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Note

^{13}C-N.m.r. spectra of some benzoylated derivatives of cellobiose, lactose, and maltose

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Recently, the ^{13}C-n.m.r. spectra of monosaccharides and disaccharides and their acetylated derivatives have been reviewed[1,2], but there are few references in the literature on benzoylated derivatives[3–6]. Petráková and Schram[6,7] reported a good correlation between the α and β effect for acetylated and methylated xylopyranosides, but stated that it was not possible to get adequate correlations for xylopyranose benzoates, as the conformation of all compared compounds was not the same.

We herein report the ^{13}C-n.m.r. data for nine benzoylated derivatives of disaccharides; namely, octa-*O*-benzoyl-β-cellobiose (**1**), octa-*O*-benzoyl-β-lactose (**4**), octa-*O*-benzoyl-β-maltose (**7**), 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-cellobiose (**2**), 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-lactose (**5**), 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-maltose (**8**), 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-3-*O*-methyl-β-cellobiose (**3**), 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-3-*O*-methyl-β-lactose (**6**), and methyl hepta-*O*-benzoyl-β-maltoside (**9**), and correlate these data with the conformation of the compounds in solution, as determined by ^{1}H-n.m.r. spectroscopy. They showed a $^4C_1$(D) conformation for both parts of the disaccharide molecules, with a slight deformation in the nonreducing β-D-galactopyranosyl group of lactose[8,9].

The ^{13}C-n.m.r. signals of the octa-*O*-benzoyl-β-disaccharides **1**, **4**, and **7**, were assigned by correlation with the signals of the structurally related hexopyranosyl derivatives[4], penta-*O*-benzoyl-α- and -β-D-glucopyranose[4], and of structurally related acylated compounds[5,10,11]. The signals of octa-*O*-benzoyl-β-cellobiose (**1**) were assigned by correlation with the spectrum of 1,2,3,4,6-penta-*O*-benzoyl-β-D-glucopyranose as shown in Fig. 1. The signals for the reducing residue of the disaccharide showed a good coincidence, except for the chemical shift of C-4, which participates in the glycosidic linkage, and whose signal showed a downfield shift of 6.72 p.p.m. Similar influences were reported by Gagnaire *et al.*[10] for acetylate disaccharides. The signals for the nonreducing group of the molecule

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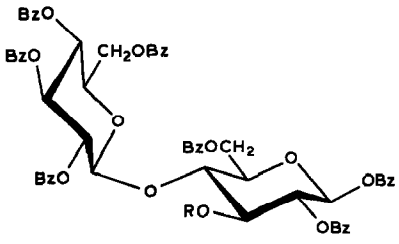
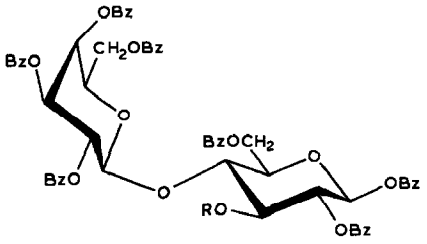
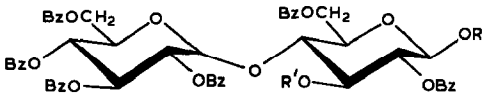


1 R = Bz
4 R = OH
7 R = Me



2 R = Bz
5 R = OH
8 R = Me



3 R = R' = Bz
6 R = Bz, R' = OH
9 R = Me, R' = Bz

agreed well, except for C-1′, which participates in the glycosidic linkage. Haverkamp *et al.*[12] also reported that the skeleton carbon atoms distant from the glycosidic linkage showed in permethylated disaccharides almost identical behavior.

The signals of octa-*O*-benzoyl-β-lactose (**4**) were assigned by correlation with 1,2,3,4,6-penta-*O*-benzoyl-β-D-glucopyranose[4], and the expected difference of the chemical shift for C-4, due to the glycosidic linkage, was observed. The assignment of the signals for the nonreducing group was corroborated by comparison of our results with those of Kováč *et al.*[5] for methyl 2,3,4-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-β-D-galactopyranoside.

