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PARTIAL BENZOYLATION OF 2,1′:4,6-DI-*O*-ISOPROPYLIDENE-SUCROSE

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ABSTRACT

Partial benzoylation of 2,1′:4,6-di-*O*-isopropylidenesucrose (**1**) with 1.1 mol. equiv. of benzoyl chloride in pyridine gave the 6′-benzoate **2** (13%), 3′-benzoate **3** (7%), and 3′,6′-dibenzoate **4** (10%); 51% of **1** was recovered. With 1.4 mol. equiv., the percentages were **1**, 20; **2**, 20; **3**, 12; and **4**, 19. The 3′,4′,6′-tribenzoate **5** (3%), 3,3′,6′-tribenzoate **6** (4%), and tetrabenzoate **7** (4%) were also formed. With 2.1 mol. equiv., 50% of **4** was obtained; with 3.1 mol. equiv., the percentages were **4**, 24; **5**, 19; **6**, 15; and **7**, 15. Removal of the acetal groups from **4** and monobenzoylation gave 6,3′,6′-tri-*O*-benzoylsucrose. Removal of the acetal groups from **5**, **6**, and **7** gave 3′,4′,6′-tri-*O*-benzoylsucrose, 3,3′,6′-tri-*O*-benzoylsucrose, and 3,3′,4′,6′-tetra-*O*-benzoylsucrose, respectively.

INTRODUCTION

As part of a programme concerned with the synthesis of selectively benzoylated sucrose derivatives, we have studied the partial benzoylation of 2,1′:4,6-di-*O*-isopropylidenesucrose[1–3] (**1**). In particular, we were interested in achieving substitution at position 3′ (fructose ring). After the three primary positions, positions 2 (glucopyranosyl ring) and 3′ (fructofuranosyl ring) are the most reactive[4]. In agreement with these results, Hough and co-workers[5] have shown that the selective tosylation of sucrose gave the 2,6,1′,6′-tetratosylate as the major tetrasubstituted derivative. Also, selective tosylation of 3,6′-di-*O*-acetyl-2,1′:4,6-di-*O*-isopropylidenesucrose gave the 3′-tosylate as the major product[2]. We now describe the benzoylation of **1** using 1–3 mol. equiv. of benzoyl chloride.

DISCUSSION

Treatment of **1** at 0° with 1.1 mol. equiv. of benzoyl chloride in pyridine gave a mixture of products which was partitioned between dichloromethane and water; 51% of **1** was recovered from the aqueous phase. T.l.c. of the dichloromethane extract revealed four major components, the slowest migrator corresponding to **1**.

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TABLE I

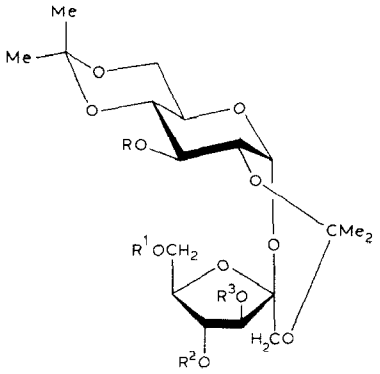
^{1}H-N M R DATA FOR COMPOUNDS **1–7**, **11–15**, AND **26**

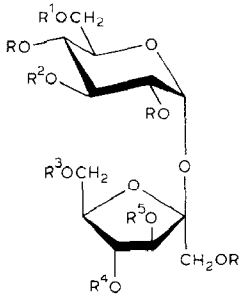
Compound[a]	*Chemical shifts (δ) (first-order couplings, Hz, in parentheses)*											
	H-1 ($J_{1,2}$)	*H-3* ($J_{2,3}$) ($J_{3,4}$)	*H-3'* ($J_{3',4'}$)	*H-4'* ($J_{4',5'}$)	*H-2–6 H-1',H-3'–6' OH*	*OH*	*Aryl*	*OAc*				CMe_2
								C-3	*C-4'*	*C-6'*	*C-3'*	
1[b]	6.26d (3.3)		(7.7)	4.58t (7.7)	3.45–4.40m	5.20d, 5.41s (8.8)						1.44, 1.51 1.51, 1.51
2[d]	6.18d (3.2)				3.25–4.80m	2.16s	7.25–8.15m					1.27, 1.46 1.50, 1.50
3[c]	6.20d (3.1)		5.15d (7.5)	4.90t (7.5)	3.50–4.20m	2.45–3.50 (broad 3H)	7.25–8.15m					1.36, 1.43 1.50, 1.50
4[e]	6.15d (3.3)		5.05d (6.2)	4.58t (6.2)	3.45–4 60m	2.47d (1.5)	7 25–8.15m					1.40, 1.43 1 53, 1.53
5[e]	6.13d (2.4)		5.53d (4.6)	5.82dd (2.4)	3.45–4.75m	2.38s	7 15–8.30m					1.38, 1 41 1.48, 1 52
6[d]	6.25d (3.5)	5.70t (9.0) (9.0)	4.93d (6.4)		3.50–4.75m		7.25–8.35m					1 21, 1.31 1.45, 1.45
7[b]	6.23d (3.6)	5.40t (9.2) (9.2)	5.57d (4.9)	5.83dd (3.3)	3.65–4.80m		7.25–8.25m					1 21, 1.28 1.40, 1 45

