Synthesis of Fluorinated Branched-chain Sugars

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Treatment of (*E*)-3-deoxy-3-*C*-ethoxycarbonyl(formylamino)methylene-1,2 : 5,6-di-*O*-isopropylidene-α-D-glucofuranose with trifluoro(fluoro-oxy)methane gives branched-chain sugars bearing a fluorine atom at the branch point. Some reactions of these fluorinated sugars are described.

BRANCHED-CHAIN sugars [1] and fluoro-sugars [2] have been reported as constituents of a number of antibiotics. We describe here the synthesis of branched-chain sugars carrying a fluorine atom at the branch point.

(*E*)-3-Deoxy-3-*C*-ethoxycarbonyl(formylamino)methylene-1,2 : 5,6-di-*O*-isopropylidene-α-D-glucofuranose (1) [3] was treated with trifluoro(fluoro-oxy)methane at −75 °C in dichloromethane (containing *ca.* 0.3% ethanol) to give a mixture of the fluorinated oxo-ester (2) and the fluorinated ethoxy-ester (4). When dry, ethanol-free dichloromethane was used as solvent the fluorinated *N*-formylimine (3) was the only product isolated. The formation of these products can be explained by the mechanism proposed [4] for the attack of trifluoro(fluoro-oxy)methane on activated double bonds. The fluorocarbocation which is formed by attack of the π-electrons of the olefin on fluorine is stabilized by the amide nitrogen atom. With traces of water and ethanol present in the solvent it gives the oxo-ester (2) on hydrolysis and the ethoxy-ester (4) on attack by ethanol. In dry ethanol-free solvent the intermediate is deprotonated to give the *N*-formylimine (3).

The configurations at C-3 of compounds (2)—(4) were determined from their n.m.r. spectra: the values of $J_{2,F}$ (*ca.*15 Hz) and $J_{4,F}$ (*ca.* 27 Hz) for all three compounds clearly show [5,6] that they are D-*gluco*-derivatives.†

Only a few examples of *N*-acylimines have been described [7,8] and little is known about their chemical properties. The *N*-formylimine (3) decomposed unless protected from moisture and stored at −5 °C.

Compound (3) was converted into the more stable oxo-ester (2) by mild hydrolysis. Under more forcing conditions the 5,6-*O*-isopropylidene group was also removed to give compound (5), which was converted into the crystalline methyl ester (6) by transesterification.

From compound (5) the *xylo*-derivative (8) was prepared by cleavage of the 5,6-glycol system and reduction of the resulting aldehyde.

Reduction of compound (3) with lithium aluminium hydride gave a crystalline compound (11) of which the stereochemistry at the new asymmetric centre is not known. As we have already found [3] for compound (1), the low-field n.m.r. spectrum of the amido-alcohol (11) showed the complex spin–spin coupling pattern which can arise from the partial double bond character of the [C(O)–N] bond. Compound (11) exists in deuteriochloroform solution as a mixture of the *cis*- and *trans*-isomers (with reference to the *N*-formyl group): the formyl proton signal appears as two broad peaks each integrating for 0.5 H at τ 1.80(s) and 2.06 (d, $J_{NH,CHO\text{-}trans}$ 11 Hz). The latter signal collapsed to a singlet on addition of D_2O. The low-field n.m.r. spectrum of compound (4) similarly showed the presence of *cis*- and *trans*-amide species.

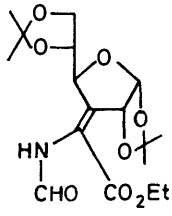
Some compounds with modified C-3 branches were also prepared from the oxo-ester (2). Reduction with lithium aluminium hydride gave an epimeric mixture of glycols (12). Cleavage of the glycol system gave an aldehyde which was reduced with sodium borohydride to the *C*-hydroxymethyl derivative (13), and oxidized

† For naming these sugars which bear unequal geminal substituents we use the system whereby the substituent having the highest priority according to the Sequence Rule is thought of as replacing the hydroxy-group at the carbon atom concerned.

