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PREPARATION AND CALCULATED CONFORMATIONS OF THE 2′-, 3′-, 4′-, AND 6′-DEOXY, 3′-*O*-METHYL, 4′-EPI, AND 4′- AND 6′-DEOXY-FLUORO DERIVATIVES OF METHYL 4-*O*-α-D-GALACTOPYRANOSYL-β-D-GALACTOPYRANOSIDE (METHYL β-D-GALABIOSIDE)*

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ABSTRACT

The glycosyl chlorides of the 3-*O*-methyl (**6**) and 4-deoxy-4-fluoro (**8**) *O*-benzylated derivatives of D-galactopyranose and 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose were condensed with methyl 2,3,6-tri-*O*-benzoyl-β-D-galactopyranoside to give, after deprotection, the 3′-*O*-methyl (**23**), 4′-deoxy-4′-fluoro (**25**), and 4′-epi (**27**) derivatives, respectively, of methyl β-D-galabioside (**1**). The glycosyl fluorides of 2,3,4-tri-*O*-benzyl-D-fucopyranose and the 3-deoxy (**12**) and 4-deoxy (**16**) *O*-benzylated derivatives of D-galactopyranose were condensed with methyl 2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (**21**), to give, after deprotection, the 6′-deoxy (**31**), 3′-deoxy (**34**), and 4′-deoxy (**37**) derivatives of **1**, respectively. The 2′-deoxy (**41**) derivative of **1** was prepared by *N*-iodosuccinimide-induced condensation of 3,4,6-tri-*O*-acetyl-D-galactal and **21** followed by deprotection. Treatment of methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,3-di-*O*-benzoyl-α-D-galactopyranosyl)-β-D-galactopyranoside with Et_2NSF_3 (DAST), followed by deprotection, provided the 6′-deoxy-6′-fluoro (**46**) derivative of **1**. Molecular mechanics calculations yielded conformations for **23**, **25**, **27**, **31**, **34**, **37**, **41**, and **46** with small deviations from the calculated conformation for **1** (Φ_H/Ψ_H: −40°/−6°).

INTRODUCTION

We have described the synthesis[1a,b] and conformational analysis[1b,c] of a series of derivatives of methyl 4-*O*-α-D-galactopyranosyl-β-D-galactopyranoside [methyl β-D-galabioside (**1**)] with hydroxyl groups of the "reducing" galactose residue replaced by hydrogen or fluorine, as well as by *O*- and *C*-methyl groups. We now report a series of derivatives of **1** modified in the terminal galactose residue, namely, the 2′-deoxy (**41**), 3′-deoxy (**34**), 3′-*O*-methyl (**23**), 4′-deoxy (**37**), 4′-

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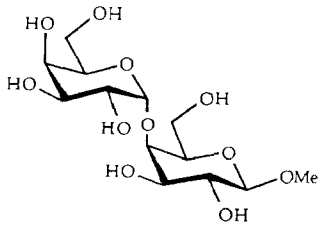
deoxy-4′-fluoro (**25**), 4′-epi (**27**), 6′-deoxy (**31**), and 6′-deoxy-6′-fluoro (**46**) derivatives. The set of analogues was designed to investigate the binding epitope[2a] of the tetrasaccharide globoside (and derivatives) towards the adhesin[2b] of uropathogenic *E. coli*[3a,3b], but is also of interest in studies of the binding of the toxin of *Shigella dysenteriae*[3c], verotoxin[3d] from *E. coli*, and antibodies towards tumor-associated antigens of Burkitt's lymphoma[3e].

In a comparative study of the biological activities of receptor-active analogues of carbohydrates, it is important that they have similar, low-energy conformations so that the observed biological activity can be considered in relation to the presence (or absence) of individual functional groups. The conformations of **1** and the analogues modified in the "reducing" unit were calculated using both the HSEA approach[1c] and molecular mechanics (MM2)[1b]. In the present paper, calculations were made using the MM2 program.



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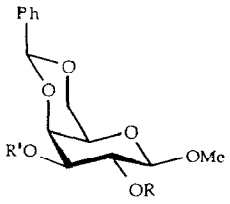
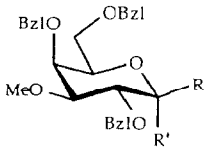
RESULTS AND DISCUSSION

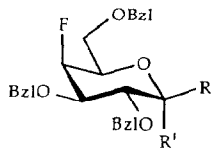
2,4,6-Tri-*O*-benzyl-3-*O*-methyl-D-galactopyranose (**6**) was prepared from methyl 4,6-*O*-benzylidene-β-D-galactopyranoside[1a,4] (**2**). Partial methylation of **2** under conditions of phase-transfer catalysis gave the 3- (**3**, 32%) and 2-methyl ether (**4**, 22%). The enhanced reactivity in **2** of HO-3, as compared to that of HO-2, has been utilised for regioselective 3-*O*-benzylation[1a] (47%), 3-*O*-benzoylation[1a,5] (80%), and 3-*O*-(methylthio)thiocarbonylation[1a] (60%). Hydrogenolysis of **3** and treatment of the product with benzyl bromide–sodium hydride–*N,N*-dimethylformamide gave the tribenzyl ether **5** (86%), hydrolysis of which with M aqueous hydrogen chloride in acetic acid then gave **6** (69%).



2 R = R′ = H
3 R = H, R′ = Me
4 R = Me, R′ = H



5 R = OMe, R′ = H
6 R, R′ = H, OH

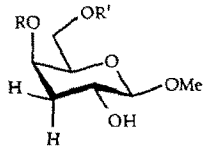


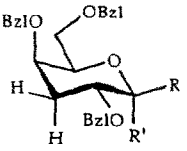
7 R = OMe, R′ = H
8 R, R′ = H, OH

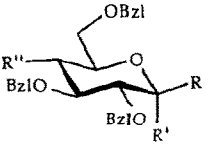
Similar hydrolysis of methyl 2,3,6-tri-*O*-benzyl-4-deoxy-4-fluoro-β-D-galactopyranoside[6] (**7**) gave 2,3,6-tri-*O*-benzyl-4-deoxy-4-fluoro-D-galactopyranose (**8**, 55%), and 21% of **7** was recovered.

2,4,6-Tri-*O*-benzyl-3-deoxy-D-*xylo*-hexopyranoside (**12**) was prepared from methyl 4,6-*O*-benzylidene-3-deoxy-β-D-*xylo*-hexopyranoside[1a] (**9**) by hydrogenolysis (→**10**, 96%), treatment with benzyl bromide–potassium hydroxide–toluene (→**11**, 64%), and hydrolysis (→**12**, 81%).

2,3,6-Tri-*O*-benzyl-4-deoxy-D-*xylo*-hexopyranoside (**16**) was prepared from methyl 2,3,6-tri-*O*-benzyl-β-D-glucopyranoside[7] (**13**) by treatment[8] with sodium hydride–imidazole–tetrahydrofuran followed by addition of carbon disulfide and methyl iodide (→**14**, 92%), reduction[8] with tributyltin hydride (→**15**, 98%), and hydrolysis (→**16**, 82%).







9 R, R' = CHPh
10 R = R' = H

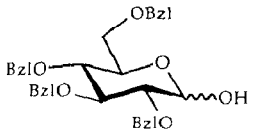
11 R = OMe, R' = H
12 R, R' = H, OH

13 R = OMe, R' = H, R'' = OH
14 R = OMe, R' = H, R'' = OCSSMe
15 R = OMe, R' = R'' = H
16 R, R' = H, OH, R'' = H

With electron-attracting substituents in the sugar ring, more severe conditions are required for hydrolysis than with electron-donating groups, as exemplified by the hydrolyses of the 4-deoxy-4-fluoro-derivative **7** (4 h, 110°, 55%), the 3-*O*-methyl derivative **5** (1 h, 100°, 69%), and the 3- and 4-deoxy derivatives **11** and **15** (~3 h, 80°, ~80%). Hydrolysis of oligosaccharide methyl glycosides can result in partial hydrolysis of interglycosidic bonds. We have reported[9,10] the preparation of 2-trimethylsilylethyl glycosides of mono- →tetra-saccharides and their transformations into 1-*O*-acyl (with retention of the initial anomeric configuration) and hemiacetal sugars[10]. The 2-trimethylsilylethyl group was stable to most of the reaction conditions used in carbohydrate synthesis, and the 1-*O*-acyl and hemiacetal sugars could be isolated in yields of 78–99% and 88–96%, respectively[10].