11[d]	6.13d (3.6)	5.22t (9.8) (9.8)	5.17d (6.2)	5.44dd (4.1)	3.25–4.70m	7.20–8.15m	2.05s	2.05s		2.25s	1.26, 1.40 1.45, 1.45
12[d]	6.12d (3.9)	5.14t (9.0) (9.0)	5.33d (5.8)	5.44dd (5.1)	3.25–4.55m	7.25–8.30m	1.98s	2.04s	2.09s		1.26, 1.40 1.45, 1.46
13[d]	6.14d (3.5)	5.13t (9.0) (9.0)	5.35d (5.1)	5.58dd (3.7)	3.40–4.75m	7.15–8.25m	1.99s	2.06s			1.25, 1.30 1.40, 1.45
14[d]	6.17d (3.5)	5.15t (9.0) (9.0)	5.55d (5.0)	5.79dd (4.0)	3.35–4.90m	7.20–8.30m	2.00s				1.30, 1.30 1.40, 1.45
15[d]	6.19d (3.6)	5.38t (9.3) (9.3)	5.36d (4.6)	5.60dd (3.6)	3.30–4.80m	7.20–8.35m		2.08s			1.18, 1.27 1.40, 1.43
26[bf]	6.09d (3.6)	5.22t (9.6) (9.6)	5.16d (5.9)	5.31dd (4.3)	3.45–4.45m		2.04s	2.06s	2.09s	2.24s	1.26, 1.40 1.45, 1.46

[a]In $CDCl_3$. [b]At 270 MHz. [c]At 300 MHz. [d]At 90 MHz. [e]At 250 MHz. [f]For comparison.

Column chromatography of the mixture gave the 3′,6′-dibenzoate **4** (10%), the 3′-benzoate **3** (7%), and the 6′-benzoate **2** (13%). The structures of **2–4** were established by ^{1}H- and ^{13}C-n.m.r. and mass spectroscopy. Thus, the ^{1}H-n.m.r. spectrum of **4** (Table I) showed signals at δ 6.15 (d, H-1) and 5.05 (d, H-3′). Since the latter signal appeared to lower field than those of the other ring protons, the benzoate groups were attached to C-3′ and C-6′. That the two benzoate groups were on the same moiety of the sucrose molecule was confirmed by the mass spectrum of the di-acetate **13** of **4** (Table II). C.i.-m.s. of **13** gave a molecular weight of 714, and e.i.-m.s. gave fragment ions at *m/z* 699 $(M - Me)^+$, 397 (ketofuranosyl cation), and 245 (hexopyranosyl cation). The ^{1}H-n.m.r. spectrum of **13** (Table I) showed, in addition to a signal at δ 5.35 (d, H-3′), signals at 5.13 (t, H-3) and 5.58 (dd, H-4′) in the δ 5.0–6.0 region.





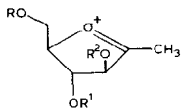
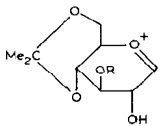
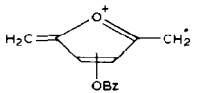
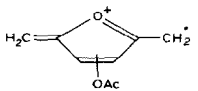
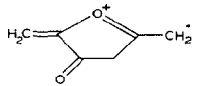
1 R = R^1 = R^2 = R^3 = H
2 R = R^2 = R^3 = H, R^1 = Bz
3 R = R^1 = R^2 = H, R^3 = Bz
4 R = R^2 = H, R^1 = R^3 = Bz
5 R = H, R^1 = R^2 = R^3 = Bz
6 R^2 = H, R = R^1 = R^3 = Bz
7 R = R^1 = R^2 = R^3 = Bz
11 R = R^2 = R^3 = Ac, R^1 = Bz
12 R = R^1 = R^2 = Ac, R^3 = Bz
13 R = R^2 = Ac, R^1 = R^3 = Bz
14 R = Ac, R^1 = R^2 = R^3 = Bz
15 R^2 = Ac, R = R^1 = R^3 = Bz
26 R = R^1 = R^2 = R^3 = Ac

16 R = R^1 = R^2 = R^4 = H, R^3 = R^5 = Bz
18 R = R^2 = R^4 = H, R^1 = R^3 = R^5 = Bz
20 R = R^1 = R^2 = H, R^3 = R^4 = R^5 = Bz
22 R = R^1 = R^4 = H, R^2 = R^3 = R^5 = Bz
24 R = R^1 = H, R^2 = R^3 = R^4 = R^5 = Bz
17 R = R^1 = R^2 = R^4 = Ac, R^3 = R^5 = Bz
19 R = R^2 = R^4 = Ac, R^1 = R^3 = R^5 = Bz
21 R = R^1 = R^2 = Ac, R^3 = R^4 = R^5 = Bz
23 R = R^1 = R^4 = Ac, R^2 = R^3 = R^5 = Bz
25 R = R^1 = Ac, R^2 = R^3 = R^4 = R^5 = Bz
27 R = R^1 = R^2 = R^3 = R^4 = R^5 = Ac

The ^{1}H-n.m.r. spectrum (Table I) of the monobenzoate **3** contained a signal at δ 5.15 (d, H-3′), at lower field than those of the other ring protons except for that of H-1, indicating that the benzoate group was at position 3′. In comparison, the monobenzoate **2** showed no signals in this region, apart from that at δ 6.18 (d, H-1), and was therefore the 6′-benzoate. The ^{13}C-n.m.r. spectra of **2** and **3** (Table III) also supported the assigned structures. Substitution at O-6′ in **2** resulted in a