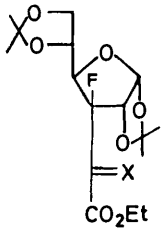
[1] H. Grisebach and R. Schmid, *Angew. Chem. Internat. Edn.*, 1972, **11**, 159.
[2] A. B. Foster and J. H. Westwood, *Pure Appl. Chem.*, 1973, 147; P. W. Kent in 'Carbon–Fluorine Compounds,' CIBA Foundation Symposium, Elsevier, Amsterdam, 1972, p. 169.
[3] A. J. Brink and A. Jordaan, *Carbohydrate Res.*, 1974, **34**, 1.
[4] D. H. R. Barton, L. S. Godinho, R. H. Hesse, and M. M. Pechet, *Chem. Comm.*, 1968, 805.
[5] A. B. Foster, R. Hems, and L. D. Hall, *Canad. J. Chem.*, 1970, **48**, 3937.
[6] J. S. Brimacombe, A. B. Foster, R. Hems, J. H. Westwood, and L. D. Hall, *Canad. J. Chem.*, 1970, **48**, 3946.
[7] N. Toshima, M. Saeki, and H. Hirae, *Chem. Comm.*, 1971, 1424.
[8] F. Kluge and R. Muschaweck, Ger. Offen. 1,907,113 (*Chem. Abs.*, 1970, **73**, 98965y).

with potassium permanganate to a carboxylic acid which formed a crystalline methyl ester (14) with diazomethane.

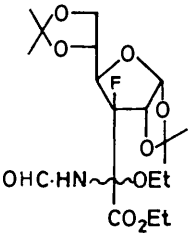
Mild hydrolysis of compound (13) gave the 5,6-diol (7) which was converted into the *xylo*-compound (9) by glycol cleavage and reduction. Acetylation of compound (9) gave a crystalline diacetate (10).



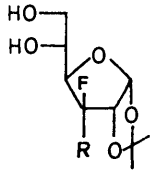
(1)



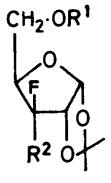
(2) X = O
(3) X = N·CHO



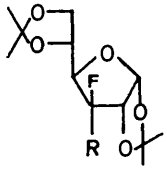
(4)



(5) R = CO·CO$_2$Et
(6) R = CO·CO$_2$Me
(7) R = CH$_2$·OH



(8) R^1 = H, R^2 = CO·CO$_2$Et
(9) R^1 = H, R^2 = CH$_2$·OH
(10) R^1 = Ac, R^2 = CH$_2$·OAc



(11) R = CH(NH·CHO)·CH$_2$·OH
(12) R = CH(OH)·CH$_2$·OH
(13) R = CH$_2$·OH
(14) R = CO$_2$Me

The use of compounds such as (9) and (10) for the preparation of nucleosides containing fluorine and compounds related to nucleocidin [9-(4-fluoro-5-*O*-sulphamoylpentofuranosyl)adenine] is being investigated.

EXPERIMENTAL

All solvent extracts were dried (Na_2SO_4), filtered, and evaporated below 50 °C *in vacuo*. T.l.c. and column chromatography were performed on silica gel (Merck GF_{254}) [100 g of silica per g of residue for column separations]. M.p.s were determined on a hot-stage apparatus. I.r. spectra were measured for solutions in chloroform with a Perkin-Elmer 237 spectrophotometer, and n.m.r. spectra were recorded on a Varian HA-100 instrument with tetramethylsilane as internal standard for solutions in $CDCl_3$. Optical rotations were measured for solutions in chloroform with a Bendix-NPL automatic polarimeter type 143 (*c* 1.0 ± 0.3) and mass spectra were determined with an A.E.I. MS9 spectrometer by direct insertion. For syrups, microanalytical figures are only given when a syrup could be distilled under high vacuum by use of Kugelröhr. Accurate mass measurements were made on the $M^+ - 15$ peaks of unstable syrups.

