A Study of ¹³CH Coupling Constants in Hexopyranoses

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Proton decoupled and undecoupled ¹³C n.m.r. spectra have been measured on a number of hexopyranoses. The direct coupling constants between the anomeric carbon atoms and protons {^1J[¹³C-H(1)]} were found to be *ca.* 160 in the β-anomers and *ca.* 170 Hz in the α-anomers; the difference of *ca.* 10 Hz between pairs of anomers was found in almost all cases. Chemical shifts and ^1J(¹³CH) values of the other carbon atoms in the pyranose rings were also measured.

WE previously reported that the coupling constant between ¹³C(1) and H(1) {^1J[¹³CH(1)]} in pyranose derivatives of carbohydrates could be used for the assignment of anomeric configuration since pyranoses with an axial H(1) have a ^1J[¹³CH(1)] value which is *ca.* 10 Hz lower than the corresponding value in compounds with

Apparently acylation increases the value slightly. This effect is also found for the other direct coupling constants (Table).

Free sugars, *i.e.* pyranoses with a hydroxy-group at C(1), also give ^1J[¹³CH(1)] values of 160 (β-pyranoses) and 170 Hz (α-pyranoses).[1]

(1)   (2)   (3)   (4)

(5)   (6)   (7)   (8)   (9)
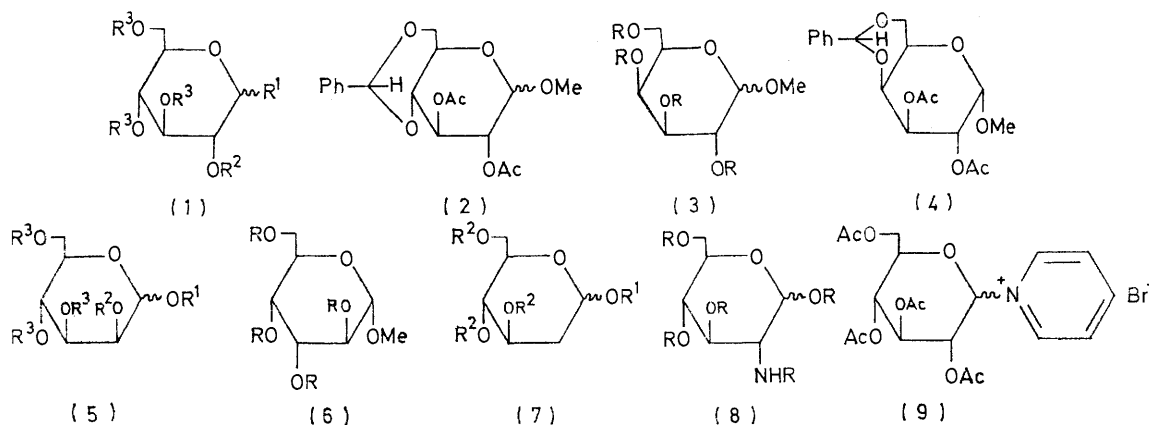
an equatorial H(1).[1] A larger number of pyranose derivatives have now been studied and, in addition to the ^1J[¹³CH(1)] values, other direct coupling constants have been measured.

In the Table ^1J[¹³CH(1)] values are given for a number of methyl glycopyranosides, and it is seen that α-glycosides, with equatorial H(1), give a value of 170 Hz whereas β-glucosides, with axial H(1), give 160 Hz. In acetylated glycosides the coupling constants are the same or 1 Hz higher. Benzoylated methyl α-D-glucopyranoside give a ¹³CH(1) coupling constant of 173 Hz.

