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TOTAL SYNTHESIS OF HIGHER-CARBON SUGARS: SYNTHESIS OF METHYL 3,4,5-TRI-*O*-ACETYL-1,7-DI-*O*-BENZYL-α-DL-*gluco*-HEPT-2-ULOPYRANOSIDE

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ABSTRACT

2-(2-Benzyloxy-1-hydroxyethyl)-5-benzyloxymethylfuran [obtained by the reaction of 2-benzyloxymethylfuran with butyl glyoxylate, reduction of the resulting hydroxyester with lithium aluminium hydride, followed by benzylation of the primary hydroxyl group] was converted into methyl 1,7-di-*O*-benzyl-3,4-dideoxy-α- and -β-DL-hept-3-en-2-ulopyranosid-5-uloses. Carbonyl-reduction of the uloses and inversion of configuration at C-5 in the resulting alcohols afforded four stereoisomeric 3,4-unsaturated methyl hept-2-ulosides. Epoxidation of the α-*erythro* isomer, ring-opening of the resulting oxirane, and then acetylation yielded the title compound.

INTRODUCTION

Amongst the naturally occurring sugars are C_7, C_8, and C_9 ketoses[1]. Several 2-heptuloses have been isolated from natural sources[2] and synthesised by isomerisation of the appropriate aldoheptose or selective oxidation of the appropriate heptitol obtained by elongation of the carbon chain of aldohexoses. Although stereoselective total syntheses of various aldoses have been described[3,4], few ketoses have been thus obtained[5] and none was a higher-carbon sugar[2], *i.e.*, contained more than six carbon atoms.

We have reported that the general method of synthesis of monosaccharides from furan compounds[6] can be applied to the preparation of hex-2-uloses[7] (**1**→**2**, R=H), the most common type of keto sugar[8]. We now describe the stereoselective synthesis from a non-sugar precursor (**1**→**2**, R=CH_2OH) of a racemic *gluco*-hept-2-ulose derivative.

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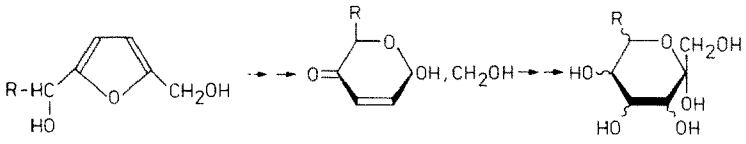
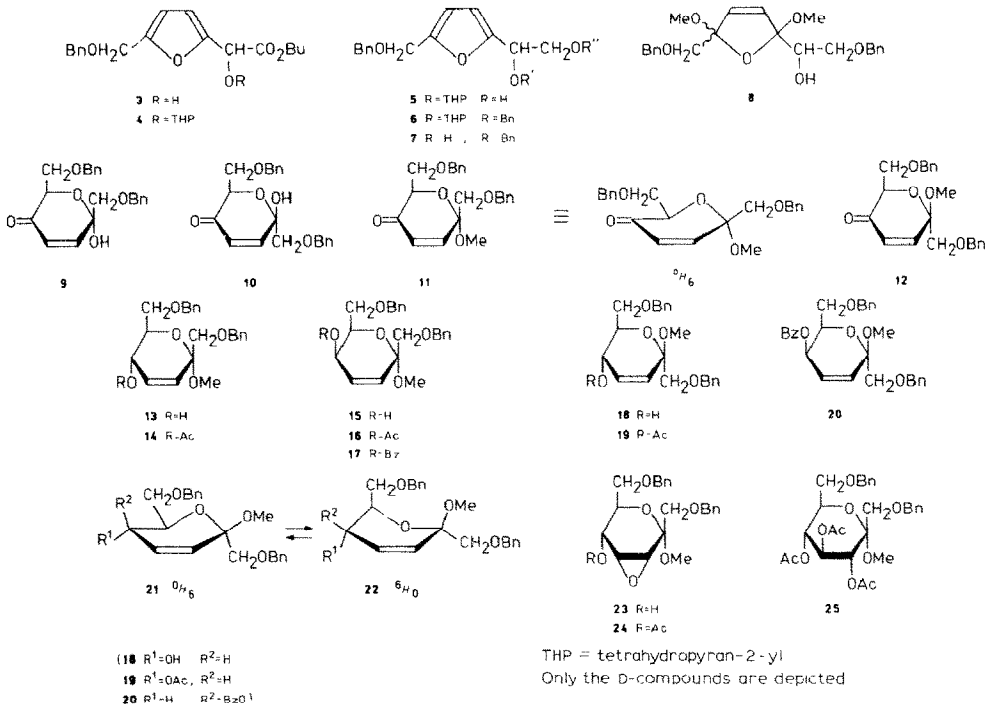


