Preparation of Some 2-Deoxy- and 2,6-Dideoxy-glycosyl Fluorides

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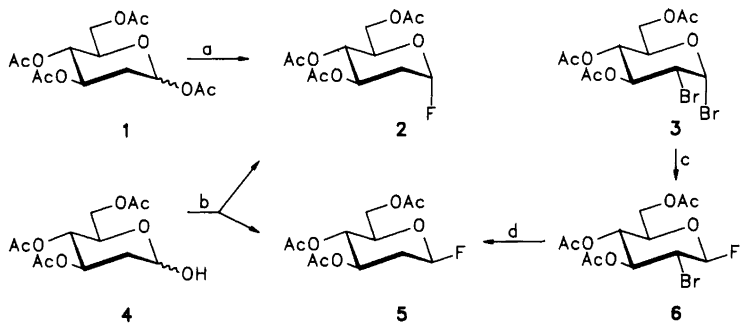
Treatment of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-*arabino*-hexose (**1**) and 1,3,4-tri-*O*-acetyl-2,6-dibromo-2,6-dideoxy-D-glucose (**7**) with HF·pyridine gave the corresponding α-glycosyl fluorides **2** and **9**, respectively, whereas treatment of 3,4,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexose (**4**) and of 3,4-di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-D-glucose (**8**) with diethylaminosulfur trifluoride (DAST) led to mixtures of the α- and β-fluorides **2** and **5**, and **9** and **12**, respectively. The 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-β-D-glucopyranosyl fluoride (**6**) was obtained as the only product from treatment of 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-glucopyranosyl bromide (**3**) with silver fluoride. Similarly, the 3,4-di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-α-D-glucopyranosyl bromide (**17**) gave the corresponding β-fluoride (**12**) by treatment with silver fluoride. The 3,4-di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-D-mannopyranosyl derivatives (**19**, **20**, **21**) all gave the 3,4-di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-α-D-mannopyranosyl fluoride (**22**) by the three methods mentioned. The bromodeoxy-glucosyl fluorides **6**, **9**, **12** and **22** were converted into 2-deoxy- and 2,6-dideoxy-α- or -β-glycosyl fluorides (**5**, **11** and **16**) by treatment with tributylstannane. Deacetylation of the glycosyl fluorides **9** and **22** gave the deprotected fluorides, 2,6-dibromo-2,6-dideoxy-α-D-gluco- (**10**) and -D-mannopyranosyl fluoride (**23**), respectively. Benzylation of the glucosyl fluoride **10** gave the 3,4-di-*O*-benzylated fluoride **15**, whereas the mannosyl fluoride **23** reacted to give the mono-*O*-benzylated 3,6-anhydro sugar **14** as the only product.

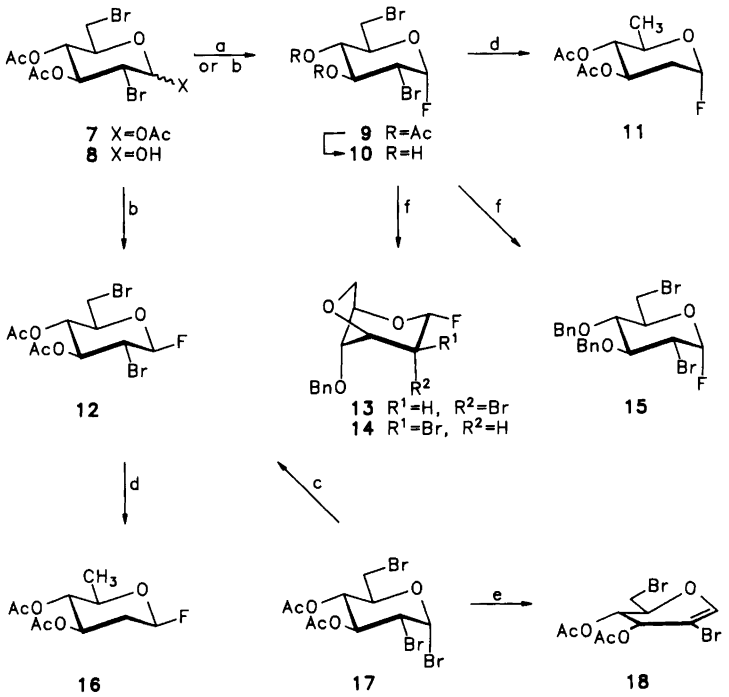
2-Deoxy- and 2,6-dideoxy-sugars are both structural features of oligosaccharides with pharmaceutical and biological relevance. Therefore, 2-deoxy and 2,6-dideoxy saccharides are glycosyl donors of great interest. A series of differently activated deoxy compounds have been synthesized and tested for their glycosylation potential, but in most cases mixtures of α- and β-glycosides were obtained.[1–4] Hence, 2-deoxy-glycosyl fluorides may be of interest with regard to possible stereoselective glycosylations by way of Lewis acid catalysis. Some approaches to the synthesis of 2-deoxy fluorides have been described previously.[5–10] In the present paper some facile methods for the stereoselective preparation of some α- and β-2-deoxy- and -2,6-dideoxyglycosyl fluorides are reported.

