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SYNTHESIS OF CRYSTALLINE DERIVATIVES OF 3-DEOXY-D-*gluco*-HEPTOFURANOSE*

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ABSTRACT

Benzoylation of D-*glycero*-D-*gulo*-heptono-1,4-lactone afforded 2,3,5,6,7-penta-*O*-benzoyl-D-*glycero*-D-*gulo*-heptono-1,4-lactone, which, by 3-deoxygenation, gave 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-D-*gluco*-heptono-1,4-lactone (**4**) in 80% overall yield. In a similar way, 2,5,6,7-tetra-*O*-acetyl-3-deoxy-D-*gluco*-heptono-1,4-lactone was prepared. Disiamylborane reduction of compound **4** gave crystalline 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-β-D-*gluco*-heptofuranose (**6**), which was acetylated to give crystalline 1-*O*-acetyl-2,5,6,7-tetra-*O*-benzoyl-3-deoxy-β-D-*gluco*-heptofuranose (**7**). Upon treatment of **6** with diazomethane–boron trifluoride etherate, methyl 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-β-D-*gluco*-heptofuranoside (**8**) was obtained. From the reaction mixture, the benzoylated β,β′-furanosyl disaccharide **11** was isolated. A higher yield (90%) of **8** was obtained by treatment of **7** with methanol and tin(IV) chloride. On *O*-debenzoylation of **8**, methyl 3-deoxy-β-D-*gluco*-heptofuranoside was obtained. Compound **11** was the sole product (82% yield) when **6** was treated with boron trifluoride-etherate in dichloromethane. *O*-Debenzoylation of **11** afforded crystalline 3-deoxy-β-D-*gluco*-heptofuranosyl 3-deoxy-β-D-*gluco*-heptofuranoside. *O*-Debenzoylation of **6** with sodium methoxide in chloroform afforded crystalline 3-deoxy-D-*gluco*-heptose, whose tautomeric equilibrium was studied by ^{13}C-n.m.r. spectroscopy.

INTRODUCTION

Among the components of the core oligosaccharide of bacterial lipopolysaccharides are aldoheptoses. 6-Deoxyheptoses were found in lipopolysaccharides from *Yersinia pseudotuberculosis*[1] and *Eubacterium saburreum*[2]. As far as we know, no other deoxyheptoses have been described as natural sugars. We now report the first synthesis of 3-deoxy-D-*gluco*-heptose (**10**), which was obtained crystalline from

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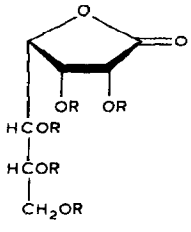
commercially available D-*glycero*-D-*gulo*-heptono-1,4-lactone (**1**). We had previously described the synthesis of deoxy sugars *via* β-elimination reactions occurring on benzoylation of aldonolactones[3,4]. The elimination of benzoylated 1,4-lactones in pyridine is, however difficult to control, because the 2,3-unsaturated lactones initially formed readily undergo further eliminations[5-7], decreasing the yield of the monounsaturated derivative and, consequently, that of its hydrogenation product, the 3-deoxylactone. For this reason, an alternative procedure[8] was employed in order to obtain 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-D-*gluco*-heptono-1,4-lactone[9] (**4**) from **1**.

Crystalline derivatives of 3-deoxy-D-*gluco*-heptofuranose were synthesized in high yields from the intermediate 3-deoxylactone **4**. In addition, we studied the tautomeric equilibrium of 3-deoxy-D-*gluco*-heptose in water.



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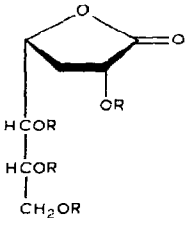
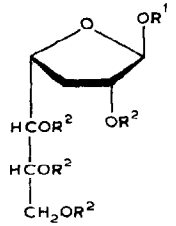
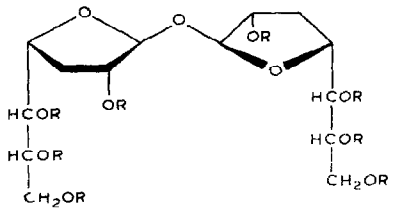
3 R = Ac



4 R = Bz
5 R = Ac



6 R^1 = H, R^2 = Bz
7 R^1 = Ac, R^2 = Bz
8 R^1 = CH_3, R^2 = Bz
9 R^1 = CH_3, R^2 = H
10 R^1 = R^2 = H



11 R = Bz
12 R = H
Ac = CH_3CO—
Bz = C_6H_5CO—

RESULTS AND DISCUSSION

3-Deoxygenation of 2,3,5,6,7-penta-*O*-benzoyl-D-*glycero*-D-*gulo*-heptono-1,4-lactone[10] (**2**) was performed as reported by Bock *et al.*[8] for acetylated aldono-

1,4-lactones. 2,5,6,7-Tetra-*O*-benzoyl-3-deoxy-D-*gluco*-heptono-1,4-lactone (**4**) was obtained in 92% yield. Compound **4** had previously been prepared in our laboratory[5,9] by stereospecific, catalytic hydrogenation of 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-D-*arabino*-hept-2-enono-1,4-lactone obtained, together with the di- and tri-unsaturated derivatives[7], by direct benzoylation of **1**. Hydrogenation was almost quantitative, but compound **4** could not be obtained in more than 50% total yield from D-*glycero*-D-*gulo*-heptono-1,4-lactone (**1**).