TABLE II

MASS-SPECTRAL DATA FOR COMPOUNDS **7**, **11**–**15**, AND **26**

m/z *of principal fragments (% of base peak)*							*Assignment*	
7	**11**	**12**	**13**	**14**	**15**	**26**[a]		
			732[b]				$M + NH_4^+$	
823 (1.1)	637 (0.9)	637 (1.5)	699 (3.2)	761 (1.1)	761 (0.3)	575 (1.4)	$[M - Me]^+$	
459 (1.1)				459 (0.5)				
			397 (0.5)		397 (1.0)			R = R¹ = R² = Bz R = R² = Bz, R¹ = Ac R = Bz, R¹ = R² = Ac R² = Bz, R = R¹ = Ac R = R¹ = R² = Ac
	335 (1.0)							
		335 (1.6)						
						273 (1.8)		
307 (14.6)					307 (7.1)			R = Bz R = Ac
	245 (10.1)	245 (1.8)	245 (9.0)	245 (8.0)		245 (8.8)		
214 (26.8)			214 (1.7)	214 (26.3)	214 (1.2)			
	152 (46.9)	152 (5.8)	152 (28.9)		152 (26.8)	152 (30.8)		
110 (1.9)	110 (0.6)	110 (3.5)	110 (26.7)	110 (2.9)	110 (17.0)	110 (30.3)		
105 (100)	105 (68.5)	105 (100)	105 (71.0)	105 (100)	105 (100)		$PhCO^+$	
	43 (100)	43 (79.8)	43 (100)	43 (11.8)	43 (17.0)	43 (100)	$MeCO^+$	

[a]For comparison. [b]Chemical-ionisation mass spectrometry.

TABLE III

^{13}C-N M R CHEMICAL SHIFTS (p.p.m.) FOR COMPOUNDS[a] **2–7** AND **11–15**

Atom	**2**	**3**	**4**	**5**	**6**	**7**	**11**	**12**	**13**	**14**	**15**
C-2′	103.7	103.8	104.7	105.1	105.1	105.3	104.8	105.1	105.2	105.3	105.3
C-1	91.2	91.2	91.2	91.6	91.4	92.0	91.7	91.8	91.8	91.9	91.9
C-5′	79.8	84.6	81.7	80.4	82.9	80.6	79.9	80.3	80.3	80.5	80.3
C-3′	79.5	81.1	81.5	78.0	82.0	78.0	77.3[b]	77.6[b]	77.9	77.9	78.0
C-4′	78.3	73.7	77.0	78.5	77.3	78.6	77.7[b]	77.8[b]	77.9	78.6	78.0
C-4[c]	73.9	72.9	74.0	73.8	72.2	72.1	71 9	71 9	71.9	71.9	72 1
C-2[c]	73.4	72.2	73.0	72.7	71.6	71.6	71.6	71.5	71.5	71.5	71.6
C-3	69.7	70.4	70 5	70.2	71.4	71.6	70.8	70.9	70.9	70.9	71.6
C-5	63.9	64.1	63.9	63.9	64.4	64.4	64.5	64.4	64.4	64.4	64.4
C-1′	66.6	66.7	66.1	66.5	66.1	66.3	66.1	66.1	66.1	66.3	66.2
C-6′	65.9	62.0	65.9	64.9	65.6	65.2	65.6	64.8	65.2	65.3	65.2
C-6	62.3	61.5	62.2	62.0	62.2	62.1	62.2	62.1	62.1	62.1	62.1
Acetal	102.2	102.1	101.8	101.7	101.6	101.6	101.5	101.5	101.5	101.5	101.5
carbons	100.1	100.0	99.8	99.6	99.7	99.5	99.7	99.5	99.5	99.5	99.5
Acetal	29.1	29.1	29.2	29.1	29.0	28.9	29.1	29.0	29.0	29.0	29.0
methyl	25.3	25.5	25.5	25.6	25.3	25.5	25.5	25.5	25.5	25.5	25.4
carbons	24.2	24.2	24.2	24.1	23.9	23.9	23.9	23.9	23.9	23.9	23.9
	19.2	19.2	19.2	19.2	19.0	19.1	19.1	19.1	19.1	19.1	19.1

[a]In $CDCl_3$. [b,c]Assignments may be reversed.

significant shift (4.6 p.p.m.) to low field[6] of the signal for C-4′ compared with the corresponding signal in **3**. Comparison of the mass spectra of the tri-acetate derivatives (**11** and **12**, respectively) of **2** and **3** showed fragment ions at *m/z* 335 (ketofuranosyl cation) and 245 (hexopyranosyl cation), confirming that the fructofuranosyl ring was benzoylated. The ^{1}H-n.m.r. spectra of **11** and **12** (Table I) were also consistent with the assigned structures. Thus, the H-3′ doublet of **12** is shifted (0.16 p.p.m.) to low-field by the 3′-benzoate group compared with that of **11** and also compared with that of the diacetal tetra-acetate **26** (Table I). The presence of a benzoate group at position 6′ (**11**) or 3′ (**12**) causes a downfield shift (0.13 p.p.m.) in the signal for H-4′.

