Carbohydrate Research, 174 (1988) 354–359
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Note

A ^{1}H- and ^{13}C-n.m.r. spectroscopic analysis of six pseudohexoses*

KLAUS BOCK, JOSÉ FERNANDEZ BOLANOS GUZMAN,
Department of Organic Chemistry, The Technical University of Denmark, DK-2800 Lyngby (Denmark)

AND SEIICHIRO OGAWA
Department of Applied Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi, Kohoku-ku, Yokohama 223 (Japan)

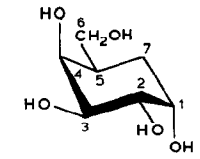
(Received June 16th, 1987; accepted for publication, August 11th, 1987)

The application of ^{1}H- and ^{13}C-n.m.r. spectroscopy in the structural and conformational analysis of carbohydrates and their derivatives has been reviewed[1,2]. We now report a complete analysis of the ^{1}H- and ^{13}C-n.m.r. parameters of the six pseudohexoses related to α- (**1**) and β-DL-galactopyranose (**2**), α- (**3**) and β-DL-glucopyranose (**4**), and α- (**5**) and β-DL-mannopyranose (**6**) for solutions in D_2O. Pseudohexose is the term given to a hexopyranose in which the ring oxygen is replaced by CH_2. The data are compared with those for the corresponding methyl hexosides (**7–12**) in order to evaluate the influence of the ring oxygen. ^{1}H-N.m.r. data on some pseudohexoses have been discussed briefly[3], but recently Paulsen and von Deyn[4] have published data on pseudo-α- and -β-D-glucopyranose which accord with the data now presented. The use of a 500-MHz spectrometer rather than a 400-MHz instrument allowed the data to be interpreted more accurately, particularly for pseudo-β-D-glucopyranose (**4**). Paulsen and von Deyn[4] also reported ^{1}H-n.m.r. data for pseudo-α- and -β-L-idopyranose. Watkins *et al.*[5] have recently described the X-ray structure of pseudo-β-DL-glucopyranose penta-acetate.

Recent synthetic work[6–10] has made the pseudohexoses **1–6** available and the ^{1}H- and ^{13}C-n.m.r. spectra have now been measured at 500 and 125.7 MHz, respectively. The ^{1}H-n.m.r. data, for 0.1M solutions in D_2O at 300 K, are shown in Table I. The assignments are based on homonuclear COSY experiments[11] which allowed unambiguous assignment of all the signals. The determination of the *J* values was made on a first-order basis from the one-dimensional spectra, except for protons where the chemical shift coincidence resulted in second-order spectra. The proton-decoupled ^{13}C-n.m.r. spectra were recorded likewise and the results are given in Table II. The assignments were based on heteronuclear shift correlation experiments (CHORTLE)[12] and were unambiguous, except those for C-2 and C-3 of

*Dedicated to Professor Hans Paulsen.

0008-6215/88/$ 03.50



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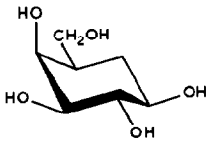

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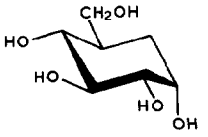

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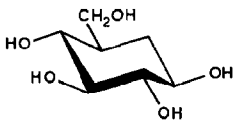

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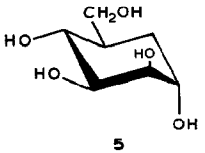

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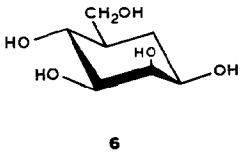

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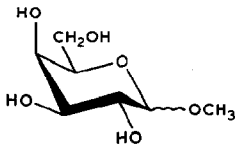

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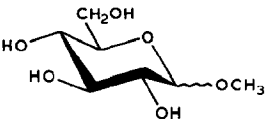

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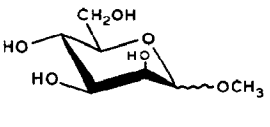

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pseudo-α-DL-galactopyranose (**1**) due to the chemical shifts of the H-2 and H-3 signals being identical. The assignments given were based on the long-range carbon–proton coupling constants, which are given together with the one-bond carbon–proton couplings for **1–6** (Table II). The ^{13}C-n.m.r. data for the corresponding methyl hexosides **7–11** are given in Table III.