1 R=H or CH_2OH 2

RESULTS AND DISCUSSION

The starting material was the C_7 furan derivative, 2-(2-benzyloxy-1-hydroxyethyl)-5-benzyloxymethylfuran (**7**) obtained by a route analogous to that used for the synthesis of 2-(2-benzyloxy-1-hydroxyethyl)furan[9]. Reaction of benzyl furfuryl ether with butyl glyoxylate in the presence of toluene-*p*-sulphonic acid yielded the butyl glycolate derivative **3**, which was tetrahydropyranylated (→**4**) and then reduced with lithium aluminium hydride to give the triol **5**. Benzylation of **5** (→**6**) followed by removal of the tetrahydropyranyl group afforded **7**, which was then transformed[10] into the dihydropyran system.

Treatment of **7** with bromine in methanol gave the *cis,trans*-2,5-dimethoxy-2,5-dihydrofuran derivative **8**. Although the isomers could be isolated by column chromatography (see Experimental), the *cis,trans*-mixture was used for preparative purposes. Hydrolysis of **8** with aqueous 1% sulphuric acid at room temperature yielded the 2,5-diulose as a mixture of α (**9**) and β (**10**) anomers which had i.r.



3 R=H
4 R=THP

5 R=THP R'=H
6 R=THP R'=Bn
7 R=H, R'=Bn

8

9 10 11 12

13 R=H
14 R=Ac

15 R=H
16 R=Ac
17 R=Bz

18 R=H
19 R=Ac

20

21 22

18 R^1=OH R^2=H
19 R^1=OAc, R^2=H
20 R^1=H R^2=BzO

23 R=H
24 R=Ac

25

THP = tetrahydropyran-2-yl
Only the D-compounds are depicted

absorptions for hydroxyl (3400 cm^{-1}) and an enone system (1695, 1630 cm^{-1}). The ^{1}H-n.m.r. spectrum contained all the signals expected, in particular two AB systems centred at δ 6.31 and 6.47 and assigned[10] to H-3 and H-4, respectively. The relative intensities of these signals indicated an $\alpha\beta$-ratio of ~1:1. The assignment of the ^{1}H-n.m.r. signals to the appropriate anomers was not possible directly since there was no proton at position 2. When the above ~1:1 mixture of **9** and **10** was equilibrated in aqueous 1% sulphuric acid, the isomer ratio changed to 9:1 (^{1}H-n.m.r.) during 24 h, with the signals for H-3 and H-4 of the major isomer appearing at higher field. Since the anomeric effect and the pseudo-equatorial position of the benzyloxymethyl group at position 2 favour the α configuration, this was assigned to the major isomer.

Treatment of the 9:1 mixture of the 2,5-diuloses **9** and **10** with methyl iodide–silver oxide gave a high yield of the methyl ulosides **11** and **12**, which were isolated by column chromatography but to which the configurations could not be assigned directly. Glycosidation[11] of glyc-2-enopyranos-4-uloses with methyl orthoformate catalysed by boron trifluoride yielded the methyl ulosides in a ratio corresponding approximately to that of the equilibrium mixture. Similar treatment of the 9:1 mixture of **9** and **10** gave an 8:1 (^{1}H-n.m.r.) mixture of anomers, of which the less mobile in t.l.c. was the major product and, being thermodynamically the more stable, it was assigned the α configuration (**11**).

Reduction of the $\alpha\beta$-mixture **11** + **12** gave the three alcohols **13** (83%), **15** (3%), and **18** (7%), to which configurations were assigned on the basis of stereochemical considerations and the ^{1}H-n.m.r. data of their acetates. The course of hydride reduction of α,β-unsaturated ketones depends on the stereoelectronic factors[12] so that, in the absence of steric hindrance, the preponderant product arises by axial approach of the hydride to the carbonyl group. This course of reduction holds also for the enone system in the pyranosid-4-uloses[13]. Therefore, for the α-glucoside **11**, which occurs mainly in the $^oH_6$ conformation, the *α-erythro* alcohol **13** is the major, and the *α-threo* alcohol **15** is the minor, product. These configurations were confirmed by the coupling constants of the acetates **14** ($J_{5,6}$ 9.4, $J_{4,5}$ 1.9, $J_{3,5}$ 1.7 Hz) and **16** ($J_{5,6}$ 2.2, $J_{4,5}$ 5.2 Hz), indicating the pseudo-axial and pseudo-equatorial position of H-5, respectively.