Reaction of (E)-3-*Deoxy*-3-C-*ethoxycarbonyl*(*formylamino*)-*methylene*-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (1) *with Trifluoro*(*fluoro-oxy*)*methane*.—(a) *In analytical grade dichloromethane*. Compound (1) (4.69 g) was dissolved in dichloromethane (250 ml; Merck analytical grade containing *ca.* 0.3% ethanol), powdered calcium oxide (2 g) was added, and the mixture was then cooled to −75 °C. Trifluoro(fluoro-oxy)methane was slowly bubbled through the stirred solution until all starting material had disappeared (t.l.c.). The mixture was allowed to warm to 25 °C and was then poured into saturated aqueous sodium hydrogen carbonate (100 ml). The organic phase was dried and evaporated to give a mixture which was chromatographed with chloroform–methanol 20 : 1 as eluant to give 3-deoxy-3-C-*ethoxalyl*-3-*fluoro*-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (2) (3.020 g) as an oil, $[\alpha]_D^{22}$ +42°, $\nu_{max.}$ 1 740 and 1 735 cm^{-1} (CO and ester), τ 3.97 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 5.08 (1 H, q, $J_{2,1}$ 4, $J_{2,F}$ 14.5 Hz, H-2), 5.25 (1 H, q, $J_{4,5}$ 8, $J_{4,F}$ 27 Hz, H-4), 5.64 (2 Hz, q, J 7 Hz, CH_2·CH$_3$), 5.79—6.01 (3 H, m, H-5, -6, and -6′), 8.5—8.7 (12 H, 4s, 4CH$_3$), and 8.62 (3 H, t, J 7 Hz, CH$_2$·CH_3), *m/e* 347 ($M^+ - 15$) and 289 ($M^+ - CO_2Et$) (Found: C, 52.8; H, 6.2. $C_{16}H_{23}FO_8$ requires C, 53.0; H, 6.4%).

Further elution gave 3-*deoxy*-3-*fluoro*-3-C-*ethoxy*(*ethoxycarbonyl*)(*formylamino*)*methyl*-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (4) (1.1 g), as needles from acetone–hexane, m.p. 152—155°, $[\alpha]_D^{21}$ +23°, $\nu_{max.}$ 1 740 (ester) and 1 695 cm^{-1} (amide), τ 1.69 (½ H, *d*, $J_{NH,CHO\text{-}trans}$ 11.5 Hz, C*H*O), 1.79 (½ H, s, CHO), 2.53 (½ H, s, NH), 2.97 (½ H, d, $J_{NH,CHO\text{-}trans}$ 11 Hz, NH), 4.18 (1 H, d, $J_{1,2}$ 3.5 Hz, H-1), 5.11 (1 H, q, $J_{4,5}$ 6.5, $J_{4,F}$ 27.5 Hz, H-4), 5.33 (1 H, q, $J_{2,1}$ 3.5, $J_{2,F}$ 14.5 Hz, H-2), 6.18—7.50 (5 H, m, H-5, -6, and -6′, CH_2·CH$_3$), 6.31 (2 H, q, J 7 Hz, CH_2·CH$_3$), and 8.53—8.76 (18 H, m, 2CH$_2$·CH_3, 4CH$_3$), *m/e* 420 ($M^+ - 15$), 406 (M^+ — Et), and 362 ($M^+ - CO_2Et$) (Found: C, 52.4; H, 6.9; N, 3.2. $C_{19}H_{30}FNO_9$ requires C, 52.4; H, 6.9; N, 3.2%).

(b) *In ethanol-free, dry dichloromethane*. Compound (1) (742 mg) in dichloromethane (50 ml; Merck analytical grade distilled from P_2O_5) and powdered calcium oxide (200 mg) was treated with trifluoro(fluoro-oxy)methane. The cold mixture (−75 °C) was poured into saturated aqueous sodium hydrogen carbonate (100 ml) and the mixture was worked up as described in (a) to give 3-*deoxy*-3-C-*ethoxycarbonyl*(*formylimino*)*methyl*-3-*fluoro*-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (3) (720 mg) as an unstable oil, $[\alpha]_D^{22}$ +119°, $\nu_{max.}$ 1 740 (ester) and 1 690 cm^{-1} (imide), τ 0.68 (1 H, d, $J_{CHO,F}$ 3 Hz, CHO), 3.98 (1 H, d, $J_{1,2}$ 4 Hz), 5.06 (1 H, q, $J_{2,F}$ 13, $J_{2,1}$ 4 Hz, H-2), 5.12 (1 H, q, $J_{4,5}$ 6, $J_{4,F}$ 27 Hz, H-4), 5.6—5.8 (3 H, m, CH_2·CH$_3$, H-5), 5.94 (2 H, d, $J_{5,6}$ 6 Hz, H-6 and -6′), 8.45—8.8 (12 H, 4CH$_3$), and 8.58 (3 H, t, J 7 Hz, CH$_2$·CH_3) (Found: *m/e*, 374.123. $C_{17}H_{24}O_8F$ requires $M - CH_3$, 374.125).

