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Note

Carbon-13 n.m.r. studies on D-glucopyranose acetates. Studies on D-glucopyranose tetraacetates and 2,3; 5,6-di-*O*-isopropylidene-α-D-mannofuranosyl-D-glucopyranose tetraacetates

HAJIME KOMURA, AKIRA MATSUNO, YOSHIHARU ISHIDO*,
Department of Chemistry, Faculty of Science, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152 (Japan),

KATSUHIKO KUSHIDA, AND KIYOSHI AOKI
The Application Laboratory, Nippon Electric Varian, Yotsuya, Fuchu-shi, Tokyo 183 (Japan)
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We can find only a few, systematic carbon-13 n.m.r. studies on protected simple carbohydrates (permethylated[1,2] or peracetylated[3–7] derivatives), in contrast to those on nonprotected derivatives. However, it is important to study the correlations between structure and chemical shifts of the skeletal carbon atoms for routine structural determinations of reaction products in synthetic carbohydrate chemistry.

In this article, we focus on the chemical-shift changes caused to D-glucopyranosyl skeletal carbon atoms by changing one of the five acetoxyl groups of 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**1**) to a hydroxyl group (by deacetylation) or to a 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranosyloxy group (mannofuranosylation)*, and two such groups of 1,2,3,4,6-penta-*O*-acetyl-α-D-glucopyranose (**2**).

EXPERIMENTAL

Carbon-13 n.m.r. spectra. — Spectra were measured at room temperature in chloroform-*d* with tetramethylsilane (internal standard) with a Varian NV-14 (15.1 MHz) or CFT-20 (20 MHz) spectrometer in the pulsed, Fourier-transform mode under proton-noise decoupling, and in the deuterium-lock mode. Signals were assigned by partial decoupling, by selective proton irradiation, or by reference to published data: compounds **1** (ref. 3), **2** (ref. 3), and 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranose[8] (**10**).

*We selected α-D-mannofuranosyl-D-glucopyranoses for determining the shift on glycosylation, because the resonance lines arising from each skeleton appear in quite a different range and make assignment of the lines easy (see Table I). The differences between the shift by mannofuranosylation and by glucopyranosylation will be reported elsewhere.

Materials. — D-Glucopyranose penta- and tetra-acetates were prepared according to known procedures: **1** (ref. 9), **2** (ref. 9), 2,3,4,6- (**3**) (ref. 10), 1,3,4,6- (**4**) (ref. 11), 1,2,4,6- (**5**) (ref. 12), 1,2,3,6- (**6**) (ref. 13), and 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose[14] (**7**), 2,3,4,6- (**8**) (ref. 15), and 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose[16] (**9**). The 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranosyl-D-glucopyranose tetraacetates; 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranosyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**11**); 1,3,4,6-tetra-*O*-acetyl-2- (**12**), 1,2,4,6-tetra-*O*-acetyl-3- (**13**), 1,2,3,6-tetra-*O*-acetyl-4- (**14**), and 1,2,3,4-tetra-*O*-acetyl-6-*O*-(2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranosyl)-β-D-glucopyranose (**15**); 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranosyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (**16**), and 1,3,4,6-tetra-*O*-acetyl-2-*O*-(2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranosyl)-α-D-glucopyranose (**17**) were synthesized by condensation of 2,3;5,6-di-*O*-isopropylidene-1-*O*-phenoxycarbonyl- or -1-*O*-(2,2,2-trichloroethoxycarbonyl)-α-D-mannofuranose[17] with the corresponding D-glucopyranose tetraacetates. Details of the syntheses will be reported elsewhere.

DISCUSSION

Chemical shifts of the D-glucopyranose tetraacetates **3–9**, and 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranosyl D-glucopyranose tetraacetates **11–17** are given in Table I, together with data for the reference compounds **1**, **2**, and **10**.

The shifts of the resonance position for the respective skeletal carbon atoms of the carbohydrate are indicated as $\Delta\delta^{OR}$, defined as follows:

$\Delta\delta^{OR} = \delta$ (compound in question) $- \delta$ (standard compound having an OR group). Thus $\Delta\delta_n^{OAc}$ denotes the chemical-shift change on the *n*th carbon atom following deacetylation or replacement of an acetyl group by a 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranosyl group. Downfield shifts are indicated by positive values.