The electronegativity of the substituent at C(1) affects the coupling constants. Thus thioglycosides have lower ^1J[¹³CH(1)] values than O-glucosides. The N-phenyl glycoside (1β; R¹ = NHPh, R² = R³ = Ac) has a smaller constant than the more electronegative N-p-nitrophenyl glycoside. In 1-O-acetyl compounds the ¹³CH(1) coupling constant is increased *ca.* 5 Hz in both anomers relative to that of the methyl glycosides. When the electronegativity of the substituent at C(1)

[1] K. Bock, I. Lundt, and C. Pedersen, *Tetrahedron Letters*, 1973, 1037.

is increased further, as in the glycosyl halides, the coupling constants of both anomers are increased by 12—16 Hz relative to the methyl glycosides; but the difference of ca. 10 Hz between pairs of anomers is still found. Tetra-O-acetyl-β-D-glucopyranosyl pyridinium bromide (9β) has a $^1J[^{13}CH(1)]$ value of 163 Hz in agreement with those of other β-anomers. The corresponding α-anomer has the same coupling constant. This is in agreement with the work of Duvette and Horton [2] who found that this compound does not adopt the $^4C_1$ conformation and has H(1) axially oriented.

Changes in the substituent at C(2) in the pyranose ring do not affect the $^1J[^{13}CH(1)]$ value appreciably as seen from the 2-deoxy-D-$arabino$-hexose derivatives (7) and from the 2-O-methyl- (1; $R^2 = OMe$) and 2-deoxy-2-amino-derivatives (8).

Several authors have discussed the effect of lone electron pairs on ^{13}CH coupling constants, and the available evidence indicates that directly bonded ^{13}CH coupling constants are increased when neighbouring lone pairs are present close to the proton.[3-8] This effect may explain the differences in $^1J[^{13}CH(1)]$ values between anomers since an equatorial H(1), which is close to the lone pairs of the pyranoid ring oxygen atom, has a larger coupling constant than the axial H1.

The exocyclic substituent at C(1) also carries lone pairs the position of which could influence the coupling constant. The fact that $^1J[^{13}CH(1)]$ varies very little through a rather large number of free sugars and methyl glycosides (Table) perhaps indicates that the OH or OMe groups at C(1) have very nearly the same orientation in these compounds.

In addition to the $^1J[^{13}CH(1)]$ values discussed above other $^1J(^{13}CH)$ values have also been measured (Table). Most of these fall into a rather narrow range (143—149 Hz) in unacylated glycosides. In acylated sugars the range is somewhat larger. It has, however, not been possible to correlate these coupling constants with the configurations of the corresponding carbon atoms.

Schwarcz and Perlin [9] studied vicinal and geminal ^{13}CH coupling constants from the ^1H spectra of ^{13}C-enriched carbohydrates. These couplings are of course also observable in the undecoupled ^{13}C spectra and their values vary from 0 to ca. 8 Hz. However, because of the complexity of the undecoupled ^{13}C spectra, and since the protons are strongly coupled in most of the compounds discussed here, it is not possible to measure these smaller coupling constants on a first-order basis.

In tetra-O-acetyl-α- and -β-D-glucopyranosyl fluoride a

number of $^{13}C^{19}F$ coupling constants have been observed. These and corresponding constants of other glycosyl fluorides will be discussed separately.

For many of the compounds in the Table chemical shifts have been assigned by other workers. The values given here are in many cases slightly different from those reported previously because of different measuring conditions. Thus internal references were used in the present work whereas most previous workers used external references. Assignment of chemical shifts to the compounds which were not studied previously was fairly straightforward using principles that are now well established.[10]

The signal of the anomeric carbon atom is always found at lowest field and normally C(1) of a β-pyranose is at lower field than that of an α-pyranose.[11] There are, however, exceptions to this. Thus, C(1) of tetra-O-acetyl-β-D-glucopyranosyl chloride is found at 87·1 p.p.m. whereas the corresponding α-anomer has this signal at 89·5. A similar reversal of shifts is found in α- and β-D-mannopyranose.[1,12] In such cases $^1J[^{13}CH(1)]$ values are useful as a supplement to the chemical shifts for the assignment of anomeric structure. The signals of C(4) and C(6) remain almost constant throughout the series of compounds described here and they are therefore readily assigned in most cases. The signals of C(3) and C(5) are often closely situated and the assignment may then be difficult.