Results and discussion

Treatment of the tetra-*O*-acetyl-2-deoxy-D-*arabino*-hexose (**1**) with HF·pyridine in dichloromethane at −20 °C, afforded the corresponding α-fluoride **2** as the sole product (Scheme 1). This reaction is comparable to that previously described by Hall *et al.*[5] However, in the present case the use of HF·pyridine instead of pure HF, was advantageous since it is much easier to handle. In order to obtain the corresponding β-fluoride **5**, 3,4,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexose (**4**) was treated with diethylaminosulfur trifluoride (DAST) as described by Posner *et al.*,[11] to give the anomeric fluorides in a β:α ratio of 5:1. Chromatographic separation gave the desired 2-deoxy-β-glucosyl fluoride **5**.



a: HF*pyridine; b: DAST; c: AgF; d: Bu_3SnH

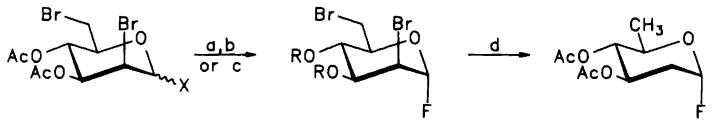


In contrast, treatment of the triacetate of 2-bromo-2-deoxy-α-D-glucosyl bromide (**3**) with silver fluoride in acetonitrile, furnished the corresponding 2-bromo-2-deoxy-β-D-glucosyl fluoride **6** as the only product. Subsequent reduction of this with tributylstannane yielded the β-glucosyl fluoride **5**. When 1,3,4-tri-*O*-acetyl-2,6-dibromo-2,6-dideoxy-D-glucopyranose (**7**) was reacted at room temperature with HF·pyridine in dichloromethane (Scheme 2), the α-fluoride **9** was formed selectively. This could easily be reduced with tributylstannane to afford the 3,4-di-*O*-acetyl-2,6-dideoxy-α-D-*arabino*-hexopyranosyl fluoride (**11**). Deacetylation of the fluoride **9** with sodium methoxide gave the unprotected compound **10**. Benzylation of this fluoride could be performed under various conditions without affecting the anomeric site.[12] Thus, benzylation with KOH in refluxing THF[13] resulted in the formation of 3,4-di-*O*-benzyl-2,6-dibromo-2,6-dideoxy-α-D-glucopyranosyl fluoride (**15**), while treatment with NaH and benzyl bromide in DMF afforded the 3,6-anhydro sugar **13** as a result of internal substitution of the C-6 bromine.

In order to prepare the β-D-glucosyl fluoride **12**, the 2,6-dibromo-1-hydroxy compound **8** was treated with DAST; but, as with the reaction of **4** with DAST, a mixture of α- and β-fluorides (1:6) was obtained, which then had to be separated by chromatography. Alternatively, displacement of the α-anomeric bromine with fluoride should lead to **12**. First, the method described by Kreuzer *et al.*[14,15] using the inexpensive KHF_2 was tried; however, on treatment of the glucosyl bromide **17** or of the mannosyl bromide **21** with KHF_2, only the 1,2-unsaturated sugar **18** was obtained. Consequently, silver fluoride first described by Helferich *et al.*[16] was tested for this conversion. The α-bromide **17** was stirred with AgF in anhydrous acetonitrile, to give 3,5-di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-β-D-glucopyranosyl fluoride (**12**) in quantitative yield. This compound could be treated with tributylstannane to give 3,4-di-*O*-acetyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl fluoride (**16**).