The hemiacetals **6** and **8** were converted[1b] into the corresponding glycosyl chlorides, using oxalyl chloride–*N*,*N*-dimethylformamide. Subsequent glycosidation of methyl 2,3,6-tri-*O*-benzoyl-β-D-galactopyranoside[11] (**20**), using silver trifluoromethanesulfonate as promoter, gave, apart from minor by-products, the 3'-*O*-methyl (**22**, 45%) and 4'-deoxy-4'-fluoro (**24**, 42%) derivatives of methyl β-D-galabioside (**1**). Glycosidation of **20** with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl chloride (prepared from **17**[12]) gave an inseparable αβ-mixture of disaccharide derivatives. Debenzoylation and chromatography gave the α- (**26**, 30%) and β-glucosides (**28**, 52%). Higher stereoselectivities in α-glucosidations of glycosyl

acceptors with reactivities similar to that of **20** have been reported with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl chloride[13a], fluoride[13b], trichloroacetimidate[13c], and xanthate[13d]. Removal of the protecting groups from **22, 24,** and **26** then gave methyl 4-*O*-(3-*O*-methyl-α-D-galactopyranosyl)-β-D-galactopyranoside (**23**, 86%), methyl 4-*O*-(4-deoxy-4-fluoro-α-D-galactopyranosyl)-β-D-galactopyranoside (**25**, 92%), and methyl 4-*O*-α-D-glucopyranosyl-β-D-galactopyranoside (**27**, 75%), respectively.



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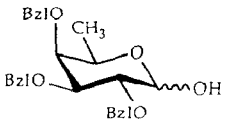

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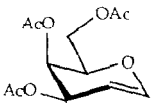

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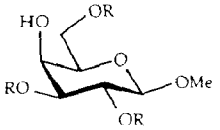
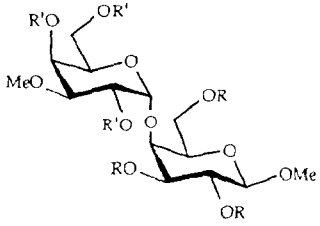
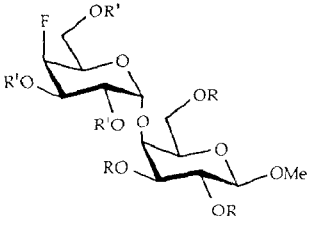


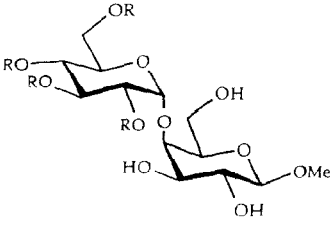
20 R = Bz
21 R = Bzl



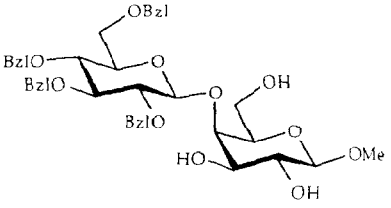
22 R = Bz, R' = Bzl
23 R = R' = H



24 R = Bz, R' = Bzl
25 R = R' = H



26 R = Bzl
27 R = H



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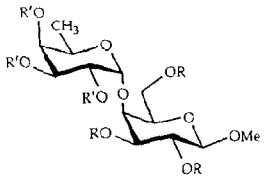
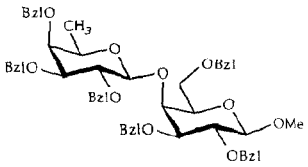
2,3,4-Tri-*O*-benzyl-D-fucopyranose[14] (**18**) was converted (t.l.c.) into the corresponding glycosyl chloride on treatment with excess of oxalyl chloride–*N*,*N*-dimethylformamide[1b], but the chloride underwent hydrolysis during the aqueous work-up. Treatment of **18** with oxalyl chloride and a catalytic amount[15] of *N*,*N*-dimethylformamide gave (t.l.c.) only a low yield of the glycosyl chloride. Conversion of **18** into the corresponding β-1-xanthate and attempted condensation[13d] with the

glycosyl acceptors **20** and **21**, using boron trifluoride etherate as catalyst, resulted in extensive decomposition.

Treatment[16] of **18** with diethylaminosulfur trifluoride[17] (DAST) gave an $\alpha\beta$-mixture of glycosyl fluorides in almost quantitative yield. The stereoselectivity of Lewis acid-catalysed glycosidations is almost independent of the anomeric composition of the glycosyl fluoride[18]. Therefore, the $\alpha\beta$-mixture was reacted[13b] immediately with **20**[11] in tetrahydrofuran, using stannous chloride and silver perchlorate as catalysts, to give the disaccharide derivative **29** (31%). Under similar conditions, reaction with **21** gave a mixture of the α (**30**, 56%) and β disaccharide (**32**, 10%) derivatives. Similar condensation of **21** with the glycosyl fluorides prepared from **12** gave **33** (71%) and **35** (15%), whereas the glycosyl fluorides obtained from **16** gave **36** (50%) and **38** (27%).



29 R = Bz, R' = Bzl
30 R = R' = Bzl
31 R = R' = H



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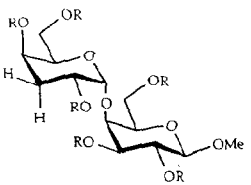
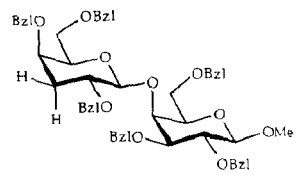


33 R = Bzl
34 R = H



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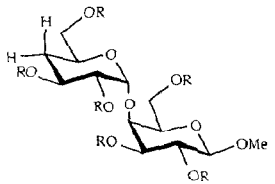
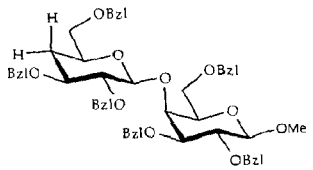


36 R = Bzl
37 R = H



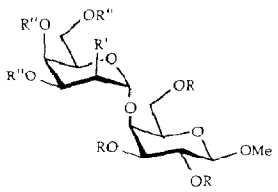
38

Alkylated (*e.g.*, benzylated) glycosyl halides have been used extensively as glycosyl donors in the synthesis of α-glycosides[20]. In the preparation of analogues of methyl β-D-galabioside (**1**), α-galactosidation[11] of HO-4 of modified methyl β-D-galactopyranosides using 2,3,4,6-tetra-*O*-benzyl-D-galactopyranosyl chloride (2 equiv.) gave higher yields[1b] (70–85%) and was less sensitive to the reaction conditions than when the corresponding galactosyl bromide was used[1a] (3 equiv., 40–50% yields). Substitution of an *O*-benzyl group for *O*-methyl or fluorine did not alter significantly the properties of the glycosyl chloride (*cf.* the preparation of **22** and **24**), whereas substitution by hydrogen gave less stable chlorides. The use of glycosyl fluorides (1.5 equiv.) circumvented this problem and gave α-glycosides in yields of 50–70%. Glycosidation with glycopyranosyl halides having an axial 4-*O*-benzyloxy or fluorine substituent gave glycosides with an $\alpha\beta$ ratio of >4.7:1, whereas, if a

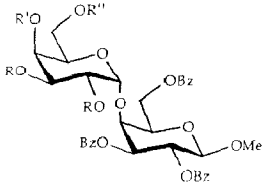
4-deoxy or an equatorial 4-*O*-benzyl group was present, lower $\alpha\beta$-ratios (2:1 and 1:2, respectively) were obtained

Hydrogenolysis of **30, 33,** and **36** then gave methyl 4-*O*-α-D-fucopyranosyl-β-D-galactopyranoside[11] (**31**, 90%), methyl 4-*O*-(3-deoxy-α-D-*xylo*-hexopyranosyl)-β-D-galactopyranoside (**34**, 91%), and methyl 4-*O*-(4-deoxy-α-D-*xylo*-hexopyranosyl)-β-D-galactopyranoside (**37**, 89%), respectively.

