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A Study of ^{13}C—^{19}F Coupling Constants in Glycosyl Fluorides

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Proton decoupled ^{13}C NMR spectra of a number of glycosyl fluorides gave information about the $^{13}C-^{19}F$ coupling constants. The $^{1}J\{^{13}C1F\}$ values were found to be negative and to be numerically higher in α-pyranosyl fluorides than in β-pyranosyl fluorides. An axial substituent at C2 in a pyranosyl fluoride increases both $^{2}J\{^{13}C2F\}$ and $^{1}J\{^{13}C1F\}$. $^{3}J\{^{13}C3F\}$ values are higher in β-pyranosyl fluorides than in α-fluorides indicating a Karplus type of relation. In furanosyl fluorides both $^{1}J\{^{13}C1F\}$ and $^{2}J\{^{13}C2F\}$ were found to be smaller when the fluorine atom and the substituent at C2 are *trans* than when they are *cis*-oriented.

Since a rather large number of glycosyl fluorides have been prepared in connection with other work [1] and since relatively few $^{13}C-^{19}F$ coupling constants have been described [2] it was decided to measure ^{13}C NMR spectra of a number of glycosyl fluorides, to see whether $^{13}C-^{19}F$ coupling constants showed a stereochemical dependance. $^{1}H-^{19}F$ coupling constants have been found to give valuable configurational information in carbohydrate derivatives.[3]

Proton decoupled ^{13}C NMR spectra have therefore been measured on a number of glycopyranosyl and furanosyl fluorides (Tables 1 and 2). These spectra give the ^{13}C chemical shifts and the $^{13}C-^{19}F$ coupling constants.

The signals were assigned by the principles generally used for pyranoses [4] or by selective proton decoupling.[5] The chemical shifts of the pyranosyl fluorides are very similar to those of other pyranoses.[6] The furanosyl fluorides mostly have C1 at slightly lower field than the corresponding pyranoses. Most noticeable in the spectra of the furanosyl fluorides is the low field position of the signals of C2 and C4. The assignment of C2 in furanosyl fluorides is easy because of its rather large coupling to fluorine.

The one bond $^{13}C-^{19}F$ coupling constant of the pyranosyl fluorides is in almost all cases 10 Hz higher in α-fluorides than in β-fluorides. This might indicate that the lone pair electrons of the ring-oxygen affect the coupling constant.[6] The α-fluorides, with an axial fluorine atom, have a numerically larger coupling constant than the β-fluorides. We have, however, found by selective decoupling of H1 in (*α-1b*) that the sign of $^{1}J\{^{13}C1F\}$ is opposite to that of $^{2}J_{HF}$, and the latter has been found to be positive.[7] This is in accordance with the results found by Weigert and Roberts.[8] Thus pyranosyl fluorides with an equatorial fluorine have a higher $^{1}J_{C1F}$ value than those with an axial fluorine atom in agreement with the results obtained for $^{1}J\{^{13}CH1\}$ values.[6]

The $^{2}J\{^{13}C2F\}$ value in α- and β-pyranosyl fluorides is found to be *ca.* 25 Hz when the substituent at C2 is equatorial. When, however, this substituent is axial, as in D-mannose derivatives, $^{2}J\{C2F\}$ is 35 – 40 Hz. Selective decoupling of H2 in (α-1b) showed that $^{2}J\{^{13}C2F\}$ is positive. An axial substituent at C2 also increases (numerically decreases) the $^{1}J\{C1F\}$ values as seen, *e.g.*, by comparison of (*α-1b*) and (*α-3b*).

This may explain why the anomeric tetra-*O*-acetyl-D-mannopyranosyl fluorides (α- and *β-3b)* have almost the same $^{1}J\{C1F\}$ values. The xylopyranosyl fluorides (α- and β-7) have different conformations,[9] both with an axial fluorine atom. In (*β-7*), which has an axial substituent at C2, $^{1}J\{^{13}C1F\}$ is only 222.8 Hz whereas it is 228.5 Hz in (α-7).