Acidic Hydrolysis of Compound (3).—(a) *Acetic acid in aqueous ethanol*. Compound (3) (2 g) was dissolved in aqueous acetic acid (2%; 20 ml) and ethanol (30 ml). After 18 h at 25 °C the solution was poured into cold saturated aqueous sodium hydrogen carbonate (200 ml) and the mixture was extracted with chloroform (4 × 50 ml).

Removal of solvent gave an oil (1.9 g) identical (i.r. and mass spectral and chromatographic behaviour) with compound (2).

(b) *Sulphuric acid in aqueous ethanol.* Compound (3) (500 mg) was stirred for 72 h with aqueous sulphuric acid (0.8%; 12 ml) and ethanol (12 ml). The solution was neutralized with solid sodium hydrogen carbonate and the solvent was removed. The residue was extracted with chloroform (50 ml). The extract was dried and evaporated to leave 3-*deoxy*-3-C-*ethoxalyl*-3-*fluoro*-1,2-O-*isopropylidene*-α-D-*glucofuranose* (5) as an oil, $[\alpha]_D^{21}$ −13°, $\nu_{max.}$ 3 450 (OH) and 1 735 cm^{-1} (CO and ester), τ 3.94 (1 H, d, $J_{1,2}$ 4 Hz, H-1); 5.18 (1 H, q, $J_{2,1}$ 4, $J_{2,F}$ 11 Hz, H-2), 5.32br (1 H, OH), 5.66 (2 H, q, J 7 Hz, CH_2CH_3), 5.60—5.90 (3 H, m, H-4, -5, and -6), 6.08—6.26 (1 H, m, H-6′), 7.27br (1 H, OH), 8.40 (3 H, s, CH_3), 8.58 (3 H, s, CH_3), and 8.63 (3 H, t, 7 Hz, CH_2CH_3), *m/e* 307 (M^+ − 15) and 249 (M^+ − CO_2Et) (Found: C, 48.4, H, 5.9. $C_{13}H_{19}FO_8$ requires C, 48.5; H, 5.9%).

3-*Deoxy*-3-*fluoro*-3-C-*methoxalyl*-1,2-O-*isopropylidene*-α-D-*glucofuranose* (6).—The ethyl ester (5) (135 mg) was stirred for 18 h at 25 °C in dry methanol (5 ml) in which sodium (50 mg) had been dissolved. The mixture was filtered through a short column of Amberlite IRC-50 ion-exchange resin and the solvent was removed to give the *methyl ester* (6) as an oil which crystallized from acetone–hexane as plates, m.p. 124°, $[\alpha]_D$ −17°, $\nu_{max.}$ 3 450 (OH) and 1 745 cm^{-1} (CO and ester), τ 3.93 (1 H, d, $J_{1,2}$ 3.5 Hz, H-1), 5.17 (1 H, q, $J_{2,1}$ 3.5, $J_{2,F}$ 12 Hz, H-2), 5.43br (1 H, OH, disappears on addition of D_2O), 5.33—5.70 (2 H, m, H-4 and -5), 5.84 (2 H, m, H-6 and -6′), 6.11 (3 H, s, OCH_3), 7.50br (1 H, disappears on addition of D_2O, OH), 8.40 (3 H, s, CH_3), and 8.58 (3 H, s, CH_3), *m/e* 293 (M^+ − 15) and 249 (M^+ − CO_2Me) (Found: C, 46.9; H, 5.7. $C_{12}H_{17}FO_8$ requires C, 46.8; H, 5.6%).