With 1.4 mol. equiv. of benzoyl chloride, less **1** (20%) remained, but more **2** (20%), **3** (12%), and **4** (20%) were obtained as well as the tribenzoates **5** and **6** and the tetrabenzoate **7**. With 2 mol. equiv. of benzoyl chloride, **1** gave 50% of **4** as well as **5–7**; only traces of the monobenzoates were isolated. With 3 mol. equiv. of benzoyl chloride, **1** gave **4–7** in approximately equal amounts (combined yield, 73%). The R_F values (t.l.c.) of **4–7** were 0.22, 0.32, 0.78, and 0.90, respectively; the marked difference in R_F of the tribenzoates **5** and **6** is noteworthy.

The ^{1}H-n.m.r. spectrum of the tribenzoate **5** showed signals at δ 5.53 (H-3′) and 5.82 (H-4′), in good agreement with the values obtained for the tetrabenzoate **7**. The H-3′ doublets for **5** and **7** were shifted to lower field compared with the corresponding signals in the 3′,6′-dibenzoate **4** and the 3′-benzoate **3**, presumably due to the 4′-benzoate group. There were no other signals in the region δ 5.0–6.0

TABLE IV

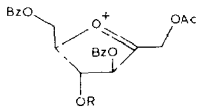
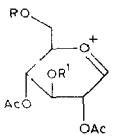
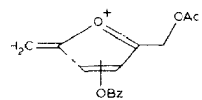
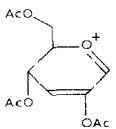
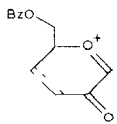
^{1}H-N M R DATA FOR COMPOUNDS **16–25** AND **27**

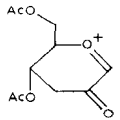
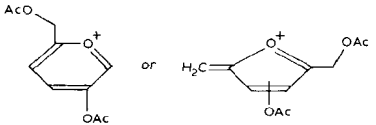
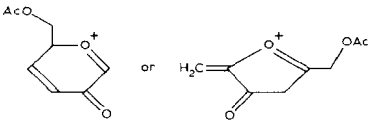
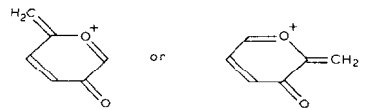
Compound[a]	*Chemical shifts (δ) (first-order couplings, Hz, in parentheses)*											
	H-1 ($J_{1,2}$)	*H-2* ($J_{2,3}$)	*H-3* ($J_{3,4}$)	*H-4* ($J_{4,5}$)	*H-3'* ($J_{3',4'}$)	*H-4'* ($J_{4',5'}$)	*H-2–6 H-1', H-4'–6' OH*	*OH*	*Aryl*	*OAc*		
16[bc]	5.43d		3.66t		5.66d	5.53t	3.35–5.00m		7.40–8.20m			
	(3.8)		(9.5)		(8.0)	(8.0)						
18[de]	5.53d		3.66t		5.53d	4.55t	3.40–4.70m		7.55–8.20m			
	(3.8)		(9.6)		(6.9)	(6.9)						
20[bf]	5.50d				6.00d	6.04t	3.35–5.10m		7.15–8.20m			
	(3.6)				(5.7)	(5.7)						
22[f]	5.49d		5.40t		5.53d		3.45–5.00m	3.20 s (5 H)	7.25–8.30m			
	(3.3)		(9.9)		(7.2)							
24[g]	5.50d		5.11t		5.83d	5.92t	3.55–4.90m	2.00–3.55	7.20–8.35m			
	(3.6)		(9.5)		(4.8)	(4.8)		(broad 4 H)				
17[e]	5.69d	4.93dd	5.39dd	5.02dd	5.75d	5.65dd	4.00–4.70m		7.40–8.15m	1.94	1.97	2.00
	(3.6)	(10.4)	(9.2)	(10.4)	(6.4)	(6.6)				2.08	2.08	2.12
19[e]	5.74d	4.91dd	5.41dd	5.16dd	5.71d	5.64dd	4.10–4.70m		7.35–8.15m	1.91	1.96	1.97
	(3.6)	(10.4)	(9.2)	(10.1)	(5.8)	(5.9)				2.08	2.13	
21[e]	5.73d	4.95dd	5.41dd	5.03dd	5.93d	5.89t	4.05–4.80m		7.30–8.15m	1.95	1.97	2.01
	(3.5)	(10.4)	(9.2)	(10.4)	(6.2)	(6.2)				2.09	2.12	
23[e]	5.74d	5.11dd	5.68dd	5.21dd	5.77d	5.69dd	4.05–4.75m		7.35–8.20m	1.85	1.89	2.09
	(3.6)	(10.4)	(9.7)	(10.1)	(6.4)	(6.6)				2.09	2.13	
25[e]	5.78d	5.13dd	5.70dd	5.23dd	5.96d	5.93t	4.10–4.85m		7.35–8.20m	1.85	1.91	2.11
	(3.6)	(10.4)	(9.6)	(10.2)	(6.3)	(6.3)				2.13		
27[h]	5.69d	4.87dd	5.45dd	5.08dd	5.45d	5.36dd	4.05–4.45m			2.02	2.05	2.10
	(3.6)	(10.4)	(9.2)	(9.6)	(5.6)	(6.1)				2.10	2.10	2.12
										2.12	2.18	

[a]In $CDCl_3$ unless otherwise stated. [b]In CD_3OD. [c]At 250 MHz. [d]In $CDCl_3/CD_3OD$. [e]At 270 MHz. [f]At 90 MHz. [g]At 300 MHz. [h]For comparison[8,9].