The signals for octa-*O*-benzoyl-β-maltose (**7**) were assigned by correlation with the signals of 1,2,3,4,6-penta-*O*-benzoyl-α- and -β-D-glucopyranose[4], with the expected shifts for C-4 and -1′. The signals for the other compounds **2, 3, 5, 6, 8,** and **9** were assigned by correlation with those of the corresponding octa-*O*-benzoyl derivatives. All the assignments are listed in Table I.

The comparative analysis of pairs of these compounds allowed a good general correlation, with expected important differences for the chain carbon atoms due to the change of substituents such as hydroxyl, methyl, and benzoyl. The correlation of the signals for the octabenzoates of β-cellobiose (**1**) and β-lactose (**4**) (a, Table II) showed a coincidence of <0.4 p.p.m. for the reducing residues and

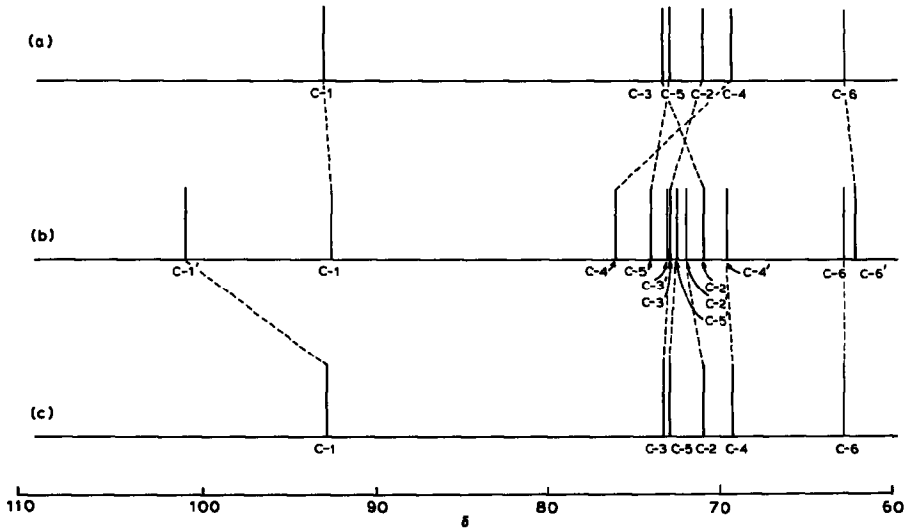


Fig. 1. Comparison of the spectra of octa-*O*-benzoyl-β-cellobiose (**1**, b), 1,2,3,4,6-penta-*O*-benzoyl-β-D-glucopyranose (a and c).

expected differences for the inversion at C-4′ due to the D-*galacto* configuration, and important differences for C-2′ and -6′. The deviation of the nonreducing group of **4** from the $^4C_1$(D) conformation has to be taken in consideration.

In the correlation of the signals of **1** and **7** (b, Table II) the change due to the glycosidic linkage at C-4 was obtained. The influence on the neighbouring C-3 and -5 is not symmetric, as expected by the different substitutions. For the nonreducing group, the greatest differences were as expected for C-1′, -3′, and -5′, and as reported for the acetylated derivatives[10].

The comparison of the octa-*O*-benzoyl and hepta-*O*-benzoyl derivatives of β-cellobiose (**1** and **2**) (c, Table II) shows an important difference of −9.23 p.p.m. for the signal assigned to C-3, where the benzoyloxy group was exchange for an hydroxyl group. Important differences in the signals for vicinal carbon atoms could be verified, even when they were not of the same magnitude.

The difference of −1.06 p.p.m. for the signal assigned to C-1′ can be explained by the interaction with the free hydroxyl group, which affects directly the chemical shift. This suggestion is supported by the correlation with the signals of the 3-*O*-methyl derivative **3** (f, Table II), which showed only a small difference for C-1′, but a large one for the signal of C-3. A similar observation was made for correlation of the signals of the β-lactose derivatives **4** with those of **5** and **6** (d, f, Table II). The differences observed with the signal for C-6′ are due to different rotamers as seen from the coupling constants in the ^{1}H-n.m.r. spectra.

The correlation of the signals for the maltose derivatives **7** and **8** (e, Table II) showed that the change from a 3-benzoyloxy to an hydroxyl group only gave a difference of −2.49 p.p.m. for C-3 and a small change for C-1′ (−0.44 p.p.m.).