In acetylated compounds the signals of the carbon atoms are shifted to higher field relative to those of the unacetylated compounds,[13] but their relative positions remain largely unchanged. However, acetylation of methyl α-D-altropyranoside causes profound changes in the spectral pattern, probably because of conformational changes analogous to those observed when idose derivatives are acetylated.[14] The assignment of shifts to the carbon atoms of the α-pyridinium compound (9a) was difficult because of the reversed conformation of this compound.

EXPERIMENTAL

Spectra were obtained at 22·63 MHz with a Bruker WH-90 instrument, equipped with a computer with 12 K memory (8 K for spectrum accumulation), using 10 mm sample tubes at 30°. Unacylated carbohydrates were measured in D_2O solution, acylated compounds in deuteriochloroform; the solutions were ca. 20%. Chemical shifts are given relative to tetramethylsilane. They were measured from proton-decoupled spectra relative to internal dioxan (10%) (67·4 p.p.m.) in D_2O solution or to internal

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Chemical shifts (p.p.m.) and observed first-order coupling constants (±1 Hz) of hexopyranoses

Compound	C(1) $^1J_{1CH}$	C(2) $^1J_{2CH}$	C(3) $^1J_{3OH}$	C(4) $^1J_{4OH}$	C(5) $^1J_{5OH}$	C(6) $^1J_{6OH}$	Me $^1J_{OH}$	Ref.
(1α; R¹ = OMe, R² = R³ = H)	99·9	72·2	73·9	70·4	71·9	61·5	55·6	9, 11
	170	148	147	145	146	145	144	
(1α; R¹ = OMe, R² = R³ = Ac)	96·3	68·2	70·4	66·8	69·7	61·6	55·6	15
	172	151	151	145	151	148	143	
(1α; R¹ = OMe, R² = R³ = Bz)	96·8	69·4	70·3	67·5	71·8	62·9	55·4	
	173	153	152	145	145	147	143	
(2α)[17]	98·7	72·6	70·0	80·1	63·4	69·8	56·3	
	171	145	146	142	144	146	138	
(1β; R¹ = OMe, R² = R³ = H)	103·7	73·7	75·5	70·3	75·5	61·7	57·8	11, 15
	160	145	143	141	143	145	144	
(1β; R¹ = OMe, R² = R³ = Ac)	101·1	70·9	71·4ᵃ	68·1	72·5ᵃ	61·6	56·6	15
	161	151	140	153	149	148	143	
(2β)[18]	101·0	72·0	71·7	78·1	66·0	68·2	57·0	
	162	145ᵇ	145ᵇ	140	143ᵇ	145	142	
(1β; R¹ = OPh, R² = R³ = Ac)	98·8	71·1	71·8ᵃ	68·2	72·5ᵃ	61·8		
	163	153	143ᵇ	152ᵇ	150ᵇ	148		
(3α; R = H)	99·8	69·9	70·2	68·9	71·2	61·8	55·6	12, 16
	170	146	145	146	143	143	143	
(3α; R = Ac)	96·5	67·0ᵃ	67·6ᵃ	65·7ᵃ	67·6ᵃ	61·2	54·8	
	171	145	150	143	150	150	143	
(4)[19]	97·3	67·8	68·2	73·6	61·8	68·7	55·2	
	172	142ᵇ	146ᵇ	146	146ᵇ	141, 152	142	
(3β; R = H)	104·1	71·2	73·3	69·1	75·3	61·4	57·4	12
	160	146	141	146	141	144	144	
(3β; R = Ac)	101·5	68·5	70·2ᵃ	66·8	70·6ᵃ	61·0	56·6	
	161	157	142	153	146	150	143	
(5α; R¹ = Me, R² = R³ = H)	101·0	70·8	70·1	67·0	72·7	61·2	55·3	11, 12
	170	144	147	145	145	144	144	
(5α; R¹ = Me, R² = R³ = Ac)	98·1	68·8ᵃ	68·0ᵃ	65·8	69·1ᵃ	62·1	54·9	
	171	154ᵇ	148ᵇ	148ᵇ	156	148	143	
(6; R = H)	101·1	69·8ᵃ	70·4ᵃ	65·0	70·6ᵃ	61·6	55·8	12
	170	147	147	145	147	145	143	
(6; R = Ac)	98·2	64·6ᵃ	66·6	64·1ᵃ	68·9	62·2	55·0	
	170	148ᵇ	156	148ᵇ	155	148	143	
(5α; R¹ = R² = R³ = Ac)	90·4	68·6ᵃ	68·2ᵃ	65·4	70·5	62·0		
	176							
(1β; R¹ = SMe, R² = R³ = Ac)	82·3	68·7	73·5	68·0	75·5	61·8		
	156							
(1β; R¹ = SEt, R² = R³ = Ac)	83·2	69·6	73·7	68·2	75·6	61·9		
	153							
(1α; R¹ = NHPh, R² = R³ = Ac)[20]	80·1	65·8	71·0	68·5	72·1	61·7		
	165							
(1β; R¹ = NHPh, R² = R³ = Ac)[20]	84·0	70·4	72·1	68·7	72·8	62·0		
	155							
(1β; R¹ = p-NO₂C₆H₄NH, R² = R³ = Ac)[21]	82·6	70·8	72·4	68·4	72·4	61·8		
	160							
(1β; R¹ = N₃, R² = R³ = Ac)[22]	87·3	70·3	72·2	67·6	73·6	61·4		
	160	140	150	145	145	148		
(9α)[23]	87·9	67·5ᵃ	68·9	68·3ᵃ	75·6	62·4		
	163							
(9β)[23]	92·6	72·8ᵃ	68·9ᵃ	68·2ᵃ	67·5ᵃ	62·4		
	163							

