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Fluorine Chemical Shifts in Some Monosaccharide Derivatives.

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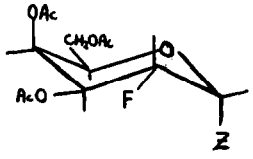
Considerable attention has already been devoted to deducing structural evidence from ^{1}H-^{1}H and ^{1}H-^{19}F coupling constants for a number of acetylated glycosyl fluorides.[1-4] The ^{19}F n.m.r. parameters show important stereochemical dependencies and potentially provide sensitive criteria for the assignment of the configuration of fluorine atoms in cyclic structures. Hitherto in the sugar series details of the chemical shifts ϕ_c are known only for anomeric fluorine, and these values generally fall in the range +130 to +150 p.p.m. (with reference to $CFCl_3$).[1,2] This relatively wide variation reflects the influence of different electronegative environments on ^{19}F responses as for example, in the inherent axial-equatorial ^{19}F shift difference ($\delta_{a,e}$) reported to be 12.1 p.p.m. for D-glucosyl fluoride tetraacetates.[2-4] The present communication is concerned with distinctive chemical shifts for fluorine attached to C(2) and C(1), and for fluorine in the glycosidic trifluoromethyl groups.

Treatment of di-O-acetyl-D-xylal in $CFCl_3$ with CF_3OF at -70° gave the following four products[5] which were separated chromatographically on a silica column: trifluoromethyl 3,4-di-O-acetyl-2-deoxy-2-fluoro-α-D-xyloside (VIII, 5% yield, m.p. 150° $[\alpha]_D^{24}$ +130° $CHCl_3$ (this and following determinations) Tm 13.0 mins (from 110° 2°/min)*); trifluoromethyl 3,4-di-O-acetyl-2-deoxy-2-fluoro-β-D-lyxoside (IV, 26%, Tm 15.2 mins (from 110°, 2°/min), $[\alpha]_D^{24}$ -120°, not cryst.); 3,4-di-O-acetyl-2-deoxy-2-fluoro-α-D-xylopyranosyl fluoride (VII, 5% not cryst, Tm 14.0 mins (from 110°, 2°/min) and 3,4-di-O-acetyl-2-deoxy-2-fluoro-α-D-lyxopyranosyl fluoride (III, 42%, m.p. 109-111° Tm 16.5 mins (from 110°, 2°/min) $[\alpha]_D^{24}$ -114°). Products VIII, IV, and III were each homogeneous by g.l.c. having elementary analyses fully in agreement with the

*Chromatographic retention times (Tm) are quoted for a Pye 104 Chromatograph model 24 with a column of diatoport-S-80-100 mesh (Hewlett Packard) /3% S.E. 30 (Applied Science Laboratories Inc.) and an argon flow of 40 $cm.^3$/minute. The starting temperature and temperature gradient is given in each case.

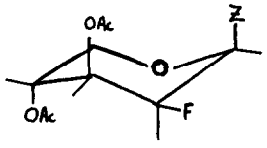
structures proposed. (Product VII was mixed with small amounts of VIII, but not such as to preclude n.m.r. measurements).

Proton and ^{1}H-^{19}F couplings indicate that the lyxo (III and IV) and arabino (V and VI) products exist in the ^{1}C conformation, under the influence of a powerful anomeric effect to which is attributed the same conformation of 2,3,4-tri-O-acetyl-α-D-xylopyranosyl fluoride.[6] The α-xylo products (VII and VIII) have the usual C-1 conformation, as do the 2-fluorogalactose derivatives (I and II). Similar findings are reported for 2-fluoroglucose derivatives.[7]



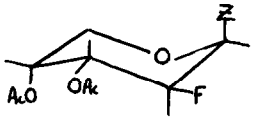
Galacto-derivatives (C-1)

I(Z = F); II(Z = OCF_3)



