Supporting Information

Fragmentation of carbohydrate anomeric alkoxyl radicals: a new synthesis of 1,1-difluoro-1-iodo alditols

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Structural data and procedures for the synthesis of compounds: **1-12**.

General Methods. Melting points were determined with a hot-stage apparatus. Optical rotations were measured at the sodium line at ambient temperature in $CHCl_3$ solutions. IR spectra were recorded in CCl_4 solutions. NMR spectra were determined at 400 MHz for ^1H and 100.6 MHz for ^{13}C in $CDCl_3$ unless otherwise stated, in the presence of TMS as internal standard. Mass spectra were determined at 70 eV. Merck silica gel 60 PF (0.063–0.2 mm) was used for column chromatography. Circular layers of 1 mm of Merck silica gel 60 PF_{254} were used on a Chromatotron for centrifugally assisted chromatography. Commercially available reagents and solvents were analytical grade or were purified by standard procedures prior to use. All reactions involving air- or moisture-sensitive materials were carried out under a nitrogen atmosphere. The spray reagents for TLC analysis were conducted with 0.5% vanillin in H_2SO_4–EtOH (4:1) and further heating until development of color.

General procedure for the synthesis of 2-deoxy-2,2-difluoropyranoses. To a solution of the corresponding 2-deoxy-2-fluoro-hex-1-enitol (1 mmol) in THF (10 mL) and H_2O (1 mL), was added F-TEDA-BF_4 (Selectfluor^{TM}) (1.5 mmol). The reaction was stirred at room temperature for 14 h and refluxed for 30 m. Once cooled, the reaction mixture was then poured into water and extracted with ethyl acetate. The organic layer was dried and concentrated in vacuo. Column chromatography of the residue (*n*-hexane-EtOAc mixtures) afforded the required fluorohydrin compounds.

General procedure for the ARF reaction. A solution of the difluorohydrin (1 mmol) in CH_2Cl_2 (50 mL) containing (diacetoxyiodo)benzene (1.5 mmol) and iodine (1 mmol) was irradiated with two 80 W tungsten-filament lamps at room temperature. The reaction mixture was then poured into water and extracted with CH_2Cl_2. The organic layer was washed with 10% aqueous sodium thiosulfate, dried and concentrated in vacuo. Chromatotron chromatography of the residue (hexanes–EtOAc mixtures)

afforded the required 1,1-difluoro-1-iodo compounds. No special precautions need to be taken to exclude light during chromatography and workup, and these compounds can be stored indefinitely under nitrogen at –20 °C in the dark.

3,4,6-Tri-*O*-acetyl-2-deoxy-2,2-difluoro-D-*lyxo*-hexopyranose (1). Syrup (39 %). IR 3611, 1758, 1371, 1235, 1124 cm^{-1}; ^1H NMR (500 MHz) 2.06 (3H, s), 2.10 (3H, s), 2.15 (3H, s), 4.15 (1H, dd, J = 6.6, 11.4 Hz), 4.18 (1H, dd, J = 6.6, 11.4 Hz), 4.56 (1H, ddd, J = 1.2, 6.6, 6.6 Hz), 5.29 (1H, dd, J = 5.7 Hz, $^3J_{FH}$ = 3.4 Hz), 5.40–5.50 (2H, m); ^{13}C NMR 20.4 (CH_3), 20.7 (2 × CH_3), 61.5 (CH_2), 65.7 (CH, dd, $^2J_{CF}$ = 18.4, 19.1 Hz), 66.4 (CH), 67.4 (CH), 91.9 (CH, dd, $^2J_{CF}$ = 29.2, 32.5 Hz), 114.2 (C, dd, $^1J_{CF}$ = 251.5, 252.7 Hz), 169.7 (C), 170.5 (C), 170.7 (C); MS (EI) *m/z* (rel intensity) 309 (M^+ – OH, 4), 279 (5), 103 (100). HRMS Calcd for $C_{12}H_{15}F_2O_7$ 309.078585, found 309.077065. Anal. Calcd for $C_{12}H_{16}F_2O_8$: C, 44.18; H, 4.94. Found: C, 43.91; H, 5.09.