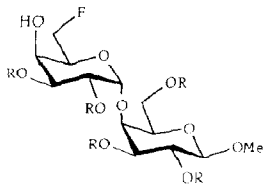
N-Iodosuccinimide-induced condensation[21] of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-hex-1-enitol[22] (**19**) with **21**[19] in acetonitrile gave the 2′-deoxy-2′-iodo-α-glycoside **39** (86%), whereas reaction with **20**[11] proceeded slowly and gave several by-products. Hydrogenolysis of the iodine in **39** in the presence of triethylamine, then of the benzyl ethers in acetic acid, gave the 2′-deoxy-α-glycoside **40** (65%), which was deacetylated to give methyl 4-*O*-(2-deoxy-α-D-*lyxo*-hexopyranosyl)-β-D-galactopyranoside (**41**, 68%).



39 R = Bzl, R′ = I, R″ = Ac
40 R = R′ = H, R″ = Ac
41 R = R′ = R″ = H



42 R = H, R′, R″ = CHPh
43 R = Bz, R′, R″ = CHPh
44 R = Bz, R′ = R″ = H



45 R = Bz
46 R = H

Benzoylation (→**43**, 97%) of methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(4,6-*O*-benzylidene-α-D-galactopyranosyl)-β-D-galactopyranoside[11] (**42**) and then removal of the 4′,6′-*O*-benzylidene group, using boiling methanolic iodine[23] (1%), gave the diol **44** (87%). Treatment of **44** with 1.05 equiv. of DAST[17], as described[1b] for the preparation of methyl 2,3-di-*O*-benzoyl-6-deoxy-6-fluoro-β-D-galactopyranoside, gave the 6′-deoxy-6′-fluorogalabioside derivative **45** (71%), which was debenzoylated to give methyl 4-*O*-(6-deoxy-6-fluoro-α-D-galactopyranosyl)-β-D-galactopyranoside (**46**, 84%).

Approximate conformations for methyl β-D-galabioside (**1**) and the analogues **23, 25, 27, 31, 34, 37, 41,** and **46** were calculated by the HSEA-approach[24] using the interactive program SUGAR[25]. After addition of lone pairs to the oxygen atoms, the atomic co-ordinates for these conformations were used as input (*via* the MIMIC[26] program) for molecular mechanics calculations using the MM2-85[27] program. The oxygen lone pairs were omitted in a previous conformational study of the 2-deoxy-, 6-deoxy-, 6-*O*-methyl-, and 6-deoxy-6-fluoro analogues of methyl β-D-galabioside[1b].

Intramolecular hydrogen bonds are present between HO-6 and HO-2′ of **1** in solution in methyl sulfoxide[1c] and between HO-3 and O-5′ in the galabiose crystal[28]. These hydrogen bonds had an important influence on the conformations obtained

TABLE I

CALCULATED[a] MINIMUM ENERGY CONFORMATIONS FOR METHYL β-D-GALABIOSIDE (**1**) AND THE ANALOGUES **23, 25, 27, 31, 34, 37, 41,** AND **46**

Compound	Φ_H[b] (°)	Ψ_H[c] (°)	ω_1[d] (°)	ω_2[e] (°)
1	−40	−6	67	63
1[g]	−40	−16	63	63
1[h]	−39	−15	68	63
23	−38	−5	68	62
25	−38	−3	68	62
27	−39	−10	67	−53
31	−40	−16	66	
34	−40	−9	67	63
37	−39	−10	67	−54
41	−39	−7	66	62
46	−40	−18	66	65[f]

[a]Calculated using the program SUGAR[25] and refinement of the data with the MM2-85 program[27]. [b]Φ_H = H-1′–C-1′–O-1′–C-4. [c]Ψ_H = H-4–C-4–O-1′–C-1′. [d]ω_1 = O-5–C-5–C-6–O-6. [e]ω_2 = O-5′–C-5′–C-6′–O-6′. [f]ω_2 = O-5′–C-5′–C-6′–F-6′ for **46**. [g]Calculated[1b] using the program SUGAR[25] and refinement of the data with the MM2-82 program[27]. [h]Calculated[1c] using the program GESA[36].

from the MM2-85 calculations. The conformation adopted by **1** in aqueous solution was shown to lack intramolecular hydrogen bonds, and to involve the *gauche-trans* conformation for the 5-hydroxymethyl group[1c]. Thus, in order to avoid the influence of intramolecular hydrogen bonding in the present calculations, the 5-hydroxymethyl group was kept in the *gauche-trans* conformation (*i.e.*, with HO-6 oriented away from HO-2′), and the torsional angle H–O-3–C-3–H-3 was kept at 60° (*i.e.*, HO-3 was oriented away from O-5′).

The calculated conformations, as described by the torsional angles of the glycosidic linkage (Φ_H and Ψ_H) and of the C-5–C-6 and C-5′–C-6′ bonds (ω_1, and ω_2, respectively), were similar for **1, 23, 25, 27, 31, 34, 37, 41,** and **46** (*cf.* Table I). Thus, the dihedral angles Φ_H and Ψ_H varied by 2° and 15° between the minimum energy conformations of these compounds. This finding is in good agreement with the results of previous investigations of analogues of **1**, modified in the β-galactosidic unit, using either the HSEA-approach[1c] or SUGAR in combination with MM2-82[1b].

A comparison of the conformations calculated for **1** by the different approaches (MM2-85, MM2-82, and HSEA) showed small variations in Φ_H and Ψ_H (1° and 10°; *cf.* Table I). All three conformations are in agreement with n.m.r. data[1c].

In **1, 23, 25, 27, 31, 34, 37, 41,** and **46**, there was marked deshielding of H-5′ ($\delta_{H\text{-}5'}$: see Table II), as compared to the 3-deoxy analogue[1c] of **1** ($\delta_{H\text{-}5'}$ 3.97 p.p.m.) or methyl α-D-galactopyranoside[29] ($\delta_{H\text{-}5}$ 3.78 p.p.m.). This deshielding requires[24a] H-5′ to be in van der Waals contact with O-3 (separation <2.7 Å) and supports the

TABLE II

SELECTED INTER-ATOMIC DISTANCES IN THE CALCULATED MINIMUM ENERGY CONFORMATIONS, AND δ(H-5'), FOR METHYL β-D-GALABIOSIDE (**1**) AND THE ANALOGUES **23, 25, 27, 31, 34, 37, 41,** AND **46**

Compound	*O-3/O-5'* *(Å)*	*O-6/O-2'* *(Å)*	*H-4/H-1'* *(Å)*	*O-3/H-1'* *(Å)*	*O-3/H-5'* *(Å)*	*δ(H-5')* *(p.p.m.)*
1	3.13	4.72	2.21	4.14	2.61	4.34
23	3.12	4.70	2.18	4.11	2.63	4.30
25	3.07	4.74	2.17	4.07	2.63	4.48
27	3.26	4.74	2.23	4.23	2.60	4.11
31	3.42	4.80	2.30	4.34	2.57	4.45
34	3.19	4.69	2.23	4.19	2.63	4.22
37	3.26	4.75	2.23	4.22	2.60	4.35
41	3.15		2.19	4.14	2.63	4.20
46	3.46	4.80	2.32	4.36	2.56	[a]

[a]Not determined.

calculated H-5'–O-3 distances (2.56–2.63 Å). Table II also shows calculated H-4–H-1' and O-3–H-1' interatomic distances that are in accord with a previous investigation of similar compounds[1c]. The calculated O-3–O-5' and O-6–O-2' interatomic distances were >3 Å, which is too long for hydrogen bonds to be present.

As concluded earlier from n.m.r. and calculational studies[1c], analogues of **1** modified at a single hydroxyl group display calculated conformations similar to those determined for **1**. Therefore, n.m.r. investigations of **23, 25, 27, 31, 34, 37, 41,** and **46** were not performed.