The deacetylation shifts ($\Delta\delta^{OAc}$) calculated by reference to the standard compound **1** are summarized in Table II, together with two deacetylation shifts based on **2**. Typical shifts are not observed at the deacetylated position (α-carbon; $\Delta\delta_\alpha^{OAc} = +0.4$ to $+0.8$ p.p.m.), but on the adjacent carbon atom(s) (β-carbon; $\Delta\delta_\beta^{OAc} = +2$ to $+3$ p.p.m.), in contrast to the cyclohexanol equatorial acetates ($\Delta\delta_\alpha^{OAc} =$ approximately -3, $\Delta\delta_\beta^{OAc} =$ approximately $+4$ p.p.m.)[18] and acetoxy steroids ($\Delta\delta_\alpha^{OAc} = -1$ to -4, $\Delta\delta_\beta^{OAc} = +1$ to $+4$ p.p.m.)[19]. These differences may be due to interactions between the substituent to be changed and nearby substituents, especially on β-carbon atoms. Consequently, for the D-glucopyranose acetates, it is deduced that the primary upfield shift caused by deacetylation as observed in cyclohexanol acetates, and the downfield shift caused by the changes in interaction with the neighboring substituents, are practically cancelled out and result in only a small downfield shift on the α-carbon atom.

Deacetylation of the acylal acetoxyl group of **1** and **2**, to give **3** and **8**, respectively, causes a significant shift ($\Delta\delta_1^{OAc} = +3.6$ p.p.m. for **3**, and $\Delta\delta_5^{OAc} = -3$ p.p.m.

TABLE I

^{13}C-N.M.R. CHEMICAL SHIFTS[a] OF THE CARBOHYDRATE SKELETAL CARBONS OF D-GLUCOPYRANOSE PENTA- AND TETRA-ACETATES, AND 2,3;5,6-DI-*O*-ISOPROPYLIDENE-α-D-MANNOFURANOSYL D-GLUCOPYRANOSE TETRAACETATES

Compounds	*Glucopyranosyl moiety*[b]						*Mannofuranosyl moiety*[b]					
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
1	91.8	70.5	72.9	68.0	72.9	61.6						
2	89.2	69.4	70.0	68.1	70.0	61.6						
3	95.4	73.3	72.7	68.7	72.1	62.2						
4	93.8	71.3	75.1	68.0	72.6	61.8						
5	91.9	72.9*	73.3*	70.4	72.9*	62.1						
6	91.9	70.5	75.2*	68.5	75.0*	62.7						
7	91.9	70.6	72.9	68.4	75.1	61.0						
8	90.0	71.4	70.2	68.8	67.0	62.2						
9	91.5	69.8	73.2	68.0	69.8	61.9						
10							101.2	85.6	79.7	80.1	73.4	66.5
11	98.8	71.5	72.9*	68.2	72.4*	61.9	107.2	85.1	79.4	81.2	72.9*	66.8
12	94.0	74.5	73.0*	68.3	72.6*	61.6	106.8	85.2	79.4	81.1	73.0*	66.5
13	92.2	70.6*	78.1	70.3*	72.8**	61.7	108.3	85.3	79.5	81.0	73.2**	66.2
14	91.7	70.5	74.9*	73.5**	75.0*	62.6	109.3	85.5	79.6	81.6	73.1**	66.7
15	91.9	70.5	73.3*	68.0	73.5*	64.5	106.4	85.1	79.5	80.5	73.3*	66.7
16	91.4	70.2*	70.1*	68.6**	68.2**	61.8	102.4	84.9	79.6	81.1	73.0	66.7
17	88.9	72.1	70.8	68.5	69.9	61.8	104.8	85.1	79.4	81.3	73.0	66.8

[a]Chemical shifts in p.p.m. from internal Me_4Si, measured in $CDCl_3$. [b]Assignments of the resonances indicated by * or ** may be interchanged.

TABLE II

DEACETYLATION SHIFTS ($\Delta\delta^{OAc}$)[a] FOR THE D-GLUCOPYRANOSE ACETATES

Compound	*Deacetylation position*	$\Delta\delta^{OAc}$ (*p.p.m.*)					
		C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
3	1	+3.6	+2.8	−0.2	+0.7	−0.8	+0.6
4	2	+2.0	+0.8	+2.2	0	−0.3	+0.2
5	3	+0.1	+2.4	+0.4	+2.4	0	+0.5
6	4	+0.1	0	+2.3	+0.5	+2.1	+1.1
7	6	+0.1	+0.1	0	+0.4	+2.2	−0.6
8	1	+0.8	+2.0	+0.2	+0.7	−3.0	+0.6
9	2	+2.3	+0.4	+3.2	−0.1	−0.2	+0.3

[a]Calculated as $\delta(3-7) - \delta(1)$, or $\delta(8 \text{ or } 9) - \delta(2)$; downfield shift is indicated by a positive value.