Compound	C(1) ¹J₁OH	C(2) ¹J₂CH	C(3) ¹J₃CH	C(4) ¹J₄CH	C(5) ¹J₅OH	C(6) ¹J₆OH	Me ¹JCH	Ref.
(1α; R¹ = F, R² = R³ = Ac)²⁴	103·5 / 186	69·9	69·1	67·1 / 155	69·6	61·0 / 150	¹JCF 228	
(1β; R¹ = F, R² = R³ = Ac)²⁵	105·7 / 178	70·6	71·4	67·0 / 145	71·5 / 150	61·3 / 150	¹JCF 218	
(1α; R¹ = Cl, R² = R³ = Ac)	89·5 / 184	70·2ᵃ / 150	70·3ᵃ / 150	66·8 / 151	68·8ᵃ / 155	60·4 / 148		
(1β; R¹ = Cl, R² = R³ = Ac)	87·1 / 171	72·4 / 150	73·0ᵃ / 155	67·2 / 155	74·9ᵃ / 145	61·2 / 149		
(1α; R¹ = Br, R² = R³ = Ac)	86·5 / 185	70·4ᵃ / 148	72·0ᵃ / 148	67·0 / 150	70·0ᵃ / 150	60·8 / 147		
(7α; R¹ = R² = H)ᶜ	92·1 / 170	38·3 / 130	68·8ᵃ / 145	72·0 / 148	72·8ᵃ / 147	61·6 / 143		15
(7β; R¹ = R² = H)ᶜ	94·1 / 162	40·5 / 130	71·4ᵃ / 148	71·7ᵃ / 148	76·8 / 142	61·9 / 143		15
(7α; R¹ = Me, R² = H)²⁶	98·9 / 170	37·5 / 130	69·0 / 145	71·8 / 146	72·8 / 144	61·6 / 144	55·2 / 143	
(7β; R¹ = Me, R² = H)²⁶	101·3 / 161	39·0 / 130	70·3 / 144	71·9 / 145	76·7 / 142	61·8 / 143	57·4 / 143	
(7α; R¹ = R² = Ac)²⁷	90·2 / 175	33·5 / 130, 134	68·0ᵃ / 144	68·2ᵃ / 150	69·7 / 150	61·5 / 149		
(7β; R¹ = R² = Ac)²⁷	90·5 / 165	34·6 / 132	68·0 / 150	69·8 / 148	72·5 / 143	61·7 / 148		
(1α; R¹ = OH, R² = Me, R³ = H)ᶜ	90·1 / 169	81·3 / 145	72·8ᵃ / 148	70·5 / 144	72·0ᵃ / 150	61·4 / 148	58·4 / 143	
(1β; R¹ = OH, R² = Me, R³ = H)ᶜ	96·5 / 162	84·4 / 148	76·6ᵃ / 145	70·5 / 144	76·1ᵃ / 145	61·5 / 148	60·9 / 143	
(1α; R¹ = AcO, R² = Me, R³ = Ac)²⁸	88·4 / 175	77·8 / 148	71·3ᵃ / 148	67·7 / 150	69·4ᵃ / 150	61·4 / 148	58·9 / 143	
(1β; R¹ = AcO, R² = Me, R³ = Ac)²⁸	93·0 / 165	79·4 / 146	73·6ᵃ / 145	67·7 / 150	71·9ᵃ / 144	61·2 / 148	60·1 / 142	
(5α; R¹ = R³ = H, R² = Me)²⁹ᶜ	91·5 / 170	81·4 / 151	70·9 / 146	68·1 / 148	73·2 / 146	61·9 / 145	59·6 / 143	
(5β; R¹ = R³ = H, R² = Me)²⁹,ᶜ	94·8 / 160	82·3	74·3	67·9	77·1	69·1	62·8	
(5α; R¹ = R³ = Ac, R² = Me)	90·4 / 176	76·7 / 146ᵇ	70·6 / 145ᵇ	65·5 / 150ᵇ	70·6 / 145ᵇ	62·0 / 150	59·3 / 142	
(5β; R¹ = R³ = Ac, R² = Me)²⁹	91·6 / 163	76·8 / 148	72·5 / 145ᵇ	65·3 / 147	72·4 / 145ᵇ	61·7 / 150	61·1 / 141	
(8α; R = H)ᶜ	89·9 / 171	55·3	70·5	70·5	72·4	61·3		
(8β; R = H)ᶜ	93·5 / 163	57·8	72·8	70·5	76·9	61·3		
(8α; R = Ac)	90·1 / 177	50·5	69·2	67·4	70·1	61·3		