3-*Deoxy*-3-C-*ethoxalyl*-3-*fluoro*-1,2-O-*isopropylidene*-α-D-*xylofuranose* (8).—Compound (5) (1.057 g, 3.28 mmol) was dissolved in ethanol (50 ml). Sodium periodate (702 mg, 3.28 mmol) in water (10 ml) was added and the mixture was stirred overnight. Ethylene glycol (0.25 ml) was added and the solution stirred for 1 h before removal of solvent. The residue was extracted with chloroform (2 × 100 ml), and the solvent was removed to leave an oil which was dissolved in ethanol (20 ml). Sodium borohydride (30 mg, 0.8 mmol) was added in small portions and the mixture was stirred for 2 h. Some starting material was still present (t.l.c.); more sodium borohydride (30 mg, 0.8 mmol) was added and the mixture was stirred for 1 h. Removal of solvent left a residue which was extracted with chloroform (2 × 200 ml). Evaporation of the extract left an oil (910 mg) which was purified by column chromatography with chloroform–methanol 19 : 1 as eluant to give the *oxo-ester* (8) as an oil, $[\alpha]_D^{21}$ +20°, $\nu_{max.}$ 3 500 (OH) and 1 730 cm^{-1} (CO and ester), τ 4.05 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 5.20—5.70 (1 H, m, H-4), 5.32 (1 H, q, $J_{2,1}$ 4, $J_{2,F}$ 12 Hz, H-2), 5.69 (2 H, q, J 7 Hz, CH_2·CH_3), 6.19 (2 H, d, $J_{4,5}$ 5 Hz, H-5 and -5′), 6.70br (1 H, disappears on addition of D_2O, OH), 8.45 (3 H, s, CH_3), 8.64 (3 H, s, CH_3), and 8.65 (3 H, t, J 7 Hz, CH_2·CH_3) (Found: *m/e*, 277.075. $C_{12}H_{17}FO_7$ requires M − CH_3, 277.072).

3-*Deoxy*-3-*fluoro*-3-C-(1-*formylamino*-2-*hydroxyethyl*)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (11).—Lithium aluminium hydride (600 mg, 16 mmol) was added in small portions to a stirred solution of compound (3) (1.1 g, 2.8 mmol) in dry tetrahydrofuran (80 ml) at 0 °C and the solution was then allowed to warm to 25 °C. After 5 h the mixture was treated with tetrahydrofuran–water (1 : 1; 6 ml), stirred for 50 min, and filtered. Removal of solvent left a yellow oil (1 g) which was purified by column chromatography with ethyl acetate as eluant to give *compound* (11) (400 mg) as an oil which crystallized from ethyl acetate–hexane as needles, m.p. 129—130°, $\nu_{max.}$ 3 400 (NH and OH) and 1 690 cm^{-1} (amide), τ 1.80 (½ H, s, CHO), 2.06 (½ H, d, $J_{NH,CHO\text{-}trans}$ 11 Hz, CHO, collapses to a singlet on addition of D_2O), 4.13 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 5.0—6.0 (8 H, m, H-2, -4, -5, -6, and -6′, side-chain CH·CH_2), 8.43 (3 H, s, CH_3), 8.61 (3 H, s, CH_3), and 8.65 (6 H, s, $2CH_3$), *m/e* 334 (M^+ − 15) (Found: C, 51.7; H, 6.8. $C_{15}H_{24}FNO_7$ requires C, 51.6; H, 6.9%).