for **8**), together with the typical downfield shifts on β-carbon atoms. As regards comparing the $\delta\Delta_2^{OAc}$ values of **3** and **8** with other, normal $\Delta\delta_\beta^{OAc}$ values, the interactions between C-1 and C-2 substituents seem to be similar to those in the other examples. Therefore, the larger downfield shifts observed at C-1 of **3** may be attributed to larger changes in the interaction between the C-1 equatorial substituent and the lone-pair electron lobes of the pyranoid ring-oxygen atom in *gauche* relationship, in contrast to the smaller downfield shift observed on C-1 of **8**, in which smaller interactions are expected between the axial substituent and the electron lobes, one being in *gauche* and the other in *anti* relationship.

A significant upfield shift in C-5 of **8** was observed, together with a set of smaller, downfield shifts on the adjacent carbon atoms (C-4 and C-6). A similar tendency may be observed in the β anomer **3**, but the upfield shift on C-5 is very small. Although this set of shifts resembles the shift observed upon the hydrolysis of ethers to the corresponding alcohols (upfield shift on the α-carbon atom and a downfield shift on β-carbon atoms[20,21]), we could not find any positive evidence for the presence of an intermediate 2,3,4,6-tetra-*O*-acetyl-*aldehydo*-D-glucose in equilibrium with **3** and **8**.

Deacetylation of the primary acetoxyl group of **1** to give **7** causes, in addition to the typical downfield shift of C-5 (β-carbon atom), a small upfield shift ($\Delta\delta_6^{OAc} = -0.6$ p.p.m.) on the α-carbon atom. This different shift-tendency observed at C-6 may be explained by a contribution of smaller downfield shift resulting from the smaller decrease of steric interactions between the less-hindered primary (C-6) substituent and the neighboring groups.

Summarizing the deacetylation shifts for the glucopyranose pentaacetates, a typical downfield shift (2–3 p.p.m.) and small downfield shift (up to 1 p.p.m.) may be observed on the β- and α-carbon atoms, respectively, except with primary or acylal acetoxyl groups. (Fig. 1).

Table III summarizes the shifts observed when an acetyl group is replaced by a 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranosyl group ($\Delta\delta^{OAc}$; mannofuranosyl-

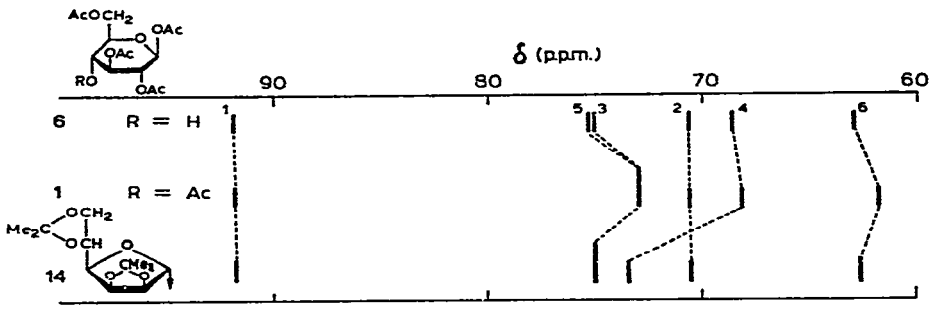

Fig. 1. Resonance positions of skeletal carbon atoms of 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**1**), 1,2,3,6-tetra-*O*-acetyl-β-D-glucopyranose (**6**), and 1,2,3,6-tetra-*O*-acetyl-4-*O*-(2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranosyl)-β-D-glucopyranose (**14**). (D-Glucopyranosyl moieties only.)

TABLE III

2,3;5,6-DI-*O*-ISOPROPYLIDENE-α-D-MANNOFURANOSYLATION SHIFTS ($\Delta\delta^{OAc}$)[a] OF THE D-GLUCOPYRANOSYL MOIETY, CALCULATED FROM 2,3;5,6-DI-*O*-ISOPROPYLIDENE-α-D-MANNOFURANOSYL D-GLUCOPYRANOSE TETRAACETATES

Compound	*Mannosylation position*	$\Delta\delta^{OAc}$ (*p.p.m.*)					
		C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
11	1	+7.0	+1.0	0	+0.2	−0.5	+0.3
12	2	+2.2	+4.0	+0.1	+0.3	−0.3	0
13	3	+0.2	+0.1	+5.2	+2.3	−0.1	+0.1
14	4	−0.1	0	+2.0	+5.5	+2.1	+1.0
15	6	+0.1	0	+0.4	0	+0.6	+2.9
16	1	+2.2	+0.8	+0.1	+0.5	−1.8	+0.2
17	2	−0.3	+2.7	+0.8	+0.4	−0.1	+0.2