EXPERIMENTAL

General methods. — ^{1}H- {$CDCl_3$ (internal Me_4Si) or D_2O [internal sodium 3-(trimethylsilyl)propanesulfonate]} and ^{19}F-n.m.r. spectra [$CDCl_3$ or D_2O (external trifluoroacetic acid); chemical shifts (Φ) in p.p.m. upfield from the signal for $CFCl_3$] were recorded with a Varian XL-300 spectrometer. Optical rotations were measured with a Perkin–Elmer 141 polarimeter. Compounds were recrystallised from ethyl acetate–heptane unless otherwise stated. Melting points were determined with a Reichert melting-point microscope and are uncorrected. T.l.c. was performed on Kieselgel 60 F_{254} (Merck) with detection by u.v. light or charring with sulfuric acid. Column chromatography was performed on Kieselgel 60 (Merck, 230–400 mesh). Organic solutions were dried over Na_2SO_4. Methyl 4,6-*O*-benzylidene-β-D-galactopyranoside[1a,4] (**2**), methyl 2,3,6-tri-*O*-benzyl-4-deoxy-4-fluoro-β-D-galactopyranoside[6] (**7**), methyl 4,6-*O*-benzylidene-3-deoxy-β-D-*xylo*-hexopyranoside[1a] (**9**), methyl 2,3,6-tri-*O*-benzyl-β-D-glucopyranoside[7] (**13**), 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose[12] (**17**), 2,3,4-tri-*O*-benzyl-α-D-fucopyranose[14] (**18**), 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-hex-1-enitol[22] (**19**), methyl 2,3,6-tri-*O*-benzoyl-β-D-galactopyranoside[11] (**20**), methyl 2,3,6-tri-*O*-benzyl-β-D-galacto-

pyranoside[19] (**21**), and methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(4,6-*O*-benzylidene-α-D-galactopyranosyl)-β-D-galactopyranoside[11] (**42**) were prepared as described. 2,4,6-Tri-*O*-benzyl-3-*O*-methyl-D-galactopyranosyl chloride, 2,3,6-tri-*O*-benzyl-4-deoxy-4-fluoro-D-galactopyranosyl chloride, and 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl chloride were prepared from the corresponding hemiacetals **6, 8,** and **17**[12], as described for 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl chloride[1b]. 2,4,6-Tri-*O*-benzyl-3-deoxy-D-*xylo*-hexopyranosyl fluoride, 2,3,6-tri-*O*-benzyl-4-deoxy-D-*xylo*-hexopyranosyl fluoride, and 2,3,4-tri-*O*-benzyl-D-fucopyranosyl fluoride were prepared[16] by treatment of the corresponding hemiacetals **12, 16,** and **18**[14] (1 mmol, respectively) in dry tetrahydrofuran (4.5 mL) with diethylaminosulfur trifluoride[17] (DAST, 140 μL, 1.15 mmol) at −45° under nitrogen. The reaction was monitored by t.l.c. (ethyl acetate–heptane, 1:2) at room temperature. Methanol (15 μL) was added to each reaction mixture, the solvent was evaporated, and the crude glycosyl fluoride was used without further purification. Satisfactory elemental analyses could not be obtained for the amorphous compounds **23, 25, 27, 31, 34, 37, 41,** and **46,** but their purity was established by t.l.c. and ^{1}H-n.m.r. spectroscopy.

The conformational calculations were performed on a VAX 11/780 computer. Formula **1** was built with the SUGAR program[25], using co-ordinates for the α- and β-D-galactopyranoside units taken from a library of energy minimised (MM2-82[27]) monosaccharide crystal structures, and then modified to give the analogues **23, 25, 27, 31, 34, 37, 41,** and **46** using the MIMIC program[26]. Atomic co-ordinates were calculated for the disaccharides using the SUGAR program[25], and entered, *via* the MIMIC program[26], into the MM2-85 program[27]. Prior to the molecular mechanics calculations, lone pairs were added to the oxygen atoms. CH_2OH-5 in the disaccharide derivatives was assigned in the *gauche-trans* conformation based on data for methyl 6(*S*)-^{2}H-β-D-galactopyranoside[30] [60% *gauche-trans* calculated[31] from $J_{5,6}$ (ref. 30)], and from the 6(*S*)-deuterated analogue[1c] of **1** [58% *gauche-trans* calculated[31] from $J_{5,6}$ (ref. 1c)]. CH_2OH-5′ in **23, 25, 34,** and **41** and CH_2F-5′ in **46**, with HO-4′ or F-4′ axial, were assigned the *gauche-trans* conformation based on the results from methyl α-D-galactopyranoside specifically deuterated at C-6 (47% *gauche-trans*, 39% *trans-gauche*)[31]. CH_2OH-5′ in **27** (HO-4′ equatorial, $J_{5',6'}$ 3.2 Hz) and **37** (4′-deoxy, $J_{5',6'}$ 5.1 and 3.7 Hz) was assigned the *gauche-gauche* conformation based on the $J_{5',6'}$ values and on the results from methyl α-D-glucopyranoside specifically deuterated[31] at C-6 (57% *gauche-gauche*, 38% *gauche-trans*). The H-3–C-3–O-3–H torsional angle was set to 60° in order to avoid intramolecular hydrogen bonding between O-3 and O-5′. The H-1–C-1–O-1–C(H_3) torsional angle was set at 60° as required by steric demands[32] and by the exo-anomeric effect[33]. The C-2′–C-3′–O-3′–C(H_3) torsional angle in **23** was set at 180°, based on the results from methyl 3-*C*-ethyl-β-D-galactopyranoside[1c], thus eliminating 1,3-diaxial-like interactions[34] with HO-2′ and HO-4′.

*Methyl 4,6-*O*-benzylidene-3-* (**3**) *and -2-*O*-methyl-β-*D*-galactopyranoside* (**4**). — Aqueous sodium hydroxide (1.25M; 20 mL) was added to **2**[1a,4] (1.00 g, 3.55 mmol), tetrabutylammonium hydrogensulfate (0.24 g, 0.70 mmol), and methyl

iodide (0.64 mL, 10.3 mmol) in dichloromethane (60 mL). The mixture was boiled under reflux with vigorous stirring for 48 h and three portions of methyl iodide (each 0.64 mL, 10.3 mmol) were added after 6, 24, and 32 h, respectively. The aqueous phase was extracted with dichloromethane (40 mL), and the combined extracts were dried and concentrated. Column chromatography (ethyl acetate) of the residue gave **3** (340 mg, 32%) and **4** (227 mg, 22%).

Compound **3** had m.p. 216–217°, $[\alpha]_D^{25}$ +25° (*c* 0.79, chloroform). ^{1}H-N.m.r. data ($CDCl_3$, plus 1 drop of D_2O): δ 5.56 (s, 1 H, PhC*H*), 4.37 (dd, 1 H, *J* 12.3 and 1.3 Hz, H-6), 4.33 (dd, 1 H, *J* 3.5 and 1.1 Hz, H-4), 4.27 (d, 1 H, *J* 7.8 Hz, H-1), 4.11 (dd, 1 H, *J* 12.3 and 1.8 Hz, H-6), 3.94 (dd, 1 H, *J* 9.8 and 7.8 Hz, H-2, shifted to δ 5.31 on acetylation), 3.59 (s, 3 H, MeO), 3.53 (s, 3 H, MeO), 3.45 (q, 1 H, *J* 1.5 Hz, H-5), 3.34 (dd, 1 H, *J* 9.8 and 3.2 Hz, H-3).

Anal. Calc. for $C_{15}H_{20}O_6$: C, 60.8; H, 6.8. Found: C, 60.7; H, 6.8.

Compound **4** had m.p. 169–171°, $[\alpha]_D^{25}$ −29° (*c* 0.69, chloroform). ^{1}H-N.m.r. data ($CDCl_3$, plus 1 drop of D_2O): δ 5.56 (s, 1 H, PhC*H*), 4.35 (dd, 1 H, *J* 12.4 and 1.6 Hz, H-6), 4.23 (d, 1 H, *J* 7.6 Hz, H-1), 4.21 (dd, 1 H, *J* 4.1 and 1.3 Hz, H-4), 4.08 (dd, 1 H, *J* 12.4 and 2.1 Hz, H-6), 3.66 (dd, 1 H, *J* 9.6 and 4.1 Hz, H-3, shifted to δ 4.82 on acetylation), 3.63 (s, 3 H, MeO), 3.58 (s, 3 H, MeO), 3.45 (q, 1 H, *J* 1.6 Hz, H-5), 3.32 (dd, 1 H, *J* 9.6 and 7.6 Hz, H-2).