In β-pyranosyl fluorides, which have the fluorine atom and C3 *trans*-oriented, the $^{3}J\{^{13}C3F\}$ value is 4 – 10 Hz whereas it is only 0 – 6 Hz in α-fluorides, in which the fluorine

Table 1. ^{13}C chemical shifts (ppm) and $^{13}C-^{19}F$ coupling constants (Hz) of glycopyranosyl fluorides.

Compound	C1 ^1J(C1F)	C2 ^2J(C2F)	C3 ^3J(C3F)	C4 ^4J(C4F)	C5 ^3J(C5F)	C6	OCH_3 J(CF)
α-*1a*[10]	108.23 222.2	71.89 24.85	73.25	69.44	75.03 2.9	61.04	[b]
β-*1a*[11]	110.02 211.3	75.97 22.1	73.56[a] 2.2	69.91	76.86[a] 4.30	61.36	[b]
α-*1b*[12]	103.65 228.92	69.90 24.29	69.16	67.13	69.66 4.39	60.99	
β-*1b*[13]	105.97 218.96	70.81 22.25	71.77[a] 3.81	67.26	71.63[a] 2.05	61.53	
α-*1c*[14]	103.93 229.9	78.39 23.4	71.01	67.45	69.54 4.4	61.30	58.84 [b]
β-*1c*[14]	108.43 217.38	80.27 24.93	72.53 10.59	67.67	71.29 4.77	61.48	59.62 1.83
α-*1d*[15]	103.90 227.4	72.01 24.7	77.74	68.42	70.00 4.6	61.43	60.20
β-*1d*[15]	106.06 218.3	71.00 27.8	79.55 5.9	67.90	72.11 3.8	62.21	58.60 [b]
α-*2*[16]	104.25 228.3	67.30 24.1	67.28	66.86	68.79 3.7	61.10	
β-*2*[16]	107.20 217.29	69.15 24.88	70.08 10.54	66.61 1.20	71.33 4.68	61.42	
α-*3b*[16]	104.71 223.1	67.55 39.7	68.08 1.8	64.95	70.82 3.1	61.72	
β-*3b*	104.05 223.6	67.75 25.0	68.37 5.9	66.36	72.71 4.4	62.72	[b]
α-*3c*[14]	104.6 224.1	75.9 35.2	70.1 ~1	64.8	70.0 2.9	61.4	59.5 [b]
α-*3d*[15]	104.96 221.19	65.87 39.55	76.12	66.35	70.94 2.9	62.01	57.74 [b]
α-*4*[16,17]	104.26 226.74	67.68 38.76	66.18 0.91	63.99 0.5	66.39 2.44	62.03	
β-*4*[16,17]	105.03 227.35	67.13 22.89	67.72	64.52 1.12	74.70	63.17 2.13	
5[17]	104.5 224.7	64.6 36.6	65.4	65.1	65.8 2.9	61.8	[b]
6e[15]	103.76 227.7	70.77 24.7	69.52	72.74	67.86 4.6	17.12	
6f[15]	104.68 221.3	67.79 41.3	68.08 2.1	69.76	68.72 3.1	17.1	

Table 1. Continued.

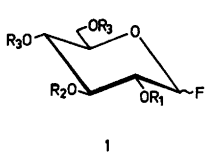
α-*7*[12]	103.8 228.5	70.3 23.4	68.8	68.0	60.1 4.4	*b*
β-*7*[18]	105.27 222.8	67.03 36.0	67.10 2.8	66.82 0.6	60.56 3.4	
8[18]	104.6 227.1	67.5 26.4	68.1	66.4	62.4 2.8	*b*

[a] May be reversed. [b] Digital resolution only ± 1.5 Hz.

Table 2. ^{13}C chemical shifts (ppm) and coupling constants (Hz) of glycofuranosyl fluorides.

