Note

Improved synthesis of the 2-, 3-, and 4-deoxy derivatives from methyl β -D-galactopyranoside*

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A number of forces may play roles in the binding of carbohydrate antigens to immunoglobulins. We have previously shown¹ that the major part of the binding energy of the interaction between several anti-galactan monoclonal antibodies and their homologous carbohydrates may arise from hydrogen bonding. This is indicated by the binding pattern shown by a great number of derivatives of methyl β -D-galactopyranoside (mono- and oligo-saccharides), many of them having fluorine substituted for hydroxyl groups at certain positions. To refine this investigation, we will examine the binding pattern of these immunoglobulins with deoxygenated ligands related to β -D-galactan. Here, we describe the syntheses of a series of deoxy analogs of methyl β -D-galactopyranoside.

The preparation of the title compounds by the previously described methods involves tedious, multistep procedures giving only moderate yields of the desired products. In view of new chemistry and blocking strategies developed since the last of any of these compounds was reported², we decided to develop a general approach to the synthesis of 2-, 3-, and 4-deoxy derivatives of methyl β -D-galactopyranoside (1). The most conventional approach to deoxygenation of a carbohydrate, *i.e.*, the hydrogenolysis of a corresponding halogeno derivative³⁻⁶, was considered first. To prepare the 4-deoxy derivative 9, an approach was chosen similar to that described for preparation of the corresponding α anomer⁷. In anticipation that side reactions^{6,8} might be minimized, methyl 2,3,6-tri-O-benzoyl- β -Dgalactopyranoside⁹ (2), rather than the corresponding D-gluco derivative⁶, was converted into the 4-O-(p-bromophenylsulfonyl) derivative 3, which was then treated with potassium iodide in Me₂SO. Several products were formed, and the desired compound 4 was obtained in a yield of only 45%. A small proportion of the corresponding D-galacto derivative⁶ (5) was also obtained. The physical constants of 4