Anal. Calc. for $C_{15}H_{20}O_6$: C, 60.8; H, 6.8. Found: C, 60.4; H, 6.7.

*Methyl 2,4,6-tri-*O*-benzyl-3-*O*-methyl-β-*D*-galactopyranoside* (**5**). — Pd/C (10%, 150 mg) was added to a solution of **3** (245 mg, 0.83 mmol) in acetic acid (10 mL). The mixture was hydrogenated for 3 h at atmospheric pressure, then filtered through Celite, and concentrated. Freeze-drying of a solution of the syrupy residue in water (5 mL) gave amorphous methyl 3-*O*-methyl-β-D-galactopyranoside that was dissolved in dry *N,N*-dimethylformamide (5 mL). Sodium hydride (50% in oil, 180 mg, 3.74 mmol) was added to the solution at 0°, followed by benzyl bromide (445 μL, 3.74 mmol) after 10 min, and the mixture was stirred for 30 min at 60°. Methanol (305 μL) was added and, after 30 min, the mixture was diluted with ether (40 mL), washed with water (4 × 10 mL), dried, and concentrated. Column chromatography (ethyl acetate–heptane, 1:5) of the residue gave **5** (340 mg, 86%), m.p. 56–58°, $[\alpha]_D^{25}$ −16° (*c* 0.78, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 4.25 (d, 1 H, *J* 7.7 Hz, H-1), 3.91 (bd, 1 H, *J* 2.9 Hz, H-4), 3.70 (dd, 1 H, *J* 9.7 and 7.7 Hz, H-2), 3.53 (s, 3 H, MeO), 3.50 (s, 3 H, MeO), 3.26 (dd, 1 H, *J* 9.7 and 2.9 Hz, H-3).

Anal. Calc. for $C_{29}H_{34}O_6$: C, 72.8; H, 7.2. Found: C, 72.8; H, 7.2.

*2,4,6-Tri-*O*-benzyl-3-*O*-methyl-*D*-galactopyranose* (**6**). — A solution of **5** (3.56 g, 7.45 mmol) in acetic acid–M aqueous hydrogen chloride (7:2, 90 mL) was stirred for 1 h at 100°, then diluted with dichloromethane (250 mL), washed with saturated aqueous sodium hydrogencarbonate (3 × 100 mL), dried, and concentrated. Column chromatography (ethyl acetate–heptane, 1:3) of the residue gave **6** (2.39 g, 69%), m.p. 56–60°, $[\alpha]_D^{25}$ +5° (*c* 0.55, chloroform).

Anal. Calc. for $C_{28}H_{32}O_6$: C, 72.4; H, 6.9. Found: C, 71.9; H, 7.0.

*2,3,6-Tri-*O*-benzyl-4-deoxy-4-fluoro-*D*-galactopyranose* (**8**). — Hydrolysis of

7[6] (2.64 g, 5.66 mmol) for 4 h at 110°, as described for **6**, and column chromatography (ethyl acetate–heptane, 1:3) of the product gave **8** (1.40 g, 55%), isolated as a syrup, and recovered **7** (0.56 g, 21%). Compound **8** had $[\alpha]_D^{25}$ +8° (*c* 0.75, chloroform). ^{19}F-N.m.r. data ($CDCl_3$): Ø 217 (dt, *J* 50.2 and 27.1 Hz, F-4), 220 (dt, *J* 50.4 and 30.7 Hz, F-4).

Anal. Calc. for $C_{27}H_{29}FO_5$: C, 71.7; H, 6.5. Found: C, 71.9; H, 6.7.

*Methyl 3-deoxy-β-*D-xylo-*hexopyranoside* (**10**). — Debenzylidenation of **9**[1a] (1.83 g, 6.88 mmol) for 10 h, as described for **5**, and recrystallisation (ethyl acetate–ethanol, 3:1; two crops) of the product gave **10** (1.18 g, 96%), m.p. 176–179°, $[\alpha]_D^{25}$ −66° (*c* 0.49, water). ^{1}H-N.m.r. data (D_2O): δ 4.30 (d, 1 H, *J* 8.1 Hz, H-1), 3.97 (t, 1 H, *J* 3.1 Hz, H-4), 3.55 (s, 3 H, MeO), 2.18 (ddd, 1 H, *J* 13.8, 5.1, and 3.3 Hz, H-3*e*), 1.71 (ddd, 1 H, *J* 13.8, 12.1, and 3.0 Hz, H-3*a*).

Anal. Calc. for $C_7H_{14}O_5$: C, 47.2; H, 7.9. Found: C, 47.0; H, 8.0.

*Methyl 2,4,6-tri-*O*-benzyl-3-deoxy-β-*D-xylo-*hexopyranoside* (**11**). — Benzyl bromide (6.1 mL, 51 mmol) was added to a refluxing mixture of **10** (1.07 g, 6.01 mmol) and finely powdered potassium hydroxide (2.52 g, 45.0 mmol) in dry toluene (40 mL). The mixture was boiled under reflux for 24 h, then filtered, washed with water (2 × 20 mL), dried, and concentrated. Column chromatography (ethyl acetate–heptane, 1:5) of the residue gave **11** (1.73 g, 64%), isolated as a syrup, $[\alpha]_D^{25}$ −40° (*c* 0.73, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 4.32 (d, 1 H, *J* 7.6 Hz, H-1), 3.55 (s, 3 H, MeO), 2.32 (ddd, 1 H, *J* 14.0, 4.9, and 3.4 Hz, H-3*e*), 1.46 (ddd, 1 H, *J* 14.0, 11.6, and 2.7 Hz, H-3*a*).

Anal. Calc. for $C_{28}H_{32}O_5$: C, 75.0; H, 7.2. Found: C, 75.3; H, 7.3.

*2,4,6-Tri-*O*-benzyl-3-deoxy-*D-xylo-*hexopyranoside* (**12**). — Hydrolysis of **11** (1.50 g, 3.34 mmol) for 3.5 h at 80°, as described for **6**, and column chromatography (ethyl acetate–heptane, 1:3) of the product gave **12** (1.18 g, 81%), m.p. 72–75°, $[\alpha]_D^{25}$ −12° (*c* 0.72, chloroform).

Anal. Calc. for $C_{27}H_{30}O_5$: C, 74.6; H, 7.0. Found: C, 75.1, H, 7.2.

*Methyl 2,3,6-tri-*O*-benzyl-4-*O*-[(methylthio)thiocarbonyl]-β-*D-*glucopyranoside* (**14**). — To a solution of **13**[7] (4.65 g, 10.0 mmol) in dry tetrahydrofuran (30 mL) were added imidazole (12 mg) and sodium hydride (50% in oil; 960 mg, 20.0 mmol), and the mixture was stirred for 1 h at room temperature[8]. Carbon disulfide (4.8 mL) was added and stirring was continued for 1 h. Methyl iodide (1.19 mL) was added, the reaction was continued for 20 min, and dichloromethane (150 mL) was added. The mixture was washed with water (50 mL) and saturated aqueous sodium hydrogencarbonate (40 mL), dried, and concentrated. Column chromatography (ethyl acetate–heptane, 1:10) of the residue gave **14** (5.54 g, 93%), m.p. 65–66°, $[\alpha]_D^{25}$ +18° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.98 (dd, 1 H, *J* 9.9 and 9.2 Hz, H-4), 4.38 (d, 1 H, *J* 7.3 Hz, H-1), 3.76 (t, 1 H, *J* 9.2 Hz, H-3), 3.60 (s, 3 H, MeO), 3.51 (dd, 1 H, *J* 8.8 and 7.8 Hz, H-2), 2.52 (s, 3 H, MeS).

Anal. Calc. for $C_{30}H_{34}O_6S_2$: C, 65.0; H, 6.2. Found: C, 64.7; H, 6.2.