The stereochemical relation of the alcohols **13** and **15** was confirmed by their interconversion. Thus, treatment of **13** with the triphenylphosphine–diethyl azodicarboxylate–benzoic acid reagent proceeded[14] with inversion of configuration at C-5 to give the benzoate **17**, saponification of which gave **15**. The product **18** ($J_{5,6}$ 7.5, $J_{4,5}$ 2.4 Hz) was derived from the β-anomer **12** and therefore had the *β-erythro* configuration. Application of the above reagent to **18** gave the *β-threo* benzoate **20** ($J_{5,6}$ 2.1, $J_{4,5}$ 5.7 Hz). It is assumed that for **19** and **20**, as for **13** (**14**) and **15** (**16**), the $^oH_6$ conformation **21** is energetically favoured despite the destabilising anomeric effect which is outweighed by the 1,3-diaxial interaction of $BnOCH_2$ and MeO and the allylic tension $A^{1,3}$ of $BnOCH_2$ in the ^6H_o conformation **22**. However, comparison of the $J_{5,6}$ values for the acetates **14** (9.4 Hz) and **19** (7.5 Hz) indicates the presence of an appreciable amount of the ^6H_o form of the β-anomer **19**.

TABLE I

^{1}H-NMR DATA (100 MHz)

Compound	Solvent	Chemical shifts (δ, Me_4Si = 0)										Coupling constants (Hz)							
		H-1,1'	H-3	H-4	H-5	H-6	H-7,7'	2 OCH_2	2 C_6H_5	OCH_3	OAc	OH	$J_{1,1'}$	$J_{3,4}$	$J_{3,5}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{6,7'}$	$J_{7,7'}$
9	CCl_4	3.50–3.90	6.68	5.95	—		4.2–4.6	4.47,4.50	7.22	—	—	3.4	[a]	10.4	—	—	—	[a]	[a]	[a]
10			6.89	6.05	—			4.56		—	—		[a]	10.2	—	—	—	[a]	[a]	[a]
11	C_6D_6	3.26,3.62	6.87	5.96	—	4.5–4.2	3.72,3.85	4.26,4.33	7.15	3.14	—	—	10.5	10.4	—	—	—	3.2	5.25	[a]
12	C_6D_6	3.49	6.42	6.02	—	4.5–4.7	3.60,4.00	4.19,4.30	7.12	3.20	—	—	—	10.5	—	—	—	3.1	5.5	10.5
13	C_6D_6	3.48,3.69	5.82	6.04	3.90–4.18		3.69	4.29,4.34	7.15	3.24	—	2.75	10.5	10.2	~1	1.5	[a]	[a]	[a]	[a]
14	C_6D_6	3.28;3.66	5.75	6.13	5.50	4.35	3.52	4.30,4.35	7.18	3.26	1.62	—	10.2	10.2	1.7	1.9	9.4	4.2	—	—
15	C_6D_6	3.40	5.72	6.02	4.15	3.65	3.75	4.19,4.34	7.12	3.16	—	2.50	—	10.2	—	5.7	[a]	[a]	[a]	[a]
16	C_6D_6	3.35;3.60	6.22	6.00	5.05	3.60	3.22	4.32,4.34	7.18	3.25	1.62	—	10.2	10.2	—	5.2	2.2	4.0	—	—
17	C_6D_6	3.42,3.70	6.30	6.10	5.35	4.42	3.70	4.29[b],4.27[b]	7.12[c],8.00[d]	3.27	—	—	10.2	10.0	—	5.2	2.4	6.5	—	—
18	C_6D_6	3.64	6.05	5.56	3.95–4.15		3.59	4.31,4.33	7.15	3.14	—	3.10	—	10.5	[a]	[a]	[a]	[a]	[a]	[a]
19	C_6D_6	3.60	5.72	5.99	5.48	4.30	3.58	4.32,4.34	7.17	3.17	1.64	—	—	10.4	1.5	2.4	7.5	4.5	—	—
20	$CDCl_3$	3.58	5.91	6.50	5.28	4.00	3.58	4.56[e],4.44[e]	7.10[c],7.95[d]	3.31	—	—	—	10.2	—	5.7	2.1	6.4	—	—
24	$CDCl_3$	3.69,3.88	3.6–3.2		5.11	4.00	3.48	4.59[f],4.37[f] 4.47	7.27	3.30	1.98	—	10.75	[a]	[a]	1.7	10.0	3.5	—	—
24	C_6D_6	3.56,3.35	3.15	3.34	5.25	4.37	3.67	4.40[b],4.42[b] 4.30	7.15	3.22	1.62	—	10.25	4.2	1.5	1.5	9.75	3.9	—	—
25	$CDCl_3$	4.44	5.26	5.47	5.07	3.88	3.56	4.52,3.52	7.27	3.30	1.92,1.88 1.85	—	11.7	9.7	—	9.0	9.7	4.1	—	—

[a]Could not be obtained from the spectrum [b]Centre of the AB system, J_{AB} = 12.0 Hz [c]3 H [d]2 H [e]Centre of the AB system, J_{AB} = 11.7 Hz [f]Centre of the AB system, J_{AB} = 12.25 Hz

Stereoselective functionalisation of the double bond in the 3,4-unsaturated hept-2-ulopyranosides opens a route to the 2-ketoheptoses as was demonstrated by the synthesis of the *α-gluco* isomer.