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¹H-N.M.R. CHEMICAL SHIFTS

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4.684d $5.343dd$ $2.682dd$ $2.039ddd$ $5.542bs$ $4.256bt$ $4.632dd$ $4.327d$ 8 $1.78-1.69m$ $2.25-2.17m$ $3.96-4.10m$ 8 $4.344t$ $4.455dd$ $4.334dd$ $1.79-1.67m$ $2.178-1.69m$ $2.25-2.17m$ $3.96-4.10m$ 8 8 $4.334dd$ $1.79-1.67m$ $2.14-2.05m$ 3.83 $3.74m$ $3.722t$ $4.531dd$ $4.562dd$ $1.71-1.62m$ $2.06-1.97m$ h h h h h $4.562dd$ $1.71-1.62m$ $2.06-1.97m$ h h h h h $1.71-1.62m$ $2.06-1.97m$ h $5.873bd$ $4.200dd$ $4.700dd$ $1.71-1.62m$ $2.064t$ $4.485dd$ $4.322dd$ $4.204dd$ h $4.700dd$ $1.71-1.62m$ $5.866t$ $4.485dd$ $4.322dd$ $4.200ddd$ 4.74 $4.35dd$ $2.288t$ $4.419dd$ $4.352dd$ $4.290ddd$ 4.74 $4.35dd$ $2.288t$ $4.307dd$ $4.303dd$ 4.78 $4.357dd$ $2.288t$ <th>14</th> <th>4.966d</th> <th>4.768dd</th> <th></th> <th>f</th> <th></th> <th>5.674dd</th> <th></th> <th>f</th> <th>4.494dd</th> <th>4.652dd</th> <th>3.595s</th>	14	4.966d	4.768dd		f		5.674dd		f	4.494dd	4.652dd	3.595s
4.327d 8 $1.78-1.69m$ $2.25-2.17m$ $3.96-4.10m$ 8 8 4.327d $5.851dd$ $5.72dd$ $1.78-1.69m$ $2.25-2.17m$ $3.96-4.10m$ 8 8 4.811d $5.851dd$ $6.078dd$ $6.078dd$ $5.112bd$ $4.344t$ $4.455dd$ 4.384dd $1.79-1.67m$ $2.14-2.05m$ 3.83 $3.74m$ $3.722t$ $4.531dd$ 4.562dd $1.71-1.62m$ $2.06-1.97m$ h h h h $1.71-1.62m$ $2.06-1.97m$ h h h h h $1.71-1.62m$ $2.05-1.97m$ h h h h h h $1.71-1.62m$ $2.$	15	4.684d	5.343dd		2.682dd	2.039ddd	5.542bs		4.256bt	4.632dd	4.485dd	3.584s
4.811d 5.851dd 6.078dd 6.112bd 4.344t 4.455dd 4.384dd 1.79-1.67m 2.14-2.05m 3.33 3.74m 3.72t 4.531dd 4.562dd 1.71-1.62m 2.06-1.97m h h 3.72t 4.531dd 1.71-1.62m 2.06-1.97m h 5.49-5.44m 5.873bd 4.500dd 4.500dd 1.71 2.33-2.25m 5.49-5.44m 5.873bd 4.204t 4.500dd 1.71 3.580t 1.71-1.62m 2.06-1.97m h 4.500dd 1.71 2.33-2.25m 5.49-5.44m 5.873bd 4.204t 4.500dd 1.71 3.580t 1.71-1.62m 2.04-5.44m 5.873bd 4.204t 4.70 1.412d 3.580t 4.419dd 4.322dd 4.320dd 4.74 4.473d 5.886t 4.419dd 4.330m 4.088m 4.621m 4.355dd 2.288m 1.697m 4.330m 4.058m 4.621m	16 ^d	4.327d	8		1.78-1.69m	2.25-2.17m	3.96-4.10m		8	8	8	3.580s
4.384d 1.79-1.67m 2.14-2.05m 3.83 3.74m 3.72zt 4.531dd 4.562dd 1.71-1.62m 2.06-1.97m h 3.72zt 4.531dd 1 2.33-2.25m 2.06-1.97m h 5.49-5.44m 5.873bd 4.204t 4.500dd 1 2.33-2.25m 5.49-5.44m 5.873bd 4.204t 4.500dd 1 2.33-2.25m 5.49-5.44m 5.873bd 4.204t 4.500dd 1 3.580t 1 4.240dd 4.200dd 4.70 4.451d 5.266t 4.419dd 4.322dd 4.72 4.473d 5.886t 4.419dd 4.352dd 4.72 4.355dd 2.218m 1.697m 4.330m 4.058m 4.621m	17	4.811d	5.851dd		6.078dd		6.112bd		4.344t	4.455dd	4.767dd	3.612s
4.562dd 1.71–1.62m 2.06–1.97m h h h h h 1 2.33–2.25m 5.49–5.44m 5.873bd 4.204t 4.500dd 1 2.33–2.25m 5.49–5.44m 5.873bd 4.204t 4.500dd 4.127d 3.580t 1 4.24dd 4.20dd 1 4.70 4.451d 5.266t 4.485dd 4.322dd 4.72 4.74 4.473d 5.886t 4.419dd 4.352dd 4.72 4.355dd 2.218m 1.697m 4.330m 4.058m 4.621m	18	4.384dd	1.79–1.67m		3.83		3.74m		3.722t	4.531dd	4.653dd	3.503s
· i 2.33-2.25m 5.49-5.44m 5.873bd 4.204t 4.500dd 4.127d 3.580t / / 4.700dd / 4.700dd 4.451d 5.266t 4.485dd 4.485dd 4.322dd 4.70 4.473d 5.886t 4.419dd 4.352dd 4.723ddd 4.72 4.355dd 2.218m 1.697m 4.330m 4.058m 4.621m	194	4.562dd	1.71–1.62m	2.06–1.97m	Ч		ų		ų	Ч	Ч	3.545s
4.127d 3.580t <i>i</i> 4.70 4.451d 5.266t 4.485dd 4.73 4.451d 5.266t 4.485dd 4.74 4.473d 5.886t 4.419dd 4.352dd 4.72 4.355dd 2.218m 1.697m 4.330m 4.058m 4.621m	20	· ·	2.33-2.25m		5.49-5.44m		5.873bd		4.204t	4.500dd	i	3.649s
4.451d 5.266t 4.485dd 4.74 4.473d 5.886t 4.419dd 4.352dd 4.230ddd 4.72 4.473d 5.886t 4.419dd 4.352dd 4.239ddd 4.72 4.355dd 2.218m 1.697m 4.330m 4.058m 4.621m	22	4.127d	3.580t		<i>i</i> .		4.240dd		j	4.70	4.58m	3.550s
4.473d 5.886t 4.419dd 4.352dd 4.239ddd 4.72 4.355dd 2.218m 1.697m 4.330m 4.058m 4.621m	53	4.451d	5.266t		4.485dd		4.322dd		4.220ddd	4.74	4.62m	3.481s
4.355dd 2.218m 1.697m 4.330m 4.058m 4.658m 4.621m	2	4.473d	5.886t		4.419dd		4.352dd		4.239ddd	4.72	4.67m	3.486s
	52	4.355dd	2.218m	1.697m	4.330m		4.058m		4.058m	4.621m	4.621m	3.494s
	aDaab multi	nlicitiae. h. h.	rood d double	t m multinlet	· · cinclet ·	trinlet bMass	torol in chlorof	man h man	othomas in a	diantad CMA	-	tooo ai boan

^aPeak multiplicities: b, broad, d, doublet, m, multiplet, s, singlet, t, triplet. ^bMeasured in chloroform-d, unless otherwise indicated. ^cMeasured in acctone- d_6 . ^dMeasured in D₂O. ^c4-Proton multiplet, δ 3.793–3.609. *Z*-Proton multiplet, δ 5.05–4.85. ^{s4}-Proton multiplet, δ 3.736–3.662. ^h5-Proton multiplet, δ 3.912– 3.603. ¹2-Proton multiplet, 84.774-4.700. ¹2-Proton multiplet, 84.161-4.110.