The analogous acetylated compound, 2,5,6,7-tetra-*O*-acetyl-3-deoxy-D-*gluco*-heptono-1,4-lactone (**5**), was also prepared by 3-deoxygenation of the fully acetylated lactone **3**, in order to compare the spectral data (see Table I). As could be expected for 1,4-lactones[11], C-1 resonates at lower field than the benzoate carbonyl groups. From the remaining lactone carbon atoms, the more deshielded one was C-4, the signal of which is shifted upfield for the 3-deoxy derivatives **4** and **5**. Signals for C-5 and C-6 could not be unambiguously assigned for compounds **2** and **3**, but a downfield shift for C-5 may be postulated for compounds **4** and **5**, because of the disappearance of the steric crowding produced by the acyloxy group[11] on C-3.

Diisoamylborane reduction[10] of compound **4** afforded the anomeric 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-D-*gluco*-heptofuranoses in 95% yield, with a preponderance of the β anomer **6**, which was obtained pure by recrystallization. The ^{1}H-n.m.r. spectrum of **6** showed a singlet for H-1 at δ 5.63. The anomeric-carbon signal appears at δ 101.1 in the ^{13}C-n.m.r. spectrum (see Table I), which agrees with a *trans* relationship[12] for C-1 and C-2. Assignments for C-2 and C-4 were confirmed by selective irradiation at δ 5.32 (H-2). However, C-5 and C-6 could not be unambiguously determined, as the corresponding signals in the ^{1}H-n.m.r. spectrum appeared at a similar frequency (δ 5.9). The β:α ratio (8:1) for the crude preparation was estimated by averaging the integrated intensities of the ^{13}C-n.m.r. resonances of C-1 and C-3 for each anomer, which appeared at δ 95.2 and 30.1, respectively, for the α anomer, and at δ 101.1 and 32.1 for the β form.

On acetylation of **6**, crystalline 1-*O*-acetyl-2,5,6,7-tetra-*O*-benzoyl-3-deoxy-β-D-*gluco*-heptofuranose (**7**) was obtained in 96% yield. As could be expected[13] (see Table I), acetylation induces an upfield shift on the signals of C-1 (1.1 p.p.m.) and C-2 (1.1 p.p.m.). The observed deshielding of C-4 (1.6 p.p.m.) can be explained by 1,3-interaction between H-4 and the acetoxyl group if **7** adopts the $^1T_0$ conformation, as do configurationally related compounds[4,6,13].

Upon methylation of **6** with diazomethane–boron trifluoride etherate[14] under conditions reported to prevent acyl migration, the anomeric methyl 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-D-*gluco*-heptofuranosides were obtained in 64% yield (β:α ratio 7:1, determined by ^{1}H-n.m.r. spectroscopy). The β anomer **8** was purified by recrystallization. From the reaction mixture, a nonreducing disaccharide derivative (**11**) could also be isolated. It was observed that increasing the concentration of boron trifluoride etherate favored the formation of **11**.

A better yield (90%) of **8** was obtained by treatment of the 1-*O*-acetyl

TABLE I

^{13}C-N.M.R. CHEMICAL SHIFTS OF COMPOUNDS **2–12** (P.P.M.)

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-7*	*CH_3O*	*Acyl group*
2	168.9	70.5	70.0	76.3	68.4[a]	68.3[a]	62.0		165.8, 165.0, 164.8, 164.5, 164.3 (C=O)
3	170.1	69.1[a]	69.0[a]	76.1	68.6[a]	67.9[a]	61.1		169.5, 169.4, 169.1, 168.8 (C=O); 20.5, 20.2, 19.9 (CH_3CO)
4	171.0	70.4[a]	30.8	74.4	71.0[a]	68.1	62.4		165.8, 165.1 (C=O)
5	171.0	69.6[a]	30.4	74.0	70.0[a]	67.7	61.4		170.2, 169.7, 169.5, 169.3 (C=O); 20.8, 20.6, 20.5 (CH_3CO)
6	101.1	78.8	32.1	76.6	72.5[a]	71.7[a]	63.0		166.1, 165.9, 165.8, 165.5 (C=O)
7	100.0	77.7	32.3	78.2	72.0[a]	71.6[a]	62.8		168.8, 165.5, 165.2 (C=O); 21.0 (CH_3CO)
8	107.0	76.0	32.3	78.1	71.8[a]	71.3[a]	63.1	54.6	166.0, 165.8, 165.3 (C=O)
9	110.2	74.7	35.1	78.0	73.6[a]	72.5[a]	64.8	54.5	
10 α-*p*	92.6	69.6	33.3	64.3	74.4	70.6	63.9		
10 β-*p*	99.4	70.2	38.0	65.7[a]	77.6	67.5[a]	63.9		
10 α-*f*	95.8	73.4	32.0	77.2	72.2[a]	71.9[a]	64.1		
10 β-*f*	103.1	76.1	34.5	78.0	72.9[a]	72.6[a]	64.1		
11	101.4	76.6	32.4	78.2	71.9[a]	71.6[a]	62.9		165.9, 165.6, 165.3 (C=O)
12	105.6	75.2	34.9	79.0	72.9[a]	72.8[a]	64.1		

[a]The assignments may have to be interchanged.

derivative **7** with methanol and tin(IV) chloride[15], conditions reported as being suitable for the efficient preparation of alkyl ribofuranosides bearing the *trans*-1,2 relationship.