TABLE V

MASS-SPECTRAL DATA FOR COMPOUNDS **17, 19, 21, 23, 25,** AND **27**

m/z *of principal fragments (% of base peak)*						*Assignment*	
17	**19**	**21**	**23**	**25**	**27**[a]		
820[b]		882[b]				$M + NH_4^+$	
455 (15.6)	455 (8.3)	517 (20.8)	455 (5 7)	517 (6.3)			R = Bz R = Ac
331 (29.3)	393 (15.0)	331 (34.6)	393 (6.9)	393 (14.7)	331 (23.8)[c]		R = Bz, R^1 = Ac R = Ac, R^1 = Bz R = R^1 = Ac
273 (14.9)	273 (9.7)	273 (23.4)	273 (8.3)	273 (11.2)			
271 (2.2)		271 (9.4)	271 (0.9)	271 (1.4)	271 (1.2)[c]		
	231 (15.9)						

229 (1.0)		229 (2.2)	229 (0.6)	229 (0.4)	229 (0.9)	
211 (3.8)	211 (1.0)	211 (4.8)	211 (1.3)	211 (0.9)	211 (23.5)	
169 (46.8)	169 (4.1)	169 (54.5)	169 (18.4)	169 (25.4)	169 (41.5)	
109 (30.3)	109 (11.2)	109 (28.5)	109 (14.8)	109 (16.2)	109 (29.2)	
105 (89.7)	105 (100)	105 (100)	105 (100)	105 (100)		$PhCO^+$
43 (100)	43 (52.3)	43 (97.5)	43 (46.9)	43 (29.9)	43 (100)	$MeCO^+$

[a]For comparison[11]. [b]Chemical-ionisation mass spectrometry. [c]Plus corresponding ketofuranosyl cation.

and hence **5** was assigned the 3′,4′,6′-tribenzoate structure. This was confirmed by the mass spectrum of the mono-acetate (**14**) of **5** which gave fragment ions at *m/z* 459 (ketofuranosyl cation) and 245 (hexopyranosyl cation), indicating that the fructofuranosyl ring carried the three benzoate groups. The ^{1}H-n.m.r. spectrum of **14** was similar to that of **5** except that a signal at δ 5.15 (H-3) was now observed.

The ^{1}H-n.m.r. spectrum of the tribenzoate **6** indicated that it was substituted at positions 3, 3′, and 6′. This assignment was supported by the mass spectrum of the mono-acetate (**15**) of **6**, which gave fragment ions at *m/z* 397 (ketofuranosyl cation) and 307 (hexopyranosyl cation) that confirmed the presence of a benzoate group on the glucopyranosyl moiety. A comparison of the ^{1}H-n.m.r. spectra of **15**, the 3′,6′-dibenzoate diacetate **13**, and the 3′,4′,6′-tribenzoate monoacetate **14** showed that the signal for H-3 (δ 5.38) in **15** was at lower field than the corresponding signal for **13** or **14** (δ 5.13 and 5.15, respectively), indicating the presence of a 3-benzoate group in **15**. The signal for H-4′ (δ 5.60) was at higher field than the corresponding signal for **14** (δ 5.79) and similar to the signal for H-4′ in **13** (δ 5.58), indicating that C-4′ was unsubstituted in the parent compound.

Removal of the acetal groups from **4** with aqueous trifluoroacetic acid[7] gave the crystalline dibenzoate **16**. The ^{1}H-n.m.r. spectrum (Table IV) of **16** showed the expected low-field signal (d) for H-3′ at δ 5.66. There were no other signals in this region, apart from that at δ 5.43 (d, H-1), and therefore the only secondary hydroxyl group substituted was at position 3′. Under the reaction conditions employed, benzoate migration was unlikely and so the product was the 3′,6′-dibenzoate **16**. The mass spectrum (Table V) of the hexa-acetate (**17**) of **16** contained fragment ions at *m/z* 455 and 273 (ketofuranosyl cations) and 331 and 271 (hexopyranosyl cations), confirming that the fructofuranosyl moiety was di-*O*-benzoylated. Comparison of the ^{1}H-n.m.r. spectra of **17** and sucrose octa-acetate[8,9] (**27**) showed that the signals for H-3′ and H-4′ in **17** had been shifted to lower field, the latter due to the deshielding effect of the 3′- and 6′-benzoate groups.

The 3′,6′-dibenzoate **16** could be conveniently prepared (22% from **1**) by treating the products of a dimolar benzoylation of **1** with aqueous trifluoroacetic acid (see Experimental).

Monobenzoylation of **16** gave a mixture which t.l.c. showed to contain two major components, namely, **16** and **18**, which were subsequently isolated in yields of 43 and 19%, respectively. The ^{1}H-n.m.r. spectrum (Table IV) of **18** was very similar to that of **16**, with a low-field signal at δ 5.53 (d, H-3′). The mass spectrum of the penta-acetate (**19**) of **18** contained fragment ions at *m/z* 455 and 273 (ketofuranosyl cations) and 393 and 231 (hexopyranosyl cations), indicating that the glucopyranosyl moiety carried a benzoate group. Thus, assuming that there was no 6′→1′ benzoate migration, then **18** is 6,3′,6′-tri-*O*-benzoylsucrose.