TABLE II

¹H-n.m.r. coupling constants (Hz)

••	4	ŝ	9	٢	æ	6	13	13 14 15	15	16	17	18	19	20	33	23	24	52
7.9	7.8	7.9	7.9	8.0	7.5	7.9	7.9	6.9	7.8	8.0	7.9	a	q	c	7.9	8.0	7.8	q
10.5	9.5	9.6	10.1	10.2	U U	8.9	10.3	4.3	e	U	10.0	v	υ	c	7.9	8.0	7.8	f
3.2	10.4	4.3	2.9	3.2	v	U	3.5	4.1	8	c	3.4	c	c	2.3	5.4	5.6	5.4	J
$\overline{\nabla}$	10.8	1.0	0	0	c	U	$\overline{\nabla}$	1.9	$\overline{\nabla}$	U	V	v	c	U	2.2	2.0	2.1	U U
7.3	4.6	5.9	U U	ն	ç	U	6.6	6.3	6.8	v	6.3	6.6	c	6.4	c	7.1	7.3	υ
6.0	2.0	6.6	J	c	ç	ç	5.6	6.5	6.1	J	6.3	6.6	U	6.4	c	5.1	5.4	Ú,
11.2	12.1	11.4	J	c	υ	c	11.3	11.4	11.1	U	11.4	11.3	U	11.3	J	с	c	S

	R ⁵ R ³ R ⁴ CI		ç)Me	Me ₂ C		OMe		
	R1	R ²	R ³	R ⁴	R ⁵	R6	_	R ¹	R ²
1	ОН	н	он	OH	н	Н	21	ОН	н
2	OBz	н	OBz	OH	н	Bz	22	OH	Bz
3	OBz	н	OBz	OBs	н	Bz	23	OBz	Bz
4	OBz	н	OBz	н	I	Bz	24	Oltc	Bz
5	OBz	н	OBz	I	н	Bz	25	н	Bz
6	OBz	Н	OBz	OTf	н	Bz			
7	OBz	н	OBz	OItc	н	Bz	Bn == be		
8	OBz	Н	OBz	н	н	Bz	Bz ≕ be Bs 4-	•	enylsulfonyl
9	OH	Н	OH	Н	н	Н			- ylthiocarbonyl
10	OH	Н	OBn	ОН	H	Н	Pab == 4 Tf == F ₃		zo)benzoyl
11	OBz	Н	OBn	OBz	н	Bz	II — F ₃	0302	
12	OBz	H	OH	OBz	Н	Bz			
13	OBz	Н	OTf	OBz	н	Bz			
14	OBz	I	н	OBz	н	Bz			
15	OBz	Н	Н	OBz	H	Bz			
16	OH	Н	Н	OH	н	Н			
17	OBz	Н	OItc	OBz	н	Bz			
18	н	н	ОН	OH	Н	Bz			
19	н	н	OH	OH	н	н			
20	н	н	OPab	OPab	Н	OPab			

and 5 agreed essentially with the reported values⁶, and the structures were fully supported by the ¹H-n.m.r. data (see Tables I and II). In another approach, the 4-O-(trifluoromethylsulfonyl) derivative 6 was treated with iodide ion under much milder conditions. In this case, compound 4, the only product (t.l.c.), was isolated crystalline in 78% yield. The iodo derivative 4 was hydrogenolyzed in the presence of 20% palladium-on-charcoal catalyst, to give the fully protected deoxy derivative 8. O-Debenzoylation (Zemplén) of 8 afforded the target glycoside 9, the physical constants of which agreed well with the literature values⁶.

Easy access¹⁰ to methyl 2,4,6-tri-O-benzoyl- β -D-galactopyranoside (12) made it possible to synthesize the 3-deoxy derivative 16, via the 3-O-triflyl derivative 13, in a way analogous to that just described for the preparation of 9. The resulting 16 showed physical constants in accord with the published data³, and its n.m.r. characteristics (not previously recorded), as well as those of its intermediates, fully supported the anticipated structures.

