Carbohydrate Research, 38 (1974) 47–59

CONFORMATIONAL STUDIES ON PERTRIMETHYLSILYL DERIVATIVES OF SOME 6-DEOXYALDOHEXOPYRANOSES AND OF FOUR LESS-COMMON ALDOHEXOPYRANOSES BY 220-MHz P.M.R. SPECTROSCOPY. SUBSTITUENT AND CONFIGURATIONAL EFFECTS ON THE CHEMICAL SHIFTS OF THE RING PROTONS

Dirk G. Streefkerk*, Marius J. A. de Bie, and Johannes F. G. Vliegenthart**
Laboratory of Organic Chemistry, Croesestraat 79, University of Utrecht,
Utrecht (The Netherlands)
(Received May 15th, 1974; accepted for publication, May 24th, 1974)

ABSTRACT

The complete interpretation of 220-MHz p.m.r. spectra and the accurate chemical shifts and coupling constants, obtained after computer simulation of the spectra, of the per-*O*-trimethylsilyl (Me_3Si) derivatives of a number of 6-deoxyaldohexopyranoses and of β-D-altro-, β-D-allo-, and α- and β-D-talo-pyranose are given. By means of an adapted Karplus equation, the structure of the derivatives has been studied in detail. All of the pyranoid rings occur in the $^4C_1$(D) or $^1C_4$(L) chair conformation. The preferred conformation of the C-5–CH_2OSiMe_3 group in the four aldohexopyranoses was found to be dependent on the configuration at C-4. By comparison of Me_3Si-aldohexopyranoses with the corresponding 6-deoxy analogues, it was found that the 6-$OSiMe_3$ group has no marked effect on the conformation of the ring. The influence of this group on the chemical shifts of the ring protons is discussed in terms of electric field and inductive effects. Rules are presented for the estimation of the chemical shifts of the ring protons of Me_3Si-aldohexopyranoses and Me_3Si-6-deoxyaldohexopyranoses.

INTRODUCTION

In the framework of our studies on the structure in solution of per-*O*-trimethylsilyl (Me_3Si) derivatives of mono- and oligo-saccharides by high-resolution p.m.r.[1–5], we have investigated the Me_3Si derivatives of some 6-deoxyaldohexopyranoses and of β-D-altro, β-D-allo-, and α- and β-D-talo-pyranose. P.m.r. data on 6-deoxyaldohexopyranoses are sparse in the literature. The p.m.r. spectrum of Me_3Si-α-L-rhamnopyranose has been published without details[6]. The normal chair conformations[7], $^1C_4$(L) or $^4C_1$(D), have been found for α- and β-L-fucopyranose[8], for methyl Me_3Si-4-*O*-*p*-cumaroyl-α-L-rhamnopyranoside[9], and for the pyranoid rings in 6,6′-dideoxy-

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*Present address: C.S.I.R. Carbohydrate Research Unit, Department of Chemistry, University of Cape Town (South Africa).

**To whom all correspondence should be addressed.

α,α-trehalose hexa-acetate[10]. Furthermore, the chemical shifts and coupling constants of the methyl group of several 6-deoxyaldohexopyranose derivatives in different solvents have been described[11]. The $^{4}C_{1}$ (D) conformation has been proposed for the four aldohexopyranoses as free sugars in aqueous solution[12] and for penta-*O*-acetyl-β-D-allopyranose in chloroform[13].

We now report the use of accurate p.m.r. data for Me_3Si-6-deoxyaldohexopyranoses to estimate the conformation of these compounds. The Me_3Si-6-deoxyaldohexopyranoses are compared with the corresponding Me_3Si-aldohexopyranoses to determine the effect of the replacement of a hydrogen atom at C-6 by $OSiMe_3$ on the deformation of the ring and on the chemical shifts of the ring protons.

RESULTS

Spectrum interpretation

(*a*) *Me_3Si-6-deoxyaldohexopyranoses.* — 220-MHz p.m.r. spectra of the 1,2,3,4-tetrakis-*O*-trimethylsilyl derivatives of 6-deoxy-α-D-glucopyranose (**1**), 6-deoxy-β-D-glucopyranose (**2**), α-L-rhamnopyranose (**3**), β-L-rhamnopyranose (**4**), α-L-fucopyranose (**5**), and β-L-fucopyranose (**6**) were recorded for solutions in acetone-d_6. Each spectrum can be subdivided into the following groups of signals: (*1*) four strong, sharp singlets for the Me_3Si-methyl groups at δ 0.1–0.2; (*2*) a doublet for the C-5–Me group at δ 1.07–1.21; (*3*) multiplets for the non-anomeric protons at δ 3.1–4.1; (*4*) a doublet for the anomeric proton at δ 4.4–5.0 p.p.m.