Reaction of the *α-erythro* alcohol **13** with *m*-chloroperbenzoic acid gave **23** as the sole product (t.l.c.). Introduction of the oxirane ring *cis* to the hydroxyl group[15], to give the *α-allo* epoxide **23**, was confirmed by the $J_{4,5}$ value of 1.7 Hz for the acetate **24**, which indicated[16] a *cis*-relationship of H-4,5.

Cleavage of the oxirane ring in 3,4-anhydro-2-ulosides is highly regioselective[7]. Due to the combined influence of the polar effect of the anomeric center[17] and steric hindrance of $BnOCH_2$-2, attack of the nucleophile at C-4 is favoured even in 3,4-anhydro-2-ulosides for which, in the preponderant conformation, diaxial[17] opening of the epoxide should lead to attack at C-3. Treatment of **23** with barium hydroxide and acetylation of the product gave the triacetate **25** as the sole product (t.l.c.). The *α-gluco* configuration of **25** was demonstrated by the ^{1}H-n.m.r. data (Table I), which showed H-3,4, H-4,5, and H-5,6 to be *trans*-diaxial.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Boiling points refer to the bath temperatures. I.r. spectra were recorded for films or KBr discs with a Unicam SP-200 spectrometer. ^{1}H-N.m.r. spectra (internal Me_4Si) were recorded with a Varian HA-60-IL or Jeol JNM-4H-100 spectrometer, and mass spectra with an LKB 900 spectrometer. G.l.c. was performed on a Willy Giede gas chromatograph 18/3. Silica gel Schuchardt (100–200 mesh) was used for column chromatography. Reactions and chromatography were monitored by t.l.c. on silica gel G (Merck). Organic solutions were dried over anhydrous $MgSO_4$.

Butyl 2-(5-benzyloxymethyl-2-furyl)glycolate (**3**). — Butyl glyoxylate (91 g, 0.70 mol) was added dropwise to a solution of 2-benzyloxymethylfuran (150 g, 0.80 mol) and toluene-*p*-sulphonic acid (0.65 g) in benzene (150 mL) at room temperature. After 12 h, the mixture was diluted with benzene (200 mL), washed with aqueous sodium hydrogencarbonate and water, and then concentrated. Distillation of the residue from a small quantity of barium oxide gave **3** (111.5 g, 55%), b.p. 170°/0.4 Torr; ν_{max}^{film} 3500 (OH), 1750 cm^{-1} (C=O). ^{1}H-N.m.r. data (C_6D_6): δ 7.2 (bs, 5 H, Ph), 6.16 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-3 furan), 6.0 (d, 1 H, H-4 furan), 5.08 (s, 1 H, $CHCO_2$), 4.30 (s, 2 H, OCH_2furyl), 4.20 (s, 2 H, OCH_2Ph), 3.9 (t, 2 H, OCH_2), 1.9–1.2 (m, 4 H, CH_2CH_2), 0.65 (t, 3 H, CH_3).

Anal. Calc. for $C_{18}H_{22}O_5$: C, 67.7; H, 7.2. Found: C, 67.7; H, 7.2.

Butyl 2-(5-benzyloxymethyl-2-furyl)-O-(tetrahydropyran-2-yl)glycolate (**4**). — 3,4-Dihydro-2*H*-pyran (16.8 g, 0.20 mol) was added dropwise to a stirred suspension of toluene-*p*-sulphonic acid (0.54 g) in **3** (57 g, 0.18 mol) at ~0°. After 30 min, the mixture was diluted with ether (250 mL), washed with aqueous sodium hydrogencarbonate and water, and then concentrated. A portion (0.2 g) of the residue (72 g, ~100%) was eluted with benzene through a short column of silica gel (5 g)

to yield an analytical sample of **4** (0.17 g); ν_{max}^{film} 1760 (C=O), 1205, 1130, 1080 cm^{-1} (C–O). ^{1}H-N.m.r. data (CCl_4): δ 7.2 (s, 5 H, Ph), 6.3–6.1 (m, 2 H, H-3,4 furan), 5.19 (s, 1 H, $CHCO_2$), 4.80* and 4.65* (m, 1 H, H-2 pyran), 4.44 (s, 2 H, OCH_2furyl), 4.37 (s, 2 H, OCH_2Ph), 4.08 (t, 2 H, OCH_2), 4.0–3.3 (m, 2 H, H-6,6′ pyran), 1.9–1.1 (m, 10 H, CH_2CH_2 and $CH_2CH_2CH_2$), 0.90 (t, 3 H, CH_3).