A suitable starting-material for the synthesis of the 2-deoxyglycoside 19 appeared to be methyl 6-O-benzoyl-3,4-O-isopropylidene- β -D-galactopyranoside (22). This compound was used by $Flowers^{11}$ in disaccharide syntheses, but details of its preparation or characterization had not been reported. We obtained compound 22 by selective benzovlation of methyl 3,4-O-isopropylidene- β -D-galactopyranoside (21; see ref. 12). A small proportion of the 2,6-di-O-benzovl derivative¹³ 23, formed along with 22 during benzoylation of 21, was also isolated. Both compounds 22 and 23 were obtained crystalline, and fully characterized. Treatment of 22 with trifluoromethanesulfonic anhydride, as described for the preparation of 6and 13, yielded a sharp-melting, crystalline material, m.p. 105° (dec.), which was homogeneous by t.l.c. and gave correct analytical data required for methyl 6-Obenzoyl-3,4-O-isopropylidene-2-O-(trifluoromethylsulfonyl)- β -D-galactopyranoside. The n.m.r. spectra of the substance showed, however, that it was a mixture of two compounds. Because isolation of the desired compound by recrystallization was unsuccessful, this approach was not pursued further, and we turned our attention to the possibility of deoxygenating carbon atom 2 in 22 via the corresponding imidazol-1-ylthiocarbonyl derivative $^{14-16}$. Compound 22 showed poor reactivity towards thiocarbonyldiimidazole (TCDI), as shown by t.l.c., but imidazolethiocarbonylation preceded by butylstannylation was successful. In this way, the crystalline thiocarbonyl derivative 24 was obtained in a yield of 86%. Reduction of 24 with tributyltin hydride gave the crystalline deoxy sugar 25 in 73% yield. Treatment of 25 with dilute acetic acid produced crystalline 18, and O-debenzoylation of 18 yielded material which crystallized readily. The compound shows a negative specific optical rotation ($[\alpha]_D - 16^\circ$), whereas methyl 2-deoxy- α -D-lyxo-hexopyranoside has been reported^{17,18} to show $[\alpha]_{D}$ +169 to +181°. A direct comparison of physical constants with literature data could not be made, as methyl 2-deoxy- β -D-lyxo-hexopyranoside was previously obtained in amorphous state only^{3,18}, and n.m.r. data for the compound have not been published. The corresponding tri-O-[4-(phenylazo)benzoyl] derivative 20 shows a m.p. close to that reported¹⁸ for a compound derived from amorphous, putative 19. However, the reported assignment of the (incomplete) ¹H-n.m.r. data is at some variance with our more-complete data reported here. Based on the analytical data found for this material and a comparison of the splitting pattern observed for H-1 and H-2 in its ¹H-n.m.r. spectrum (see Tables I and II) with that observed in the spectra of α - and β -linked 2,6-dideoxy-Dlyxo-hexopyranose^{19,20}, we assigned to it structure **19**.

Prompted by the ease of preparation of **19** via **24**, we applied the same method of deoxygenation to the synthesis of 3- and 4-deoxy derivatives **9** and **16**. Preparation of the intermediate compounds **8** and **15** via **7** and **17**, respectively, was uneventful. Thus, judging by the yields obtained and the simplicity of the operations involved, we find that the deoxygenation via imidazol-1-ylthiocarbonyl derivatives definitely superior to the conversions developed earlier. A high-yielding deoxygenation in the D-galactose series involving a dithiocarbonate derivative has recently been described by Kihlberg et al.²¹.

EXPERIMENTAL

General methods. — Melting points were determined on a Kofler hot stage. Unless otherwise stated, optical rotations were measured at 25° for solutions in chloroform, using a Perkin-Elmer automatic polarimeter, Model 241 MC. Preparative chromatography was performed by gradient elution from columns of Silica Gel 60 (Merck, Cat. No. 9385). All reactions were monitored by thin-layer chromatography (t.l.c.) on glass slides coated with silica gel (Analtech or Whatman). Elutions were conducted with solvent mixtures of appropriately adjusted polarity, consisting of: A, carbon tetrachloride-ethyl acetate; B, carbon tetrachloride-ethyl acetateacetone; C, toluene-ethyl acetate; D, dichloromethane-methanol; and E, carbon tetrachloride-acetone. ¹³C-N.m.r. and ¹H-n.m.r. spectra were routinely recorded at 25° with a Varian XL 300 spectrometer. Proton-signal assignments were made by first-order analysis of the spectra, supported by selective homonuclear decoupling experiments, and carbon-signal assignments were made by mutual comparison of the spectra. Unambiguous assignment of lines in the ${}^{13}C$ -n.m.r. spectrum of 19 was achieved by a heteronuclear ¹H-¹³C correlation 2D n.m.r. experiment (HETCOR), using a GE 300 WB (NT Series) spectrometer. Solvents for compounds used in measurements are reported in Tables I and II, as required. ¹³C-N.m.r. chemical shifts found in the spectra recorded for solutions in CDCl₃ and D₂O are reported using Me₄Si and methanol as internal standards (δ_{MeOH} vs. $\delta_{Me,Si}$ 49.0). Desorptive c.i. mass spectra were recorded using ammonia as the reagent gas and a Finnigan 4500 spectrometer. Palladium-on-charcoal (20%) catalyst was a product of Engelhardt Industries. N,N'-Thiocarbonyldiimidazole (TCDI, 97% purity) was purchased from Fluka Chemical Company, and used as supplied. Solutions in organic solvents were dried with anhydrous sodium sulfate, and concentrated or evaporated at $<40^{\circ}/2$ kPa.