The p.m.r. data for compounds **1–6** were obtained from a first-order, sub-spectral analysis. The data for the protons attached to the carbon skeleton (*3* and *4*) were refined by calculation of theoretical spectra in an interactive, iterative procedure with the spin-simulation program SIMEQ[14] until a good agreement was obtained between the observed and calculated spectra. In these calculations, the spin system was treated as an eight-spin system: X_3ABCDE (X_3 representing the protons of the C-5–Me group, and A–E the protons H-1–H-5). All vicinal coupling constants were taken to be positive. The refined p.m.r. parameters are given in Tables I and II.

(*b*) *Me_3Si-aldohexopyranoses.* — The 220-MHz p.m.r. spectra of the 1,2,3,4,6-pentakis-*O*-trimethylsilyl derivatives of β-D-altropyranose (**7**), β-D-allopyranose (**8**), α-D-talopyranose (**9**), and β-D-talopyranose (**10**) were recorded for solutions in acetone-d_6. The accurate p.m.r. parameters of **7** were obtained as described for **1–6**. The spectrum of **8** was complex. However, by comparison with the spectrum of **8** recorded at 300 MHz, a straightforward analysis was possible. The spectra of **9** and **10** were poorly resolved. A better spectral dispersion was obtained for solutions in benzene-d_6, and the complete sets of parameters were thereby derived. Starting with the latter data, the spectra of the acetone solutions of **9** and **10** could be interpreted. The parameters of H-3,4,5,6′ of compound **9** in acetone could not be determined exactly, because they have apparently the same chemical shifts. Computer simulation of the spectra revealed that H-2 and H-4 of **9** and **10** have a long-range coupling in both solvents. The p.m.r. data of **7–10** are summarized in Tables I and II.

TABLE I

CHEMICAL SHIFTS (δ, P.P.M.) OF METHINE, METHYLENE, METHYL AND Me_3SiO-METHYL PROTONS OF Me_3Si-6-DEOXYALDOHEXOPYRANOSES AND Me_3Si-ALDOHEXOPYRANOSES IN ACETONE-d_6

Compound	*Parent sugar*	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*C-5–CH₃*	*Me_3SiO-methyl groups (number of protons)*				
1	6-Deoxy-α-D-Glc*p*	4.98	3.39	3.72	3.12	3.74			1.14	0.155 (9)	0.160 (9)	0.162 (9)	0.165(9)	
2	6-Deoxy-β-D-Glc*p*	4.51	3.18	3.39	3.15	3.35			1.21	0.151 (9)	0.156 (9)	0.165 (9)	0.171(9)	
3	α-L-Rha*p*	4.86	3.72	3.82	3.58	3.65			1.14	0.139(18)	0.151 (9)	0.170 (9)		
4	β-L-Rha*p*	4.83	3.79	3.54	3.51	3.23			1.19	0.129 (9)	0.135(18)	0.168 (9)		
5	α-L-Fuc*p*	4.96	3.80	3.91	3.71	4.05			1.07	0.141(18)	0.147 (9)	0.159 (9)		
6	β-L-Fuc*p*	4.50	3.54	3.56	3.67	3.69			1.15	0.126 (9)	0.149 (9)	0.155 (9)	0.173(9)	
7	β-D-Alt*p*	5.09	3.59	3.83	3.96	3.70	3.64	3.78		0.126 (9)	0.130 (9)	0.147(18)	0.155(9)	
8	β-D-All*p*[a]	4.85	3.32	4.00	3.67	3.72	3.64	3.78		0.108 (9)	0.134 (9)	0.142 (9)	0.145(9)	0.164(9)
9	α-D-Tal*p*	4.97	3.44	[b]	[b]	[b]	3.73	[b]		0.107 (9)	0.123 (9)	0.137 (9)	0.149(9)	0.162(9)
10	β-D-Tal*p*	4.74	3.71	3.70	3.76	3.46	3.66	3.73		0.109(18)	0.120 (9)	0.153 (9)	0.188(9)	
9	α-D-Tal*p*[c]	5.33	3.50	3.85	3.80	4.12	3.91	4.08		0.126(18)	0.287(18)	0.306 (9)		
10	β-D-Tal*p*[c]	4.53	3.71	3.26	3.77	3.33	3.86	3.93		0.171(18)	0.190 (9)	0.221 (9)	0.274(9)	

[a] Data from 300-MHz spectrum. [b] Complex multiplet between 3.87 and 3.90 p.p.m. [c] Recorded in benzene-d_6.