Anal. Calc. for $C_{23}H_{30}O_6$: C, 68.6; H, 7.5. Found: C, 68.7; H, 7.5.

2-Benzyloxymethyl-5-[2-hydroxy-1-(tetrahydropyran-2-yloxy)ethyl]furan (**5**). — A solution of **4** (70 g, 0.17 mol) in ether (200 mL) was added dropwise to a stirred suspension of lithium aluminium hydride (6.5 g, 0.17 mol) in ether (200 mL). After 15 min, the excess of reductant was decomposed by successive addition of water (6 mL), aqueous 15% sodium hydroxide (6 mL), and water (18 mL). Insoluble material was collected and washed thrice with ether, and the combined filtrates and washings were concentrated to give **5** (57 g, 99%). An analytical sample, obtained as in the preceding experiment, had ν_{max}^{film} 3450 (OH), 1110, 1070 cm^{-1} (C–O).

Anal. Calc. for $C_{19}H_{24}O_5$: C, 68.6; H, 7.0. Found: C, 68.1; H, 7.0.

Two diastereoisomers were isolated by column chromatography (benzene–ether, 9:1).

Diastereoisomer more mobile in t.l.c., ^{1}H-n.m.r. data (CCl_4): δ 7.24 (s, 5 H, Ph), 6.17 (s, 2 H, H-3,4 furan), 4.67 (dd, 1 H, $J_{1,2}$ 7, $J_{1,2'}$ 5 Hz, H-1), 4.53 (m, 1 H, H-2 pyran), 4.43 (s, 2 H, OCH_2furyl), 4.35 (s, 2 H, OCH_2Ph), 3.78 (dd, 1 H, H-2), 3.75 (dd, 1 H, H-2′), 4.05–3.25 (m, 2 H, H-6,6′ pyran), 2.62 (s, 1 H, OH), 1.8–1.4 (m, 6 H, $CH_2CH_2CH_2$).

Diastereoisomer less mobile in t.l.c., ^{1}H-n.m.r. data (CCl_4): δ 7.24 (s, 5 H, Ph), 6.20 (ABq, 2 H, J 3.2 Hz, H-3,4 furan), 4.76 (m, 1 H, H-2 pyran), 4.62 (t, 1 H, J 5.7 Hz, H-1), 4.43 (s, 2 H, OCH_2furyl), 4.35 (s, 2 H, OCH_2Ph), 3.75 (d, 2 H, J 5.7 Hz, H-2,2′), 4.05–3.20 (m, 2 H, H-6,6′ pyran), 1.8–1.4 (m, 6 H, $CH_2CH_2CH_2$).

2-Benzyloxymethyl-5-[2-benzyloxy-1-(tetrahydropyran-2-yloxy)ethyl]furan (**6**). — To a solution of **5** (51 g, 0.154 mol) in dry methyl sulfoxide (200 mL) was added a suspension of powdered sodium hydroxide (14 g, 0.35 mol) in methyl sulfoxide (20 mL). The mixture was stirred for 0.5 h and then benzyl chloride (22 g, 0.174 mol) was added dropwise. After stirring for a further 12 h, the mixture was poured into ice–water (500 g) and extracted with ether, and the extract was washed with water and concentrated to yield **6** (63 g, 93%). An analytical sample, obtained as in the preceding experiment, had ν_{max}^{film} 1500, 880 (furan), 1460, 740, 700 (C_6H_5), 1120, 1080 cm^{-1} (C–O). ^{1}H-N.m.r. data (CCl_4): δ 7.25 (bs, 10 H, 2 Ph), 6.18 (s, 2 H, H-3,4 furan), 4.90 (m, 1 H, H-1 of diastereoisomer A) and 4.80 (t, 1 H, J 3.2 Hz, H-1 of diastereoisomer B), 4.55 (m, 1 H, H-2 pyran), 4.48 (s, 2 H, OCH_2), 4.42 (s, 2 H, OCH_2), 4.34 (s, 2 H, OCH_2), 3.72 (d, 2 H, J 3.2 Hz, H-2,2′), 3.95–3.30 (m, 2 H, H-6,6′ pyran), 2.0–1.0 (m, 6 H, $CH_2CH_2CH_2$).