Methyl 2,3,6-tri-O-benzoyl-4-O-(p-bromophenylsulfonyl)- β -D-galactopyranoside (3). — A mixture of 2 (lit.⁹, 5.06 g, 10 mmol), pyridine (25 mL), and pbromobenzenesulfonyl chloride (5.11 g, 20 mmol) was stirred overnight at 50°. Conventional processing gave the product 3 (6.10 g, 85%), which crystallized from ethanol. Recrystallization of a portion from the same solvent gave material having m.p. 178–179°, $[\alpha]_D$ +65° (c 0.5); ¹³C-n.m.r. data: δ 102.2 (C-1), 69.0 (C-2), 71.6 (C-3), 75.7 (C-4), 70.9 (C-5), 61.8 (C-6), and 57.0 (OCH₃).

Anal. Calc. for C₃₄H₂₉BrO₁₁S: C, 56.28; H, 4.03; Br, 11.01; S, 4.42. Found: C, 56.34; H, 4.03; Br, 11.10; S, 4.41.

Methyl 2,3,6-tri-O-benzoyl-4-deoxy-4-iodo- β -D-glucopyranoside (4) and methyl 2,3,6-tri-O-benzoyl-4-deoxy-4-iodo- β -D-galactopyranoside (5). — (a) A mixture of compound 3 (0.363 g, 0.5 mmol) and potassium iodide (1.66 g, 10 mmol) in Me₂SO (5 mL) was heated overnight at 110° (bath). T.l.c. (solvent B) then showed that all of the 3 had been consumed, and that one major and several minor products had been formed. The mixture was partitioned between water and dichloromethane, the organic layer was washed with an aqueous solution of sodium thiosulfate, dried, and concentrated, and the residue was chromatographed (solvent *B*), to give, first, a small amount of **5**; m.p. 166° (lit.⁶ 163–164°); ¹³C-n.m.r. data: δ 102.7 (C-1), 67.7 (C-2), 72.1, 71.2, 71.0 (C-3,5,6), 33.5 (C-4), and 56.8 (OCH₃).

Eluted next was the major product 4 (0.145 g, 45%); m.p. 144.5–145° (from methanol), $[\alpha]_D$ +49° (c 0.2), (lit.⁶ m.p. 131–133°, $[\alpha]_D$ +19.9°); ¹³C-n.m.r. data: δ 102.2 (C-1), 75.8, 75.3, 72.8 (C-2,3,5), 24.0 (C-4), 65.5 (C-6), and 57.0 (OCH₃).

Anal. Calc. for C₂₈H₂₅IO₈: C, 54.56; H, 4.11; I, 20.59. Found: C, 54.67; H, 4.11; I, 20.67.

Both compounds 4 and 5 produced a peak at m/z 634 (M + 18)⁺ in their c.i.m.spectra.

(b) Potassium iodide (0.996 g, 6 mmol) was added to a solution of 6 (1.277 g, 2.0 mmol) in acetonitrile (15 mL). The mixture was heated for 3 h at 50°; t.l.c. then showed that the reaction was complete and that only one product had been formed. After concentration, the concentrate was partitioned between dichloromethane and water, and the organic layer was dried and concentrated. Chromatography (solvent A), and crystallization from methanol, yielded 4 (0.957 g, 78%); m.p. 144.5–145°.

Methyl 2,3,6-tri-O-benzoyl-4-O-(trifluoromethylsulfonyl)- β -D-galactopyranoside (6). — Trifluoromethanesulfonic anhydride (0.42 mL, 2.5 mmol) was slowly added at -10° to a solution of 2 (0.506 g, 1 mmol) in pyridine (5 mL), the mixture was stirred for 1 h at 0°, ice-water (20 mL) was added, and the mixture was extracted with dichloromethane. The extract was dried and concentrated, and the residue was chromatographed (solvent A). Crystallization from ethanol gave **6** (0.524 g, 83%); m.p. 142-143°, [α]_D +22° (c 0.8); ¹³C-n.m.r. data: δ 102.4 (C-1), 68.7 (C-2), 70.8, 70.4 (C-3,5), 81.0 (C-4), 61.0 (C-6), and 57.3 (OCH₃): c.i.m.s.: m/z 656 (M + 18)⁺.

Anal. Calc. for C₂₉H₂₅F₃O₁₁S: C, 54.55; H, 3.95; F, 8.93; S, 5.02. Found: C, 54.23; H, 4.17; F, 8.63; S, 5.19.

Methyl 2,3,6-tri-O-benzoyl-4-O-(imidazol-1-ylthiocarbonyl)- β -D-galactopyranoside (7). — A mixture of 2 (0.506 g, 1 mmol) and TCDI (0.3 g, 1.6 mmol) in toluene (15 mL) was boiled for 3 h under reflux, cooled, and concentrated, the residue was chromatographed (solvent A), and the product crystallized from ethanol, to give 7 (0.45 g, 75%); m.p. 150.5–151°, $[\alpha]_D$ +112° (c 0.6); ¹³C-n.m.r. data: δ 102.4 (C-1), 69.7 (C-2), 71.1, 71.4 (C-3,5), 76.3 (C-4), 61.5 (C-6), and 57.2 (OCH₃); c.i.m.s.: m/z 617 (M + 1)⁺.