TABLE II

COUPLING CONSTANTS (Hz) OF METHINE, METHYLENE, AND METHYL PROTONS OF Me_3Si-6-DEOXY- AND Me_3Si-ALDOHEXOPYRANOSES IN ACETONE-d_6

Compound	*Parent sugar*	$J_{1,2}$	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{5,Me}$
1	6-Deoxy-α-D-Glc*p*	3.1	9.2		8.6	9.2				6.5
2	6-Deoxy-β-D-Glc*p*	7.2	8.8		8.8	8.9				6.4
3	α-L-Rha*p*	2.1	2.5		8.9	9.0				6.0
4	β-L-Rha*p*	0.9	2.2		9.2	8.7				6.2
5	α-L-Fuc*p*	3.0	9.5		2.6	1.1				6.5
6	β-L-Fuc*p*	6.7	~9.5		1.0	0.7				6.3
7	β-D-Alt*p*	1.3	4.3		2.7	9.0	5.2	2.3	−11.0	
8	β-D-All*p*[a]	7.4	2.5		2.2	9.4	4.9	1.6	−11.0	
9	α-D-Tal*p*	4.7	3.0	~−0.8	~3.0	~2.0	4.0	~8.0	−9.6	
10	β-D-Tal*p*	1.4	~2.9	~−0.8	2.9	1.6	6.2	6.5	−9.5	
9	α-D-Tal*p*[b]	4.6	3.0	~−0.7	3.0	~3.0	4.0	8.0	−9.6	
10	β-D-Tal*p*[b]	1.4	3.2	~−0.7	3.2	1.6	6.1	6.6	−9.5	

[a] Data from 300-MHz spectrum. [b] Recorded in benzene-d_6.

The structure of the Me_3Si derivatives

(*a*) *Me_3Si-6-deoxyaldohexopyranoses* **1–6**. — To characterize the type of ring conformation, fourteen ideal conformations were considered: 2 chair (*C*), 6 boat (*B*), and 6 skew-boat (*S*) conformations[15]. For each conformation, the dihedral angles between the ring protons were estimated from Dreiding molecular models, and the corresponding vicinal coupling constants were calculated by using a modified Karplus equation[1]:

$$J_{HH'} = (6.6-1.0\cos\phi+5.6\cos 2\phi)(1-\sum_{i=1}^{4} f_i \Delta X_i),$$

in which ϕ is the dihedral angle between the protons in the fragment H–C–C′–H′; $\Delta X_i = X_R - X_H$ represents the difference in electronegativity X between a substituent R and hydrogen; f_i amounts to 0.15 when the dihedral angle θ between R and H in H–C–C′–R is larger than 90°, and 0.05 when θ is smaller than 90°. The following values for X, as determined by the method of Cavanaugh and Dailey[16], were used: $X_H = 2.1$; $X_{OSiMe_3} = 3.4$; $X_{-C-O-} = 2.5$; $X_{CH_3} = 2.5$, and $X_{O_r} = 3.3$. Comparison of the observed coupling constants of tetrakis-Me_3Si-α-L-fucopyranose (**5**) with the calculated values (Table III) shows that only for the $^1C_4$(L) conformation is a good agreement found between both series. In any other conformation, at least one calculated coupling constant deviates substantially from the experimental value. This points to a strong preponderance of the $^1C_4$(L) conformation. Calculations for compounds **2**, **3**, **4**, and **6** gave similar results: only the $^1C_4$ (L series) or $^4C_1$ (D series) conformation shows a good fit of the calculated with the observed coupling constants (Table IV). However, for compound **1**, the $^1S_3$(D) conformation has also to be taken into consideration, because the theoretical coupling constants (4.2, 8.9, 10.5, and

9.0 Hz) agree reasonably well with the observed values (3.1, 9.2, 8.6, and 9.2 Hz). In general, the actual conformations are not ideal, a flattening of the chair conformations in pyranoid rings has been found in several cases (*cf.* Ref. 17). Calculations on non-ideal conformations show that the fit of the coupling constants of the $^4C_1$(D) conformation with the observed data improves, whereas for the $^1S_3$(D) conformation the agreement diminishes, thus favouring the $^4C_1$(D) conformation for compound **1**.

TABLE III

CALCULATED, VICINAL COUPLING-CONSTANTS IN TETRAKIS-Me_3Si-α-L-FUCOPYRANOSE (5) IN DIFFERENT CONFORMATIONS[a]

Conformation		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
Chair *C1*(L)	$^4C_1$(L)	1.7	2.4	2.1	2.5
1C(L)	$^1C_4$(L)	2.0	10.8	2.1	1.9
Boat	$^{1,4}B$(L)	2.0	3.2	2.1	2.5
	$^{2,5}B$(L)	1.7	2.4	5.2	1.9
	$^{3,O}B$(L)	3.8	10.8	2.1	5.5
	$B_{1,4}$(L)	1.7	3.2	2.1	1.9
	$B_{2,5}$(L)	2.0	10.8	5.2	2.5
	$B_{3,O}$(L)	3.8	2.4	2.1	5.5
Skew Boat	$^1S_5$(L)	1.1	8.9	5.2	1.4
	$^OS_2$(L)	4.2	10.5	5.2	4.6
	$^3S_1$(L)	4.2	8.9	1.2	4.6
	$^5S_1$(L)	1.0	0.7	5.2	1.1
	^2S_O(L)	4.2	3.8	5.2	4.6
	$^1S_3$(L)	4.9	0.7	1.2	6.1
$J_{HH'}$ observed[b]		3.0	9.5	2.6	1.1

[a]For nomenclature of conformations, see ref. 7. [b]See Table II.