In order to study the influence of the 2-bromo substituent in Lewis-acid-catalysed glycosylation reactions, it was of interest to synthesize the analogous α- and β-fluorides in the 2,6-dibromo-manno series. However, only the α-fluoride was obtained. Thus, on treatment of 1,3,4-tri-*O*-acetyl-2,6-dibromo-2,6-dideoxy-D-mannopyranose (**19**) with HF·pyridine, or its anomerically unblocked counterpart **20** with DAST (Scheme 3), 3,4-di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-α-D-mannopyranosyl fluoride (**22**) was obtained as the single product. This was also the case when the α-D-mannopyranosyl bromide **21** was treated with silver fluoride; no β-fluoride could be detected. The bromine atoms of **22** were removed reductively by treatment with tributylstannane, to give the α-fluoride **11**. Compound **22** could readily be deacetylated to give the 2,6-dibromo-2,6-dideoxy-α-D-mannopyranosyl fluoride (**23**). However, benzylation of **23** with KOH in THF led exclusively to the formation of the 3,6-anhydro sugar **14**. Obviously, the 3,6-anhydro derivatives **13** or **14** can only be formed from the $^1C_4$ (D) chair conformation. The activation energy to reach this conformation must be lower for the manno derivative **23** than for the gluco isomer **10**, since the bromine in the manno derivative will adopt an equatorial orientation.

In summary, we have described methods of preparing glycosyl fluorides. On treatment of 1-*O*-acetates with HF·pyridine only α-fluorides were obtained, whereas sugar



19 X=OAc
20 X=OH
21 X=αBr

22 R=Ac
23 R=H

11

a: HF•pyridine; b: DAST; c: AgF; d: Bu_3SnH

derivatives with a free 1-OH group, when treated with DAST, yielded α,β-mixtures of glycosyl fluorides. Anomerically pure glycosyl fluorides were obtained from the corresponding α-bromides by treatment with silver fluoride, which yielded 1,2-*trans* products. Thus 2-bromo-2-deoxy-α-D-mannopyranosyl and β-D-glucopyranosyl fluorides could be prepared.

The glycosyl fluorides described above were used as glycosyl donors for glycosylation studies. The results of these experiments will be discussed in a future paper.

Experimental

Melting points are uncorrected. Optical rotations were measured on a Perkin Elmer 241 polarimeter. NMR spectra were obtained on Bruker WH-90, AM-500, WM-270 and WM-400 NMR instruments with $SiMe_4$ as an internal standard. Column chromatography was performed on silica gel 60 (230–400 mesh, Merck 9835) using the flash technique.

*3,4,6-Tri-*O*-acetyl-2-deoxy-α-*D*-arabino-hexopyranosyl fluoride* (**2**). Tetra-*O*-acetyl-2-deoxy-D-*arabino*-hexopyranose (**1**) (1.0 g) was dissolved in dry CH_2Cl_2 (10 ml), and HF·pyridine (70 %) (1 ml) was added at −25 °C. The reaction was complete after 10 h (TLC, toluene–EtOAc 4:1). CH_2Cl_2 (20 ml) was then added and the mixture washed twice with H_2O, neutralized with aq. $NaHCO_3$, dried ($MgSO_4$), and concentrated to a syrup, which was purified by chromatography (toluene–EtOAc–Et_3N 60:10:0.5), to yield the crystalline fluoride **2** (0.82 g, 93 %), m.p. 74 °C; $[\alpha]_D^{20}$ + 73.9° (*c* 1.3, $CHCl_3$) [lit.[5] m.p. 73–74 °C; $[\alpha]_D^{20}$ + 67° (*c* 2.2, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$): δ 5.75 (H-1, ddd, $J_{1,F}$ 50.1, $J_{1,2e}$ 1.4, $J_{1,2a}$ 2.8 Hz), 5.32 (H-3, ddd, $J_{3,4}$ 9.6 Hz), 5.10 (H-4, dd, $J_{4,5}$ 9.5 Hz), 4.34 (H-6, dd, $J_{5,6}$ 2.1, $J_{6,6'}$ 12.5 Hz), 4.15 (H-5, dd, $J_{5,6'}$ 4.5 Hz), 4.11 (H-6', m), 2.5 (H-2e, m, $J_{2e,F}$ 5.0, $J_{2e,2a}$ 13.7, $J_{2e,3}$ 5.4 Hz), 1.89 (H-2a, m, $J_{2a,F}$ 38.6, $J_{2a,3}$ 11.6 Hz), 2.07, 2.05, 2.02 (3 OAc). ^{13}C NMR ($CDCl_3$): δ 105.5 (C-1, d, J_{C_1F} 218.4 Hz), 69.8 (C-3, d, J_{C_3F} 2.3 Hz), 67.4, 67.6 (C-4, C-5), 61.2 (C-6), 33.9 (C-2, d, J_{C_2F} 26.3 Hz), 169.8, 169.3, 169.5, 20.1, 20.5 and 19.9 (OAc).