2-Deoxy-2,2-difluoro-3,4,6-tri-*O*-methyl-D-*lyxo*-hexopyranose (2). Syrup. ^1H NMR (500 MHz) 3.40 (3H, s), 3.56 (3H, s), 3.62 (3H, s), 3.57–3.72 (5H, m), 4.28 (1H, dd, J = 7.5 Hz, $^3J_{FH}$ = 4.6 Hz), 5.21 (1H, dd, J = 7.5 Hz); ^{13}C NMR 59.1 (CH_3), 60.0 (CH_3), 61.6 (CH_3), 69.3 (2 × CH), 71.5 (CH_2), 76.9 (CH, dd, $^2J_{CF}$ = 17.2, 26.9 Hz), 91.9 (CH, dd, $^2J_{CF}$ = 27.6, 27.8 Hz), 117.0 (C, t, $^1J_{CF}$ = 250.0 Hz); MS (EI) *m/z* (rel intensity) 242 (M^+, <1), 167 (7), 138 (8), 119 (19), 107 (88), 101 (100); HRMS Calcd for $C_9H_{16}F_2O_5$ 242.096588, found 242.094666. Anal. Calcd for $C_9H_{16}F_2O_5$: C, 44.63; H, 6.66. Found: C, 44.57; H, 6.70.

3,4-Di-*O*-acetyl-2,6-dideoxy-2,2-difluoro-L-*arabino*-hexopyranose (3). Crystalline solid (65 %). IR 3615, 3472, 2964, 1764, 1376, 1233, 1078 cm^{-1}; ^1H NMR (500 MHz) 1.21 (3H, d, J = 6.3 Hz), 2.04 (3H, s), 2.12 (3H, s), 3.92 (1H, br s), 4.20 (1H, ddd, J = 6.3, 6.3, 9.9 Hz), 4.94 (1H, t, J = 9.9 Hz), 5.16 (1H, d, $^3J_{FH}$ = 5.7 Hz), 5.55 (1H, ddd, J = 9.9 Hz, $^3J_{FH}$ = 4.6, 20.8 Hz); ^{13}C NMR (125.7 MHz) 17.1 (CH_3), 20.5 (CH_3), 20.6 (CH_3), 65.9 (CH), 68.7 (CH, dd, $^2J_{CF}$ = 19.0, 19.4 Hz), 72.6 (CH, dd, $^3J_{CF}$ = 5.8, 8.5 Hz), 91.2 (CH, dd, $^2J_{CF}$ = 31.0, 32.7 Hz), 115.8 (C, dd, $^1J_{CF}$ = 244.5, 245.1 Hz), 168.8 (C), 170.1 (C); MS (EI) *m/z* (rel intensity) 251 (M^+ – OH, 8), 181 (11), 164 (11), 148 (44), 103 (100). HRMS Calcd for $C_{10}H_{13}F_2O_5$ 251.073105, found 251.071659. Anal. Calcd for $C_{10}H_{14}F_2O_6$: C, 44.78; H, 5.26. Found: C: 44.80; H, 5.17.

3,4-Di-*O*-acetyl-2,6-dideoxy-2,2-difluoro-L-*lyxo*-hexopyranose (4). Syrup (75 %) anomeric mixture (3:1). Major isomer: IR 3610, 2940, 1753, 1368, 1237, 1117, 1090 cm^{-1}; ^1H NMR (500 MHz) 1.18 (3H, d, J = 6.6 Hz), 2.08 (3H, s), 2.16 (3H, s), 4.26 (1H,

d, J = 3.9 Hz), 4.50 (1H, dddd, J = 1.6, 6.6, 6.6, 6.6 Hz), 5.21 (1H, dd, J = 3.9 Hz, $^3J_{FH}$ = 6.2 Hz), 5.27 (1H, dd, J = 1.6, 3.9 Hz), 5.44 (1H, ddd, J = 3.9 Hz, $^3J_{FH}$ = 6.0, 22.3 Hz); ^{13}C NMR (125.7 MHz) 15.8 (CH_3), 20.4 (CH_3), 20.5 (CH_3), 64.6 (CH), 66.1 (CH, t, $^2J_{CF}$ = 19.0 Hz), 69.7 (CH), 91.8 (CH, dd, $^2J_{CF}$ = 28.6, 35.3 Hz), 114.3 (C, t, $^1J_{CF}$ = 252.2 Hz), 169.9 (C), 171.1 (C); MS (EI) *m/z* (rel intensity) 251 (M^+ – OH, 5), 233 (5), 209 (4), 163 (24), 148 (95), 135 (81), 130 (60), 120 (91), 103 (100); HRMS Calcd for $C_{10}H_{13}F_2O_5$ 251.073105, found: 251.072880. Anal. Calcd for $C_{10}H_{14}F_2O_6$: C, 44.78; H, 5.26. Found: C: 44.51; H, 5.46.

