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Note

Partial benzoylation of 1,5-anhydroxylitol

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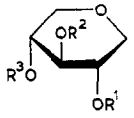
In previous publications on the selective benzoylation of methyl 6-deoxy-β-D-glucopyranoside[1], 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol[2], and 1,5-anhydro-D-glucitol[3], we reported that, among the secondary hydroxyl groups, the 3-hydroxyl groups are the most reactive. In connection with these studies, this communication describes the partial benzoylation of 1,5-anhydroxylitol (**1**).

Treatment of **1** with one molar equivalent of benzoyl chloride in pyridine at −40° gave a complex mixture, shown by quantitative t.l.c. to consist of the 2,3,4-tribenzoate **2** (1.6%), the 2,4-dibenzoate **3** (14.5%), the 2,3-dibenzoate **4** (30.1%), the 3-benzoate **5** (16.6%), and the 2-benzoate **6** (37.2%).

After chromatographic separation, the structure of **2** was established by comparison with an authentic specimen prepared from **1** with an excess of benzoyl



	R^1	R^2	R^3
1	H	H	H
2	Bz	Bz	Bz
3	Bz	H	Bz
4	Bz	Bz	H
5	H	Bz	H
6	Bz	H	H
7	Bz	Ac	Bz
8	Bz	Bz	Ac
9	Ac	Bz	Ac
10	Bz	Ac	Ac
11	Bz	Bz	Ts
12	Ts	Bz	Ts

TABLE I

CHEMICAL SHIFTS (δ) AND COUPLING CONSTANTS (Hz) OF BENZOYLATED 1,5-ANHYDROXYLITOL IN CHLOROFORM-*d* AT 60 MHz

Compound:	**2**	**3**	**5**[a]	**6**[a]	**7**	**8**	**9**	**10**	**11**	**12**
H-1*ax*	3.65 q	3.46 q	3.33 q	3.9–4.1 m	3.52 q	3.52 q	3.45 q	3.53 q	3.57 q	3.42 q
H-5*ax*						3.43 q		3.35 q	3.40 q	
H-1*eq*	4.30 q	4.13 q	3.93 q		4.22 q	4.30 q	4.07 q	4.23 q	4.28 q	4.23 q
H-5*eq*						4.12 q		4.05 q	4.18 q	
H-2	5.33 sex	5.07 sex	3.4–3.9 m	4.93 sex	5.28 sex	4.9–5.5 m	5.07 sex	4.7–5.2 m	5.17 sex	4.53 sex
H-4									4.67 sex	
H-3	5.83 t	4.13 m	5.07 t		5.60 t	5.65 t	5.43 t	5.40 t	5.58 t	5.38 t
OH		3.45 d	4.35 d	4.25 d 4.60 d						
Acetyl-Me					1.95 s	2.00 s	1.95 s	2.05 s 2.02 s		
Tosyl-Me									2.17 s	2.15 s
$J_{1ax,2}$	8	8	7	8	8	8	8	8	8	10
$J_{1eq,2}$	4	4	4	5	5	5	4	5	4	5
$J_{1ax,1eq}$	12	12	11		11	11	10	10	12	11
$J_{2,3}$	8	8	8	8	8	8	9	9	8	9
$J_{3,4}$	8	8	8	8	8	8	9	9	8	9
$J_{4,5ax}$	8	8	7		8	8	8	8	10	10
$J_{4,5eq}$	4	4	4		5	5	4	5	5	5
$J_{5ax,5eq}$	12	12	11		11	11	10	12	12	11
J_{OH}		~5	5	4 3						

[a]In acetone-d_6.