A comparison of the ^{1}H-n.m.r. chemical shifts and J values given in Table I with the values reported[1] for the corresponding methyl hexosides show no unexpected results. The resonances of H-1 and H-5 are shifted up-field by ~1.1 and ~2.0 p.p.m., respectively, due to the lack of the ring oxygen atom, whereas all other chemical shift differences are <0.2 p.p.m. This result, together with the $^{3}J_{H,H}$ values, strongly supports the conclusion that each compound adopts an almost unperturbed $^{4}C_{1}$ chair conformation.

However, the J values for H-5,6,6′ in **1–6** are somewhat different from those found[1] for the corresponding methyl hexosides **7–12**, which indicate that the rotamer populations for the C-5–C-6 bond are different[13]. This is based on the assumption that the assignment of the signals for H-6_{proR} and H-6_{proS} is correct. The present results are based on the same order of chemical shifts as those found for the corresponding methyl glycosides.

Based on these assumptions, the results in Table I indicate that the "gt" rotamer[13] preponderates in **1** and **2** and that an appreciable amount of the "gg"

TABLE I

^{1}H-N.M.R. DATA[a] FOR THE PSEUDOHEXOSES

Compound	*Chemical shifts (p.p.m.)*								
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*H-7*	*H-7'*
α-Gal (**1**)	4.11	3.72	3.72	4.09	2.03	3.64	3.52	1.68	1.55
β-Gal (**2**)	3.57	3.55	3.44	4.04	1.79	3.67	3.54	1.79	1.39
α-Glc (**3**)	4.10	3.43	3.59	3.29	1.88	3.73	3.68	1.92	1.47
β-Glc (**4**)	3.58	3.24	3.30	3.32	1.64	3.77	3.63	2.01	1.28
α-Man (**5**)	4.00	3.94	3.70	3.55	1.83	3.73	3.67	1.76	1.69
β-Man (**6**)	3.82	4.05	3.48	3.52	1.57	3.80	3.63	1.82	1.59

	Observed first-order coupling constants (Hz)											
	$J_{1,2}$	$J_{1,7}$	$J_{1,7'}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{5,7}$	$J_{5,7'}$	$J_{7,7'}$
α-Gal (**1**)		3.2	2.5				8.0	6.2	11.0	3.2	13.5	14.8
β-Gal (**2**)				9.8	3.2	0.9	7.8		11.0			
α-Glc (**3**)	3.0	3.0	3.0	10.0	9.5	10.0	3.5	5.5	11.5	3.0	13.0	15.0
β-Glc (**4**)	9.0	3.8	11.5	9.0			3.5	6.0	11.5	3.2	10.0	13.5
α-Man (**5**)	3.0	3.0	3.0	3.2	10.0	10.0	3.5	6.2	11.8	3.0	12.5	15.0
β-Man (**6**)	2.8	2.2	11.0	2.9	10.0	10.0	3.0	6.0	11.5			

[a]Measured at 500 MHz on 0.1M solutions in D_2O at 300 K (internal acetone, 2.22 p.p.m.).

rotamer is present for **3–6**, but that the population of the "tg" rotamer is low for all compounds, as also found for the hexosides[13].

A comparison of the ^{13}C-n.m.r. chemical shifts (Table II) for **1–6** with the data published[2] for the corresponding methyl glycosides **7–12** shows significant differences only for C-1 and C-5 (23–25 and 33–36 p.p.m., respectively). All other chemical shift differences are in the range 1–3 p.p.m. and do not suggest any major conformational differences between the two classes of compounds.

A comparison of the $^1J_{C,H}$ values for the pseudohexoses **1–6** (Table II) and the methyl glycosides **7–11** (Table III) shows that the difference of 10 Hz between the $J_{C\text{-}1,H\text{-}1}$ values for pyranosides[14] does not occur in the pseudohexoses, reflecting the effect[14] of the ring oxygen. However, there appears to be a consistent difference of 4–5 Hz between the $^1J_{C,H}$ values for the pseudohexoses with axial (141–144 Hz) and equatorial C–H bonds (147–148 Hz). This difference is not found with the same consistency for the hexopyranosides (Table III), but has been observed and discussed in connection with glycopyranosyl azides[15] and KDO derivatives[16].