*2,3,6-Tri-*O*-acetyl-2-deoxy-β-*D*-arabino-hexopyranosyl fluoride* (**5**). *(a) From* **4**. To a solution of 3,4,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexopyranose (**4**)[17] (1.0 g) in dry THF (20 ml), was added DAST (0.5 ml) at −30 °C. The mixture was stirred at room temperature for 30 min (TLC, EtOAc–hexane 4:1); CH_3OH (2 ml) was then added at −30 °C and stirring was continued for 30 min. After concentration the product was purified as described above to give 0.72 g (75 %) of the β-fluoride **5** and 0.13 g (14 %) of the α-fluoride **2**. The NMR spectra were identical with those described above and below, respectively.

(b) From **6**. To a solution of the fluoride **6** (see below) (2.5 g) and α,α'-azobis(isobutyronitrile) (300 mg) in dry toluene (20 ml), tributylstannane (2.8 ml) was added in one portion under N_2-atmosphere, and kept at 70 °C for 2 h. The mixture was concentrated, and submitted to chromatography (EtOAc–hexane 1:3; 250 ml, followed by EtOA–hexane 1:2). The product 1.68 g (85 %) (m.p. 66–73 °C) was recrystallized from Et_2O–hexane to give colourless crystals; m.p. 74–75 °C; $[\alpha]_D^{20}$ + 16.7° (*c* 0.8, $CHCl_3$). Anal: $C_{12}H_{17}FO_7$: C, H. ^{1}H NMR ($CDCl_3$): δ 5.53 (H-1, ddd, $J_{1,F}$ 52.0, $J_{1,2e}$ 2.8, $J_{1,2a}$ 6.5 Hz), 5.08 (H-4, t, $J_{4,5}$ 7.5 Hz), 5.03 (H-3, ddd, $J_{3,4}$ 7.5 Hz), 4.32 (H-6, dd, $J_{6,6'}$ 12.0 Hz), 4.28 (H-6', dd), 3.87 (H-5, ddd, $J_{5,6}$ 5.5, $J_{5,6'}$ 4 Hz), 2.43 (H-2e, m, $J_{2e,F}$ 8.0, $J_{2e,3}$ 5.0, $J_{2e,2a}$ 13.5 Hz), 1.98 (H-2a, m, $J_{2a,3}$ 7.5, $J_{2a,F}$ 10.0 Hz), 2.10, 2.07, 2.06 (3×OAc). ^{13}C NMR ($CDCl_3$): δ 105.5 (C-1, d, J_{C_1F} 215.0 Hz), 72.0 (C-5, d, J_{C_5F} 2.9 Hz), 67.6 (C-3, d, J_{C_3F} 9.4 Hz), 67.4 (C-4), 62.5 (C-6), 33.3 (C-2, d, J_{C_2F} 23.5 Hz).