Removal of the acetal groups from **5**–**7**, in the normal manner, gave the 3′,4′,6′-tribenzoate **20**, the 3,3′,6′-tribenzoate **22**, and the 3,3′,4′,6′-tetrabenzoate **24**, respectively. The ^{1}H- and ^{13}C-n.m.r. spectra (Tables IV and VI) of **20**, **22**, and **24**, and their acetylated derivatives **21**, **23**, and **25**, respectively, were in agreement

TABLE VI

^{13}C-N.M.R. CHEMICAL SHIFTS (p.p.m.) FOR COMPOUNDS[a] **16–25**

Atom	**16**[b]	**18**[c]	**20**	**22**[b]	**24**	**17**	**19**	**21**	**23**	**25**
C-2′	105.2	104.7	105.7	105.3	105.7	103.9	104.3	104.0	103.9	104.0
C-1	93.3	92.2	92.6	93.6	92.7	90.0	90.3	90.2	90.3	90.4
C-5′	81.4	80.9	79.7	81.3	80.0	78.9	79.1	79.3	78.4	79.3
C-3′	80.3	80.2	78.2	80.4	78.5	76.6	77.0	76.7	77.0	76.7
C-4′	75.6	74.9	77.6	75.7	77.7	75.5	75.7	76.3	75.6	76.3
C-3	75.1	74.1	74.2	77.7	77.4	70.0	70.0	70.0	70.2	70.2
C-5	74.6	72.1	73.1	74.8	73.5	68.8	68.7	68.9	69.0	69.1
C-2	73.2	71.4	71.9	71.5	70.7	70.2	70.2	70.0	70.4	70.5
C-4	71.5	70.5	69.9	69.6	69.5	68.5	68.7	68.6	68.3	68.4
C-6′	67.5	65.7	64.8	67.6	64.8	64.5	64.2	64.7	64.5	64.7
C-1′	65.1	64.9	64.5	64.8	64.7	64.0	64.0	64.1	63.9	64.0
C-6	62.7	64.6	61.7	62.3	62.2	62.0	62.2	62.1	62.0	62.1

[a]In $CDCl_3$ unless otherwise stated. [b]In CD_3OD. [c]In $CD_3OD/CDCl_3$.

with the assigned structures. Thus, the ^{1}H-n.m.r. spectrum (CD_3OD) of **20** showed low-field signals at δ 6.00 (d, H-3′) and 6.04 (t, H-4′), and that ($CDCl_3$) of **22** signals at δ 5.53 (d, H-3′) and 5.40 (t, H-3). The ^{1}H-n.m.r. spectra of the penta-acetate **21** and the tetra-acetate **25** were very similar, with the signals for H-3′ and H-4′ appearing at lower field than those for the other ring protons. The signals at δ 5.70 (dd) and 5.68 (dd) in the ^{1}H-n.m.r. spectra of the tetrabenzoate **25** and the 3,3′,6′-tribenzoate **23** were assigned to H-3, and appeared downfield by 0.29 and 0.27 p.p.m., respectively, compared with the corresponding signal in **21**, indicating that position 3 was benzoylated. The mass spectra of **21** and **25** contained a fragment ion at *m/z* 517 (tri-*O*-benzoylated ketofuranosyl cation), and **23** and **25** gave a fragment ion at *m/z* 393 (mono-*O*-benzoylated hexopyranosyl cation).

The foregoing results indicate that the order of reactivity of the hydroxyl groups in **1**, towards esterification, is HO-6′ > HO-3′ ⩾ HO-4′ ≃ HO-3. The greater reactivity of HO-3′ compared with those of HO-3 and HO-4′ accords with results[4] on the partial benzoylation of sucrose, whereby substitution of HO-2 and HO-3′ is greatly preferred to the other secondary hydroxyl groups.

EXPERIMENTAL

General methods. — In addition to the data given in the preceding paper[4], i.r. spectra were recorded with a Perkin–Elmer Model 157G spectrometer. Column and flash chromatography[10] were performed on silica gel 9385 (Merck, 0.040–0.063 mm). T.l.c. was performed with dichloromethane–ethyl acetate–ethanol (6:3:1) unless otherwise stated. ^{1}H-N.m.r. spectra (internal Me_4Si) were recorded with Jeol FX90Q, Jeol FX270Q, Bruker WM-250, and Bruker WH-300 spectrometers (see Tables I and IV); ^{13}C-n.m.r. spectra (22.50 MHz) were recorded with a Jeol FX90Q spectrometer (see Tables III and VI). Mass spectra are recorded in Tables II and V.

*2,1′:4,6-Di-*O*-isopropylidenesucrose* (**1**). — A solution of 2,1′:4,6-di-*O*-iso-

propylidenesucrose tetra-acetate[1-3] (**26**, 1 g) in methanol (25 mL) was treated with sodium (catalytic quantity). After 2 h, t.l.c. revealed two components with mobilities lower than that of **26**. After a further 20 h, only the component of lowest mobility remained, and the solution was neutralised with solid carbon dioxide and concentrated to dryness. A solution of the residue in dichloromethane was filtered and concentrated to give **1** (80%). Recrystallisation from ethyl acetate–light petroleum gave **1**, m.p. 161–163°, $[\alpha]_D^{25}$ +25° (*c* 2, methanol); lit.[3] $[\alpha]_D$ +25.5° (methanol).