TABLE IV

OBSERVED AND CALCULATED VICINAL COUPLINGS, FOR IDEAL $^4C_1$(D) [OR $^1C_4$(L)] CHAIR CONFORMATIONS OF THE Me_3Si DERIVATIVES 1–10

Compound	*Parent sugar*	*Observed*				*Calculated*			
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
1	6-Deoxy-α-D-Glc*p*	3.1	9.2	8.6	9.2	2.0	10.8	10.8	11.0
2	6-Deoxy-β-D-Glc*p*	7.2	8.8	8.8	8.9	10.3	10.8	10.8	11.0
3	α-L-Rha*p*	2.1	2.5	8.9	9.0	2.0	2.1	10.8	11.0
4	β-L-Rha*p*	0.9	2.2	9.2	8.7	1.7	2.1	10.8	11.0
5	α-L-Fuc*p*	3.0	9.5	2.6	1.1	2.0	10.8	2.1	1.9
6	β-L-Fuc*p*	6.7	~9.5	1.0	0.7	10.3	10.8	2.1	1.9
7	β-D-Alt*p*	1.3	4.3	2.7	9.0	1.7	2.4	2.1	11.0
8	β-D-All*p*	7.4	2.5	2.2	9.4	10.3	2.1	2.1	11.0
9	α-D-Tal*p*	4.7	3.0	~3.0	~2.0	2.0	2.1	2.1	1.9
10	β-D-Tal*p*	1.4	~2.9	2.9	1.6	1.7	2.1	2.1	1.9

TABLE V

CALCULATED DIHEDRAL ANGLES $\phi_{HH'}$ FOR Me_3Si-6-DEOXYALDOHEXOPYRANOSES AND Me_3Si-ALDOHEXOPYRANOSES

Parent sugar	$\phi_{1,2}$	$\phi_{2,3}$	$\phi_{3,4}$	$\phi_{4,5}$
A 6-Deoxyaldohexopyranoses				
6-Deoxy-α-D-Glc*p* (**1**)	49	156	151	155
6-Deoxy-β-D-Glc*p* (**2**)	144	153	153	153
α-L-Rha*p* (**3**)	59	56	154	153
β-L-Rha*p* (**4**)	73	59	156	151
α-L-Fuc*p* (**5**)	50	158	55	71
β-L-Fuc*p* (**6**)	141	~158	74	79
B Aldohexopyranoses[a]				
α-D-Glc*p*	50	154	151	156
β-D-Glc*p*	145	149	150	151
α-D-Man*p*	59	56	156	154
β-D-Man*p*	73	54	154	155
α-D-Gal*p*	49	158	55	67
β-D-Gal*p*	144	143	63	72
C Aldohexopyranoses				
β-D-Alt*p* (**7**)	66	46	55	153
β-D-All*p* (**8**)	146	56	59	156
α-D-Tal*p* (**9**)	36	52	~52	~59
β-D-Tal*p* (**10**)	64	~53	53	63

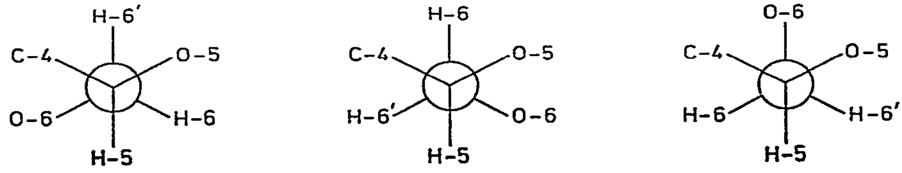
[a] Ref. 1.

To study the ring conformation in more detail, the dihedral angles (Table VA) between the ring protons were calculated from the coupling constants $J_{1,2}$, $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ (Table II). For comparison, the dihedral angles of corresponding Me_3Si-aldohexopyranoses[1] are summarized in Table VB. The close similarity between both series of angles demonstrates that the conformation of the ring is not affected by the presence or absence of an $OSiMe_3$ group at C-6, and that the deviations from the ideal-chair conformation are almost equal in both series of compounds.