Anal. Calc. for $C_{26}H_{30}O_5$: C, 73.9; H, 7.2. Found: C, 73.9; H, 7.3.

*Two diastereoisomers.

2-Benzyloxymethyl-5-(2-benzyloxy-1-hydroxyethyl)furan (**7**). — A solution of **6** (29 g, 0.069 mol) and toluene-*p*-sulphonic acid (0.14 g) in dry methanol (400 mL) was left for 4 h at room temperature, filtered through a column of alumina, and concentrated to give **7** (23 g, ~100%). Column chromatography (benzene–ether 9:1) yielded an analytical sample; ν_{max}^{film} 3450 (OH), 1120, 1070 cm^{-1} (C–O). ^{1}H-N.m.r. data (C_6D_6): δ 7.2 (s, 5 H, Ph), 6.10 (ABq, 2 H, *J* 3.5 Hz, H-3,4 furan), 4.32 (s, 2 H, OCH_2furyl), 4.26 (s, 2 H, OCH_2Ph), 3.56 (d, 2 H, *J* 5.7 Hz, H-2,2'), 3.28 (bs, 1 H, OH), 4.82 (t, 1 H, *J* 5.7 Hz, H-1).

Anal. Calc. for $C_{21}H_{22}O_4$: C, 74.5; H, 6.5. Found: C, 74.7; H, 6.7.

2-(2-Benzyloxy-1-hydroxyethyl)-5-benzyloxymethyl-2,5-dimethoxy-2,5-dihydrofuran (**8**). — To a solution of **7** (34 g, 0.1 mol) in ether (200 mL) and methanol (100 mL) at −45° was added dropwise with stirring a solution of bromine (6.2 mL, 0.12 mol) in methanol (50 mL). The mixture was stirred at −45 to −35° for 30 min, neutralised with gaseous ammonia, and concentrated. The residue was diluted with water and extracted with benzene, and the extract was concentrated to yield crude **8** (37.5 g, 94%) as a *cis,trans*-mixture, the less-mobile (t.l.c.) being the major isomer. Column chromatography (benzene–ether, 9:1) of a portion (0.5 g) on silica gel (10 g) gave an analytical sample; ν_{max}^{film} 3500 (OH), 1630 (C=C), 1460, 738 (C_6H_5), 1110, 1030 cm^{-1} (C–O). ^{1}H-N.m.r. data (CCl_4): major isomer, δ 7.26 (s, 10 H, 2 Ph), 5.90 (ABq, 2 H, *J* 5.7 Hz, H-3,4 furan), 4.49 and 4.47 (2 s, each 2 H, 2 OCH_2Ph), 3.92 (m, 1 H, H-1), 3.75–3.25 (m, 4 H, 2 CH_2), 3.27 and 3.22 (2 s, each 3 H, 2 OMe); minor isomer, δ 7.23 (bs, 10 H, 2 Ph), 5.85 (ABq, 2 H, *J* 5.6 Hz, H-3,4 furan), 4.42 (s, 4 H, 2 OCH_2Ph), 3.9–3.3 (m, 5 H, H-1, 2 CH_2), 3.25 and 3.19 (2 s, each 3 H, 2 OMe), 2.8 (s, 1 H, OH).

Anal. Calc. for $C_{23}H_{28}O_6$: C, 69.0; H, 7.0. Found: C, 69.0; H, 7.0.

*1,7-Di-*O*-benzyl-3,4-dideoxy-α-* (**9**) *and -β-*DL*-hept-3-en-2-ulopyranos-5-ulose* (**10**). — A mixture of **8** (20.0 g, 0.05 mol) and aqueous 1% H_2SO_4 (25 mL) was made homogeneous with acetone and left at room temperature for 2 h. The solution was brought to pH 5 with solid $NaHCO_3$, the acetone was evaporated *in vacuo*, and the residue was extracted with benzene. Concentration of the extract gave an amorphous mixture (17.7 g, 100%) of **9** and **10** in the ratio ~1:1 (^{1}H-n.m.r.), which decomposed on distillation or column chromatography and had ν_{max}^{film} 3400 (OH), 1695, 1630 (C=C–C=O), 1500, 1460, 740 (C_6H_5), 1100, 1030 cm^{-1} (C–O).

The mixture (0.5 g) of **9** and **10** and aqueous 1% sulphuric acid (1 mL) was made homogeneous with acetone at room temperature and monitored by ^{1}H-n.m.r. spectrometry. After 24 h, equilibrium had been attained with a 9:1 ratio of **9** and **10**.