*Methyl 2,3,6-tri-*O*-benzyl-4-deoxy-β-*D-xylo-*hexopyranoside* (**15**). — A solution of **14** (4.78 g, 8.62 mmol) in dry toluene (50 mL) was added, under argon, to

a refluxing solution of tributyltin hydride (3.20 mL, 12.1 mmol) in toluene (40 mL) during 1 h[8]. The solution was boiled under reflux for 16 h and then concentrated. Column chromatography (ethyl acetate–heptane, 1:4) of the residue gave **15** (3.80 g, 98%), isolated as a syrup, $[\alpha]_D^{25}$ −4° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 4.28 (d, 1 H, *J* 7.8 Hz, H-1), 3.60 (s, 3 H, MeO), 3.33 (dd, 1 H, *J* 8.7 and 7.8 Hz, H-2), 2.15 (ddd, 1 H, *J* 1.8, 5.1, and 1.3 Hz, H-4*e*), 1.49 (bq, 1 H, *J* 12.0 Hz, H-4*a*). δ 4.28 (d, 1 H, *J* 7.8 Hz, H-1), 3.60 (s, 3 H, MeO), 3.33 (dd, 1 H, *J* 8.7 and 7.8 Hz, H-2), 2.15 (ddd, 1 H, *J* 12.8, 5.1, and 1.3 Hz, H-4*e*), 1.49 (bq, 1 H, *J* 12.0 Hz, H-4*a*).

Anal. Calc. for $C_{28}H_{32}O_5$: C, 75.0; H, 7.2. Found: C, 74.8; H, 7.4.

*2,3,6-Tri-O-benzyl-4-deoxy-*D-xylo-*hexopyranoside* (**16**). — Hydrolysis of **15** (1.93 g, 4.30 mmol) for 2.5 h at 80°, as described for **6**, and column chromatography (ethyl acetate–heptane, 1:2) of the product gave **16** (1.53 g, 82%), m.p. 75–81°, $[\alpha]_D^{25}$ +50° (*c* 1, chloroform).

Anal. Calc. for $C_{27}H_{30}O_5$: C, 74.6; H, 7.0. Found: C, 74.8; H, 7.0.

*Methyl 2,3,6-tri-O-benzoyl-4-O-(2,4,6-tri-O-benzyl-3-O-methyl-α-*D-*galactopyranosyl)-β-*D-*galactopyranoside* (**22**). — A mixture of **20**[11] (954 mg, 1.89 mmol), silver trifluoromethanesulfonate (727 mg, 2.83 mmol), and molecular sieves (4 Å, 1.2 g) was dried overnight at 0.1 Torr. Dry toluene (27 mL) and 2,4,6-trimethylpyridine (374 μL, 2.83 mmol) were added with stirring and the mixture was cooled to −40° under nitrogen. A solution of freshly prepared 2,4,6-tri-*O*-benzyl-3-*O*-methyl-D-galactopyranosyl chloride (~1.5 mmol) in dry toluene (4.5 mL) was added with protection from light, and the mixture was allowed to attain room temperature, then filtered through Celite, and diluted with dichloromethane (100 mL)[11]. The solution was washed with M hydrochloric acid (20 mL) and saturated aqueous sodium hydrogencarbonate (20 mL), dried, and concentrated. Column chromatography (ethyl acetate–heptane, 1:5) of the residue gave **22** (640 mg, 45%), isolated as a syrup, and recovered **20** (496 mg). Compound **22** had $[\alpha]_D^{25}$ +42° (*c* 0.43, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.76 (dd, 1 H, *J* 10.4 and 7.7 Hz, H-2), 5.20 (dd, 1 H, *J* 10.4 and 2.8 Hz, H-3), 4.90 (d, 1 H, *J* 3.6 Hz, H-1′), 4.62 (d, 1 H, *J* 7.7 Hz, H-1), 4.39 (bd, 1 H, *J* 2.8 Hz, H-4), 4.32 (dd, 1 H, *J* 9.8 and 4.7 Hz, H-6 or H-6′), 4.10 (bs, 1 H, H-4′), 4.05 (bt, 1 H, *J* 6.8 Hz, H-5 or H-5′), 3.98 (dd, AB-type, 1 H, *J* 10.3 and 3.6 Hz, H-2′), 3.90 (dd, AB-type, 1 H, *J* 10.3 and 2.6 Hz, H-3′), 3.55 (s, 3 H, MeO), 3.54 (s, 3 H, MeO), 3.36 (dd, 1 H, *J* 9.5 and 8.5 Hz, H-6 or H-6′), 2.84 (dd, 1 H, *J* 8.3 and 4.9 Hz, H-5 or H-5′).

Anal. Calc. for $C_{56}H_{56}O_{14}$: C, 70.6; H, 5.9. Found: C, 70.4; H, 6.1.

*Methyl 4-O-(3-O-methyl-α-*D-*galactopyranosyl)-β-*D-*galactopyranoside* (**23**). — A solution of **22** (628 mg, 0.660 mmol) in dichloromethane–methanolic 0.1M sodium methoxide (1:1, 16 mL) was stirred for 6 h at room temperature, then neutralised with Duolite (H^+) resin, and concentrated. Pd/C (10%, 400 mg) was added to a solution of the crude methyl 4-*O*-(2,4,6-tri-*O*-benzyl-3-*O*-methyl-α-D-galactopyranosyl)-β-D-galactopyranoside in acetic acid (10 mL). The mixture was hydrogenated for 5 h at atmospheric pressure, then filtered through Celite, and concentrated. Column chromatography (ethanol–dichloromethane, 1:3) of the residue gave, after freeze-drying, amorphous **23** (210 mg, 86%), $[\alpha]_D^{25}$ +121° (*c* 1.4, water). ^{1}H-N.m.r. data (D_2O): δ 4.93 (d, 1 H, *J* 3.6 Hz, H-1′), 4.36 (d, 1 H, *J*

7.9 Hz, H-1), 4.30 (t, 1 H, *J* 6.4 Hz, H-5′), 4.28 (bd, 1 H, *J* 3.2 Hz, H-4′), 4.01 (bd, 1 H, *J* 2.9 Hz, H-4), 3.85 (dd, 1 H, *J* 10.0 and 3.6 Hz, H-2′), 3.71 (dd, 1 H, *J* 10.4 and 2.9 Hz, H-3), 3.57 (dd, 1 H, *J* 10.0 and 3.2 Hz, H-3′), 3.56 (s, 3 H, MeO-1), 3.51 (dd, 1 H, *J* 10.4 and 7.9 Hz, H-2), 3.42 (s, 3 H, MeO-3′).

*Methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,3,6-tri-*O*-benzyl-4-deoxy-4-fluoro-α-*D*-galactopyranosyl)-β-*D*-galactopyranoside* (**24**). — Glycosidation[11] of **20** (784 mg, 1.55 mmol) with 2,3,6-tri-*O*-benzyl-4-deoxy-4-fluoro-D-galactopyranosyl chloride (~1.6 mmol), as described for **22**, gave, after column chromatography (ethyl acetate–heptane, 1:5; repeated with ether–toluene, 1:25) of the product, **24** (614 mg, 42%), isolated as a syrup, $[\alpha]_D^{25}$ +54° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.72 (dd, 1 H, *J* 10.6 and 7.8 Hz, H-2), 5.23 (dd, 1 H, *J* 10.6 and 2.7 Hz, H-3), 5.03 (dd, 1 H, *J* 50.1 and 1.7 Hz, H-4′), 4.91 (d, 1 H, *J* 3.4 Hz, H-1′), 4.63 (d, 1 H, *J* 7.8 Hz, H-1), 4.42 (bd, 1 H, *J* 2.7 Hz, H-4), 4.33 (ddd, 1 H, *J* 29.9, 9.5, and 5.1 Hz, H-5′), 4.15 (ddd, 1 H, *J* 27.7, 10.1, and 2.3 Hz, H-3′), 4.06 (t, 1 H, *J* 7.0 Hz, H-5), 3.91 (dd, 1 H, *J* 10.1 and 3.4 Hz, H-2′), 3.54 (s, 3 H, MeO), 3.35 (t, 1 H, *J* 9.2 Hz, H-6′), 2.96 (ddd, 1 H, *J* 8.6, 5.2, and 1.6 Hz, H-6′). ^{19}F-N.m.r. data ($CDCl_3$): Ø 221 (dt, *J* 49.9 and 29.0 Hz, F-4′).

Anal. Calc. for $C_{55}H_{53}FO_{13}$: C, 70.2; H, 5.7. Found: C, 70.2; H, 5.6.