Anal. Calc. for C₃₂H₂₈N₂O₉S: C, 62.33; H, 4.58; N, 4.54; S, 5.20. Found: C, 62.39; H, 4.61; N, 4.48; S, 5.16.

Methyl 2,3,6-tri-O-benzoyl-4-deoxy- β -D-xylo-hexopyranoside (8). — (a) A mixture of 4 (0.924 g, 1.5 mmol), 20% palladium-on-charcoal catalyst (0.46 g), and NaHCO₃ (0.252 g, 3 mmol) in DMF (20 mL) was stirred overnight in a hydrogen atmosphere. After conventional processing, the crude product was chromatographed (solvent C) to give 0.56 g (76%) of amorphous, major product 8; $[\alpha]_D$ +53° (c 0.8); ¹³C-n.m.r. data: δ 102.2 (C-1), 72.6, 71.6, 69.7 (C-2,3,5), 33.3 (C-4), 65.9 (C-6), and 56.9 (OCH₃); c.i.m.s.: m/z 508 (M + 18)⁺.

Anal. Calc. for C₂₈H₂₆O₈: C, 68.56; H, 5.34. Found: C, 68.60; H, 5.38.

Under the same conditions, compound 5 did not react, as shown by t.l.c.

(b) A solution of compound 7 (0.616 g, 1 mmol) in toluene (20 mL) was added to a reflxing solution of tributyltin hydride (0.5 mL, 1.5 mmol) in toluene (50 mL). The mixture was boiled under reflux until t.l.c. (solvent C) showed that the reaction was complete (~ 0.5 h). After concentration, the residue was chromatographed (solvent C), to give 8 in almost theoretical yield.

Methyl 4-deoxy- β -D-xylo-hexopyranoside (9). — M Methanolic sodium methoxide (1 mL) was added to a solution of 8 (0.54 g, 1.1 mmol) in methanol (50 mL), and the solution was kept overnight at room temperature. One product was formed, as shown by t.l.c. (solvent D). After neutralization of the base with Amberlite IR-120 (H⁺) ion-exchange resin, the solution was concentrated with addition of toluene, to remove methyl benzoate, and crystallization of the residue from methanol-ethyl acetate gave 9 (0.124 g, 63%); m.p. 148–148.5°, $[\alpha]_D$ –38° (c 0.4, water), (lit.⁶ m.p. 146–147°, $[\alpha]_D$ not reported; lit.³ m.p. 143°, $[\alpha]_D$ –35.5°); ¹³Cn.m.r. data: δ 103.7 (C-1), 75.1, 72.7, 70.6 (C-2,3,5), 35.1 (C-4), 63.7 (C-6), and 57.2 (OCH₃); c.i.m.s.: m/z 179 (M + 1)⁺.

Anal. Calc. for C₇H₁₄O₅: C, 47.19; H, 7.92. Found: C, 47.29; H, 7.96.

Methyl 2,4,6-tri-O-benzoyl-3-O-(trifluoromethylsulfonyl)- β -D-galactopyranoside (13). — Compound 12 (1.013 g, 2 mmol) was dissolved in pyridine (10 mL), and trifluoromethanesulfonic anhydride (1 mL, 1.667 g, 5.8 mmol) was slowly added at -10° . The solution was kept for 1 h at -10° and then for 2 h at room temperature. The yellow solution was poured into ice-water (50 mL), and the mixture was extracted with dichloromethane (3 × 40 mL); the extracts were combined, dried, and concentrated, and the concentrate was subject to chromatography (solvent A), giving 13 (0.95 g, 75%) as a colorless glass; $[\alpha]_D$ +41° (c 0.5); ¹³Cn.m.r. data: δ 102.1 (C-1), 70.9, 69.1, 68.1 (C-2,4,5), 83.2 (C-3), 61.9 (C-6), and 57.2 (OCH₃); c.i.m.s.: m/z 656 (M + 18)⁺.

Anal. Calc. for C₂₉H₂₅F₃O₁₁S: C, 54.55; H, 3.95; F, 8.93; S, 5.02. Found: C, 54.87; H, 3.81; F, 8.94; S, 5.21.

Methyl 2,4,6-tri-O-benzoyl-3-deoxy-3-iodo- β -D-gulopyranoside (14). — A mixture of compound 13 (3.31 g, 5.18 mmol) and potassium iodide (1.72 g, 10.3 mmol) in acetonitrile (50 mL) was heated overnight at 60° (bath), cooled, and concentrated; the residue was extracted with toluene (300 mL), the extract concentrated, and the concentrate chromatographed (solvent A), to give the major product 14 (2.47 g, 77%) as a colorless glass; $[\alpha]_D$ +61° (c 0.6); ¹³C-n.m.r. data: δ 101.2 (C-1), 72.3, 70.3, 68.6 (C-2,4,5), 27.9 (C-3), 63.1 (C-6), and 57.1 (OCH₃); c.i.m.s.: m/z 634 (M + 18)⁺.