The patterns of the C–H long-range coupling constants follow the proposed rules[17,18] and make it possible to assign the carbon atoms which give well resolved signals both for the pseudohexoses **1–6** and the methyl glycosides **7–11** (Tables II and III). The large $^2J_{C\text{-}6,H\text{-}5}$ values observed for the galactopyranosides, not shown by the glucopyranosides due to the relatively large population of the "gg" rotamers in the *gluco* compared to the *galacto* compounds, are also seen clearly for the

TABLE II

^{13}C-N.M.R. CHEMICAL SHIFTS[a] AND ^{13}C–^{1}H COUPLING CONSTANTS[b] FOR THE PSEUDOHEXOSES

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-7*
	69.3	71.8	72.0	70.8	37.0	63.3	28.3
	147.8	143.0	142.5	148	126	143	129
α-Gal (**1**)	6.0 H-7	5.0 H-1	5.2 H-1	m[c]	m	6.5 H-5	m
	1.3 H-7′	5.0 H-7	5.2 H-2			2.0 H-4	
		5.0 H-3	5.2 H-4			2.0 H-7	
		5.0 H-4				2.0 H-7′	
	72.6	75.7	74.9	70.3	39.3	63.1	29.6
	143.0	144	143.0	147	128	142.5	128
β-Gal (**2**)	5.0 H-2	m	4.5 H-2	m	m	7.0 H-5	m
	5.0 H-7		4.5 H-4				
	5.0 H-7′						
	69.6	74.6	75.2	73.9	38.8	63.1	29.6
	148.5	141.0	143	143	127.5	142.5	128
α-Glc (**3**)	6.0 H-7	m	m	m	m	2.3 H-5	4.5 H-1
						2.3 H-4	4.5 H-5
						2.3 H-7	4.5 H-6
						2.3 H-7′	
	71.8	77.7	77.5	73.3	40.8	62.9	32.4
	143.5	143.5	144	143	126	143.6	129.0
β-Glc (**4**)	4.5 H-7′	3.4 H-3	5.2 H-2	m	m	2.3 H-5	m
	4.5 H-7	3.4 H-1	5.2 H-4			2.3 H-4	
	4.5 H-2	3.4 H-7	2.0 H-1			2.3 H-7	
	2.0 H-3		or H-5			2.3 H-7′	
	or H-5						
	69.8	73.4	73.1	71.1	39.5	63.3	29.1
	147.8	147.0	143	144	127.5	143.6	128
α-Man (**5**)	5.0 H-7′	5.0 H-7	m	m	m	2.0 H-5	m
	4.0 H-2	4.0 H-1				2.0 H-4	
						2.0 H-7	
						2.0 H-7′	
	69.5	73.8	74.9	70.7	41.1	63.3	29.4
	143.0	147.0	141	143	128	143.3	129.8
β-Man (**6**)	5.0 H-7′	6.0 H-7	5.1 H-4	m	m	2.0 H-5	m
	5.0 H-7	2.0 H-7′	5.1 H-2			2.0 H-4	
						2.0 H-7	
						2.0 H-7′	

[a]Measured at 125.7 MHz on 0.1M solutions in D_2O at 300 K (internal 1,4-dioxane, 67.4 p.p.m.). [b]Measured using the gated technique to ±0.5 Hz. [c]Unresolved multiplet.

pseudohexoses. The results accord with the conclusions based on the $J_{5,6}$ values as discussed above.

Thus, the solution behavior of the pseudohexoses is similar to that of the corresponding methyl glycosides and the n.m.r. data presented above will make it easier to interpret the results from biological systems where the pseudohexoses are used as analogs for normal carbohydrate derivatives.