Compound	C1 ^1J(C1F)	C2 ^2J(C2F)	C3 ^3J(C3F)	C4 ^4J(C4F)	C5 ^3J(C5F)	C6	OCH_3 J(CF)
α-*9b*[19]	106.88 234.19	78.21 19.61	73.13	76.65 1.17	67.55 0.7	62.35	
β-*9b*[19]	111.51 228.46	78.96 35.36	71.69	80.39 2.46	68.15	62.51	
α-*9c*[15]	107.73 233.8	86.15 18.9	73.95	76.78 1.2	67.75 0.9	62.55	58.91 0.9
β-*9c*[15]	112.15 226.5	87.00 31.4	71.59	80.14 2.4	68.48	62.79	57.93
α-*9d*[15]	106.68 231.6	77.74 19.5	77.74	81.11 1.5	68.74 1.2	62.46	58.06
β-*9d*[15]	112.26 227.3	77.81 34.5	81.67 0.7	81.94 2.6	69.26	63.11	58.53
α-*10b*[19]	112.62 225.2	75.96 36.0	69.84 0.9	77.96 2.1	67.69 1.5	62.40	
β-*10b*[19]	106.52 236.8	71.57 20.1	68.33	77.88 2.4	67.10 1.2	62.18	
β-*10c*[15]	106.74 234.4	80.72 20.5	66.28[a]	78.06	68.35[a]	62.14	58.90 *b*
11[15]	112.27 228.0	80.23 36.8	73.83	81.63	63.17		*b*
α-*12*[15]	112.27 224.7	75.72 37.4	70.77	78.31 1.8	62.91 1.8		
β-*12*[15]	107.07 236.1	72.68 20.5	68.54 1.2	79.00 2.6	63.11		
α-*13*[20]	107.39 234.4	71.91 20.5	69.59	82.92	63.57		*b*
β-*13*[20]	112.44 225.5	75.00 35.9	71.35 1.5	81.27 2.9	64.29 0.5		
14[20,21]	112.71 225.81	80.94 40.3	76.65	84.42	63.49		

[a] May be reversed. [b] Digital resolution only ± 1.5 Hz.



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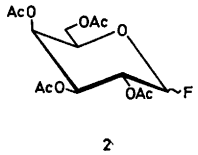

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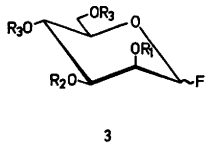

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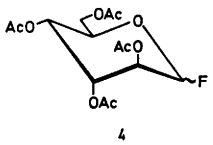

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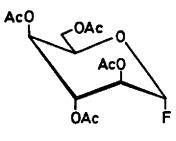

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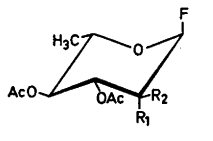

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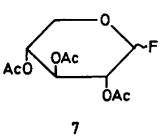

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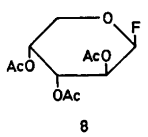

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(a) $R_1 = R_2 = R_3 = H$

(b) $R_1 = R_2 = R_3 = CH_3CO$

(c) $R_1 = CH_3$, $R_2 = R_3 = CH_3CO$

(d) $R_1 = R_3 = CH_3CO$, $R_2 = CH_3$

(e) $R_1 = H$, $R_2 = CH_3COO$

(f) $R_2 = H$, $R_1 = CH_3COO$

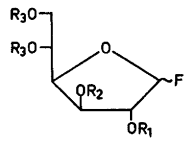
atom and C3 have a *gauche*-orientation. This may indicate a Karplus type of relation. In all pyranosyl fluorides, irrespective of anomeric structure, a $^3J\{^{13}C5F\}$ value of 2 – 5 Hz is found. In a single case (*β-2*) a small coupling was observed between the fluorine atom and C4. A small four bond coupling was also observed to the *O*-methyl group of (*β-1c*).