*Methyl 1,7-di-*O*-benzyl-3,4-dideoxy-α-* (**11**) *and -β-*DL*-hept-3-en-2-ulopyranosid-5-ulose* (**12**). — (*a*) To a solution of the 9:1 mixture of **9** and **10** (6.5 g, 18 mmol) and trimethyl orthoformate (2.65 g, 25 mmol) in ether (50 mL) at 0° was added slowly with stirring a solution of boron trifluoride etherate (0.8 g) in ether (10 mL). After 5 h at room temperature, the reaction was quenched with triethylamine, and the ether solution was washed with water and concentrated to give a mixture (4.8

g, 72%) of anomers **11** and **12**. A sample (2 g) was subjected to column chromatography (benzene–ether) on silica gel (40 g) to give **12** (0.11 g, 5.6%); ν_{max}^{film} 1690, 1635 (C=C–C=O), 1500, 1460, 735, 690 (C_6H_5), 1100, 1050 cm^{-1} (C–O). See Table I for the ^{1}H-n.m.r. data.

Further elution yielded **11** (0.92 g, 46%); ν_{max}^{film} 1690, 1630 (C=C–C=O), 1560, 1455, 730, 685 (C_6H_5), 1100, 1050 cm^{-1} (C–O). See Table I for the ^{1}H-n.m.r. data.

Anal. Calc. for $C_{22}H_{24}O_5$: C, 71.7; H, 6.6. Found: C, 71.5; H, 6.6.

(*b*) Silver oxide (8.8 g, 63 mmol) was added to a solution of the 9:1 mixture of **9** and **10** (7.5 g, 21 mmol) in dry ether (100 mL). The mixture was stirred for 8 h at room temperature, insoluble material was collected and washed with ether, and the combined filtrate and washings were concentrated to give a mixture (7.0 g, 90%) of **11** and **12** which was identical with the sample obtained in (*a*).

*Methyl 1,7-di-*O*-benzyl-3,4-dideoxy-α-*DL-erythro-*hept-3-en-2-ulopyranoside* (**13**). — A solution of **11** (9.2 g, 25 mmol) containing ~10% of **12** in tetrahydrofuran (20 mL) was added with stirring to a solution of sodium borohydride (0.475 g, 12.5 mmol) in tetrahydrofuran (40 mL) and water (40 mL) at ~0°. The mixture was stirred for 30 min at room temperature and then neutralised with acetic acid, the tetrahydrofuran was evaporated, and the aqueous layer was extracted with benzene. Concentration of the extract gave a mixture of three (t.l.c.) compounds as a thick oil (9.2 g). Column chromatography (benzene–ether, 9:1) of the mixture gave a mixture (1.46 g, 16%) of the two minor products, and homogeneous **13** (7.67 g, 83%); ν_{max}^{film} 3500 (OH), 1660 (C=C) 1455, 740 (C_6H_5), 1100 cm^{-1} (C–O). See Table I for the ^{1}H-n.m.r. data.

Conventional treatment of **13** with acetic anhydride–pyridine gave the acetate **14**; ν_{max}^{film} 1720, 1230 (OAc), 1650 (C=C), 1455, 740, 695 (C_6H_5), 1100, 1040 cm^{-1} (C–O). See Table I for the ^{1}H-n.m.r. data.

Anal. Calc. for $C_{24}H_{28}O_6$: C, 69.9; H, 6.8. Found: C, 69.9; H, 7.0.

*Methyl 1,7-di-*O*-benzyl-3,4-dideoxy-β-*DL-erythro-*hept-3-en-2-ulopyranoside* (**18**). — The fraction (1.46 g) comprising the two minor components obtained in the preceding experiment was subjected to column chromatography (benzene–ether, 9:1) to give **18** (0.64 g, 7%); ν_{max}^{film} 3550 (OH), 1465, 745 (C_6H_5), 1100 cm^{-1} (C–O). See Table I for the ^{1}H-n.m.r. data.

Acetylation of **18** gave **19**: ν_{max}^{film} 1740, 1230 (OAc), 1455, 740 (C_6H_5), 1100, 1040 cm^{-1} (C–O). See Table I for the ^{1}H-n.m.r. data.

Anal. Calc. for $C_{24}H_{28}O_6$: C, 69.9; H, 6.8. Found: C, 70.0; H, 7.0.

*Methyl 1,7-di-*O*-benzyl-3,4-dideoxy-α-*DL-threo-*hept-3-en-2-ulopyranoside* (**15**). — Eluted second in the column chromatography in the preceding experiment was **15** (0.27 g, 3%), which was acetylated to give **16**; ν_{max}^{film} 1745, 1245 (OAc), 1470, 745 (C_6H_5), 1100, 1050 cm^{-1} (C–O). See Table I for the ^{1}H-n.m.r. data.