The anomeric-carbon signal in the ^{13}C-n.m.r. spectrum of **8** (see Table I) was deshielded 5.9 p.p.m. in comparison with the hydroxylated compound **6**. The mass spectrum further confirmed the furanoid structure of the methyl glycoside **8**. The primary fragment at *m/z* 221, which corresponds to cleavage between C-5 and the ring, was 99.8% of the base peak. The loss of the methoxyl group at C-1 from the molecular ion accounts for the cation at *m/z* 593 (7.0%) having the highest mass of the spectrum. On saturation of this signal, the molecular ion at *m/z* 624 could be detected.

Methyl 3-deoxy-β-D-*gluco*-heptofuranoside (**9**) was obtained by debenzoylation of **8** with sodium methoxide in methanol at low temperature. Neutralization of the base was carried out with solid carbon dioxide, in order to avoid the partial hydrolysis (of the glycoside) observed on treatment with cationic resins. The downfield shifts for C-1 (3.2 p.p.m.), C-3 (2.8 p.p.m.), C-5, C-6, and C-7 (1.7 p.p.m.) when compared with those for **8** (see Table I) may be explained by the decrease in steric hindrance on debenzoylation. On the other hand, C-2 was shielded by 1.3 p.p.m. on removal of the (more electronegative) benzoyl group, whereas the C-4 signal showed no significant shift.

Compound **11**, isolated as a by-product on treatment of 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-β-D-*gluco*-heptofuranose (**6**) with diazomethane–boron trifluoride-etherate, was characterized as the benzoylated β,β′-furanoid disaccharide. The chemical shifts observed in the ^{13}C-n.m.r. spectrum (see Table I) were similar to those of compound **6** and were consistent with a symmetrical structure. Moreover, the disaccharide **11** was obtained in 82% yield on treatment of **6** with boron trifluoride-etherate in dichloromethane. Tin(IV) chloride, in the absence of methanol, also catalyzes the disaccharide formation. On *O*-debenzoylation, crystalline 3-deoxy-β-D-*gluco*-heptofuranosyl 3-deoxy-β-D-*gluco*-heptofuranoside (**12**) was obtained. As could be expected, no mutarotation was observed, even after 12 h. Acid hydrolysis, monitored by ^{1}H-n.m.r. spectroscopy, further confirmed the structure postulated.

Dyong *et al.*[16] also observed dimerization on treatment of acetylated reducing aldofuranoses with boron trifluoride-etherate.

Crystalline 3-deoxy-D-*gluco*-heptose (**10**) was obtained on *O*-debenzoylation of **6** with sodium methoxide in chloroform at 0°. The free sugar was synthesized in four steps from commercially available D-*glycero*-D-*gulo*-heptono-1,4-lactone (**1**) in 62% overall yield.

Tautomeric equilibrium of compound **10** in aqueous solution was studied by pulsed, Fourier-transform, ^{13}C-n.m.r. spectroscopy (see Fig. 1). Four anomeric signals were evident, at δ 103.1 (β-furanose), 99.4 (β-pyranose), 95.8 (α-furanose), and 92.6 (α-pyranose). The relative abundance of these forms is compared with the values for 3-deoxy-D-*ribo*-hexose[17] and 3-deoxy-D-*arabino*-hexose[18] in Table II.

Good agreement is observed with the *ribo*-hexose equilibrium-composition, as could be expected on taking into account the stereochemical relationship for O-1 and O-2. On the same basis, the β anomers are the more stable at equilibrium.