(*b*) *Me_3Si-aldohexopyranoses* **7–10**. — The type of ring conformation of compounds **7–10** was determined as described for the deoxy sugars. For all compounds, the $^4C_1$(D) conformation gives a good fit between the observed and the calculated coupling constants (Table IV). The $^{1,4}B$ conformation of pentakis-Me_3Si-β-D-altropyranose (**7**) has theoretical coupling constants (2.0, 3.2, 2.1, and 11.0 Hz) which are also in accordance with the experimental values. However, if the steric interaction between the bulky $OSiMe_3$ groups is taken into account and the coupling constants are calculated for less-ideal conformations, the agreement with the experimental data improves for the $^4C_1$(D) conformation and diminishes for the $^{1,4}B$ conformation. The conclusion, obtained for the pentakis-Me_3Si-D-talopyranoses (**9**) and (**10**), is corroborated by the presence of a long-range coupling between H-2 and H-4. For compound **10**, the $^1C_4$(D) conformation can be excluded because no long-range coupling occurs between H-1, H-3, and H-5. This conformation had to be considered, despite the unfavourable 1,3-diaxial interactions between Me_3SiO-1, Me_3SiO-3, and C-5–CH_2OSiMe_3, because the coupling constants of the $^1C_4$(D) conformation (2.0, 2.1, 2.1, and 2.5 Hz) fit well with the observed data.

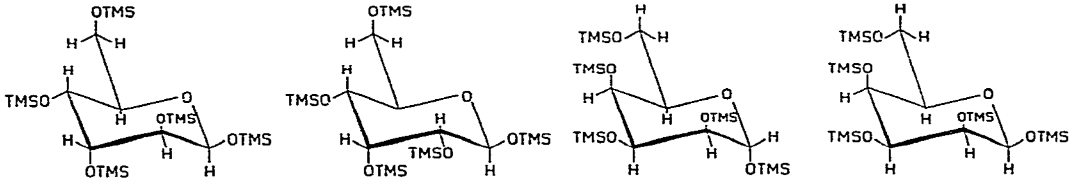
Accepting that compounds **7–10** have the $^4C_1$(D) conformation, the dihedral angles (Table VC) between the ring protons are calculated from the observed coupling constants by means of the modified Karplus equation. Comparison with the values calculated for other Me_3Si-aldohexopyranoses (Table VB) shows that similar values are found for 1,2-diaxial protons (143–156°) and 1,2-diequatorial or 1,2-axial, equatorial protons (49–72°). Therefore, the deviations from the ideal-chair conformation are not significantly different.

The preferred conformations of the C-5–CH_2OSiMe_3 group in compounds **7–10** were deduced from the coupling constants $J_{5,6}$ and $J_{5,6'}$ (Table II). The three staggered rotamers *1*, *2*, and *3* (Fig. 1), which arise by rotation around the C-5–C-6 bond, are the most important conformations. Each of these rotamers contributes to the time-averaged coupling constants[13,18]. The mole fractions of the rotamers (Table VIA) were calculated by using the values $(J_{5,6})_1 = (J_{5,6'})_2 = 2.0$ Hz; $(J_{5,6})_2 = (J_{5,6'})_1 = 11.1$ Hz; and $(J_{5,6})_3 = (J_{5,6'})_3 = 1.6$ Hz. The preference for a rotamer evidently depends on the configuration at C-4, which is in accordance with our previous finding[1] (Table VIB). In Me_3Si-gluco-, -manno-, -altro-, and -allopyranoses (Me_3SiO-4 equatorial), the rotamer *3* is strongly favoured and rotamer *1* is



1 *2* *3*

Fig. 1. The three staggered rotamers (*1*–*3*) of the C-5–CH_2OSiMe_3 group in Me_3Si-aldohexopyranoses.



7 8 9 10

TMS = Me_3Si

Fig. 2. The $^4C_1$(D) conformation of 1,2,3,4,6-pentakis-*O*-trimethylsilyl derivatives of *β*-D-allopyranose (**8**), *α*-D-talopyranose (**9**), and *β*-D-talopyranose (**10**) with the favoured rotamers of their C-5–CH_2OSiMe_3 groups.

nearly absent. However, for Me$_3$Si-galacto-, and -talo-pyranoses (Me$_3$SiO-4 axial), rotamer *1* prevails and rotamer *3* is nearly absent. The geminal coupling constants $J_{6,6'}$ also reflect these conformational preferences. According to MO calculations[19], the geminal coupling constant increases algebraically with the rotamer in which the C-6–C-5–O-5 plane bisects the axis between H-6 and H-6′ (rotamer *1*). The values of $J_{6,6'}$ for compounds **7** and **8** agree with those for Me$_3$Si-gluco- and -manno-pyranoses, and the same holds for compounds **9** and **10**, and for the Me$_3$Si-galacto-pyranoses (*cf.* Tables VIA and VIB).

The structures of compounds **7–10** are shown in Fig. 2.