3,4-Di-*O*-acetyl-2-deoxy-2,2-difluoro-L-*erythro*-pentopyranose (5). Crystalline solid (38 %) anomeric mixture (4:1). Major isomer: IR 3618, 1762, 1549, 1239, 1216, 1005 cm^{-1}; ^{1}H NMR (500 MHz) 2.13 (3H, s), 2.14 (3H, s), 3.14 (1H, d, J = 4.4 Hz), 3.80 (1H, dd, J = 3.7, 12.9 Hz), 4.23 (1H, dd, J = 2.5, 12.9 Hz), 5.22 (1H, ddd, J = 4.4 Hz, $^3J_{FH}$ = 4.4, 9.1 Hz), 5.32 (1H, m), 5.53 (1H, m); ^{13}C NMR (125.7 MHz) 20.4 (CH_3), 20.7 (CH_3), 60.7 (CH_2), 65.8 (CH, dd, $^2J_{CF}$ = 20.1, 20.5 Hz), 67.8 (CH), 91.8 (CH, dd, $^2J_{CF}$ = 30.2, 31.9 Hz), 114.1 (C, t, $^1J_{CF}$ = 252.6 Hz), 169.7 (C), 170.0 (C); MS (EI) *m/z* (rel intensity) 237 (M^+ – OH, 6), 149 (51), 135 (46), 106 (100); HRMS Calcd for $C_9H_{11}F_2O_5$ 237.057455, found: 237.055420. Anal. Calcd for $C_9H_{11}F_2O_6$: C, 42.53; H, 4.76. Found: C, 42.38; H, 4.98.

1,3,4-Tri-*O*-acetyl-5-deoxy-5,5-difluoro-2-*O*-formyl-5-iodo-D-arabinitol (6). Syrup (75%). $[\alpha]_D$ +23 (c = 0.73); IR 1762, 1736, 1370, 1230, 1198, 1056 cm^{-1}; ^{1}H NMR (500 MHz) 2.03 (3H, s), 2.13 (3H, s), 2.18 (3H, s), 3.91 (1H, dd, J = 7.4, 11.7 Hz), 4.31 (1H, dd, J = 5.0, 11.7 Hz), 5.19 (1H, ddd, J = 8.6 Hz, $^3J_{FH}$ = 5.9, 11.0 Hz), 5.52 (1H, dddd, J = 1.0, 1.7, 5.0, 7.4 Hz), 5.61 (1H, dd, J = 1.7, 8.6 Hz), 8.00 (1H, s); ^{13}C NMR 20.5 (CH_3), 20.6 (CH_3), 20.8 (CH_3), 61.6 (CH_2), 67.4 (CH), 68.3 (CH), 72.5 (CH, dd, $^2J_{CF}$ = 23.0, 24.0 Hz), 100.4 (C, t, $^1J_{CF}$ = 314.3 Hz), 159.7 (CH), 168.3 (C), 169.1 (C), 170.3 (C); MS (rel intensity) *m/z* 407 (M^+ – OCOH, 1), 393 (4), 283 (100); HRMS calcd for $C_{11}H_{14}F_2IO_6$ 406.9803, found 406.9847. Anal. Calcd. for $C_{12}H_{15}F_2IO_8$: C, 31.86; H, 3.34. Found: C, 31.95; H, 3.31.

5-Deoxy-5,5-difluoro-2-*O*-formyl-5-iodo-1,3,4-tri-*O*-methyl-D-arabinitol (7). Syrup (57%). $[\alpha]_D$ +9 (c = 0.29); IR ($CHCl_3$) 2937, 1728, 1460, 1324, 1175, 1124 cm^{-1}; ^{1}H NMR 2.98 (1H, ddd, J = 7.9 Hz, $^3J_{HF}$ = 5.0, 8.7 Hz), 3.41 (3H, s), 3.42 (3H, s), 3.53 (3H, dd, $^5J_{HF}$ = 0.8, 1.3 Hz), 3.58 (2H, d, J = 6.7 Hz), 3.63 (1H, dd, J = 2.3, 7.9 Hz), 5.42 (1H, dddd, J = 1.0, 2.3, 6.7, 6.7 Hz), 8.14 (1H, s). ^{13}C NMR 59.0 (CH_3), 60.8

(CH_3), 61.2 (CH_3), 69.6 (CH_2), 70.6 (CH), 79.4 (CH, d, $^3J_{CF}$ = 4.3 Hz), 84.8 (CH, dd, $^2J_{CF}$ = 19.4, 20 Hz), 107.9 (C, dd, $^1J_{CF}$ = 316.6, 322.4 Hz), 160.1 (CH). MS (rel intensity) 353 (M^+ – Me, 1), 337 (4), 291 (6), 265 (2), 147 (100), 115 (79); HRMS calcd. for $C_8H_{12}F_2IO_5$ 352.9698, found 352.9699. Anal. Calcd for $C_9H_{15}F_2IO_5$: C, 29.36; H, 4.11. Found: C, 29.47; H, 4.09.