Anal. Calc. for $C_{24}H_{28}O_6$: C, 69.9; H, 6.8. Found: C, 69.7; H, 6.7.

*Methyl 5-*O*-benzoyl-1,7-di-*O*-benzyl-3,4-dideoxy-α-*DL-threo-*hept-3-en-2-ulopyranoside* (**17**). — Benzoic acid (1.22 g, 0.01 mol) and triphenylphosphine (2.6 g, 0.01 mol) were added to a solution of **13** (1.85 g, 0.005 mol) in tetrahydrofuran (25

mL), followed dropwise with stirring by a solution of diethyl azodicarboxylate (1.74 g, 0.01 mol) in tetrahydrofuran (15 mL). After 1 h, the solvents were removed under reduced pressure and the residue was subjected to column chromatography (light petroleum–ethyl acetate, 9:1) to give **17** (1.94 g, 82%) as a thick liquid: ν_{max}^{film} 1730, 1260 (ester), 3050, 1600, 740 (C_6H_5), 1120, 1040 cm^{-1} (C–O). See Table I for the ^{1}H-n.m.r. data.

Anal. Calc. for $C_{29}H_{30}O_6$: C, 73.4; H, 6.4. Found: C, 73.5; H, 6.2.

*Methyl 5-*O*-benzoyl-1,7-di-*O*-benzyl-3,4-dideoxy-β-*DL*-*threo*-hept-3-en-2-ulopyranoside* (**20**). — Carbinol **18** (0.37 g, 1 mmol) was treated with benzoic acid, triphenylphosphine, and diethyl azodicarboxylate as described above, to give **20** (0.34 g, 72%); ν_{max}^{film} 1720, 1265 (ester), 3080, 1600, 740 (C_6H_5), 1100, 1070 cm^{-1} (C–O). See Table I for the ^{1}H-n.m.r. data.

Anal. Calc. for $C_{29}H_{30}O_6$: C, 73.4; H, 6.4. Found: C, 73.4; H, 6.4.

*Methyl 5-*O*-acetyl-3,4-anhydro-1,7-di-*O*-benzyl-α-*DL*-allo-hept-2-ulopyranoside* (**24**). — A solution of **13** (0.62 g, 1.44 mmol) in dichloromethane (10 mL) was treated with *m*-chloroperbenzoic acid (0.26 g, 1.50 mmol) for 4 days, filtered, and concentrated, and the residue was subjected to column chromatography (benzene–ether, 4:1) on silica gel (10 g) to give **23** (0.34 g, 62%) as a colorless, thick liquid; ν_{max}^{film} 3500 (OH), 1460, 740, 700 (C_6H_5), 1100, 1050 (C–O), 880 cm^{-1} (epoxide). ^{1}H-n.m.r. data (C_6D_6): δ 7.19 (bs, 10 H, 2 Ph), 4.39 and 4.30 (2 s, each 2 H, 2 OCH_2Ph), 4.15–3.42 (m, 8 H, H-1,1′,4,6,7,7′,OH), 3.27 (s, 3 H, OMe).

Conventional treatment of **23** with acetic anhydride–pyridine gave the acetate **24** (84%) as a thick liquid; ν_{max}^{film} 1740, 1220 (OAc), 1460, 740 (C_6H_5), 1100, 1040 (C–O), 870, 820 cm^{-1} (epoxide). See Table I for the ^{1}H-n.m.r. data.

Anal. Calc. for $C_{24}H_{28}O_7$: C, 67.3; H, 6.6. Found: C, 67.2; H, 6.8.

*Methyl 3,4,5-tri-*O*-acetyl-1,7-di-*O*-benzyl-α-*DL*-gluco-hept-2-ulopyranoside* (**25**). — The epoxide **23** (0.278 g, 0.72 mmol) was heated for 7 days under reflux with a saturated solution of barium hydroxide in 2:1 water–1,4-dioxane (30 mL). The mixture was then neutralised with carbon dioxide, insoluble material was collected and washed with water, and the combined filtrates and washings were concentrated to dryness. The residue, consisting essentially of one component (t.l.c.), was treated with acetic anhydride–pyridine. Column chromatography (benzene–ether, 5:1) of the product on silica gel (5 g) gave **25** (0.216 g, 63%); ν_{max}^{film} 1760, 1240 (OAc), 3150, 1500, 740 (C_6H_5), 1100, 1020 cm^{-1} (C–O). See Table I for the ^{1}H-n.m.r. data.

Anal. Calc. for $C_{28}H_{34}O_{10}$: C, 63.4; H, 6.5. Found: C, 63.3; H, 6.5.

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