TABLE III

^{13}C–^{1}H COUPLING CONSTANTS[a] FOR THE METHYL HEXOSIDES

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*OMe*
	170.2	145.8	144.0	146.0	142	145	143.7
α-Gal-OMe	4.3 OMe	5.2 H-3	4.5 H-1	m	m	m	3.7 H-1
(**7**)	1.6 H-5	5.2 H-4	4.5 H-2				
		1.2 H-1	4.5 H-4				
	160.5	148	144	146.0	142.0	143.5	144.5
						146.0	
β-Gal-OMe	6.1 H-2[b]	m	m	m	m	6.3 H-5	4.5 H-1
(**8**)	4.5 OMe					1.2 H-4	
	2.5 H-5						
	1.3 H-3						
	170.0	146.0	147.0	144.0	144	146.6	143.6
α-Glc-OMe	4.3 OMe	5.8 H-3	5.6 H-2	m	m	3.3 H-4[c]	3.8 H-1
(**9**)		1.0 H-1	5.6 H-4			1.7 H-5	
		1.0 H-4	3.7 H-1				
			2.0 H-5				
	161.0	145.0	143	146	143.0	144.3	144.4
						142.8	
β-Glc-OMe	6.3 H-2[b]	4.3 H-3	2.4 H-5[b]	2.3 H-6[b]	m	3.3 H-4	4.6 H-1
(**10**)	4.5 OMe		1.2 H-1	1.1 H-6		1.9 H-5	
	2.5 H-5						
	1.2 H-3						
	171.0	149.0	144.0	147	145	143	144.4
α-Man-OMe	4.3 OMe	1.8 H-1[d]	3.8 H-1[d]	m[e]	m	m	3.8 H-1
(**11**)	1.3 H-5	1.4 H-3	1.6 H-5				
	0.8 H-2						

[a]Measured at 125.7 MHz on 0.2M solutions in D_2O at 300 K, using the gated technique. Accuracy ±0.3 Hz. [b]Data in agreement with published values[19]. [c]Data in agreement with published values[20]. [d]Confirmed by selective decoupling experiments[21]. [e]Unresolved multiplet.

EXPERIMENTAL

Compounds **1–6** were available through earlier synthetic work[6–11]; pseudo-α-DL-galactose[7,8] (**1**), m.p. 169–170.5° (from ethanol) (lit.[7] 173–174°); pseudo-β-DL-galactose (**2**), prepared in the usual way[6] from the corresponding penta-acetate[9,10], had m.p. 173–174° (from ethanol) (*Anal.* Calc. for $C_7H_{14}O_5$: C, 47.19; H, 7.92. Found: C, 46.88; H, 7.67); pseudo-α-DL-glucose[6] (**3**), m.p. 142–143° (from ethanol–water) (lit.[6] m.p. 146–147°); pseudo-β-DL-glucose[6,7] (**4**), m.p. 129–130° (from ethanol–water) (lit.[7] m.p. 132–133°); pseudo-α-DL-mannose[7] (**5**), syrup; pseudo-β-DL-mannose[7] (**6**), m.p. 198–199° (from ethanol–water) (lit.[7] m.p. 198–199°). Melting points were measured with a MEL-TEMP capillary melting-point apparatus and are uncorrected.

N.m.r. spectra were recorded with a Bruker AM 500 spectrometer operating at 500 MHz for ^{1}H spectra. 0.1M Solutions in D_2O were used at 300 K (internal acetone, 2.22 p.p.m.; DOH signal at 4.75 p.p.m.). A sweep width of 5000 Hz,

using 32 k of computer memory giving a digital resolution of 0.3 Hz/pt., was used together with pulse angles of 90° (10 μs). COSY-90 experiments[11] were performed using Bruker standard software. The ^{13}C spectra were obtained on the same spectrometer operating at 125.7 MHz at 300 K (internal 1,4-dioxane, 67.4 p.p.m.). A sweep width of 25,000 Hz, using 62 k of computer memory giving a digital resolution of 0.8 Hz/pt., was used together with pulse angles of 5 μs (90° = 8.5 μs). ^{13}C–^{1}H correlation experiments were made using CHORTLE experiments[12]. Coupled carbon spectra were measured in the gated mode.

ACKNOWLEDGMENTS

The n.m.r. spectrometer was provided by the Danish Natural Science Research Council and The Carlsberg Foundation. We thank Mr. Y. Shibata and Mr. M. Orihara for the synthesis of **1–6**.

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