3-*Deoxy*-3-C-(1,2-*dihydroxyethyl*)-3-*fluoro*-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (12).—Compound (2) (650 mg) was stirred for 18 h in tetrahydrofuran (50 ml) containing lithium aluminium hydride (300 mg). Saturated aqueous sodium hydroxide (3 ml) was added dropwise and the mixture was stirred for 12 h. The solvent was removed and the residue was extracted with chloroform (2 × 250 ml). Evaporation of the extract left an oil (450 mg) which was purified by column chromatography with ethyl acetate–hexane (1 : 1) as eluant to give *compound* (12) as an oil, $\nu_{max.}$ 3 425 cm^{-1} (OH), τ 4.12 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 5.31 (1 H, q, $J_{2,1}$ 4, $J_{2,F}$ 12 Hz, H-2), 5.4—6.2 (7 H, m, H-4, -5, -6, and -6′, side-chain CH·CH_2), 6.76br (1 H, d, disappears on addition of D_2O, OH), 7.43br (1 H, disappears on addition of D_2O, OH), 8.47 (3 H, s, CH_3), 8.54 (3 H, s, CH_3), and 8.65 (6 H, s, $2CH_3$) (Found: *m/e*, 307.120. $C_{14}H_{23}FO_7$ requires M − CH_3, 307.119).

3-*Deoxy*-3-*fluoro*-3-C-*hydroxymethyl*-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (13).—Compound (12) (500 mg, 1.7 mmol) in methanol (50 ml) was oxidized with sodium periodate (400 mg, 1.7 mmol) in water (50 ml) as described for the preparation of compound (8) to give a hydrated aldehyde (570 mg), $\nu_{max.}$ 3 520 (OH) and 1 750w cm^{-1} (CO), *m/e* 275 (M^+ − 15). Reduction of the aldehyde (700 mg) with sodium borohydride (1 g) in ethanol (50 ml) for 3 h and work-up as in the preparation of compound (8) gave an oil (650 mg), which was distilled under high vacuum (Kugelrohr) to give pure *compound* (13) as an oil, $[\alpha]_D^{22}$ +20°, $\nu_{max.}$ 3 450 cm^{-1} (OH), τ 4.10 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 5.33 (1 H, q, $J_{2,1}$ 4, $J_{2,F}$ 12 Hz, H-2), 5.50—6.40 (6 H, m, H-4, -5, -6, and -6′, CH_2·OH), 7.32br (1 H, s, disappears on addition of D_2O, OH), 8.46 (3 H, s, CH_3), 8.56 (3 H, s, CH_3), and 8.63 (6 H, s, $2CH_3$), *m/e* 277 (M^+ − 15) (Found: C, 53.2, H, 7.4. $C_{13}H_{21}FO_6$ requires C, 53.4; H, 7.2%).

3-*Deoxy*-3-*fluoro*-3-C-*methoxycarbonyl*-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (14).—The hydrated aldehyde (430 mg) obtained from glycol cleavage of compound (12) was dissolved in acetone (100 ml), potassium permanganate (500 mg) was added, and the mixture was stirred for 2 h. Isopropyl alcohol (5 ml) was introduced and stirring was continued for 18 h. Chloroform (150 ml) and glacial acetic acid (1 ml) were added and the mixture was stirred for 1 h and filtered. The residue was again extracted with chloroform (150 ml) containing acetic acid (1 ml); the combined extracts were evaporated to leave an oil which was dissolved in ether (100 ml) containing an excess of diazomethane and was kept at 0 °C for 18 h. Removal of the solvent left crystalline *compound* (14) (330 mg) ,which was recrystallized from acetone–hexane to give needles, m.p. 108—109°, $[\alpha]_D^{21}$ +61°, $\nu_{max.}$ 1 755 cm^{-1} (ester), τ 4.01 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 5.32 (1 H, q, $J_{2,1}$ 4, $J_{2,F}$ 15 Hz, H-2), 5.36 (1 H, q, $J_{4,5}$ 8, $J_{4,F}$ 26 Hz, H-4), 5.60—6.0 (3 H, m, H-5, -6, and -6′),

6.16 (3 H, s, OCH_3), 8.43 (3 H, s, CH_3), 8.60 (3 H, s, CH_3), and 8.67 (6 H, s, $2CH_3$), *m/e* 305 ($M^+ - 15$) and 289 ($M^+ - OCH_3$) (Found: C, 52.5; H, 6.7. $C_{14}H_{21}FO_7$ requires C, 52.5; H, 6.6%).