2,3-Di-*O*-acetyl-1,5-dideoxy-1,1-difluoro-4-*O*-formyl-1-iodo-L-arabinitol (8). Syrup (76%). $[\alpha]_D$ –51 (*c* = 0.62); IR 2940, 1767, 1736, 1372, 1203, 1161 cm^{-1}; ^1H NMR 1.28 (3H, d, *J* = 6.4 Hz), 2.13 (3H, s), 2.23 (3H, s), 5.05 (1H, q, *J* = 6.4 Hz), 5.56 (1H, ddd, *J* = 2.0 Hz, $^3J_{FH}$ = 10.0, 12.0 Hz), 5.64 (1H, dd, *J* = 2.0, 6.4 Hz), 8.00 (1H, s); ^{13}C NMR 15.9 (CH_3), 20.5 (CH_3), 20.6 (CH_3), 67.2 (CH), 69.3 (CH), 73.5 (CH, dd, $^2J_{CF}$ = 21.8, 24.5 Hz), 98.2 (C, dd, $^1J_{CF}$ = 314.6, 315.1 Hz), 159.6 (CH), 168.8 (C), 169.3 (C); MS (rel intensity) 349 (M^+ – OCOH, 36), 267 (9), 225 (97), 205 (100); HRMS calcd for $C_9H_{12}F_2IO_4$ 348.9748, found 348.9737. Anal. Calcd for $C_{10}H_{13}F_2IO_6$: C, 30.48; H, 3.32. Found: C: 30.53; H, 3.30.

3,4-Di-*O*-acetyl-1,5-dideoxy-5,5-difluoro-2-*O*-formyl-5-iodo-L-arabinitol (9). Crystalline solid (82%). mp 76.5–78 ºC (from *n*-hexane–EtOAc); $[\alpha]_D$ –15 (*c* = 0.22); IR 2940, 1760, 1731, 1371, 1201, 1170, 1113, 1069 cm^{-1}; ^1H NMR 1.23 (3H, d, *J* = 6.2 Hz), 2.16 (3H, s), 2.17 (3H, s), 5.18 (1H, dddd, *J* = 6.2, 6.2, 6.2, 8.8 Hz), 5.32 (1H, dddd, *J* = 1.1, 2.1 Hz, $^3J_{FH}$ = 6.6, 13.0 Hz), 5.42 (1H, dd, *J* = 2.1, 8.8 Hz), 7.96 (1H, s); ^{13}C NMR 16.1 (CH_3), 20.5 (CH_3), 20.7 (CH_3), 66.9 (CH), 71.1 (CH), 72.8 (CH, dd, $^2J_{CF}$ = 23.0, 24.0 Hz), 100.8 (C, dd, $^1J_{CF}$ = 314.0, 318.0 Hz), 159.9 (CH), 168.2 (C), 169.4 (C); MS (rel intensity) *m*/*z* 267 (M^+ – I, 14), 249 (16), 225 (100), 205 (91); HRMS calcd for $C_{10}H_{13}F_2O_6$ 267.0680, found 267.0692. Anal. Calcd for $C_{10}H_{13}F_2IO_6$: C, 30.48; H, 3.32. Found: C: 30.68; H, 3.14.