*3,4,6-Tri-*O*-acetyl-2-bromo-2-deoxy-β-*D*-glucopyranosyl fluoride* (**6**). 3,4,6-Tri-*O*-acetyl-2-bromo-2-deoxy-α-D-glucopyranosyl bromide (**3**)[18] (3.0 g) was stirred with silver fluoride (3.0 g) in dry CH_3CN (30 ml) for 2 h at room temperature. Filtration and concentration of the reaction mixture left a residue which was dissolved in CH_2Cl_2, washed with aq. $NaHCO_3$, dried ($MgSO_4$), and concentrated. The syrupy product (2.6 g, 100 %) was pure according to TLC, and ^{13}C and ^{1}H NMR spectra. The β-fluoride has been described[19,20] in admixture with other isomers. ^{1}H NMR ($CDCl_3$): δ 5.41 (H-1, dd, $J_{1,F}$ 50.0, $J_{1,2}$ 7.8 Hz), 5.33 (H-3, ddd, $J_{3,F}$ 1.0, $J_{3,4}$ 9.0 Hz), 5.06 (H-4, dd, $J_{4,5}$ 10.0 Hz), 4.30 (H-6, ddd, $J_{6,6'}$ 12.0, $J_{6,F}$ 1.0 Hz), 4.12 (H-6', br dd), 3.90 (H-5, m, $J_{5,6}$ 4.8, $J_{5,6'}$ 2.8, $J_{5,F}$ 0.8 Hz), 3.89 (H-2, ddd, $J_{2,F}$ 10.5, $J_{2,3}$ 10.0 Hz), 2.09, 2.07, 2.06 (3 OAc). ^{13}C NMR ($CDCl_3$): δ 107.5 (C-1, d, J_{C_1F} 218 Hz), 73.2 (C-3, d, J_{C_3F} 8.9 Hz), 71.8 (C-5, d, J_{C_5F} 5.6 Hz), 68.0 (C-4), 61.3 (C-6), 47.3 (C-2, d, J_{C_2F} 26.6 Hz), 170.3, 169.4, 169.1, 20.5, 20.2 (OAc).

*3,4-Di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-α-*D*-glucopyranosyl fluoride* (**9**). 1,3,4-Tri-*O*-acetyl-2,6-dibromo-2,6-dideoxy-D-glucopyranose (**7**)[21] (1.0 g) was treated with HF·pyridine (70 %) (2 ml) for 12 h as described above. Purification by

chromatography (toluene–EtOAc 10:1) gave **9** as a crystalline product (0.8 g, 88 %); m.p. 134 °C; $[\alpha]_D^{20}$ + 162° (*c* 0.98, $CHCl_3$). Anal: $C_{10}H_{13}Br_2FO_5$: C, H, Br. ^{1}H NMR ($CDCl_3$): δ 5.78 (H-1, dd, $J_{1,F}$ 50.8, $J_{1,2}$ 2.5 Hz), 5.52 (H-3, dd, $J_{3,4}$ 9.2 Hz), 5.12 (H-4, dd), 4.27 (H-5, ddd, $J_{4,5}$ 10.0, $J_{5,6}$ 2.8, $J_{5,6'}$ 4.8 Hz), 3.98 (H-2, ddd, $J_{2,F}$ 25.6, $J_{2,3}$ 11.0 Hz), 3.57 (H-6, dd, $J_{6,6'}$ 11.7 Hz), 3.44 (H-6', dd), 2.09, 2.07 (2×OAc). ^{13}C NMR ($CDCl_3$): δ 105.2 (C-1, d, J_{C_1F} 229.6 Hz), 70.9 (C-3, d, J_{C_3F} 4.7 Hz), 70.3 (C-4, s), 45.4 (C-2, d, J_{C_2F} 28.2 Hz), 30.5 (C-6), 169.4, 168.9, 20.3 (OAc).

*2,6-Dibromo-2,6-dideoxy-α-*D*-glucopyranosyl fluoride* (**10**). The acetylated fluoride **9** (0.5 g) was dissolved in CH_3OH (25 ml), saturated with $Ba(OH)_2 \cdot 8H_2O$ and stirred for 15 min, then neutralized with dry ice and concentrated. Chromatography (toluene–EtOAc–Et_3N 140:70:1) gave the deacetylated fluoride **10** (0.313 g, 81 %), isolated as a slightly yellow syrup; $[\alpha]_D^{20}$ + 102.5° (*c* 0.8, $CHCl_3$). ^{1}H NMR (acetone-d_6): δ 5.66 (H-1, dd, $J_{1,F}$ 52.0, $J_{1,2}$ 2.4 Hz), 3.86 (H-2, ddd, $J_{2,F}$ 25.6, $J_{2,3}$ 10.4 Hz), 3.83 (H-5, ddd, $J_{4,5}$ 9.6, $J_{5,6}$ 2.2, $J_{5,6'}$ 5.2 Hz), 3.72 (H-3, dd, $J_{3,4}$ 8.6 Hz), 3.68 (H-5, dd, $J_{6,6'}$ 11.2 Hz), 3.57 (H-6', dd), 3.39 (H-4, dd).