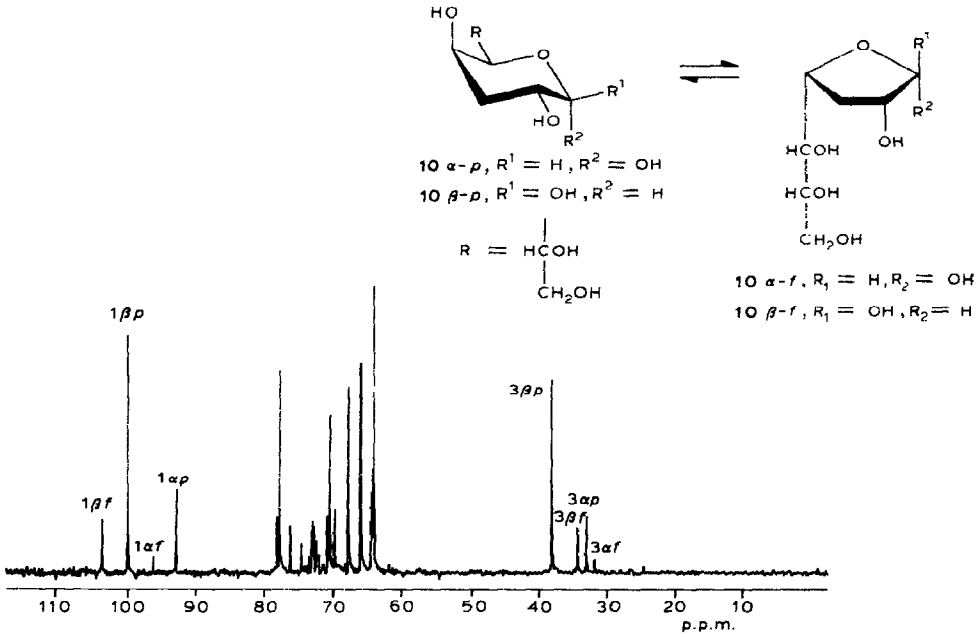


Fig. 1. ^{13}C-N.m.r. spectrum (25.2 MHz) of 3-deoxy-D-*gluco*-heptose (2M in D_2O–H_2O); 7200 pulses; spectral width, 5000 Hz; acquisition time, 0.8 s; pulse width, 30 μs; data length, 8 kilobytes.

EXPERIMENTAL

General. — Evaporations were conducted under diminished pressure at a bath temperature below 40°. Melting points were determined with a Fisher–Johns apparatus and are uncorrected. Optical rotations were determined with a Perkin–Elmer 141 polarimeter. T.l.c. was performed on 0.25-mm Silica Gel 60 (Merck 5626) coated plates with (*A*) 9:1 (v/v) toluene–ethyl acetate, (*B*) 4:1 (v/v) toluene–ethyl acetate, (*C*) 5:1 (v/v) dichloromethane–methanol, (*D*) 7:1:1 (v/v) 1-propanol–ethanol–water, and (*E*) 15:2:2:1 (v/v) acetone–chloroform–methanol–water. Compounds were visibilized by spraying with 5% (v/v) H_2SO_4–ethanol, followed by charring at 140° for a few minutes. Descending paper-chromatography was performed on Whatman No. 1 paper with 6:4:3 (v/v) 1-butanol–pyridine–water, detection being effected with silver nitrate–sodium hydroxide[10]. Dichloromethane was dried with P_2O_5, and distilled; methanol was refluxed with

TABLE II

EQUILIBRIUM COMPOSITION OF 3-DEOXY-D-*gluco*-HEPTOSE

Tautomeric form	*Composition of mixture by ^{13}C-n.m.r.*
3-Deoxy-D-*gluco*-heptose[a]	
α-pyranose	20
β-pyranose	61
α-furanose	4
β-furanose	15
3-Deoxy-D-*ribo*-hexose[b]	
α-pyranose	26
β-pyranose	51
α-furanose	6
β-furanose	17
3-Deoxy-D-*arabino*-hexose[c]	
α-pyranose	56.6
β-pyranose	25.7
α-furanose	17.6

[a]Average values from intensities for C-1 and C-3 (percentages ±2%). [b]Ref. 17. [c]Ref. 18.

magnesium for 4 h, and then distilled; bis(2-methoxyethyl) ether (diglyme) and tetrahydrofuran (THF) were dried, and distilled under nitrogen from sodium benzophenone ketyl, and boron trifluoride-etherate was distilled over CaH_2 at 2.7 kPa. The ^{1}H- and ^{13}C-n.m.r. spectra were recorded with a Varian XL-100-15 spectrometer, using a 620L-100 computer interfaced to a Sykes 700 dual-disk drive. Samples were spun in 5-mm tubes at 27°. For solutions in chloroform-*d* (compounds **2–8** and **11**) and acetone-d_6 (compound **9**), tetramethylsilane was used as the internal reference; 1,4-dioxane was used as the external standard for solutions in D_2O (compounds **10** and **12**) (δ_c 67.4 downfield from Me_4Si). The apparent coupling-constants reported are the line spacings directly observed. Signal assignments for ^{13}C-n.m.r. spectra were made on the basis of selective decoupling experiments or by comparison with literature data. Mass spectra were recorded with a Varian MAT CH7 spectrometer coupled to a Varian MAT Data-system 166.

2,3,5,6,7-Penta-O-*benzoyl*-D-glycero-D-gulo-*heptono-1,4-lactone* (**2**). — Compound **2** was obtained by benzoylation of D-*glycero*-D-*gulo*-heptono-1,4-lactone (**1**) as already described[10]; ^{1}H-n.m.r.: δ 8.08–7.09 (m, 5 BzO), 6.38–6.22 (m, H-3,5), 6.09 (d, $J_{2,3}$ 6 Hz, H-2), 5.86 (m, $J_{6,7}$ 4, $J_{6,7'}$ 6, $J_{5,6}$ 6 Hz, H-6), 5.27 (dd, $J_{3,4}$ 4, $J_{4,5}$ 6 Hz, H-4), 4.91 (dd, $J_{7,7'}$ 12 Hz, H-7), and 4.54 (dd, H-7'); for ^{13}C-n.m.r., see Table I.