*Methyl 4-*O*-(4-deoxy-4-fluoro-α-*D*-galactopyranosyl)-β-*D*-galactopyranoside* (**25**). — Deprotection of **24** (614 mg, 0.652 mmol), as described for **23**, and column chromatography (ethanol–dichloromethane, 1:3) of the product gave, after freeze-drying, amorphous **25** (215 mg, 92%), $[\alpha]_D^{25}$ +95° (*c* 1, water). ^{1}H-N.m.r. data (D_2O): δ 4.99 (d, 1 H, *J* 3.7 Hz, H-1′), 4.93 (dd, 1 H, *J* 51.0 and 2.5 Hz, H-4′), 4.48 (dt, 1 H, *J* 32.7 and 6.4 Hz, H-5′), 4.36 (d, 1 H, *J* 7.8 Hz, H-1), 4.03 (bd, 1 H, *J* 3.3 Hz, H-4), 4:00 (ddd, 1 H, *J* 29.0, 10.6, and 2.5 Hz, H-3′), 3.56 (s, 3 H, MeO), 3.50 (dd, 1 H, *J* 10.3 and 7.8 Hz, H-2). ^{19}F-N.m.r. data (D_2O): Ø 221 (dt, *J* 50.9 and 30.7 Hz, F-4′).

*Methyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-* (**26**) *and -β-*D*-glucopyranosyl)-β-*D*-galactopyranoside* (**28**). — Glycosidation[11] of **20** (200 mg, 0.395 mmol) with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl chloride (~0.59 mmol), as described for **22**, gave, after column chromatography (ether–toluene, 1:20) of the product, an inseparable mixture of the α and β disaccharides (298 mg). Debenzoylation of the mixture, as described for **23**, and column chromatography (ethyl acetate–heptane, 6:1) of the product gave **26** (66 mg, 30%) and **28** (115 mg, 52%), isolated as syrups.

Compound **26** had $[\alpha]_D^{25}$ −3° (*c* 3, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 4.70 (d, 1 H, *J* 3.7 Hz, H-1′), 4.13 (d, 1 H, *J* 7.3 Hz, H-1), 3.93 (bs, 1 H, H-4), 3.54 (s, 3 H, MeO).

Anal. Calc. for $C_{41}H_{48}O_{11}$: C, 68.7; H, 6.8. Found: C, 68.3; H, 6.6.

Compound **28** had $[\alpha]_D^{25}$ −4° (*c* 1.4, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 4.57 (d, 1 H, *J* 7.9 Hz, H-1′), 4.12 (d, 1 H, *J* 7.6 Hz, H-1), 4.08 (bd, 1 H, *J* 3.3 Hz, H-4), 3.94 (dd, 1 H, *J* 10.9 and 9.7 Hz, H-3′ or H-4′), 3.54 (s, 3 H, MeO).

Anal. Calc. for $C_{41}H_{48}O_{11}$: C, 68.7; H, 6.8. Found: C, 68.6; H, 6.8.

*Methyl 4-*O*-α-*D*-glucopyranosyl-β-*D*-galactopyranoside* (**27**). — Debenzyla-

tion of **26** (70 mg, 98 μmol), as described for **23**, and column chromatography (ethanol–dichloromethane, 3:1) of the product gave, after freeze-drying, amorphous **27** (26 mg, 75%), $[\alpha]_D^{25}$ +88° (*c* 0.54, water). ^{1}H-N.m.r. data (D_2O): δ 4.91 (d, 1 H, *J* 3.8 Hz, H-1′), 4.36 (d, 1 H, *J* 7.7 Hz, H-1), 4.11 (dt, 1 H, *J* 10.2 and 3.2 Hz, H-5′), 4.00 (d, 1 H, *J* 3.0 Hz, H-4), 3.89 (dd, AB-type, 1 H, *J* 11.4 and 7.6 Hz, H-6), 3.71 (dd, 1 H, *J* 10.2 and 3.0 Hz, H-3), 3.56 (s, 3 H, MeO), 3.51 (dd, 1 H, *J* 10.1 and 3.8 Hz, H-2′), 3.51 (dd, 1 H, *J* 10.2 and 7.7 Hz, H-2), 3.44 (dd, 1 H, *J* 10.2 and 9.1 Hz, H-4′).

*Methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,3,4-tri-*O*-benzyl-α-*D*-fucopyranosyl)-β-*D*-galactopyranoside* (**29**). — A mixture of stannous chloride (796 mg, 4.20 mmol), silver perchlorate (871 mg, 4.20 mmol), and activated molecular sieves (3 Å, 2 g) in dry tetrahydrofuran (20 mL) was stirred, under nitrogen, for 1 h at −20°. A solution of **20**[11] (1.42 g, 2.80 mmol) and freshly prepared 2,3,4-tri-*O*-benzyl-D-fucopyranosyl fluoride (~4.2 mmol) in dry tetrahydrofuran (15 mL) was added with exclusion of light, and the mixture was allowed to attain room temperature[13b]. Triethylamine (787 μL, 5.60 mmol) was added when reaction was complete, and the mixture was filtered through Celite and diluted with dichloromethane (150 mL). The solution was washed with M hydrochloric acid (40 mL) and saturated aqueous sodium hydrogencarbonate (40 mL), dried, and concentrated. Column chromatography (ethyl acetate–heptane, 1:3, repeated with ether–toluene, 1:20) of the residue gave **29** (796 mg, 31%), isolated as a syrup, $[\alpha]_D^{25}$ +62° (*c* 0.89, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.72 (dd, 1 H, *J* 10.6 and 7.8 Hz, H-2), 5.20 (dd, 1 H, *J* 10.6 and 2.7 Hz, H-3), 4.91 (d, 1 H, *J* 3.4 Hz, H-1′), 4.77 (d, 2 H, *J* 6.7 Hz, H-6), 4.63 (d, 1 H, *J* 7.8 Hz, H-1), 4.37 (bd, 1 H, *J* 2.7 Hz, H-4), 4.22 (bq, 1 H, *J* 6.4 Hz, H-5′), 4.17 (dd, 1 H, *J* 10.4 and 2.7 Hz, H-3′), 4.05 (bt, 1 H, *J* 6.7 Hz, H-5), 4.04 (dd, 1 H, *J* 10.5 and 3.4 Hz, H-2′), 3.66 (bs, 1 H, H-4′), 3.54 (s, 3 H, MeO), 0.65 (d, 3 H, *J* 6.4 Hz, H-6′).

Anal. Calc. for $C_{55}H_{54}O_{13}$: C, 71.6; H, 5.9. Found: C, 71.2; H, 5.8.

*Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4-tri-*O*-benzyl-α-* (**30**) *and -β-*D*-fucopyranosyl)-β-*D*-galactopyranoside* (**32**). — Glycosidation[13b] of **21**[19] (178 mg, 0.384 mmol) with 2,3,4-tri-*O*-benzyl-D-fucopyranosyl fluoride (~0.58 mmol) for 3.5 h at −20°, as described for **29**, gave, after column chromatography (ethyl acetate–heptane, 1:5; repeated with ether–toluene, 1:20) of the residue, **30** (189 mg, 56%) and **32** (32 mg, 10%).

Compound **30** had $[\alpha]_D^{25}$ +60° (*c* 0.66, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.00 (d, 1 H, *J* 3.0 Hz, H-1′), 4.25 (dd, 1 H, *J* 7.5 Hz, H-1), 4.09 (dd, AB-type, 1 H, *J* 10.4 and 3.0 Hz, H-2′), 4.04 (dd, AB-type, 1 H, *J* 10.4 and 2.4 Hz, H-3′), 4.00 (bd, 1 H, *J* 3.0 Hz, H-4), 3.95 (dd, 1 H, *J* 9.3 and 7.2 Hz, H-6), 3.62 (dd, 1 H, *J* 10.1 and 7.5 Hz, H-2), 3.56 (s, 3 H, MeO), 3.47 (bt, 1 H, *J* 6.6 Hz, H-5), 3.36 (dd, 1 H, *J* 10.1 and 3.0 Hz, H-3), 0.92 (d, 3 H, *J* 6.5 Hz, H-6′).

Anal. Calc. for $C_{55}H_{60}O_{10}$: C, 75.0; H, 6.9. Found: C, 75.2; H, 7.0.