*3,4-Di-*O*-acetyl-2,6-dideoxy-α-*D*-*arabino*-hexopyranosyl fluoride* (**11**). The dibromoglucosyl fluoride **9** (1.89 g) [alternatively dibromomannosyl fluoride (**22**)] was dissolved in dry toluene (65 ml) together with α,α'-azobis-(isobutyronitrile) (0.5 g) and Bu_3SnH (4.4 ml). The mixture was stirred at 70 °C for 3 h, concentrated and purified by chromatography as described above, to give **11** as a colourless syrup (1.01 g, 89.6 %); $[\alpha]_D^{20}$ + 86.9° (*c* 1.0, $CHCl_3$). Anal: $C_{10}H_{15}FO_5$: C, H. ^{1}H NMR ($CDCl_3$): δ 5.65 (H-1, dm, $J_{1,F}$ 50.8 Hz), 5.26 (H-3, ddd, $J_{2a,3}$ 11.4, $J_{2e,3}$ 5.4, $J_{3,4}$ 9.6 Hz), 4.82 (H-4, t, $J_{4,5}$ 9.6 Hz), 4.06 (H-5, dq, $J_{5,6}$ 6.0 Hz), 2.47 (H-2e, m, $J_{2e,F}$ 5.6, $J_{1,2e}$ 1.4, $J_{2e,2a}$ 14.0 Hz), 1.82 (H-2a, m, $J_{2a,F}$ 25.0, $J_{1,2a}$ 2.8 Hz), 1.23 (H-6, d), 2.10, 2.07 (2×OAc).

*3,4-Di-*O*-acetyl-2,6-dibromo-2,6-dideoxy-β-*D*-glucopyranosyl fluoride* (**12**). To the dibromoglucosyl bromide **17**[21] (2.8 g) in dry CH_3CN, was added silver fluoride (3.0 g), and the mixture was stirred for 2 h, filtered and concentrated. The residue was dissolved in CH_2Cl_2, washed with aq. $NaHCO_3$ and dried ($MgSO_4$) to give a crystalline product (2.5 g) after concentration. This was recrystallized from Et_2O–hexane to give **13** (1.8 g, 74.3 %); m.p. 107–108 °C; $[\alpha]_D^{20}$ + 96.5° (*c* 0.9, $CHCl_3$). Anal: $C_{10}H_{13}Br_2FO_5$: C, H, Br. ^{1}H NMR ($CDCl_3$): δ 5.48 (H-1, dd, $J_{1,F}$ 50.2, $J_{1,2}$ 7.8 Hz), 5.34 (H-3, ddd, $J_{3,F}$ 1.0, $J_{3,4}$ 9.0 Hz), 5.05 (H-4, dd, $J_{4,5}$ 3.5 Hz), 3.93 (H-5, m), 3.92 (H-2, ddd, $J_{2,F}$ 10.0, $J_{2,3}$ 10.0 Hz), 3.58 (H-6, br dd, $J_{5,6}$ 3.0, $J_{6,6'}$ 11.5 Hz), 3.45 (H-6', br dd, $J_{5,6'}$ 5.5 Hz), 2.10, 2.07 (2×OAc). ^{13}C NMR ($CDCl_3$): δ 107.2 (C-1, d, J_{C_1F} 218 Hz), 72.8 (C-3, d, J_{C_3F} 8.8 Hz), 72.6 (C-5, d, J_{C_5F} 5.8 Hz), 70.4 (C-4), 47.1 (C-2, d, J_{C_2F} 25.7 Hz), 29.7 (C-6), 169.4, 169.0, 20.3, 20.2 (OAc).

*3,6-Anhydro-4-*O*-benzyl-2-bromo-2-deoxy-α-*D*-manno-pyranosyl fluoride* (**14**). The dibromomannosyl fluoride **23** (0.25 g) was dissolved in dry THF (2 ml), mixed with fresh powdered KOH (0.2 g), 18-crown-6 (0.1 g) and benzyl bromide (0.2 ml), and stirred at room temperature for 2 h. Then the mixture was diluted with CH_2Cl_2 (100 ml), washed twice with H_2O, dried ($MgSO_4$), and the solvent evaporated. Purification by chromatography (hexane–EtOAc–Et_3N 180:20:1) yielded the 3,6-anhydro sugar **14** as the only product (yellow syrup, 0.194 g, 75 %); $[\alpha]_D^{20}$ −14.1° (*c* 2.08, $CHCl_3$). Anal: $C_{13}H_{14}BrFO_3$: C, H, Br. ^{1}H NMR ($CDCl_3$): δ 7.35–7.50 (5 H, Ph), 5.75 (H-1, $J_{1,F}$ 55.4 Hz), 4.78 (H-Bn), 4.61 (H-4), 4.59 (H-Bn), 4.41 (H-2, $J_{2,F}$ 14.8, $J_{1,2}$ 6.8, $J_{2,3}$ 0.7 Hz), 4.33 (H-3), 4.15 (H-6, $J_{6,6'}$ 11.0 Hz), 4.0 (H-6', H-5). ^{13}C NMR ($CDCl_3$): δ 128.8–127.3 (5 C, Ph), 109.2 (C-1, J_{C_1F} 216 Hz), 77.8 (C-5), 77.5 (C-3, J_{C_3F} 7 Hz), 73.8 (C-4), 71.8 (CH_2–Ph), 69.5 (C-6), 49.8 (C-2, J_{C_2F} 23 Hz). The NMR signals were identified by COSY and CH-correlation.