2,5,6,7-Tetra-O-*benzoyl-3-deoxy*-D-gluco-*heptono-1,4-lactone* (**4**). — Compound **2** (14.56 g, 20 mmol) was dissolved in ethyl acetate (120 mL) and hydrogenated at room temperature and 304 kPa over 10% palladium–charcoal (1.5 g) in the presence of triethylamine (8.5 mL)[8]. After 4 h, no starting material was

observed by t.l.c. (solvent *A*). The catalyst was removed by filtration, and the filtrate was successively washed with 4M hydrochloric acid, water, saturated sodium hydrogencarbonate solution, and water, and dried (magnesium sulfate). Because substantial amounts of **4** remained mixed with the catalyst, several dichloromethane washings were performed. The dichloromethane and ethyl acetate solutions were pooled and evaporated, to give crystalline 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-D-*gluco*-heptono-1,4-lactone (**4**) (refs. 5 and 9) (11.46 g, 94%). It was recrystallized from 1:2 benzene–cyclohexane; m.p. and m.m.p. 203–204°; ^{1}H-n.m.r.: δ 8.15–7.22 (m, 4 BzO), 5.90 (m, H-5,6), 5.74 (t, $J_{2,3} = J_{2,3'}$ 9 Hz, H-2), 5.06 (m, H-4), 4.95 (m, H-7), 4.57 (m, H-7'), 3.02 (m, $J_{3,4}$ 7, $J_{3,3'}$ 13 Hz, H-3), and 2.26 (m, $J_{3',4}$ 9 Hz, H-3'); for ^{13}C-n.m.r., see Table I.

*2,3,5,6,7-Penta-O-acetyl-*D-glycero-D-gulo-*heptono-1,4-lactone* (**3**). — Compound **1** was acetylated by the method described by Bock *et al.*[8]. To a solution containing 0.3 mL of 70% perchloric acid in acetic anhydride (12.6 mL) was slowly added **1** (2.08 g, 10 mmol) under stirring, while maintaining the temperature below 40° with external cooling. After 30 min at room temperature, the mixture was poured into ice–water (60 mL), and extracted with dichloromethane (4 × 75 mL). The extracts were combined, successively washed with saturated sodium hydrogencarbonate (2 × 100 mL) and water (2 × 100 mL), dried (magnesium sulfate), and evaporated to a syrup which solidified (4.06 g, 97%). The chromatographically homogeneous product (R_F 0.20, solvent *B*) was recrystallized from ethanol (3.83 g, 92%), and characterized as 2,3,5,6,7-penta-*O*-acetyl-D-*glycero*-D-*gulo*-heptono-1,4-lactone (**3**); m.p. 131–132°, $[\alpha]_D^{27}$ −29° (*c* 1.02, chloroform); ν_{max}^{Nujol} 1805 (1,4-lactone C=O) and 1740 cm^{-1} (acetyl C=O); ^{1}H-n.m.r.: δ 5.82–5.60 (m, H-2,3,5), 4.99 (m, $J_{5,6}$ 4, $J_{6,7}$ 4, $J_{6,7'}$ 6 Hz, H-6), 4.72 (dd, $J_{3,4}$ 3, $J_{4,5}$ 8 Hz, H-4), 4.37 (dd, $J_{7,7'}$ 12 Hz, H-7), 4.16 (dd, H-7'), and 2.18, 2.15, 2.13, 2.09, and 2.05 (5 s, 5 CH_3CO); for ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{17}H_{22}O_{12}$: C, 48.81; H, 5.30. Found: C, 48.88; H, 5.14.

*2,5,6,7-Tetra-O-acetyl-3-deoxy-*D-gluco-*heptono-1,4-lactone* (**5**). — Compound **3** (3.35 g, 8.0 mmol) was hydrogenolyzed as described for the benzoylated lactone **2**. 2,5,6,7-Tetra-*O*-acetyl-3-deoxy-D-*gluco*-heptono-1,4-lactone (**5**) solidified upon evaporation (2.66 g, 92%). It was recrystallized from ethanol (2.31 g, 80%); R_F 0.15 (solvent *B*); m.p. 103–104°, $[\alpha]_D^{27}$ −7.5° (*c* 1.05, chloroform); ν_{max}^{Nujol} 1790 (1,4-lactone C=O), and 1740 cm^{-1} (acetyl C=O); ^{1}H-n.m.r.: δ 5.50 (dd, $J_{2,3}$ 9, $J_{2,3'}$ 10 Hz, H-2), 5.38–5.16 (m, H-4,5), 4.70 (m, $J_{5,6}$ 9 Hz, H-6); 4.42 (dd, $J_{6,7}$ 3, $J_{7,7'}$ 12 Hz, H-7), 4.18 (dd, $J_{6,7'}$ 6 Hz, H-7'), 2.77 (m, $J_{3,3'}$ 13, $J_{3,4}$ 6 Hz, H-3), 2.17 (s, 2 CH_3CO), 2.10, 2.06 (2 s, 2 CH_3CO), and 2.05–1.70 (m, H-3'), for ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{15}H_{20}O_{10}$: C, 50.00; H, 5.59. Found: C, 49.90; H, 5.48.