Anal. Calc. for C₂₈H₂₅IO₈: C, 54.56; H, 4.09; I, 20.59. Found: C, 54.41; H, 4.11; I, 20.49.

Methyl 2,4,6-tri-O-benzoyl-3-O-(imidazol-1-ylthiocarbonyl)- β -D-galactopyranoside (17). — TCDI (0.3 g, 1.6 mmol) was added to a solution of 12 (0.506 g, 1 mmol) in toluene (15 mL), and the mixture was refluxed for 4 h. After processing as described for the preparation of **7**, compound **17** (0.54 g, 88%) was obtained as a colorless glass; $[\alpha]_D$ +67° (*c* 0.5); ¹³C-n.m.r. data: δ 102.1 (C-1), 71.1, 69.4, 67.1 (C-2,4,5), 79.4 (C-3), 61.9 (C-6), and 57.2 (OCH₃); c.i.m.s.: *m/z* 617 (M + 1)⁺.

Methyl 2,4,6-tri-O-benzoyl-3-deoxy- β -D-xylo-hexopyranoside (15). — (a) To a solution of 14 (2.28 g, 3.7 mmol) in DMF (50 mL) were added 20% palladium-oncharcoal catalyst (1.0 g) and sodium hydrogencarbonate (0.62 g, 7.4 mmol), and the mixture was stirred in a hydrogen atmosphere overnight. After conventional processing, the crude product was chromatographed (solvent C) to give 1.346 g (74%) of the major product 15 as a colorless glass: $[\alpha]_D - 17^\circ$ (c 0.4); ¹³C-n.m.r.: δ 103.3 (C-1), 68.2, 67.6 (C-2,4), 32.6 (C-3), 74.1 (C-5), 62.8 (C-6), and 56.6 (OCH₃); c.i.m.s.: m/z 508 (M + 18)⁺.

Anal. Calc. for C₂₈H₂₆O₈: C, 68.56; H, 5.34. Found: C, 68.67; H, 5.35.

(b) A solution of 17 (0.616 g, 1 mmol) in dry toluene (20 mL) was treated as described for preparation (b) of 8. When the reaction was complete (\sim 1 h), the mixture was concentrated, and the residue was chromatographed (solvent C), to give 15 in a virtually theoretical yield.

Methyl 3-deoxy-β-D-xylo-*hexopyranoside* (**16**). — A solution of **15** (0.62 g, 1.26 mmol) in methanol (40 mL) was treated as described for the preparation of **9**. Chromatography (solvent *D*), and crystallization yielded **16** (0.161 g, 73%); m.p. 177.5–179°, $[\alpha]_D = -67°$ (*c* 0.5, water), (lit.³ 173–174°, $[\alpha]_D = -69.4°$); ¹³C-n.m.r. data: δ 106.0 (C-1), 65.9, 65.6 (C-2,4), 37.3 (C-3), 78.4 (C-5), 61.4 (C-6), and 56.9 (OCH₃).

Anal. Calc. for C₇H₁₄O₅: C, 47.19; H, 7.92. Found: C, 46.96; H, 7.86.

Methyl 6-O-benzoyl- (22) and 2,6-di-O-benzoyl-3,4-O-isopropylidene- β -D-galactopyranoside (23). — Benzoyl chloride (0.64 mL, 5.5 mmol) was slowly added at -20° to a solution of compound 21 (lit.¹⁸; 1.17 g, 5 mmol) and dry pyridine (0.53 mL, 6.5 mmol) in dichloromethane (30 mL). When addition was complete, the mixture was allowed to warm to -10° and, after 15 min, it was processed in the usual way. The crude product was chromatographed (solvent *E*), to give, first, the minor product 23 (0.45 g, 21%); m.p. 123.5–125°, $[\alpha]_{\rm D}$ +30° (*c* 0.8), (lit.¹³ 121–122°, $[\alpha]_{\rm D}$ +31°); ¹³C-n.m.r. data: δ 101.5 (C-1), 77.1, 73.7, 73.4, 71.1 (C-2,3,4,5), 63.8 (C-6), and 56.6 (OCH₃); c.i.m.s.: *m/z* 460 (M + 18)⁺.

Eluted next was the major product **22** (0.935 g, 55%); m.p. 168–168.5°, $[\alpha]_D$ +11° (*c* 0.5); ¹³C-n.m.r. data: δ 103.2 (C-1), 73.7, 73.5 (C-2,4), 78.8 (C-3), 71.3 (C-5), 63.8 (C-6), and 56.9 (OCH₃); c.i.m.s.: *m/z* 356 (M + 18)⁺.