*3,4-Di-*O*-benzyl-2,6-dibromo-2,6-dideoxy-α-*D*-gluco-pyranosyl fluoride* (**15**). The dibromoglycosyl fluoride **10** (0.25 g) dissolved in dry THF (2 ml), mixed with fresh powdered KOH (0.2 g), 18-crown-6 (0.1 g) and benzyl bromide (0.2 ml), was stirred under reflux for 2 h. Then the mixture was diluted with CH_2Cl_2 (100 ml), washed twice with H_2O, dried ($MgSO_4$) and concentrated. The resulting syrup was purified by chromatography (hexane–EtOAc–Et_3N 180:20:1), to yield the dibenzylated fluoride **15** as the main product as colourless crystals; m.p. 105–108 °C (0.182 g, 46 %); $[\alpha]_D^{20}$ +132° (*c* 0.73, $CHCl_3$). Anal: $C_{20}H_{21}Br_2FO_3$: C, H, Br. ^{1}H NMR ($CDCl_3$): δ 7.30–7.10 (10 H, Ph), 5.70 (H-1, $J_{1,F}$ 51.4, $J_{1,2}$ 2.2 Hz), 4.97 (2 H, Bn), 4.79 (2 H, Bn), 4.07 (H-5, H-3), 3.92 (H-2, $J_{2,F}$ 25.3, $J_{2,3}$ 10.4 Hz), 3.73 (H-6, $J_{5,6}$ 9.4, $J_{6,6'}$ 11.8 Hz), 3.66 (H-6', $J_{5,6'}$ 3.0 Hz). A second product isolated was the 3,6-anhydro compound **13** (syrup, 0.085 g, 33 %); $[\alpha]_D^{20}$ +101° (*c* 0.63, $CHCl_3$). Anal: $C_{13}H_{14}BrFO_3$: C, H, Br. ^{1}H NMR ($CDCl_3$): δ 7.30–7.10 (5 H, Ph), 5.51 (H-1, $J_{1,F}$ 51.7 Hz), 4.48 and 4.29 (Bn), 3.71 (H-5), 3.51 (H-4, $J_{4,5}$ 10.0 Hz), 3.34 (H-6, $J_{5,6}$ 2.8, $J_{6,6'}$ 10.9 Hz), 3.22 (H-6', $J_{5,6'}$ 5.4 Hz), 3.12 (H-2, $J_{2,3}$ 3.8 Hz), 2.86 (H-3). The NMR signals were identified by COSY.

*3,4-Di-*O*-acetyl-2,6-dideoxy-β-*D*-arabino-hexopyranosyl fluoride* (**16**). The dibromo-β-fluoride **12** (1 g) was treated with Bu_3SnH and worked up as described above. Purification by chromatography yielded 0.52 g (86 %) of amorphous **16**; $[\alpha]_D^{20}$ +29.6° (*c* 1.17, $CHCl_3$). Anal: $C_{10}H_{15}FO_5$: C, H. ^{1}H NMR ($CDCl_3$): δ 5.41 (H-1, $J_{1,F}$ 51.8, $J_{1,2a}$ 7.7, $J_{1,2e}$ 2.6 Hz), 4.96 (H-3, $J_{3,4}$ 8.7 Hz), 4.80 (H-4, $J_{4,5}$ 8.9 Hz), 3.61 (H-5, $J_{5,6}$ 6.2 Hz), 2.43 (H-2e, $J_{2e,F}$ 7.8, $J_{2e,2a}$ 13.3, $J_{2e,3}$ 5.1 Hz), 1.82 (H-2a, $J_{2a,F}$ 12.8, $J_{2a,3}$ 7.4 Hz), 1.26 (H-6), 2.09, 2.07 (OAc).