*2,5,6,7-Tetra-O-benzoyl-3-deoxy-β-*D-gluco-*heptofuranose* (**6**). — To a freshly prepared solution containing 42 mmol of bis(2-butyl-3-methyl)borane (diisoamyl borane)[20] in tetrahydrofuran (21 mL) was added compound **4** (6.08 g, 10 mmol) suspended in 3:1 dichloromethane–tetrahydrofuran (40 mL). After stirring

for 22 h at room temperature, the mixture was processed as already described[3]. The organic layer solidified on evaporation. After successive evaporations with methanol (to eliminate boric acid), 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-D-*gluco*-heptofuranose was obtained as a chromatographically homogeneous solid (5.79 g, 95% yield) of R_F 0.16 (solvent *A*), 0.38 (solvent *B*). The β:α ratio estimated by ^{13}C-n.m.r. spectroscopy was 8:1. After recrystallization from ethanol–water, 4.63 g (80% yield) of compound **6** was obtained; m.p. 114–116°, $[\alpha]_D^{27}$ +28° (*c* 0.90, chloroform); ν_{max}^{Nujol} 3520 (OH) and 1720 cm^{-1} (benzoyl C=O); ^{1}H-n.m.r.: δ 8.18–7.12 (m, 4 BzO), 5.90 (m, H-5,6); 5.63 (s, $J_{1,2}$ <1 Hz, H-1), 5.53 (dd, $J_{2,3}$ 7, $J_{2,3'}$ 2 Hz, H-2); 5.10–4.50 (m, H-4,7,7'), 2.74 (m, $J_{3,3'}$ 14, $J_{3,4}$ 8 Hz, H-3), 2.11 (m, $J_{3',4}$ 6 Hz, H-3'), and 3.26 (broad, disappeared on deuteration, OH); ^{1}H-n.m.r. (Me_2SO-d_6): δ 6.73 (d, $J_{1,OH}$ 4.5 Hz, OH; disappeared on deuteration) and 6.41 (d, $J_{1,2}$ <1 Hz, H-1); for ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{35}H_{30}O_{10}$: C, 68.85; H, 4.95. Found: C, 68.74; H, 5.21.

1-O-Acetyl-2,5,6,7-tetra-O-benzoyl-3-deoxy-β-D-gluco-heptofuranose (**7**). — Compound **6** (4.27 g, 7 mmol) was dissolved in anhydrous pyridine (15 mL) at 0°, and acetic anhydride (11 mL) was added. After standing for 18 h at room temperature, it was slowly poured into ice–water (200 mL), and the mixture was stirred for 1 h. The solid obtained was collected by filtration (4.39 g, 96%); it showed a single spot in t.l.c. (R_F 0.35, solvent *A*; 0.50, solvent *B*). Upon recrystallization from ethanol, it was characterized as compound **7**; m.p. 153–154°, $[\alpha]_D^{27}$ +10° (*c* 1.09, chloroform); ^{1}H-n.m.r.: δ 8.10–7.11 (m, 4 BzO), 6.43 (s, $J_{1,2}$ <1 Hz, H-1), 5.93–5.76 (m, H-5,6), 5.42 (dd, $J_{2,3}$ 7, $J_{2,3'}$ 2.5 Hz, H-2), 5.05–4.50 (m, H-4,7,7'), 2.78 (m, $J_{3,3'}$ 14, $J_{3,4}$ 8 Hz, H-3), 2.18 (m, $J_{3',4}$ 6 Hz, H-3'), and 1.97 (s, CH_3CO); for ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{37}H_{32}O_{11}$: C, 68.09; H, 4.94. Found: C, 68.28; H, 4.96.

Methyl 2,5,6,7-tetra-O-benzoyl-3-deoxy-β-D-gluco-heptofuranoside (**8**) *and octa-O-benzoyl 3-deoxy-β-D-gluco-heptofuranosyl 3-deoxy-β-D-gluco-heptofuranoside* (**11**). — *Method A*. Compound **6** (0.50 g, 0.82 mmol) was methylated with diazomethane–boron trifluoride-etherate in dichloromethane[14]. The reaction was monitored by t.l.c. (solvent *A*) until no starting material could be detected. Polymethylene was removed by filtration, and the filtrate was successively washed with saturated sodium hydrogencarbonate solution and water, dried (magnesium sulfate), and evaporated to a syrup. T.l.c. showed a main spot (R_F 0.45, solvent *A*; 0.59, solvent *B*); upon addition of methanol, methyl 2,5,6,7-tetra-*O*-benzoyl-3-deoxy-D-*gluco*-heptofuranoside crystallized (0.33 g, 64%) as a mixture of anomers (β:α ratio, 7:1). After recrystallization from ethanol, pure **8** showed m.p. 157–158°, $[\alpha]_D^{27}$ +22° (*c* 0.87, chloroform); ^{1}H-n.m.r.: δ 8.10–7.10 (m, 4 BzO), 6.03–5.82 (m, H-5,6), 5.29 (dd, $J_{2,3}$ 7, $J_{2,3'}$ 2.5 Hz, H-2), 5.13 (s, $J_{1,2}$ <1 Hz, H-1), 5.00 (dd, $J_{6,7}$ 3, $J_{7,7'}$ 12 Hz, H-7), 4.74–4.51 (m, H-4,7'), 3.30 (s, CH_3O), 2.70 (m, $J_{3,3'}$ 14, $J_{3,4}$ 8 Hz, H-3), and 2.03 (m, $J_{3',4}$ 6 Hz, H-3'); the mixture of anomers also showed a signal at δ 3.42 (OCH_3, α anomer); for ^{13}C-n.m.r., see Table I; *m/z* (%) 593 (7.0, $M^+ - CH_3O\cdot$), 564 (1.2, $M - CH_3OCHO$), 380 (1.7, $M - 2\,C_6H_5CO_2H$), 338 (5.9,

