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Note

Synthesis and characterization of two 1,2,3,6,2′,3′,4′,6′-octa-*O*-benzoyl-β-D-hexapyranosyl-(1 → 4)β-D-allopyranoses

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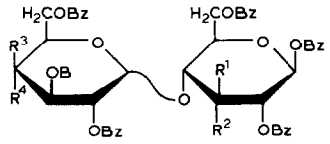
^{13}C NMR data of monosaccharides and their derivatives, such as acetates and methyl ethers[1] of oligosaccharides including disaccharides[2], and of fluorinated derivatives[3] have been published as well as data of benzoylated derivatives of cyclic and acyclic monosaccharides[4–7] and disaccharides[8–10]. In this previous work[7–10], it was possible to correlate configurational changes, deduced from the coupling constants of the ^1H NMR signals, with chemical shifts in the ^{13}C NMR spectra.

D-Allose is a rare sugar in Nature. Its synthesis[11] requires selective protection to keep OH-3 free, its substitution with a methanesulfonyl or 4-toluenesulfonyl group, and inversion at C-3. These reactions gave good yields for the β anomer, but very low yields for the α anomer due to steric hindrance.

Bhatt et al.[12] synthesized a disaccharide having a reducing residue in the *allo* configuration from methyl 2,6,2′,3′,4′,6′-hexa-*O*-benzoyl-β-lactoside by methanesulfonylation and displacement with sodium benzoate to give methyl *O*-(2,3,4-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-*O*-benzoyl-β-D-allopyranoside and by acetolysis and hydrolysis *O*-β-D-galactopyranosyl-(1 → 4)-D-allose. From methyl 2,6,2′,3′,4′,6′-hexa-*O*-acetyl-β-maltoside, Durette et al.[13] obtained by a similar reaction sequence methyl *O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-(1 → 4)-2,6-di-*O*-acetyl-3-*O*-benzoyl-β-D-allopyranose.

We report herein the synthesis of 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-3-*O*-methanesulfonyl and -(4-toluenesulfonyl) derivatives of β-cellobiose (**3** and **5**, respectively) and β-lactose (**4** and **6**, respectively) and their transformation into the octa-*O*-benzoyl derivatives having the β-D-glucopyranosyl → β-D-allopyranose (**5**) and β-D-galactopyranosyl → β-D-allopyranose (**6**) structure. The starting materials were 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-cellobiose (**1**)[15] and 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-lactose[16] (**2**), respectively, which were obtained by direct benzoylation of the disaccharides under Schotten–Baumann conditions. 4-Toluenesulfonyl and methanesulfonyl derivatives (**3–6**) were used, but the yields of the products with



1 R^1 = OH, R^2 = R^3 = H, R^4 = OBz
2 R^1 = OH, R^2 = R^4 = H, R^3 = OBz
3 R^1 = OMs, R^2 = R^3 = H, R^4 = OBz
4 R^1 = OMs, R^2 = R^4 = H, R^3 = OBz
5 R^1 = OTs, R^2 = R^3 = H, R^4 = OBz
6 R^1 = OTs, R^2 = R^4 = H, R^3 = OBz
7 R^1 = R^3 = H, R^2 = R^4 = OBz
8 R^1 = R^4 = H, R^2 = R^3 = OBz

Scheme 1.

sodium benzoate were better with the latter derivatives (**3** and **5**), and disaccharides **7** and **8** were obtained in 37 and 70% yields, respectively.

The ^{1}H NMR chemical shifts and coupling constants of compounds **3–8** are listed in Tables I and II. The assignments were confirmed by double-resonance experiments. The coupling constants showed the $^4C_1$ conformation for both units. The variation of coupling constants observed between compounds **3** and **6**, and **4** and **8** are due to the change from an equatorial to an axial substituent. The signals of H-1 and H-3 of **7** and **8** appeared superposed with the aromatic signals because the spectra were obtained with solutions in C_6D_6. In this solvent, the shifts to lower field were also observed for other benzoylated derivatives[14].