*3,4-Di-*O*-acetyl-2,6-dibromo-1,2,6-trideoxy-hex-1-eno-pyranose* (**18**). The dibromoglucosyl bromide **17**[21] (1.0 g)

was dissolved in CH_3CN (10 ml). Dry KHF_2 (1.0 g) was added and the mixture was refluxed overnight.[14,15] Filtration and concentration gave a residue (0.8 g, 95 %), containing **18**[1,18] as the main product, as seen from NMR spectra. ^1H NMR ($CDCl_3$): δ 6.8 (H-1, d, $J_{1,3}$ 0.8 Hz), 5.45 (H-3, ddd, $J_{3,4}$ 4.5, $J_{3,5}$ 1.0 Hz), 5.39 (H-4, dd, $J_{4,5}$ 4.4 Hz), 4.41 (H-5, m, $J_{5,6}$ 6.5, $J_{5,6'}$ 7.0 Hz), 3.64 (H-6, dd, $J_{6,6'}$ 10.5 Hz), 3.56 (H-6', dd). ^{13}C NMR ($CDCl_3$): δ 144.6 (C-1), 74.2, 68.5, 68.3 (C-3, C-4, C-5), 27.8 (C-6), 20.6, 20.5 (OAc).

3,4-Di-O-acetyl-2,6-dibromo-2,6-dideoxy-α-D-mannopyranosyl fluoride (**22**). 1,3,4-Tri-*O*-acetyl-2,6-dibromo-2,6-dideoxy-D-mannopyranose (**19**)[21] (1.0 g) was dissolved in dry CH_2Cl_2 (5 ml), HF·pyridine (70 %) (2 ml) was added, and the mixture was stirred at room temperature. After 12 h the mixture was worked up as described above. Chromatography gave **22** which crystallized (0.77 g, 85 %); m.p. 136 °C; $[\alpha]_D^{20}$ −14.2° (*c* 0.93, $CHCl_3$). Anal: $C_{10}H_{13}Br_2FO_5$: C, H, Br. ^1H NMR ($CDCl_3$): δ 5.86 (H-1, dd, $J_{1,F}$ 50.3, $J_{1,2}$ 1.4 Hz), 5.46 (H-4, dd, $J_{4,5}$ 9.8 Hz), 5.22 (H-3, dd, $J_{3,4}$ 9.8 Hz), 4.56 (H-2, ddd, $J_{2,F}$ 4.5, $J_{2,3}$ 4.1 Hz), 4.20 (H-5, ddd), 3.53 (H-6, dd, $J_{5,6}$ 2.9, $J_{6,6'}$ 11.6 Hz), 3.44 (H-6', dd, $J_{5,6'}$ 5.8 Hz), 2.10, 2.08 (2 OAc). ^{13}C NMR ($CDCl_3$): δ 106.6 (C-1, d, J_{C_1F} 226.7 Hz), 72.0 (C-3, d, J_{C_3F} 3.1 Hz), 67.7 (C-5), 67.2 (C-4), 46.6 (C-2, d, J_{C_2F} 34.6 Hz), 30.4 (C-6), 169.5, 169.0, 20.4 (OAc).

2,6-Dibromo-2,6-dideoxy-α-D-mannopyranosyl fluoride (**23**). The acetylated fluoride (**22**) (0.5 g) was dissolved in CH_3OH (25 ml), saturated with $Ba(OH)_2$ and stirred for 15 min. Dry ice was then added and the mixture was concentrated. The resulting syrup was purified by chromatography (toluene–EtOAc–Et_3N 140:70:1) to give 0.305 g (78 %) of the deacetylated fluoride **23** as a sligthly yellow syrup; $[\alpha]_D^{20}$ +11.3° (*c* 0.92, acetone). ^1H NMR: ($CDCl_3$): δ 5.86 (H-1, $J_{1,F}$ 50.6, $J_{1,2}$ 1.3 Hz), 4.42 (H-2), 4.10 (H-4, $J_{3,4}$ 8.2, $J_{4,5}$ 7.9 Hz), 3.95 (4 H, H-3, H-5, H-6, H-6').

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