ᵃ Assignment may be reversed.   ᵇ Measured from centre of broad multiplet.   ᶜ From mutarotated mixture.

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deuteriochloroform (76·9 p.p.m.). The pulse width was 4—5 μs, pulse intervals 1 s. Undecoupled spectra were obtained with a gated decoupling technique [30] using the Bruker B-WM 6 multi-pulse unit; repetition time was 3·0 s, decoupling time 1·1—1·4 s.

Tetra-O-*acetyl*-2-O-*methyl*-α-D-*mannopyranose*.— 2-O-Methyl-D-mannose [29] (150 mg) was acetylated in the usual manner with acetic anhydride in pyridine. The product was crystallized from ether–pentane, yield 160 mg. Recrystallization gave pure (5α; $R^1 = R^2 = Ac$, $R^2 = Me$), m.p. 130—131°, $[\alpha]_D^{25}$ 51·2° (c 1·3, $CHCl_3$) (Found: C, 49·55; H, 6·1. Calc. for $C_{15}H_{22}O_{10}$: C, 49·7; H, 6·1%), ^{1}H n.m.r.,

δ (90 MHz; $CDCl_3$) 6·29 [$J_{1,2}$ 2·1 Hz, H(1)], 3·63 [$J_{1,2}$ 2·1, $J_{2,3}$ 2·9 Hz, H(2)], 5·23 [$J_{2,3}$ 2·9, $J_{3,4}$ 9·7 Hz, H(3)], 5·40 [$J_{3,4}$ 9·7, $J_{4,5}$ 10·0 Hz, H(4)], 4·04 [$J_{4,5}$ 10·0, $J_{5,6}$ 4·7, $J_{5,6'}$ 2·3 Hz, H(5)], 4·09 [$J_{5,6}$ 4·7, $J_{6,6}$ 12·5 Hz, H(6)], and 4·24 [$J_{5,6'}$ 2·3, $J_{6,6'}$ 12·5 Hz, H(6')].

The Fourier transform instrument was provided by The Danish National Science Research Council.

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