The $^1J\{C1F\}$ values of the furanosyl fluorides (Table 2) seem to be dependent of the relative configuration of C1 and C2. When the fluorine atom and the substituent at C2 are *cis*-oriented $^1J\{C1F\}$ is numerically larger (*ca.* 6 Hz) than when the two substituents are *trans*-oriented. The $^2J\{C2F\}$ value, on the other hand, is numerically much larger when the substituents at C1 and C2 are *trans* than when they are *cis*. Selective proton decoupling of H1 and H2 has shown that the sign of $^1J\{C1F\}$ in (*α-9b*) is negative whereas $^2J\{C2F\}$ is positive, in agreement with the results found for the pyranosyl fluorides. Thus the absolute values of $^1J\{C1F\}$ and $^2J\{C2F\}$ are smallest in the furanosyl fluorides which have the fluorine atom and the substituent at C2 *cis*-oriented. It may be noted that only few of the furanosyl fluorides investigated show any coupling between fluorine and C3. A small coupling between fluorine and C4 is, on the other hand, found in almost all compounds.

EXPERIMENTAL

The ^{13}C NMR spectra were obtained on a Bruker WH-90 instrument at 22.63 MHz. The two unacylated glucosyl fluorides (α- and *β-1a*) were measured as *ca.* 20 % solutions in water using dioxane (10 %) as internal reference (67.40 ppm). All other compounds were measured as *ca.* 20 % solutions in deuteriochloroform using tetramethylsilane as internal reference. In order to measure the $^{13}C - ^{19}F$ coupling constants accurately a sweep width of 1200 Hz was used in most cases with 8K computer memory for spectrum accumulation. This gives a digital resolution of ± 0.3 Hz.

Tetra-O-acetyl-β-D-mannopyranosyl fluoride (*β-3b*). A solution of 1,3,4,6-tetra-*O*-acetyl-*β*-D-



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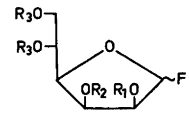

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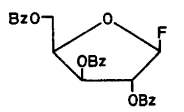

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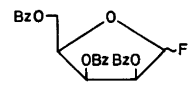

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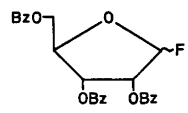

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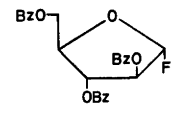

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(b) $R_1 = R_2 = R_3 = CH_3CO$

(c) $R_1 = CH_3$, $R_2 = R_3 = CH_3CO$

(d) $R_2 = CH_3$, $R_1 = R_3 = CH_3CO$

mannopyranose [22] (500 mg) in anhydrous hydrogen fluoride (2 ml) was kept at −70 °C for 30 min. It was then diluted with dichloromethane and poured on ice. The organic phase was washed with aqueous sodium hydrogencarbonate, dried and evaporated. The residue was acetylated with acetic anhydride (2 ml) in pyridine (2 ml). The product thus obtained was separated into two fractions by preparative TLC using ether-pentane (3:1) as eluent. The fastest moving fraction gave 220 mg (44 %) of tetra-*O*-acetyl-α-D-mannopyranosyl fluoride (*α-3b*), identified through its ^1H and ^{19}F NMR spectra. The next fraction yielded 33 mg (7 %) of (*β-3b*) which was crystallized from ether, m.p. 105.5 − 107 °C, $[\alpha]_D^{20}$ − 1.0 ° (*c* 1.5, $CHCl_3$). (Found: C 47.82; H 5.50. Calc. for $C_{14}H_{19}FO_9$ C 48.00; H 5.43).

A ^1H NMR spectrum in deuteriochloroform gave the following data: H1 δ 5.53; H2 5.42; H3-4 5.1 − 5.3; H5 3.90; H6 4.2 − 4.4. J_{12} 1.8 Hz; J_{23} 3.1; J_{45} 7.0; J_{56} 5.6. A ^{19}F NMR spectrum gave $\Phi = -142.0$ ppm (from $CFCl_3$); J_{1F} 50.3 Hz; J_{2F} 10.7.

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