TABLE VI

CALCULATED[a] MOLE FRACTIONS OF THE ROTAMERS *1*, *2*, AND *3* OF THE C-5–C-6 FRAGMENT IN Me$_3$Si-ALDOHEXOPYRANOSES

Parent sugar	n_1	n_2	n_3	$J_{6,6'}$
A β-D-Alt*p* (**7**)	0.06	0.38	0.56	−11.0
β-D-All*p* (**8**)	0.00	0.35	0.65	−11.0
α-D-Tal*p* (**9**)	∼0.66	∼0.22	∼0.12	−9.6
β-D-Tal*p* (**10**)	0.50	0.46	0.04	−9.5
B[a] α-D-Glc*p*	0.00	0.23	0.77	−11.5
β-D-Glc*p*	0.03	0.34	0.63	−11.0
α-D-Man*p*	0.02	0.29	0.69	−11.7
β-D-Man*p*	0.00	0.36	0.64	−11.2
α-D-Gal*p*	0.55	0.45	0.00	−9.5
β-D-Gal*p*	0.61	0.34	0.05	−9.5

[a] Ref. 1.

The influence of the Me$_3$SiO-6 group on the chemical shifts of the ring protons

The differences in chemical shifts ($\Delta\delta$) between corresponding ring protons in Me$_3$Si-6-deoxyaldohexopyranoses and Me$_3$Si-aldohexopyranoses are presented in Table VII. Replacement of a hydrogen atom at C-6 by an OSiMe$_3$ group has a profound influence on H-4, namely, a deshielding of 0.31–0.39 p.p.m. for axial positions and 0.24 p.p.m. for equatorial positions. The effect on H-5 is smaller; a shielding of 0.08–0.18 p.p.m. is observed. The chemical shifts of the more remote protons, H-1, H-2, and H-3, undergo rather small changes.

In general, to explain the substituent effect on the chemical shift of a proton, a series of factors are considered, like electric-field, inductive, anisotropic, mesomeric, and Van der Waals effects. A reasonable interpretation of the influence of an OSiMe$_3$ group at C-6 can be given in terms of electric-field and inductive effects; the changes in δ-values of H-1, H-2, and H-3 are too small and too irregular to be amenable to calculation. The electric-field effect of the OSiMe$_3$ group arises mainly from the large negative charge[20] (0.46 e) on the oxygen atom. The contribution of the Si atom to this effect can be neglected because its charge is much smaller than that of the oxygen atom and a more remote position of the Si atom is highly probable. For the calculation of the electric-field effect δ_E (in p.p.m.) on the chemical shift, the following equation[21] was used:

$$\delta_E = n_i\left(-12.5\cdot10^{-6}\sum_{i=1}^{3}\frac{q_i\cos\theta_i}{r_i^2} - 17.0\cdot10^{-6}\sum_{i=1}^{3}\frac{q_i^2}{r_i^4}\right),$$

where r_i is the length of the radius vector between the proton and the oxygen atom in rotamer i of the C-5–CH_2OSiMe_3 group, and θ_i is the angle between this vector and the C–H bond. The contributions of the three rotamers (Fig. 1) were calculated, according to their respective mole fractions (Table VIB). Using the following bond lengths: C–H = 1.07 Å, C–C = 1.54 Å, and C–O = 1.43 Å, and assuming that all carbon atoms have tetrahedral symmetry, the contributions of the electric-field effect (δ_E) on H-4 and H-5 were calculated for an ideal-chair conformation (Table VII).

TABLE VII

OBSERVED AND CALCULATED DIFFERENCES[a] IN CHEMICAL SHIFTS BETWEEN THE METHINE PROTONS IN Me_3Si-6-DEOXYALDOHEXOPYRANOSES AND Me_3Si-ALDOHEXOPYRANOSES

Configuration	*Δδ (observed)*					*δ_E (calc.)*		*$\delta_E+\delta_I$ (calc.)*	
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-4*	*H-5*	*H-4*	*H-5*
α-D-Glc*p*	+0.08	−0.01	+0.06	+0.39	−0.11	+0.14	−0.35	+0.34	−0.05
β-D-Glc*p*	+0.04	0.00	+0.06	+0.33	−0.08	+0.09	−0.35	+0.29	−0.05
α-D-Man*p*	+0.11	+0.01	+0.03	+0.35	−0.14	+0.11	−0.35	+0.31	−0.05
β-D-Man*p*	0.00	0.00	+0.05	+0.31	−0.08	+0.10	−0.35	+0.30	−0.05
α-D-Gal*p*	+0.05	+0.03	−0.03	+0.24	−0.18	+0.07	−0.39	+0.27	−0.09
β-D-Gal*p*	+0.01	+0.04	+0.08	+0.24	−0.14	+0.07	−0.40	+0.27	−0.10

[a] A positive value implies a deshielding (a negative sign, shielding) of the proton in the aldohexopyranose with respect to the 6-deoxy analogue.

It is difficult to get a good estimation of the contributions of the inductive effect (δ_I) on the chemical shift of a proton, because this effect cannot completely be separated from the electric-field effect. From comparison of chemical shift data[22] of aliphatic ethers with those of hydrocarbons, the δ_I values for H-4 and H-5 were estimated to be about +0.2 and +0.3 p.p.m., respectively. The calculated total influence ($\delta_E+\delta_I$) of the introduction of the Me_3SiO-6 group on the chemical shifts of H-4 and H-5 are also summarized in Table VII. A comparison of the observed and calculated differential shieldings shows that the magnitude of the effects, as well as the trends for the shifts in the various compounds, are reasonably well reproduced by this simple model.