2,3-Di-*O*-acetyl-1-deoxy-1,1-difluoro-4-*O*-formyl-1-iodo-L-erythritol (10). Syrup. $[\alpha]_D$ –18 (*c* = 0.27); IR 2940, 1762, 1737, 1371, 1228, 1201 cm^{-1}. ^1H NMR (500 MHz) 2.09 (3H, s), 2.20 (3H, s), 4.29 (1H, dd, *J* = 6.0, 12.4 Hz), 4.47 (1H, dd, *J* = 2.5, 12.4 Hz), 5.42 (1H, ddd, *J* = 6.0 Hz, $^3J_{FH}$ = 7.5, 13.2 Hz), 5.50 (1H, ddd, *J* = 2.5, 6.0, 6.0 Hz), 8.03 (1H, s); ^{13}C NMR (125.7 MHz) 20.6 (2 × CH_3), 60.7 (CH_2), 68.4 (CH), 74.4 (CH, dd, $^2J_{CF}$ = 23.0, 24.5 Hz), 98.6 (C, dd, $^1J_{CF}$ = 315.8, 318.8 Hz), 160.1 (CH), 168.2 (C), 169.4 (C); MS (rel intensity) *m*/*z* 335 (M^+ – OCOH, 1), 253 (9), 211 (97), 191 (100); HRMS calcd for $C_8H_{10}F_2IO_4$ 334.9592, found 334.9600. Anal. Calcd for $C_9H_{11}F_2IO_6$: C, 28.44; H, 2.92. Found: C, 28.64; H, 2.73.

1,3,4-Tri-*O*-acetyl-5-deoxy-5,5-difluoro-2-*O*-formyl-D-arabinitol (11). Syrup (87%). $[\alpha]_D$ +55 (*c* = 0.27); IR 2944, 1761, 1737, 1371, 1206, 1157 cm^{-1}; ^1H NMR 2.07 (3H, s), 2.12 (3H, s), 2.15 (3H, s), 4.03 (1H, dd, *J* = 6.8, 11.9 Hz), 4.31 (1H, dd, *J* = 4.7, 11.9 Hz), 5.20–5.28 (1H, m), 5.50–5.56 (2H, m), 5.84 (1H, dt, *J* = 3.5 Hz; $^2J_{FH}$ = 54.4 Hz), 8.05 (1H, s); ^{13}C NMR 20.4 (2 × CH_3), 20.5 (CH_3), 61.5 (CH_2), 67.2 (CH), 67.3 (CH), 67.6 (CH, dd, $^2J_{FC}$ = 23.8, 24.8 Hz), 112.7 (CH, dd, $^1J_{FC}$ = 243.6, 245.4), 159.6 (CH), 169.0 (C), 169.3 (C), 170.3 (C); MS (rel intensity) *m*/*z* 327 (M^+ + 1, 1), 281 (2), 267 (13), 253 (6), 203 (82), 178 (58), 131 (69), 115 (100); HRMS calcd for $C_{12}H_{17}F_2O_8$ 327.089149, found 327.090736. Anal. Calcd for $C_{12}H_{16}F_2O_8$: C, 44.18; H, 4.94. Found: C, 44.20; H, 5.03.

3,4-Di-*O*-acetyl-1,5,6,7,8-pentadeoxy-5,5-difluoro-2-*O*-formyl-L-*arabino*-oct-7-enitol (12). Syrup (90%). $[\alpha]_D$ +27 (*c* = 0.25); IR 2935, 1757, 1730, 1370, 1209, 1173, 1055 cm^{-1}; ^1H NMR 1.23 (3H, d, *J* = 6.4 Hz), 2.09 (3H, s), 2.13 (3H, s), 2.63 (2H, ddd, *J* = 7.0 Hz; $^3J_{FH}$ = 19.0, 19.0 Hz), 5.20 (1H, dd, *J* = 1.5, 17.0 Hz), 5.24 (1H, dd, *J* = 1.5, 10.2 Hz), 5.29–5.35 (2H, m), 5.44 (1H, ddd, *J* = 0.8, 2.7, 8.2 Hz), 5.78 (1H, dddd, *J* = 7.0, 7.0, 10.2, 17.0 Hz), 7.97 (1H, s); ^{13}C NMR 16.3 (CH_3), 20.6 (2 × CH_3), 38.4 (CH_2, t, $^2J_{FC}$ = 25.0 Hz), 67.3 (CH), 68.9 (CH, t, $^2J_{FC}$ = 28.0 Hz), 70.1 (CH), 121.0 (C, t, $^1J_{FC}$ = 246.0 Hz), 121.0 (CH_2), 127.6 (CH), 160.0 (CH), 168.9 (C), 169.7 (C); MS (rel intensity) *m*/*z* 289 (M^+ – F, 1), 262 (7), 248 (14), 193 (33), 145 (100), 103 (67); HRMS calcd for $C_{13}H_{18}FO_6$ 289.1087, found 289.1099. Anal. Calcd for $C_{13}H_{18}O_6F_2$: C, 50.65; H, 5.89. Found: C, 50.51; H, 5.89.