564 − $C_6H_5COO\cdot$ − $C_6H_5CO\cdot$), 320 (7.5, 564 − 2 $C_6H_5CO_2H$), 258 (9.6, M − 3 $C_6H_5CO_2H$); 221 (99.8, M − ·CHOBz-CHOBz-CH_2OBz), 188 (21.2), 105 (100, $C_6H_5CO^+$), 99 (93.1, 221 − $C_6H_5CO_2H$); 77 (16.1, $C_6H_5^+$), and 71 (99 − CO). On *m/z* 593 saturation, M^+ at *m/z* 624 could be observed.

Anal. Calc. for $C_{36}H_{32}O_{10}$: C, 69.22; H, 5.16. Found: C, 69.39; H, 5.40.

From the mother liquors, the disaccharide **11** (R_F 0.36, solvent *A*; 0.57, solvent *B*) was isolated (0.11 g, 22%). Upon recrystallization from 1:1 methanol–acetone, it showed m.p. 173–174°, $[\alpha]_D^{27}$ −3° (*c* 1.00, chloroform); ν_{max}^{Nujol} 1720 cm^{-1} (benzoyl C=O), and no hydroxyl signal was observed; ^{1}H-n.m.r.: δ 8.10–7.06 (m, 4 BzO), 6.00–5.8 (m, H-5,6), 5.59 (s, $J_{1,2}$ <1 Hz, H-1), 5.22 (dd, $J_{2,3}$ 7, $J_{2,3'}$ 2 Hz, H-2), 5.08–4.52 (m, H-4,7,7'), 2.72 (m, $J_{3,3'}$ 14, $J_{3,4}$ 8 Hz, H-3), and 2.03 (m, $J_{3',4}$ 7 Hz, H-3'); for ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{70}H_{58}O_{19}$: C, 69.88; H, 4.86. Found: C, 69.97; H, 5.11.

Method B. To a solution of compound **7** (1.96 g, 3 mmol) in anhydrous dichloromethane (14 mL) was added tin(IV) chloride (0.40 mL, 3.3 mmol) with stirring[15] at 0°. After standing for 10 min, anhydrous methanol (0.20 mL, 4.9 mmol) was added; no starting material could be detected by t.l.c. (solvent *A*) after 2.5 h. The mixture was slowly poured into a stirred solution of saturated sodium hydrogencarbonate (75 mL). The aqueous phase was extracted with dichloromethane (3 × 80 mL), and the organic layers were combined, washed with brine, and dried (magnesium sulfate). On evaporation, a white solid (1.84 g, 98%) was obtained; it showed a main product (R_F 0.44, solvent *A*) and traces of compound **6**; ^{1}H-n.m.r. of the crude product showed that only the β anomer **8** was obtained. After recrystallization from ethanol, compound **8** (1.69 g, 90%) showed the same constants as already given.

*Methyl 3-deoxy-β-*D*-gluco-heptofuranoside* (**9**). — A suspension of compound **8** (0.64 g, 1.0 mmol) in anhydrous methanol (20 mL) was cooled to 0°, and 0.5M sodium methoxide in methanol (6 mL) was added. After 4 h of stirring, the solution showed no starting material (by t.l.c., solvent *A*). Neutralization was effected with solid carbon dioxide, and the solution was then evaporated. The title compound was recovered from the solid mixture by dissolution with acetone. Upon evaporation of the solvent, a syrup was obtained which was extracted with benzene to eliminate methyl benzoate. Compound **9** (0.18 g, 82%), which could not be induced to crystallize, was chromatographically homogeneous (R_f 0.38, solvent *C*; 0.62, solvent *D*; 0.60, solvent *E*); $[\alpha]_D^{27}$ −105° (*c* 0.81, methanol); ^{1}H-n.m.r. (acetone-d_6): δ 4.76 (s, $J_{1,2}$ <1 Hz, H-1), 4.54 (m, $J_{3,4}$ 9, $J_{3',4}$ 4, $J_{4,5}$ 2 Hz, H-4), 4.00 (d, $J_{2,3}$ 5, $J_{2,3'}$ <1 Hz, H-2), 3.84–3.40 (m, H-5,6,7,7'), 3.28 (s, CH_3O), 2.35 (m, $J_{3,3'}$ 13.5 Hz, H-3), and 1.75 (dd, H-3'), ^{1}H-n.m.r. (D_2O): δ 4.92 (s, $J_{1,2}$ <1 Hz, H-1), 4.47 (m, $J_{3,4}$ 8, $J_{3',4}$ 6, $J_{4,5}$ 3 Hz, H-4), 4.22 (dd, $J_{2,3}$ 6, $J_{2,3'}$ 2.5 Hz, H-2), 3.90–3.50 (m, H-5,6,7,7'), 3.39 (s, CH_3O), 2.44 (m, $J_{3,3'}$ 14 Hz, H-3), and 1.80 (m, H-3'); for ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_8H_{16}O_6$: C, 46.15; H, 7.75. Found: C, 46.32; H, 7.75.