TABLE I

^{1}H NMR chemicalshifts (δ) and multiplicities of compounds **3–8** at 400 MHz

Atom	**3** [a]	**4** [a]	**5** [b]	**6** [b]	**7** [a]	**8** [a]
H-1	5.80 (d)	5.87 (d)	5.97 (d)	5.95 (d)	[c]	[c]
H-2	5.80 (dd)	5.81 (dd)	5.55 (dd)	5.58 (dd)	6.09 (dd)	6.03 (dd)
H-3	5.06 (t)	5.13 (dd)	5.23 (dd)	5.25 (t)	[c]	[c]
H-4	4.00 (dd)	4.08 (dd)	4.24 (dd)	4.41 (dd)	4.40 (dd)	4.29 (dd)
H-5	3.14 (ddd)	3.08 (ddd)	3.86 (ddd)	3.47 (ddd)	4.66 (ddd)	4.64 (ddd)
H-6a	4.48 (dd)	4.56 (dd)	4.64 (dd)	4.64 (dd)	4.90 (dd)	4.80 (dd)
H-6b	4.60 (dd)	4.47 (dd)	4.36 (dd)	4.47 (m)	4.51 (dd)	4.54 (dd)
H-1′	4.81 (d)	4.80 (d)	4.76 (d)	5.03 (d)	4.66 (d)	4.49 (d)
H-2′	5.91 (dd)	6.22 (dd)	5.11 (dd)	5.94 (dd)	5.73 (dd)	6.10 (dd)
H-3′	6.05 (t)	5.58 (dd)	5.62 (dd)	5.50 (dd)	6.11 (dd)	5.70 (dd)
H-4′	5.98 (dd)	5.92 (dd)	5.02 (dd)	5.93 (dd)	5.76 (t)	6.14 (dd)
H-5′	3.62 (ddd)	3.60 (ddd)	3.72 (ddd)	3.96 (ddd)	3.60 (ddd)	3.83 (ddd)
H-6′a	4.43 (m)	4.49 (dd)	4.40 (dd)	4.47 (m)	4.62 (dd)	4.75 (dd)
H-6′b	4.43 (m)	4.20 (dd)	4.08 (dd)	4.47 (m)	4.46 (dd)	4.24 (dd)
CH_3	2.79 (s) [d]	3.05 (s) [d]	2.50 (s) [e]	2.00 (s) [e]		

[a] Measured for a solution in C_6D_6 with Me_4Si as internal standard. [b] Measured for a solution in $CDCl_3$ with Me_4Si as internal standard. [c] Superposed with the signals for the aromatic protons. [d] Methyl of methanesulfonyl group. [e] Methyl of 4-toluenesulfonyl group.

TABLE II

Vicinal proton–proton coupling constants (Hz) of compounds 3–8

Coupling constant	3 [a]	4 [a]	5 [b]	6 [b]	7 [a]	8 [a]
$J_{1,2}$	8.5	8.2	8.0	8.0	8.6	8.5
$J_{2,3}$	9.2	9.2	9.3	8.2	3.0	3.0
$J_{3,4}$	9.2	9.3	9.4	8.2	3.0	3.0
$J_{4,5}$	9.6	9.4	9.8	9.9	9.7	9.8
$J_{5,6b}$	5.4	2.2	3.7	1.8	4.1	2.0
$J_{5,6a}$	1.7	4.8	2.0	3.5	2.0	4.4
$J_{6a,6b}$	12.0	11.8	12.5	12.4	12.1	12.0
$J_{1',2'}$	8.0	8.0	8.0	8.0	7.9	7.8
$J_{2',3'}$	9.4	10.3	9.7	10.2	9.9	10.6
$J_{3',4'}$	9.4	3.5	9.7	3.5	9.8	3.4
$J_{4',5'}$	10.0	0.5	9.9	1.0	9.8	1.1
$J_{5',6'b}$	4.0	5.6	6.7	7.0	3.2	7.2
$J_{5',6'a}$	4.0	3.6	4.2	6.6	3.0	5.8
$J_{6'a,6'b}$		11.7	11.9		12.2	11.3

[a] Measured for a solution in $CDCl_3$. [b] Measured for a solution in C_6D_6.

The ^{13}C NMR spectra of compounds 3–8 are listed in Table III were assigned by correlation with structurally related benzoylated derivatives of mono-[7] and di-saccharides[9]. The correlations of the ^{13}C NMR signals of the compounds having the same substituents but a different configuration at C-4', showed the expected small differences in the chemical shifts for the carbon atoms of the reducing residue and more important changes for the nonreducing group where the configu-

TABLE III

^{13}C NMR chemical shifts (δ) for compounds 3–8 [a]

Atom	3 [b]	4 [b]	5 [c]	6 [c]	7 [b]	8 [b]
C-1	93.13	93.18	92.49	92.37	91.97	92.03
C-2	73.90	73.99	70.63	70.54	73.25	73.40
C-3	79.33	79.54	80.11	79.91	69.85	70.52
C-4	75.47	74.84	73.66	74.31	75.36	74.86
C-5	74.01	73.99	73.25	73.60	70.66	70.78
C-6	62.67	62.74	61.92	62.15	62.98	63.49
C-1'	101.46	101.36	99.90	100.65	102.00	101.94
C-2'	71.44	70.77	71.59	70.14	72.71	70.61
C-3'	73.26	72.36	72.76	71.96	73.50	72.08
C-4'	70.23	68.68	70.12	67.84	70.17	68.71
C-5'	72.70	71.49	72.00	71.62	73.03	72.08
C-6'	62.85	61.63	63.21	61.52	63.41	62.20
CH_3	39.16 [d]	39.43 [d]	21.66 [e]	21.35 [e]		
C-arom.	127.09–133.51		127.43–144.94		124.48–133.42	
C=O	164.51–166.04		164.25–165.86		164.89–166.08	

[a] Measured at 100.63 MHz with Me_4Si as internal standard. [b] For a solution in C_6D_6. [c] For a solution in $CDCl_3$. [d] CH_3 of methanesulfonyl group. [e] CH_3 of 4-toluenesulfonyl group.

rational inversion at C-4′ is present. The change from a benzoyloxy (**7** and **8**) to a methanesulfonyl (**3** and **4**) or 4-toluenesulfonyl group (**5** and **6**) showed important displacements to lower field due to the different substituents at C-4′ and the inversion of configuration. The differences for the vicinal carbon atoms are less important.