Benzoylation of 2,1':4,6-di-O-isopropylidenesucrose (**1**). — (*a*) Benzoyl chloride (0.3 mL, 1.1 mol. equiv.) was added to a solution of **1** (1 g) in anhydrous pyridine (5 mL) at 0°. The mixture was stored at room temperature for 18 h, then treated with water (a few drops), poured into ice–water, and extracted with dichloromethane, and the extract was washed with water. T.l.c. of the extract revealed four major components, the slowest corresponding to **1**. The aqueous phase contained **1** and concentration to dryness gave **1** (0.51 g). The dichloromethane extract was dried ($MgSO_4$) and concentrated to dryness. Column chromatography of the resulting syrup (0.64 g) with ethyl acetate–light petroleum (4:1) gave, first, the 3',6'-dibenzoate **4** (178 mg, 12%), then the 3'-benzoate **3** (83 mg, 7%), and finally the 6'-benzoate **2** (160 mg, 13%); **1** was not eluted from the column.

Compound **2** was an amorphous solid, $[\alpha]_D^{25}$ +41° (*c* 3.5, chloroform); ν_{max}^{Nujol} 3420 (OH), 1720 cm^{-1} (C=O).

Anal. Calc. for $C_{25}H_{34}O_{12}$: C, 57.03; H, 6.46. Found: C, 57.08; H, 6.75.

The triacetate (**11**) of **2** was a glass, $[\alpha]_D^{25}$ +15° (*c* 2.9, chloroform); ν_{max}^{KBr} 1753, 1728 cm^{-1} (C=O).

Compound **3** was an amorphous solid, $[\alpha]_D^{25}$ −29° (*c* 2.8, chloroform); ν_{max}^{Nujol} 3440 (OH), 1720 cm^{-1} (C=O).

Anal. Calc. for $C_{25}H_{34}O_{12}$: C, 57.03; H, 6.46. Found: C, 56.98; H, 6.42.

The triacetate (**12**) of **3** was a glass, $[\alpha]_D^{25}$ +18° (*c* 2.2, chloroform); ν_{max}^{KBr} 1755 cm^{-1} (C=O).

Recrystallisation of **4** from ethyl acetate–light petroleum gave material having m.p. 121–122°, $[\alpha]_D^{20}$ −13° (*c* 1, chloroform); $\nu_{max}^{liq\ film}$ 3470 (OH), 1725 cm^{-1} (C=O).

Anal. Calc. for $C_{32}H_{38}O_{13}$: C, 60.95; H, 6.03. Found: C, 60.92; H, 6.04.

The diacetate (**13**) of **4** was a glass, $[\alpha]_D^{25}$ +16° (*c* 4.8, chloroform); ν_{max}^{Nujol} 1755 (shoulder), 1724 cm^{-1} (C=O).

(*b*) A solution of **1** (1 g) in anhydrous pyridine (5 mL) was treated with benzoyl chloride (0.38 mL, 1.4 mol. equiv.) at 0°. The mixture was kept at room temperature for 18 h, treated with water (a few drops), and concentrated to dryness. Column chromatography of the syrupy product with ethyl acetate–light petroleum (4:1) gave, first, a mixture (497 mg) containing di-, tri-, and tetra-benzoates, and then **3** (150 mg, 12%), **2** (244 mg, 20%), and **1** (198 mg, 20%). Column chromatography of the initial mixture with light petroleum–ethyl acetate (3:1) gave, first, the tetrabenzoate **7** (86 mg, 4%), and then the 3,3',6'-tribenzoate **6** (66 mg, 4%), the 3',4',6'-tribenzoate **5** (54 mg, 3%), and **4** (280 mg, 19%).

Recrystallisation of **7** from ethyl acetate–light petroleum gave a product iden-

tical with the tetrabenzoate prepared by the treatment of **1** with excess of benzoyl chloride and which had m.p. 93–95°, $[\alpha]_D^{25}$ +4° (*c* 2, chloroform); ν_{max}^{Nujol} 1725 cm^{-1} (C=O).

Anal. Calc. for $C_{46}H_{46}O_{15}$: C, 65.87; H, 5.49. Found: C, 65.42; H, 5.84.

After recrystallisation from ethyl acetate–light petroleum, **5** had m.p. 151–152°, $[\alpha]_D^{20}$ −54° (*c* 1, chloroform); ν_{max}^{Nujol} 3450 (OH), 1725 cm^{-1} (C=O).

Anal. Calc. for $C_{39}H_{42}O_{14}$: C, 63.80; H, 5.70. Found: C, 63.51; H, 6.05.

The acetate (**14**) of **5** was a glass, $[\alpha]_D^{25}$ −9° (*c* 4.4, chloroform); ν_{max}^{Nujol} 1725 cm^{-1} (C=O).

After recrystallisation from ethyl acetate–light petroleum, **6** had m.p. 198–201°, $[\alpha]_D^{20}$ +62° (*c* 1, chloroform); ν_{max}^{Nujol} 3545 (OH), 1715 cm^{-1} (C=O).

Anal. Calc. for $C_{39}H_{42}O_{14}$: C, 63.80; H, 5.70. Found: C, 64.16; H, 5.90.

The acetate (**15**) of **6** was a glass, $[\alpha]_D^{25}$ +38° (*c* 3, chloroform); ν_{max}^{Nujol} 1725 cm^{-1} (C=O).

(*c*) Benzoyl chloride (0.57 mL, 2.1 mol. equiv.) was added to a solution of **1** (1 g) in anhydrous pyridine (5 mL) at 0°. The mixture was stored at room temperature for 18 h, treated with a few drops of water, and concentrated to dryness. T.l.c. of the product showed that **1** was absent and that **4** was the major product. There were also several faster-moving components and traces of the 3′- and 6′-benzoates. Column chromatography of the mixture with light petroleum–ethyl acetate (3:1) gave, first, **7** (179 mg, 9%), and then **6** (157 mg, 9%), **5** (142 mg, 8%), and **4** (746 mg, 50%). Only traces of the monobenzoates were recovered.