chloride. The position of the benzoyl groups in **3** was assigned from the ^{1}H-n.m.r. spectrum. The H-2 and H-4 signals (δ 5.07) appeared the most downfield of the ring-proton resonances and were coincident, showing that these protons must be geminal to the symmetrically substituted, deshielding benzoyl groups. This was further proved by acetylation of **3**. The H-3 triplet resonance of the product **7** fell downfield of all other ring-proton resonances (Table I), as would be anticipated from the known tendency of an acetyloxyl group to deshield methine protons attached to the same carbon atom. As the ^{1}H-n.m.r. spectrum of **4** was unresolved, the structure of **4** was confirmed by the ^{1}H-n.m.r. spectra of its 4-acetate **8** and 4-*p*-toluenesulfonate **11**. The ^{1}H-n.m.r. spectra of **8** and **11** showed the clear dissymetry of these compounds by the slightly separated resonances for H-1*ax* and H-5*ax*, and H-1*eq* and H-5*eq*. The ^{1}H-n.m.r. spectrum of **5** showed the presence of one benzoyloxy and two hydroxyl groups. The H-3 signal appeared as a triplet downfield of all other ring protons, indicating that H-3 is deshielded by the geminal benzoyl group. The 3-benzoate **5** was converted into the symmetrical diacetate **9** and di-*p*-toluenesulfonate **12**. The ^{1}H-n.m.r. spectra of **9** and **12** supported the structure assigned to **5**. The H-3 resonance was a triplet at lowestfield, whereas the coincidental signals for H-1*ax* and H-5*ax*, H-1*eq* and H-5*eq*, and H-2 and H-4 were clearly observed at higher field as two quartets and a sextet, respectively. The structure of **6** was also established by its ^{1}H-n.m.r. spectrum. A one-proton sextet at lowest field (δ 4.93) was assigned to H-2, suggesting that the benzoyl group was attached to C-2. Further structural elucidation of **6** was obtained from the ^{1}H-n.m.r. spectrum of its acetate **10**. The lack of symmetry of this compound was clearly shown by the slightly separated resonances for H-1*ax* and H-5*ax*, and H-1*eq* and H-5*eq* at higher field.

From symmetry considerations, the hydroxyl groups at C-2 and C-4 in **1** are chemically and physically identical, and thus the reactivities of HO-2 and HO-4 are exactly the same. Therefore, it is noteworthy that the molar ratios of **3** to **4** in the dibenzoates, and of **5** to **6** in the monobenzoates, are 1:2. This result indicates that the relative reactivity of the hydroxyl group at C-2 (or C-4) is very similar to that of the hydroxyl group at C-3. This finding is in agreement with the result that deoxygenation has no activating effect on a neighboring hydroxyl group, as indicated by selective benzoylation of 1,5-anhydro-D-glucitol[3] and its 4,6-benzylidene acetal[2]. The preponderance of **4** over **3** suggests that the gauche interactions at C-2 (or C-4), between a hydroxyl group and a hydrogen atom, are almost equivalent to those at C-3, with a benzoyl group and a hydroxyl group, in benzoylation.

EXPERIMENTAL

General methods. — Melting points were determined with a Yanagimoto micro hot-stage apparatus and are uncorrected. The ^{1}H-n.m.r. spectra were recorded with a Hitachi R-24 60-MHz instrument with tetramethylsilane as the internal standard. Quantitative t.l.c. was performed on quartz rods sintered with silica gel H 60 (Merck) and glass powder (1:2). Toluene–acetone (9:1) completely resolved the benzoylation

products, and the bands were detected with an Iatron chromatoscanner TH-10 equipped with a hydrogen flame-ionization detector. Column chromatography was performed on silica gel 60 (70–230 mesh, Merck) with mixtures of benzene and acetone.

Partial benzoylation of 1,5-anhydroxylitol (**1**). — The anhydroxylitol **1** (500 mg) was dissolved in pyridine (20 mL) and benzoyl chloride (0.54 mL, 1.1 molar equivs.) was added at −40°. The solution was stirred for 3 h at −20°, maintained for 48 h at 0°, and then extracted with chloroform. The extract was washed with dilute sulfuric acid, saturated sodium hydrogencarbonate, and dried over sodium sulfate. The chloroform solution was directly used for quantitative t.l.c. analysis of the components in the mixture.

Evaporation of the solvent and column chromatography of the resultant residue gave five fractions.

1,5-Anhydro-2,3,4-tri-*O*-benzoylxylitol (**2**) crystallized from ethanol as fine needles (23 mg, 1%), m.p. 149–150°, R_F 0.68, identical with an authentic sample prepared by perbenzoylation of **1**.

1,5-Anhydro-2,4-di-*O*-benzoylxylitol (**3**) crystallized from ethanol as long needles (108 mg, 8%), m.p. 155–156°, R_F 0.50.

Anal. Calc. for $C_{19}H_{18}O_6$: C, 66.65; H, 5.31. Found: C, 66.64; H, 5.58.

1,5-Anhydro-2,3-di-*O*-benzoyl-DL-xylitol (**4**) was obtained as a foam (255 mg, 20%), R_F 0.46. Attempts to crystallize it failed.