EXPERIMENTAL

General methods.—Melting points are uncorrected. The optical rotations were determined at 20°C with a Perkin–Elmer 141 Polarimeter. TLC was performed on plates coated with Silica gel G (Merck, Darmstadt) with 9:1 benzene–EtOAc as the eluent and I_2 vapor for detection. The ^1H NMR spectra were recorded with a Bruker WH400 instrument at 400 MHz for solutions in $CDCl_3$ or C_6D_6, with Me_4Si as the internal standard. First-order coupling constants were measured from the expanded spectra. The ^{13}C NMR spectra were recorded with the same instrument with wide-band proton-decoupling. 1,2,6,2′,3′,4′,6′-Hepta-*O*-benzoyl-β-cellobiose (**1**)[15] and 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-lactose (**1**)[16] were prepared as described earlier.

*1,2,6,2′,3′,4′,6′-Hepta-*O*-benzoyl-3-*O*-methanesulfonyl-β-cellobiose* (**3**).—Compound **1** (1.0 g) was dissolved in pyridine (10 mL), methanesulfonyl chloride (2.5 mL) was added, and the mixture kept at 60°C with vigorus stirring for 5 h, until the starting material disappeared (TLC). The solution was poured into ice–water, and the precipitate filtered off after 24 h, washed, and purified from 1:1 acetone–2-propanol. Compound **3** (0.77 g, 71.5%) was obtained as an amorphous solid, mp 163–165°C, $[\alpha]_D$ +6.6° (*c* 1.1, $CHCl_3$). Anal. Calcd for $C_{62}H_{52}O_{20}S$: C, 64.81; H, 4.53; S, 2.79. Found: C, 64.81; H, 4.77; S, 2.53.

*1,2,6,2′,3′,4′,6′-Hepta-*O*-benzoyl-3-*O*-methanesulfonyl-β-lactose* (**4**).—Compound **2** (0.80 g) was treated as described for the preparation of **3** to give compound **4** (0.75 g, 86%), mp 183–185°CV, $[\alpha]_D$ +39° (*c* 1, $CHCl_3$), Anal. Calcd for $C_{62}H_{52}O_{20}S$; C, 64.81; H, 4.53; S, 2.79. Found: C, 64.79; H, 4.78; S, 2.75.

*1,2,6,2′,3′,4′,6′-Hepta-*O*-benzoyl-3-*O*-(4-toluenesulfonyl)-β-cellobiose* (**5**).—Compound **1** (1.0 g) was dissolved in pyridine (3.5 mL), 4-toluenesulfonyl chloride (1.84 g) was added, and the mixture heated to 80°C with vigorus stirring for 4 h. It was poured into ice–water, the precipitate filtered off, washed and it crystallized from 1:1 acetone–2-propanol. Owing to the presence of starting material it was separated by flash column chromatography to give **5** (0.24 g, 47%), mp 145–146°C, $[\alpha]_D$ −6.5° (*c* 1, $CHCl_3$). Anal. Calcd for $C_{68}H_{56}O_{20}S$: C, 66.66; H, 4.57; S, 2.61. Found: C, 66.68; H, 4.74; S, 2.68.

*1,2,6,2′,3′,4′,6′-Hepta-*O*-benzoyl-3-*O*-(4-toluenesulfonyl)-β-lactose* (**6**).—Compound **2** (1.0 g) was treated as described for the preparation of **5** to give **6** (0.79 g, 69.5%), mp 123–125°C, $[\alpha]_D$ +46° (*c* 1, $CHCl_3$). Anal. Calcd for $C_{68}H_{56}O_{20}S$: C, 66.66; H, 4.57; S, 2.61. Found: C, 66.91; H, 4.88; S, 2.39.

O-(*2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl)-(1 → 4)-1,2,3,6-tetra-O-benzoyl-β-D-allopyranose* (**7**).—Compound **1** (0.68 g) and sodium benzoate (0.74 g) were dissolved in DMF (24 mL) and refluxed for 18 h. The mixture was concentrated, and the solid residue extracted with water and crystallized from 1:1 acetone–MeOH to give compound **7** (0.24 g, 37%), mp 118–120°C, $[\alpha]_D$ −16.5° (*c* 1, $CHCl_3$). Anal. Calcd for $C_{68}H_{54}O_{19}$: C, 69.50; H, 4.60. Found: C, 69.45; H, 4.72.

O-(*2,3,4,6-Tetra-O-benzoyl-β-D-galactopyranosyl)-(1 → 4)-1,2,3,6-tetra-O-benzoyl-β-D-allopyranose* (**8**).—Compound **2** (1.02 g) was treated as described for the preparation of **7** to give compound **8** (0.72 g, 70%), as rectangular plates, mp 121–123°C, $[\alpha]_D$ +1.9° (*c* 1, $CHCl_3$). Anal. Calcd for $C_{68}H_{54}O_{19}$: C, 69.50; H, 4.60. Found: C, 69.37; H, 4.90.

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