Anal. Calc. for C₁₇H₂₂O₇: C, 60.35; H, 6.55. Found: C, 60.27; H, 6.60.

Methyl 6-O-benzoyl-3,4-O-isopropylidene-2-O-(imidazol-1-ylthiocarbonyl)- β -D-galactopyranoside (24). — A mixture of 22 (3.38 g, 10 mmol) and bis(tributyltin) oxide (3.0 g, 2.82 mL, 5 mmol) in dry toluene (100 mL) was refluxed for 3 h with continuous azeotropic removal of water, cooled to room temperature, TCDI (2.7 g, 15 mmol) added, and the mixture heated almost at reflux for 1 h. The mixture was concentrated to a yellow oil which was dissolved in dichloromethane (100 mL), and the solution was washed successively with M HCl (100 mL), 5% aqueous sodium hydrogencarbonate solution (100 mL), and water (100 mL), dried, concentrated, and the residue crystallized from ether, to give **24** (3.82 g, 86%); m.p. 130.5°, $[\alpha]_D$ +8° (*c* 0.2); ¹³C-n.m.r. data: δ 100.8 (C-1), 81.1 (C-2), 76.7, 73.8, 71.2 (C-3,4,5), 63.5 (C-6), and 56.8 (OCH₃); c.i.m.s.: *m/z* 449 (M + 1)⁺.

Anal. Calc. for C₂₁H₂₄N₂O₇S: C, 56.23; H, 5.39; N, 6.24; S, 7.15. Found: C, 56.32; H, 5.43; N, 6.25; S, 7.08.

Methyl 6-O-benzoyl-2-deoxy-3,4-O-isopropylidene- β -D-lyxo-hexopyranoside (25). — Compound 24 (2.69 g, 6 mmol) was treated with tributylin hydride (2.9 g, 2.8 mL, 10 mmol) as described for preparation (b) of 8. When the reaction was complete (~2 h), the mixture was processed as described for the preparation of 8, and the product crystallized from hexane to afford pure 25; m.p. 62.5–63°, $[\alpha]_D$ –18° (c 0.8). Chromatography (solvent C) of the material in the mother liquor gave a further crop of 25 (total yield 1.4 g, 73%); ¹³C-n.m.r. data: δ 100.6 (C-1), 35.5 (C-2), 72.2, 71.3, 71.1 (C-3,4,5), 64.3 (C-6), and 56.3 (OCH₃); c.i.m.s.: m/z 340 (M + 18)⁺.

Anal. Calc. for C₁₇H₂₂O₆: C, 63.34; H, 6.88. Found: C, 63.13; H, 6.89.

Methyl 6-O-benzoyl-2-deoxy- β -D-lyxo-hexopyranoside (18). — A solution of compound 25 (0.71 g, 1.45 mmol) in a mixture of 1,2-dimethoxyethane (5 mL) and 10% aqueous acetic acid (4 mL) was heated for 18 h at 60°, cooled, concentrated, and the concentrate subjected to column chromatography (solvent *D*). Compound 18 (0.59 g, 88%) crystallized from acetone; m.p. 149–151°, $[\alpha]_D$ –27° (*c* 0.4, methanol); ¹³C-n.m.r. data: δ 101.3 (C-1), 35.1 (C-2), 68.4 (C-3), 67.2 (C-4), 72.5 (C-5), 63.1 (C-6), and 56.5 (OCH₃); c.i.m.s.: *m/z* 300 (M + 18)⁺.

Anal. Calc. for C₁₄H₁₈O₆: C, 59.57; H, 6.43. Found: C, 59.66; H, 6.44.

Methyl 2-deoxy- β -D-lyxo-hexopyranoside (19). — Conventional O-debenzoylation of 18 (0.140 g, 0.5 mmol), and crystallization of the product from methanol, gave 19 (0.079 g, 89%); m.p. 125–126°, $[\alpha]_D - 16^\circ$ (c 0.5, water), (lit.³ $[\alpha]_D 0^\circ$, and lit.¹⁸ $[\alpha]_D$ not reported for the amorphous 19); ¹³C-n.m.r. data: δ 101.3 (C-1), 33.5 (C-2), 68.0 (C-3), 67.0 (C-4), 75.5 (C-5), 61.5 (C-6), and 56.6 (OCH₃); c.i.m.s.: m/z 196 (M + 18)⁺.

Anal. Calc. for C₇H₁₄O₅: C, 47.19; H, 7.92. Found: C, 47.25; H, 7.97.

The corresponding per-O-[4-(phenylazo)benzoyl] derivative **20**, prepared as described¹⁸, had m.p. 193–194° (lit.¹⁸ m.p. 187°); ¹³C-n.m.r. data: δ 101.3 (C-1), 32.5 (C-2), 69.7 (C-3), 66.7 (C-4), 71.4 (C-5), 62.7 (C-6), and 57.0 (OCH₃).

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