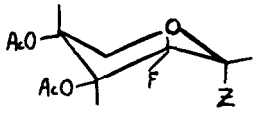
Lyxo-derivatives (1-C)

III(Z = F); IV(Z = OCF_3)



Arabino-derivatived (1-C)

V(Z = F); VI(Z = OCF_3)



xylo-derivatives (C-1)

VII(Z = F); VIII(Z = OCF_3)

Parallel series of experiments[8] with 3,4,6-tri-O-acetyl-D-galactal yielded two major products: 3,4,6-tri-O-acetyl-2-deoxy-2-fluoro-α-D-galactosyl fluoride (I, 55% yield, m.p. 68-70°; Tm 13.5 mins. (from 140°, 2°/min). $[\alpha]_D^{20}$ +130°) and trifluoromethyl 3,4,6-tri-O-acetyl-2-deoxy-2-fluoro-α-D-galactoside (II, 40%, m.p. 53-55° $[\alpha]_D^{25}$ +147° Tm 11.3 min. (from 140°, 2°/min.) and trace amounts of minor products. Similarly, 3,4-di-O-acetyl-D-arabinal yielded 3,4-di-O-acetyl-2-deoxy-2-fluoro-β-D-arabinosyl fluoride (V, Tm 13.5 min. (from 120°, 2°/min.), $[\alpha]_D^{23}$ -176 (c 0.4 $CHCl_3$), and trifluoromethyl 3,4-di-O- acetyl-2-deoxy-2-fluoro-β-D-arabinoside (VI, Tm 12.0 min. (from 120°, 2°/min.), $[\alpha]_D^{26}$ -226° (c 1.03 $CHCl_3$).

It has now been possible by use of a wide-sweep attachment (450 p.p.m. to 3000 p.p.m.) to

a JEOL (Model JNM-4H-100) spectrometer (^{19}F frequency 94 MHz) at 33° to detect and assign the chemical shifts (with reference to $CFCl_3$ as standard) (see Table). For F(1) and F(2) in I, III, V and VII, the vicinal fluorines are in an axial-equatorial relationship and give values for ϕ_cF(1a) in the range +152 to 158 p.p.m., of an order similar to values reported for other glycosyl fluorides.[1] Comparable values for ϕ_cF(2e) are far removed, in the range +211 to +223 p.p.m. and are consistent throughout the range of compounds studies. The ^{19}F-^{19}F coupling constant J[F(1a)-F(2e)] for I is found to be 20 Hz ± 1. Conventional high-resolution ^{19}F measurements on compound I, give J values for F-H coupling in good agreement with those determined from proton data, viz. J[F(1)-H(1)] 53 Hz; J[F(1)-H(2)] 23 Hz; J[F(2)-H(2)] 47 Hz; J[F(2)-H(3)] 12 Hz indicative of the C-1 conformation and α-anomeric configuration.

Fluorine atoms not attached directly to the ring as in the trifluoromethyl glycoside (II, IV, VI, VIII) have a chemical shift of +60 p.p.m. and show no evidence of coupling with the ring.

Table

^{19}F Shifts for F(1), F(2) and -OCF_3 in fluorinated monosaccharides

(ϕ_c values accurate to ± 5 p.p.m.)

Compound	ϕ_c[F(1)]	ϕ_c[F(2)]	ϕ_c[OCF_3(1)]
I	+ 157	+ 223	-
II	-	+ 211	+ 60
III	+ 156	+ 215	-
IV	-	+ 214	+ 61
V	+ 158	+ 212	-
VI	-	+ 212	+ 60
VII	+ 152	+ 220	-
VIII	-	+ 214	+ 61

The results indicate that the decisive determination of ^{19}F chemical shifts may provide a ready method for locating the position of this halogen in a cyclic structure such as a monosaccharide. High resolution measurements of ^{19}F-^{19}F coupling constants may also provide significant conformational evidence in multifluorinated monosaccharides but the interpretation may well be more complex[9] in the absence of well-founded theories relating to fluorine.

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