TABLE I

^{13}C-N.M.R. CHEMICAL SHIFTS (δ) FOR COMPOUNDS **1–9**[a]

Atom	*Compound*								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
C-1	92.58	92.37	92.40	92.69	92.37	92.40	92.29	92.20	101.56
C-2	71.02	71.62	72.30	70.90	71.54	72.05	71.29	73.54	72.37
C-3	72.85	82.08	82.81	72.96	82.06	82.97	74.91	77.40	75.09
C-4	76.00	73.23	77.80	75.60	73.03	77.46	73.02	75.67	73.42
C-5	73.95	73.58	73.58	73.97	73.61	73.50	73.73	73.71	73.77
C-6	62.21	62.12	62.32	62.19	62.92	62.32	63.29	63.23	63.62
C-1′	101.03	102.09	101.37	101.10	102.32	101.51	96.46	96.90	96.37
C-2′	72.02	71.88	72.06	69.99	69.53	70.28	71.08	71.42	71.00
C-3′	72.92	72.98	72.98	71.83	72.63	71.73	70.02	70.02	70.02
C-4′	69.60	69.22	69.61	67.65	68.12	68.10	69.24	68.90	69.24
C-5′	72.55	72.55	72.42	71.56	71.89	71.51	69.29	69.13	69.33
C-6′	62.78	63.16	62.81	61.14	62.16	61.76	62.57	62.72	62.69
OCH_3			60.60			60.38			56.84

[a]Signals for aromatic groups appeared between δ 128.03 and 133.69 and for carbonyl group between 164.40 and 166.19.

For the β-linked compounds, this value is of the order -1 p.p.m. as shown in Table II (c and d). In this case, there are two variations, the glycoside linkage and the possible interaction of the hydroxyl group with the environment of C-1′.

The small difference for the signal of C-3 was ascertained by repeating the recording of the spectrum with other instruments under different experimental conditions. Lee *et al.*[13] reported for benzyl hepta-*O*-acetyl-β-maltoside and benzyl 2,6,2′,3′,4′,6′-hexa-*O*-acetyl-β-maltoside, a ^{13}C-n.m.r. chemical shift differences of -7.4 p.p.m. for C-3. No detailed ^{1}H-n.m.r. data were given to ascertain the conformation.

An important difference for the signal of C-3 was observed (f, Table II) when we correlated the signals for compounds **1** and **3**, and **4** and **6**. The change from a benzoyloxy to a methoxy substituent at C-3 showed a strong influence on the signal of C-3 of -9.96 or -10.01 p.p.m., and slighter influences on the signals of the vicinal carbon atoms, but of different magnitude and sign. This can be attributed to the presence of different substituents at C-2 and -4. Vignon and Vottero[14] observed that the exchange of an acetoxy by a methoxy group for the acetates of β-D-glucopyranose causes a difference of -8.5 p.p.m. (C-3) and the same difference (0.9 p.p.m.) for the signals of the vicinal groups (C-2 and -4).

The correlation of the signals of the heptabenzoates of β-cellobiose (**2**) and β-lactose (**5**) (g, Table II) showed a good coincidence for the reducing residues as they have the same conformation and glycoside linkage. For the nonreducing group, the differences observed were similar to those for the octabenzoates (a, Table II). The configurational change at C-4′ showed its influence on the signal of C-2′ and -6′, but there is also a slight deformation of the $^4C_1$(D) conformation in

