the 50% probability level

4) Crystal structure of 2

Thermal ellipsoids drawn at the 35% probability level
5) HMBC spectra of 2, 5, 6 and 7
HMBC of 5
HMBC of 7
(2R)-4-bromo-3,3,4,4-tetrafluorobutane-1,2-diol (9)
(2R)-1-Benzylloxy-4-bromo-3,3,4,4-tetrafluorobutan-1-ol (10)
(2R)-2-Benzylxyo-4-bromo-3,3,4,4-tetrafluorobutan-1-ol (11)
(2R)-4-bromo-1-(naphth-2-ylmethyloxy)-3,3,4,4-tetrafluorobutan-1-ol (20)
(2S)-[(2R)-4-bromo-1-(2-naphthylmethyl)-3,3,4,4-tetrafluorobut-2-yl]-2-(6-methoxy-2-naphthyl) propanoate (21)
(2S)-[(2R)-4-bromo-1-(2-benzyl)-3,3,4,4-tetrafluorobut-2-yl]-2-(6-methoxy-2-naphthyl) propanoate (22)
(2R)-1-tert-Butyldimethylsilyloxy-4-bromo-3,3,4,4-tetrafluorobutan-2-ol (24)
(2R)-(4-bromo-2-hydroxy-3,3,4,4-tetrafluorobut-1-yl)-2,2-dimethyl propanoate (25)
(2R)-(1-benzyloxy-4-bromo-3,3,4,4-tetrafluoro)but-2-yl formate (27)
(2R)-(1-benzyloxy-4-bromo-3,3,4,4-tetrafluoro)but-2-yl benzzyloxyethanoate (32)
(2R)-(2-benzyloxy-4-bromo-3,3,4,4-tetrafluorobut-1-yl)formate (33)
(2R)-(2-benzyloxy-4-bromo-3,3,4,4-tetrafluoro)but-1-yl benzzyloxyethanoate 34
(5R)-5-Benzylxymethyl-3,3,4,4-tetrafluoro-tetrahydrofuran-2-ol 2
tetra fluoro furanose
(2R)-1-Benzzyloxy-3,4,4,-trifluorobut-3-ene-1,2-diol (30)
(5R)-2,5-Bisbenzyloxymethyl-3,3,4,4-tetrafluoro-tetrahydrofuran-2-ol (3)
(2S,5R)-5-Benzyloxy-3,3,4,4-tetrafluoro tetrahydropyran-2-ol (4) (α anomer)
(2R,5R)-5-Benzyl oxy-3,3,4,4-tetrafluoro tetrahydropyran-2-ol (4)(β anomer)
(5R)-2,5-Bisbenzyloxymethyl-3,3,4,4-tetrafluoro-tetrahydropyran-2-ol (5)
(5R)-3,3,4,4-Tetrafluoro-tetrahydropyran-2,5-diol (6)
(5R)-2,5-bishydroxymethyl-3,3,4,4-tetrafluoro-tetrahydropuran-2-ol (7)