3-*Deoxy*-3-*fluoro*-3-C-*hydroxymethyl*-1,2-O-*isopropylidene*-α-D-*glucofuranose* (7).—Compound (13) (800 mg) was dissolved in methanol (50 ml) and concentrated sulphuric acid (500 mg) and the solution kept at 20 °C for 18 h. Solid sodium hydrogen carbonate (2 g) was added with stirring and the solvent was evaporated off. The residue was extracted with chloroform (2 × 100 ml) and the solvent removed to give *compound* (7) as an oil (390 mg), $[\alpha]_D^{23}$ +16°, $\nu_{max.}$ 3 380 cm^{-1} (OH), τ 4.10 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 5.42 (1 H, q, $J_{2,1}$ 4, $J_{2,F}$ 12 Hz, H-2), 5.80—6.40 (6 H, m, H-4, -5, -6, and -6′, CH_2·OH; changes on addition of D_2O), 8.46 (3 H, s, CH_3), and 8.67 (3 H, s, CH_3) (Found: *m/e* 237.078. $C_{10}H_{17}FO_6$ requires $M^+ - CH_3$, 237.077).

3-*Deoxy*-3-*fluoro*-3-C-*hydroxymethyl*-1,2-O-*isopropylidene*-α-D-*xylofuranose* (9).—Compound (7) (375 mg) in methanol (20 ml) was oxidized with sodium periodate (316 mg, 1.5 mmol) in water (3 ml) as described for the preparation of compound (8) to give a hydrated aldehyde (360 mg), $\nu_{max.}$ 3 420 (OH) and 1 745w cm^{-1} (CHO), *m/e* 205 ($M^+ - CH_3$). Reduction of the aldehyde (355 mg) with sodium borohydride (150 mg) in ethanol (5 ml) for 16 h and work-up as in the preparation of compound (8) gave *compound* (9) as an oil (272 mg), $[\alpha]_D^{22}$ +9°, $\nu_{max.}$ 3 600 and 3 360 cm^{-1} (OH), τ 4.08 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 5.42 (1 H, q, $J_{2,1}$ 4, $J_{2,F}$ 12 Hz, H-2), 5.60—6.40 (5 H, m, H-4, -5, and -5′, CH_2·OH; changes on addition of D_2O), 6.80br (2 H, s, disappears on addition of D_2O, 2OH), 8.47 (3 H, s, CH_3), and 8.68 (3 H, s, CH_3) (Found: *m/e*, 207.066. $C_9H_{15}O_5$ requires $M - CH_3$, 207.067).

3-C-*Acetoxymethyl*-5-O-*acetyl*-3-*deoxy*-3-*fluoro*-1,2-O-*isopropylidene*-α-D-*xylofuranose* (10).—Compound (9) (202 mg) was dissolved in pyridine (3 ml) and acetic anhydride (3 ml); the mixture was kept at 20 °C for 18 h and then poured into ice–water (20 ml). The aqueous mixture was extracted with chloroform (3 × 25 ml) and the combined extracts were successively washed with ice-cold 0.5N-hydrochloric acid (3 × 20 ml), ice-cold saturated aqueous sodium hydrogen carbonate (10 ml), and water (20 ml). Removal of solvent left *compound* (10) as an oil (246 mg) which crystallized from acetone–hexane as needles, m.p. 90—92°, $[\alpha]_D^{22}$ +49°, $\nu_{max.}$ 1 745 cm^{-1} (acetate), τ 4.02 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 5.36 (1 H, q, $J_{2,1}$ 4, $J_{2,F}$ 12 Hz, H-2), 5.30—6.0 (5 H, *m*, H-4, 5, and -5′, CH_2·OAc), 7.84 (3 H, s, OAc), 7.88 (3 H, s, OAc), 8.46 (3 H, s, CH_3), and 8.63 (3 H, s, CH_3), *m/e* 291 ($M^+ - CH_3$) and 246 ($M^+ - AcOH$) (Found: C, 51.1; H, 6.5. $C_{13}H_{19}FO_7$ requires C, 51.0; H, 6.2%).

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