1,5-Anhydro-3-*O*-benzoylxylitol (**5**) crystallized from benzene–2-propanol as long needles (94 mg, 11%), m.p. 168–169°, R_F 0.19.

Anal. Calc. for $C_{12}H_{14}O_5$: C, 60.49; H, 5.93. Found: C, 60.30; H, 6.10.

1,5-Anhydro-2-*O*-benzoyl-DL-xylitol (**6**) crystallized from benzene–2-propanol–petroleum ether to give white plates (169 mg, 19%), m.p. 112–113°, R_F 0.15.

Anal. Calc. for $C_{12}H_{14}O_5$: C, 60.49; H, 5.93. Found: C, 60.44; H, 6.08.

*1,5-Anhydro-2,3,4-tri-*O*-benzoylxylitol* (**2**). — 1,5-Anhydroxylitol (**1**) (71 mg) was dissolved in pyridine (2 mL), and benzoyl chloride (0.3 mL) was added to the solution cooled in ice–water. After stirring overnight at room temperature, extraction with chloroform followed by crystallization from ethanol yielded the tribenzoate **2** as long needles (183 mg, 78%), m.p. 149–150°.

Anal. Calc. for $C_{26}H_{22}O_7$: C, 69.94; H, 4.98. Found: C, 69.67; H, 5.06.

*3-*O*-Acetyl-1,5-anhydro-2,4-di-*O*-benzoylxylitol* (**7**). — The dibenzoate **3** (63 mg) was acetylated with acetic anhydride (0.5 mL) in pyridine (1 mL). Extraction with chloroform followed by crystallization from ethanol gave **7** (61 mg, 86%), m.p. 138–139°.

Anal. Calc. for $C_{21}H_{20}O_7$: C, 65.61: H, 5.25. Found: C, 65.04; H, 5.45.

*4-*O*-Acetyl-1,5-anhydro-2,3-di-*O*-benzoyl-DL-xylitol* (**8**). — Acetylation of the dibenzoate **4** (147 mg) as described for **7** provided **8** (155 mg, 94%), m.p. 141–142° (from ethanol).

Anal. Calc. for $C_{21}H_{20}O_7$: C, 65.61; H, 5.25. Found: C, 65.87; H, 5.26.

*1,5-Anhydro-2,3-di-*O*-benzoyl-4-*O*-p-tolylsulfonyl-DL-xylitol* (**11**). — To a solu-

tion of the dibenzoate **4** (106 mg) in pyridine (1 mL) was added *p*-toluenesulfonyl chloride (180 mg). The solution was stirred for 4 days at room temperature, extracted with chloroform, and the extract evaporated. Recrystallization from chloroform–ethanol afforded **11** (148 mg, 96%) as long needles, m.p. 183–184°.

Anal. Calc. for $C_{26}H_{24}O_8S$: C, 62.88; H, 4.88; S, 6.46. Found: C, 62.76; H, 5.01; S, 6.49.

2,4-Di-O-*acetyl-1,5-anhydro-3*-O-*benzoylxylitol* (**9**). — Acetylation of the monobenzoate **5** (30 mg) as described for **7** gave **9** (40 mg, 98%). Recrystallization from ethanol–petroleum ether yielded flaky crystals, m.p. 119–120°.

Anal. Calc. for $C_{16}H_{18}O_7$: C, 59.61; H, 5.64. Found: C, 59.80; H, 5.66.

1,5-Anhydro-3-O-*benzoyl-2,4-di*-O-p-*tolylsulfonylxylitol* (**12**). — The 3-benzoate **5** (100 mg) was treated with *p*-toluenesulfonyl chloride (320 mg) in pyridine for 4 days at room temperature. Extraction with chloroform followed by crystallization from dichloromethane–ethanol gave fine needles (141 mg, 62%), m.p. 167–168°.

Anal. Calc. for $C_{26}H_{26}O_9S_2$: C, 57.12; H, 4.80; S, 11.70. Found: C, 56.91; H, 5.03; S, 11.71.

3,4-Di-O-*acetyl-1,5-anhydro-2*-O-*benzoyl*-DL-*xylitol* (**10**). — Acetylation of the monobenzoate **6** (100 mg) followed by evaporation gave a syrup (134 mg, 99%). Crystallization from ethanol afforded **10**, m.p. 103–104°.

Anal. Calc. for $C_{16}H_{18}O_7$: C, 59.61; H, 5.64. Found: C, 59.72; H, 5.66.

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