Configurational effects on the chemical shifts of the ring protons

The chemical shifts of the ring protons of Me_3Si-aldohexopyranoses and their 6-deoxy analogues show some interesting regularities, which can be interpreted in terms of shielding and deshielding effects arising from changes in configuration. By analogy with the rules described by Lemieux *et al.*[13] for per-*O*-acetylaldohexopyranoses, empirical rules can be formulated for the estimation of the chemical shifts of the ring protons. Using the observed chemical shifts of the ring protons of pentakis-Me$_3$Si-β-D-glucopyranose (all ring protons axial) as reference values (Table VIII), the following shift alterations are found for Me$_3$Si-aldohexopyranoses:

(*1*) If the proton under consideration has remained axial, (*a*) 0.20 p.p.m. must be added for an axial Me$_3$SiO group at a neighbouring carbon atom, and (*b*) 0.35 p.p.m. must be added for an axial Me$_3$SiO group at the next to neighbouring carbon atom.

(*2*) If the proton under consideration has reached the equatorial position, (*a*) 0.50 p.p.m. must be added for this configurational change, (*b*) 0.05 p.p.m. must be subtracted for an axial Me$_3$SiO group at a neighbouring carbon atom, and (*c*) 0.10 p.p.m. must be subtracted for an axial Me$_3$SiO group at the next to neighbouring carbon atom.

TABLE VIII

OBSERVED AND CALCULATED CHEMICAL SHIFTS δ (IN P.P.M.) OF RING PROTONS IN Me$_3$Si-MONOSACCHARIDES

Parent sugar	*H-1*		*H-2*		*H-3*		*H-4*		*H-5*	
	Obs.	*Calc.*	*Obs.*	*Calc.*	*Obs.*	*Calc.*	*Obs.*	*Calc.*	*Obs.*	*Calc.*
β-D-Glc*p*[a]	4.55	4.55	3.18	3.18	3.45	3.45	3.48	3.48	3.27	3.27
α-D-Glc*p*	5.06	5.05	3.38	3.38	3.78	3.80	3.51	3.48	3.63	3.62
α-D-Man*p*	4.97	5.00	3.73	3.63	3.85	4.00	3.93	3.83	3.51	3.62
β-D-Man*p*	4.83	4.75	3.79	3.68	3.59	3.65	3.82	3.83	3.15	3.27
α-D-Gal*p*	5.01	5.05	3.83	3.73	3.88	4.00	3.95	3.98	3.87	3.82
β-D-Gal*p*	4.51	4.55	3.58	3.53	3.64	3.65	3.91	3.98	3.55	3.47
β-D-Alt*p*	5.09	5.10	3.59	3.63	3.83	3.90	3.96	4.03	3.70	3.62
β-D-All*p*	4.85	4.90	3.32	3.38	4.00	3.95	3.67	3.68	3.72	3.62
α-D-Tal*p*	4.97	5.00	3.44	3.53	3.88	4.20[b]	3.88	3.88	3.88	3.82
β-D-Tal*p*	4.74	4.75	3.71	3.58	3.70	3.85	3.76	3.88	3.46	3.47
6-Deoxy-α-D-Glc*p*	4.98	5.05	3.39	3.38	3.72	3.80	3.12	3.13	3.74	3.77
6-Deoxy-β-D-Glc*p*	4.51	4.55	3.18	3.18	3.39	3.45	3.15	3.13	3.35	3.42
α-L-Rha*p*	4.86	5.00	3.72	3.63	3.82	4.00	3.58	3.48	3.65	3.77
β-L-Rha*p*	4.83	4.75	3.79	3.68	3.54	3.65	3.51	3.48	3.23	3.42
α-L-Fuc*p*	4.96	5.05	3.80	3.73	3.91	4.00	3.71	3.74	4.05	3.97
β-L-Fuc*p*	4.50	4.55	3.54	3.53	3.56	3.65	3.67	3.74	3.69	3.62

[a] Reference values. [b] Discrepancy, probably arising from multiple corrections.

Because the influence of the Me$_3$SiO-6 group is mainly restricted to the chemical shifts of H-4 and H-5, these rules can be adapted for application to the 6-deoxyaldohexopyranoses. The following additional corrections must be made (*cf.* Table VII): for H-4 in an axial position, 0.35 p.p.m. must be subtracted; and in an equatorial position, 0.24 p.p.m.; for H-5, 0.15 p.p.m. must be added.

In Table VIII, observed and calculated chemical shifts of a number of Me_3Si-monosaccharides are given. The applicability of the rules to both series of compounds supports the conclusion that all have the same conformation.