*3-Deoxy-β-*D*-gluco-heptofuranosyl 3-deoxy-β-*D*-gluco-heptofuranoside* (**12**).

— To a solution of compound **6** (0.525 g, 0.86 mmol) in anhydrous dichloromethane (4 mL), was added boron trifluoride etherate (0.2 mL, 1.62 mmol). After stirring for 6 h at room temperature, no starting material could be detected by t.l.c. (solvent *A*). The mixture was poured into saturated, aqueous sodium hydrogencarbonate (25 mL), and, after 30 min, it was extracted with dichloromethane (3 × 30 mL). The organic layer was washed with brine, dried (magnesium sulfate), and evaporated to a syrup which crystallized upon addition of methanol (yield 0.42 g, 82%). The product was characterized as the benzoylated β,β'-furanoid disaccharide **11**. Similar yields were obtained when boron trifluoride etherate was replaced by equivalent amounts of tin(IV) chloride.

Compound **11** (0.28 g, 0.23 mmol) was suspended in anhydrous methanol (4 mL), and 0.5M sodium methoxide in methanol (2 mL) was added. After stirring overnight at room temperature, the base was neutralized with Amberlite MB-3 (Sigma) in methanol, and the solution was evaporated to a syrup. After washing with dichloromethane, a chromatographically homogeneous solid (R_F 0.06, solvent *C*; 0.54, solvent *D*; 0.31, solvent *E*) was obtained (0.07 g, 84%). Upon recrystallization from 2-propanol, it showed m.p. 133–134°, $[\alpha]_D^{27}$ −132° (*c*, 0.91, water); ^{1}H-n.m.r. (D_2O): δ 5.27 (s, $J_{1,2}$ <1 Hz, H-1), 4.54 (m, $J_{3,4}$ 8, $J_{3',4}$ 6, $J_{4,5}$ 3 Hz, H-4), 4.26 (dd, $J_{2,3}$ 6, $J_{2,3'}$ 3 Hz, H-2), 3.93–3.50 (m, H-5,6,7,7'), 2.49 (m, $J_{3,3'}$ 14 Hz, H-3), 1.82 (m, H-3'); for ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{14}H_{26}O_{11}$: C, 45.40; H, 7.08. Found: C, 45.20; H, 7.01.

Hydrolysis of **12** (0.020 g) was performed with 2M deuterium chloride in D_2O (0.5 mL) at 27°, and monitored by ^{1}H-n.m.r. spectroscopy with 1,4-dioxane as an internal reference (3.70 p.p.m. downfield from Me_4Si). In the anomeric region, signals at δ 4.60 (d, $J_{1,2}$ 8 Hz) and 5.16 (d, $J_{1,2}$ 3.5 Hz), corresponding to the β- and α-pyranose forms of 3-deoxy-D-*gluco*-heptose, were observed after 45 min, together with a decrease in the signal at δ 5.27. When hydrolysis was complete, the spectrum was identical to that of 3-deoxy-D-*gluco*-heptose recorded under the same conditions (see next).

3-Deoxy-D-gluco-*heptose* (**10**). Compound **6** (1.94 g, 3.2 mmol) was dissolved in 1:1 chloroform–methanol (10 mL) at 0°, and 0.5M sodium methoxide in methanol (6 mL) was added. After standing for 3 h at 0°, no starting material was observed by t.l.c. (solvent *B*). The free sugar was recovered by water extraction (3 × 40 mL). The aqueous phase was washed with dichloromethane, and the base neutralized with Dowex 50W (H^+) ion-exchange resin. Upon evaporation, a syrup was obtained (0.51 g, 82%) that was homogeneous by paper chromatography (R_{Glc} 1.38) and t.l.c. (R_F 0.11, solvent *C*; 0.51, solvent *D*). It crystallized from 2-propanol (0.42 g, 68%), and was characterized as 3-deoxy-D-*gluco*-heptose (**10**); m.p. 126–128°, $[\alpha]_D^{27}$ +10° (at equilibrium, 12 h, *c* 1.1, water); ^{1}H-n.m.r. (after mutarotation in D_2O): δ 5.27 (s, $J_{1,2}$ <1 Hz, H-1 β-*f*), 5.16 (d, $J_{1,2}$ 3.5 Hz, H-1 α-*p*), and 4.56 (d, $J_{1,2}$ 8 Hz, H-1 β-*p*). The β-pyranose:α-pyranose:β-furanose ratios determined by integration were 68:19:13; for ^{13}C-n.m.r. after complete mutarotation, see Fig. 1.

Anal. Calc. for $C_7H_{14}O_6$: C, 43.29; H, 7.26. Found: C, 43.08; H, 7.07.

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