TABLE II

CORRELATION BETWEEN RELATED COMPOUNDS

Correlation	*Atom*											
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-1'*	*C-2'*	*C-3'*	*C-4'*	*C-5'*	*C-6'*
(a) **Δ1–4**	−0.11	0.12	−0.11	0.40	−0.02	0.02	−0.08	2.03	1.09	1.95	0.99	1.64
(b) **Δ1–7**	0.29	−0.27	−2.06	2.98	0.22	−1.08	4.57	0.94	2.90	0.36	3.26	0.21
(c) **Δ1–2**	0.21	−0.60	−9.23	2.78	0.37	0.09	−1.06	0.14	−0.06	0.38	0	−0.38
(d) **Δ4–5**	0.32	−0.64	−9.10	2.57	0.36	−0.73	−1.22	0.46	−0.80	−0.47	−0.33	−1.02
(e) **Δ7–8**	0.09	−2.25	−2.49	−2.65	0.02	0.06	−0.44	−0.34	0	0.34	0.16	−0.15
(f) **Δ1–3**	0.18	−1.28	−9.96	−1.80	0.37	−0.11	−0.34	−0.04	−0.06	−0.01	0.13	−0.03
(f) **Δ4–6**	0.29	−1.15	−10.01	−1.86	0.47	−0.13	−0.41	−0.29	0.10	−0.45	0.05	−0.62
(g) **Δ2–5**	0	0.08	0.02	0.20	−0.03	−0.80	−0.23	2.35	0.35	1.10	0.66	1.00
(h) **Δ2–8**	0.17	−1.92	4.68	−2.44	−0.13	−1.11	5.19	0.46	2.96	0.32	3.42	0.44
(i) **Δ3–6**	0	0.25	−0.16	0.34	0.08	0	−0.14	1.78	1.25	1.51	0.91	1.05
(j) **Δ7–9**	−9.27	−1.08	−0.18	−0.40	0.04	−0.33	0.09	0.08	0	0	0.04	0.12

compound **5**, as seen in the ^{1}H-n.m.r. spectrum[6]. The correlations of the signals of the heptabenzoates of cellobiose (**2**) and maltose (**8**) (h, Table II) showed magnitudes similar to those observed for the signals of the corresponding octabenzoates **1** and **7** (b, Table II).

The correlation of the signals of 3-*O*-methylheptabenzoates **3** and **6** (i, Table II) showed a good coincidence for the reducing residue and changes for the nonreducing group at C-4′, and at C-2′ and -6′, respectively, owing to the configurational inversion as stated earlier in Table II (a and g). The comparison of the signals of octa-*O*-benzoyl-β-maltose (**7**) with those of methyl hepta-*O*-benzoyl-β-maltoside (**9**) (j, Table II) showed the influence of the different group at C-1 (−9.27 p.p.m.) and at C-2 (−1.08 p.p.m.), but slight differences for the rest of the molecule. In general, it can be stated that the inversion of configuration at C-1 from α- to β-, or at C-4 from a D-*gluco* to a D-*galacto* configuration results in important changes for the signals of those carbon atoms and the respective carbon atoms in 3-position.

The effect on the ^{13}C-n.m.r. spectra of the replacement of an hydroxyl by an acetyloxy group was investigated by Terui *et al.*[15] for model compounds. They analyzed the influence of the displacement on the signals of the carbon atom where the change took place, and on the signals of the carbon atom in positions 2, 3, and 4. Most of these signals showed a shift to higher field for the carbon atom in position 1, but to lower field for the signals of the carbon atoms in positions 2 and 4. In the present study, several vicinal *O*-benzoyl groups are present and the 1-influence of the benzoyl groups has to be considered, as well as the participation of the benzoyl groups in positions 2, 3, and 4. These different effects result, in general, in a shift to a higher field than that of the free hydroxyl derivative.

From the results presented herein, it is possible to assign the ^{13}C-n.m.r. spectra of other benzoylated derivatives, if they have the same conformation (as seen by their ^{1}H-n.m.r. spectra), or to predict conformational changes, inversion in configuration, or changes of substituting groups.

EXPERIMENTAL

The compounds investigated were prepared as described in the literature. The spectra were recorded for solutions in (^{2}H)chloroform with Me_4Si as internal standard (conditions in parentheses). The signals were assigned by correlation with those of the monosaccharide derivatives: octa-*O*-benzoyl-β-cellobiose[16] (**1**; 100.1 MHz); octa-*O*-benzoyl-β-lactose[17] (**4**; 100.1 MHz); octa-*O*-benzoyl-β-maltose[18] (**7**; 100.1 MHz); 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-cellobiose[19] (**2**; 25.02 MHz); 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-lactose[20] (**5**; 25.02 MHz); 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-maltose[21] (**8**; 20 MHz); 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-3-*O*-methyl-β-cellobiose[19] (**3**; 100.1 MHz); 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-3-*O*-methyl-β-lactose[20] (**6**; 100.1 MHz); and methyl hepta-*O*-benzoyl-β-maltoside[21] (**9**; 100.1 MHz).

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