DISCUSSION

P.m.r. is widely applied for the determination of the structure of sugars and their derivatives in solution. This study shows that, in several cases, it is difficult to draw conclusions about the conformation of a pyranoid ring solely on the basis of vicinal coupling constants. The theoretical coupling constants of more than one ideal conformation may be in reasonable accordance with the experimental values. Additional evidence from long-range coupling(s), chemical-shift data, and/or considerations on ring distortions are then indispensable to make a final decision on the ring structure. As a consequence, it is an over-simplification to derive the ring conformation solely from $J_{1,2}$. Inspection of Table III makes clear that quite different conformations have almost similar $J_{1,2}$ coupling constants.

Me_3Si-aldohexopyranoses and their 6-deoxy analogues have almost the same ring structure, which illustrates that an Me_3SiO group at C-6 does not introduce a significant ring-deformation. The substituent effect of the Me_3SiO group at C-6 on the chemical shifts of the ring protons can be interpreted in terms of electric-field and inductive effects. The configurational effects on the chemical shifts of the ring protons, which arise from the alteration of the position of one or more Me_3SiO groups, attached to the ring, from equatorial to axial and *vice versa*, cannot be explained with these simple model calculations. This aspect is still under investigation.

In Me_3Si-saccharides, the rings are more deformed than in the corresponding peracetyl derivatives, as a consequence of the greater steric requirement of the Me_3Si groups[1]. However, the steric interactions of the Me_3SiO groups are not such as to prevent 1,3-diaxial orientations [*e.g.*, pentakis-Me_3Si-α-D-talopyranose (**9**)].

EXPERIMENTAL

Monosaccharides. — 6-Deoxy-D-glucose, α-D-talose, α-L-rhamnose, and α-L-fucose were obtained commercially. β-D-allose and β-D-altrose were supplied by Dr. J. M. Ballard and Dr. E. Zissis, respectively.

G.l.c. — Analytical g.l.c. was carried out on a F and M Gas Chromatograph Model 700, equipped with a dual flame-ionization detector and coiled stainless-steel columns (2.70 m × 3.2 mm) containing 3% OV-17 on Chromosorb W (HP), 80–100 mesh, at 150°. Preparative g.l.c. was performed on a Pye Gas Chromatograph Model 105 provided with a flame-ionization detector and a glass column (2.0 m × 9.6 mm) containing 10% OV-17 on Chromosorb W/NAW, 30–60 mesh, at 190°. Nitrogen was used as carrier gas.

Per-O-trimethylsilyl derivatives. — The compounds **3**, **5**, **7**, **8**, and **9** were prepared by silylation[2] of the corresponding monosaccharides. To obtain compounds

1 and **2**, 6-deoxy-D-glucose was anomerized in dry pyridine at 80° for 2 h, followed by silylation at 80°. Preparative t.l.c. on Silica gel G (Merck), using dry benzene as solvent[23], was used for the separation and isolation of both anomers. After spraying with 1% of morine in methanol, the zones were detected under u.v. light and extracted by chloroform.

Compounds **4**, **6**, and **10** were isolated from anomeric mixtures by preparative g.l.c. (**4** and **10**) or preparative t.l.c. (**6**). These mixtures were obtained after anomerization of the free sugars in water for 24 h, followed by lyophilization and subsequently silylation at room temperature. The purity of all compounds was tested by analytical g.l.c.

P.m.r. spectroscopy. — Spectra were obtained with a Varian HR-220 spectrometer (TNO Central Laboratories, Delft, The Netherlands) or a Varian HA-300 spectrometer (Laboratory of N.m.r. spectroscopy, Ghent, Belgium), operating in the field-sweep mode at a probe temperature of ~25°. Spectra of the pure Me_3Si-derivatives were recorded for 3–10% (w/v) solutions in acetone-d_6 or benzene-d_6. Spectrum simulations were run on a 16 k Varian 620 i computer coupled with an XL-100 spectrometer, using a modified and extended SIMEQ[12] spin-simulation program. Chemical shifts are given relative to tetramethylsilane (indirect to acetone-d_6: $\delta = 2.05$ p.p.m.) with an accuracy of ~0.005 p.p.m. The accuracy of the coupling constants is ~0.1 Hz.

ACKNOWLEDGMENTS

We thank Mr. E. Zissis for the gift of β-D-altrose, Dr. J. M. Ballard for the gift of β-D-allose, Ir. P. E. J. Verwiel and Mr. J. L. Hoogendoorn (TNO Central Laboratories, Delft, The Netherlands) for recording the 220-MHz p.m.r. spectra, Professor Dr. M. Anteunis and Dr. G. J. Gelan (Laboratory of N.m.r. Spectroscopy, University of Ghent, Belgium) for recording the 300-MHz p.m.r. spectrum, and Mrs. L. R. Smaling–Hakkert for technical assistance. This investigation was supported by the Netherlands Foundation for Chemical Research (SON), with financial aid from the Netherlands Organization for the Advancement of Pure Research (ZWO).

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