(*d*) Benzoyl chloride (0.87 mL, 3.1 mol. equiv.) was added to a solution of **1** (1 g) in anhydrous pyridine (5 mL) at 0°. The mixture was stored at room temperature for 18 h, treated with a few drops of water, and poured into ice–water. T.l.c. of the resulting solid with light petroleum–ethyl acetate (3:2) revealed four major components, R_F 0.22 (**4**), 0.32 (**5**), 0.78 (**6**), and 0.90 (**7**). Column chromatography of the solid product gave **7** (292 mg, 15%), **6** (262 mg, 15%), **5** (336 mg, 19%), and **4** (361 mg, 24%).

3′,6′-Di-O-benzoylsucrose (**16**). — Compound **4** (0.3 g) was treated[7] with 9:1 trifluoroacetic acid–water (3 mL). Addition of ethyl acetate gave a product (0.21 g, 81%) which was recrystallised from ethyl acetate to give **16**, m.p. 169–171°, $[\alpha]_D^{20}$ +6° (*c* 2, methanol); $\nu_{max}^{liq.\ film}$ 3350 (OH), 1735, 1695 cm^{-1} (C=O).

Anal. Calc. for $C_{26}H_{30}O_{13}$: C, 56.73; H, 5.45. Found: C, 57.01; H, 5.57.

The hexa-acetate (**17**) of **16** was a glass, $[\alpha]_D^{25}$ +37° (*c* 2.6, chloroform); ν_{max}^{Nujol} 1753, 1730 cm^{-1} (C=O).

6,3′,6′-Tri-O-benzoylsucrose (**18**). — A solution of **16** (0.4 g) in anhydrous pyridine (3 mL) was treated with benzoyl chloride (0.10 mL, 1.2 mol. equiv.) at 0°. The mixture was stored at room temperature for 18 h, treated with a few drops of water, poured into ice–water, and extracted with dichloromethane. The aqueous phase was then extracted with ethyl acetate, and the extract was dried ($MgSO_4$) and concentrated to dryness to give **16** (172 mg, 43%). T.l.c. of the dichloromethane extract revealed one major and several minor components. Column chromatography of the mixture with dichloromethane–ethyl acetate–ethanol

(6:3.5:0.5) gave **18** (90 mg, 19%), m.p. 158–162°, $[\alpha]_D^{20}$ +18° (*c* 1, chloroform); ν_{max}^{Nujol} 3465, 3350 (OH), 1725, 1710, 1693 cm^{-1} (C=O).

Anal. Calc. for $C_{33}H_{34}O_{14}$: C, 60.55; H, 5.20. Found: C, 60.45; H, 5.03.

The penta-acetate (**19**) of **18** was a glass, $[\alpha]_D^{25}$ +46° (*c* 5.5, chloroform); ν_{max}^{KBr} 1755, 1725, 1690 cm^{-1} (C=O).

3',4',6'-Tri-O-benzoylsucrose (**20**). — The diacetal **5** (0.28 g) was treated[7] with 9:1 trifluoroacetic acid–water (3 mL) to give **20** (288 mg, 85%) as a foam, $[\alpha]_D^{25}$ −52° (*c* 1, methanol); ν_{max}^{KBr} 3410 (OH), 1725 cm^{-1} (C=O).

Anal. Calc. for $C_{33}H_{34}O_{14}$: C, 60.55; H, 5.20. Found: C, 60.47; H, 5.17.

The penta-acetate (**21**) of **20** was a glass, $[\alpha]_D^{25}$ +5° (*c* 4, chloroform); ν_{max}^{KBr} 1755, 1735 cm^{-1} (C=O).

3,3',6'-Tri-O-benzoylsucrose (**22**). — The diacetal **6** (0.15 g) was treated[7] with 9:1 trifluoroacetic acid–water (2 mL). Recrystallisation of the product from dichloromethane gave **22** (80 mg, 60%), m.p. 128–130°, $[\alpha]_D^{25}$ +35° (*c* 2, methanol); ν_{max}^{KBr} 3520, 3260 (OH), 1715 cm^{-1} (C=O).

Anal. Calc. for $C_{33}H_{34}O_{14}$: C, 60.55; H, 5.20. Found: C, 60.56; H, 4.92.

The penta-acetate (**23**) of **22** was a glass, $[\alpha]_D^{25}$ +27° (*c* 3.6, chloroform); ν_{max}^{KBr} 1753, 1730 cm^{-1} (C=O).

3,3',4',6'-Tetra-O-benzoylsucrose (**24**). — The diacetal **7** (0.53 g) was treated[7] with 9:1 trifluoroacetic acid–water (5 mL). Recrystallisation of the product (455 mg, 95%) from ether–light petroleum gave **24**, m.p. 129–132°, $[\alpha]_D^{25}$ +9° (*c* 2, chloroform); ν_{max}^{KBr} 3450 (OH), 1725 cm^{-1} (C=O).

Anal. Calc. for $C_{40}H_{38}O_{15}$: C, 63.32; H, 5.01. Found: C, 63.17; H, 5.03.

The tetra-acetate (**25**) of **24** was a glass, $[\alpha]_D^{25}$ −0.7° (*c* 4.5, chloroform); ν_{max}^{Nujol} 1753, 1730 cm^{-1} (C=O).

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