[a]Calculated as $\delta(11-15) - \delta(1)$, or $\delta(16 \text{ or } 17) - \delta(2)$; downfield shift is indicated by a positive value.

ation shift) on the D-glucopyranose moiety, based on the pentaacetates **1** or **2**; Table IV gives the tetra-*O*-acetyl-D-glucopyranosylation shifts ($\Delta\delta^{OH}$; glucopyranosylation shift) of the sekeletal carbon atoms of the mannofuranosyl moiety, based on **10**, respectively. Mannofuranosylation gives typical downfield shifts of the α-carbon atom ($\Delta\delta_\alpha^{OAc} = +2.2$ to $+7.0$ p.p.m.), in addition to a smaller shift of the β-carbon atoms ($\Delta\delta_\beta^{OAc} = -0.3$ to $+2.3$ p.p.m.). These ambiguous shifts, observed especially on the β-carbon atom, may be attributed to the steric effect between the neighboring substituents and the bulky 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranosyl group; the most favored rotameric orientation around the glycosyl bond is quite different in each instance, and therefore, variation in the changes of steric interaction caused with the adjacent substituents is reflected in the wide distribution of the $\Delta\delta_\alpha^{OAc}$ and $\Delta\delta_\beta^{OAc}$ values. From this viewpoint, smaller $\Delta\delta_\alpha^{OAc}$ values correspond well to smaller downfield shifts ($\Delta\delta_\beta^{OAc} = +0.6$ to $+0.8$ p.p.m.; C-5 of **15**, C-2 of **16**, and C-3 of **17**) or even an upfield shift ($\Delta\delta_\beta^{OAc} = -0.3$ p.p.m.; C-1 of **17**) on β-carbon

atoms. The upfield shift for C-5 of **16** ($\Delta\delta_{\gamma}^{OAc} = -1.8$ p.p.m.) is attributable to the steric effect, the 1,3-diaxial interaction, or a kind of so-called γ-effect[15] between the C-1 substituent and the *syn*-axial H-5. Small shifts observed on the carbon atoms other than C_α and C_β may be due to subtle conformational change caused by insertion of the bulky mannofuranosyl group.

In conclusion, mannofuranosylation generates a typical downfield shift on the α-carbon atom (2–7 p.p.m.), and small downfield shifts on the β-carbon atoms (less than ~2 p.p.m.) (see Fig. 1), thus resembling glycosylation shifts earlier reported[5].

TABLE IV

TETRA-*O*-ACETYL-D-GLUCOPYRANOSYLATION SHIFT ($\Delta\delta^{OH}$)[a] OF THE MANNOFURANOSYL MOIETIES, CALCULATED FROM 2,3;5,6-DI-*O*-ISOPROPYLIDENE-α-D-MANNOFURANOSYL D-GLUCOPYRANOSE TETRAACETATES

Compound	*Linking to position*	$\Delta\delta^{OH}$ (*p.p.m.*)					
		C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
11	O-1 of β-D-Glc	+6.0	−0.5	−0.3	+1.1	−0.5	+0.3
12	O-2	+5.6	−0.4	−0.3	+1.0	−0.4	0
13	O-3	+7.1	−0.3	−0.2	+0.9	−0.2	−0.3
14	O-4	+8.1	−0.1	−0.1	+1.5	−0.3	+0.2
15	O-6	+5.2	−0.5	−0.2	+0.4	−0.1	+0.2
16	O-1 of α-D-Glc	+1.2	−0.7	−0.1	+1.0	−0.4	+0.2
17	O-2	+3.6	−0.5	−0.3	+1.2	−0.4	+0.3

[a]Calculated as $\delta(\mathbf{11}-\mathbf{17}) - \delta(\mathbf{10})$; downfield shift is indicated by a positive value.

Comparing the glycosylation shifts ($\Delta\delta^{OH}$) of the mannofuranosyl moiety of **12**, **13**, **14**, and **15** (Table IV), it is interesting that the order of the downfield shift observed for C-1 corresponds* well, but in reverse, to the reported orders of the nucleophilicities of the hydroxyl groups of β-D-glucopyranosides[23,24]: 6-OH>2-OH>3-OH>4-OH.

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*Perlin[22] had reported such a correlation between the carbon-13 and proton n.m.r. chemical shifts of aldopyranoses and the relative rates of oxidation of hemiacetal hydroxyl groups by bromine.

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