Compound **32** had $[\alpha]_D^{25}$ +41° (*c* 0.28, chloroform). ^{1}H-N.m.r. data: δ 4.85 (d, 1 H, *J* 7.6 Hz, H-1′), 4.28 (d, 1 H, *J* 7.6 Hz, H-1), 4.26 (bd, 1 H, *J* 3.0 Hz, H-4

or H-4′), 3.85 (dd, 1 H, *J* 10.2 and 5.5 Hz, H-6), 3.80 (dd, 1 H, *J* 9.6 and 7.6 Hz, H-2′), 3.72 (dd, 1 H, *J* 9.7 and 7.6 Hz, H-2), 3.72 (dd, 1 H, *J* 10.2 and 6.0 Hz, H-6), 3.56 (s, 3 H, MeO), 3.34 (q, 1 H, *J* 6.4 Hz, H-5′), 1.13 (d, 3 H, *J* 6.4 Hz, H-6′).

Anal. Calc. for $C_{55}H_{60}O_{10}$: C, 75.0; H, 6.9. Found: C, 75.2; H, 7.0.

*Methyl 4-*O*-α-*D*-fucopyranosyl-β-*D*-galactopyranoside*[11] (**31**). — Debenzylation of **30** (175 mg, 0.199 mmol), as described for **23**, and column chromatography (ethanol–dichloromethane, 1:2) of the product, gave, after freeze-drying, amorphous **31** (61 mg, 90%), $[\alpha]_D^{25}$ +107° (*c* 1.3, water); lit.[11] $[\alpha]_D$ +96° (*c* 0.7, water). ^{1}H-N.m.r. data (D_2O): δ 4.86 (d, 1 H, *J* 3.9 Hz, H-1′), 4.45 (q, 1 H, *J* 6.5 Hz, H-5′), 4.35 (d, 1 H, *J* 7.8 Hz, H-1), 3.95 (bd, 1 H, *J* 3.2 Hz, H-4), 3.56 (s, 3 H, MeO), 3.49 (dd, 1 H, *J* 10.0 and 7.8 Hz, H-2), 1.16 (d, 3 H, *J* 6.6 Hz, H-6).

*Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,4,6-tri-*O*-benzyl-3-deoxy-α-* (**33**) *and -β-*D*-xylo-hexopyranosyl)-β-*D*-galactopyranoside* (**35**). — Glycosidation[13b] of **21**[19] (570 mg, 1.23 mmol) with 2,4,6-tri-*O*-benzyl-3-deoxy-D-*xylo*-hexopyranosyl fluoride (~1.84 mmol) for 4 h at −20°, as described for **29**, gave, after column chromatography (ether–toluene, 1:15) of the residue, **33** (768 mg, 71%) and **35** (160 mg, 15%).

Compound **33** had $[\alpha]_D^{25}$ +22° (*c* 0.53, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.00 (d, 1 H, *J* 3.2 Hz, H-1′), 4.25 (d, 1 H, *J* 7.6 Hz, H-1), 4.10 (d, 1 H, *J* 2.9 Hz, H-4), 3.92 (dt, 1 H, *J* 11.8 and 3.7 Hz, H-2′), 3.79 (bs, 1 H, H-4′), 3.69 (dd, 1 H, *J* 10.0 and 7.6 Hz, H-2), 3.54 (s, 3 H, MeO), 3.41 (dd, 1 H, *J* 10.0 and 2.9 Hz, H-3), 2.12 (dt, 1 H, *J* 13.2 and 3.7 Hz, H-3′*e*), 1.96 (td, 1 H, *J* 12.7 and 2.1 Hz, H-3′*a*).

Anal. Calc. for $C_{55}H_{60}O_{10}$: C, 75.0; H, 6.9. Found: C, 74.7; H, 6.8.

Compound **35** had $[\alpha]_D^{25}$ −7° (*c* 1.8, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 4.88 (d, 1 H, *J* 7.6 Hz, H-1′), 4.28 (d, 1 H, *J* 7.7 Hz, H-1), 4.23 (bd, 1 H, *J* 2.8 Hz, H-4), 3.82 (dd, AB-type, 1 H, *J* 10.5 and 5.0 Hz, H-6 or H-6′), 3.74 (dd, AB-type, 1 H, *J* 10.5 and 6.3 Hz, H-6 or H-6′), 3.72 (dd, 1 H, *J* 9.7 and 7.7 Hz, H-2), 3.56 (s, 3 H, MeO), 2.36 (ddd, 1 H, *J* 14.0, 4.8, and 2.8 Hz, H-3′*e*), 1.45 (ddd, 1 H, *J* 14.0, 11.8, and 2.5 Hz, H-3′*a*).

Anal. Calc. for $C_{55}H_{60}O_{10}$: C, 75.0; H, 6.9. Found: C, 75.4; H, 7.0.

*Methyl 4-*O*-(3-deoxy-α-*D*-*xylo*-hexopyranosyl)-β-*D*-galactopyranoside* (**34**). — Debenzylation of **33** (742 mg, 0.842 mmol), as described for **23**, and column chromatography (ethanol–dichloromethane, 2:5) of the product gave, after freeze-drying, amorphous **34** (260 mg, 91%), $[\alpha]_D^{25}$ +72° (*c* 1.1, water). ^{1}H-N.m.r. data (D_2O): δ 4.88 (d, 1 H, *J* 3.7 Hz, H-1′), 4.36 (d, 1 H, *J* 7.7 Hz, H-1), 4.22 (t, 1 H, *J* 6.4 Hz, H-5′), 4.07 (bs, 1 H, H-4′), 4.05 (d, 1 H, *J* 3.1 Hz, H-4), 4.04 (ddd, 1 H, *J* 11.7, 5.6, and 3.7 Hz, H-2′), 3.88 (dd, AB-type, 1 H, *J* 11.4 and 7.5 Hz, H-6), 3.82 (dd, AB-type, 1 H, *J* 11.4 and 4.7 Hz, H-6), 3.76 (dd, 1 H, *J* 7.5 and 4.7 Hz, H-5), 3.70 (dd, 1 H, *J* 10.2 and 3.1 Hz, H-3), 3.67 (dd, AB-type, 1 H, *J* 11.5 and 5.5 Hz, H-6′), 3.62 (dd, AB-type, 1 H, *J* 11.5 and 7.1 Hz, H-6′), 3.56 (s, 3 H, MeO), 3.54 (dd, 1 H, *J* 10.2 and 7.7 Hz, H-2), 2.06–1.90 (m, 2 H, H-3′).

*Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,6-tri-*O*-benzyl-4-deoxy-α-* (**36**) *and -β-*D*-xylo-hexopyranosyl)-β-*D*-galactopyranoside* (**38**). — Glycosidation[13b] of **21**[19] (178

mg, 0.384 mmol) with 2,3,6-tri-*O*-benzyl-4-deoxy-D-*xylo*-hexopyranosyl fluoride (~0.58 mmol) for 3 h at −20°, as described for **29**, gave, after column chromatography (ethyl acetate–heptane, 1:4; repeated with ether–toluene, 1:20) of the product, **36** (170 mg, 50%) and **38** (90 mg, 27%).

Compound **36** had $[\alpha]_D^{25}$ +51° (*c* 0.47, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.05 (d, 1 H, *J* 3.4 Hz, H-1′), 4.25 (d, 1 H, *J* 7.6 Hz, H-1), 4.05 (bd, 1 H, *J* 2.9 Hz, H-4), 4.00 (dd, 1 H, *J* 9.2 and 7.1 Hz, H-6), 3.66 (dd, 1 H, *J* 10.0 and 7.6 Hz, H-2), 3.56 (s, 3 H, MeO), 3.39 (dd, 1 H, *J* 10.0 and 2.9 Hz, H-3), 3.17 (dd, AB-type, 1 H, *J* 10.1 and 4.4 Hz, H-6′), 3.12 (dd, AB-type, 1 H, *J* 10.1 and 3.8 Hz, H-6′), 2.09 (ddd, 1 H, *J* 12.8, 5.0, and 2.4 Hz, H-4′*e*), 1.63 (bq, 1 H, *J* 11.5 Hz, H-4′*a*).

Anal. Calc. for $C_{55}H_{60}O_{10}$: C, 75.0; H, 6.9. Found: C, 74.6; H, 6.9.

Compound **38** had $[\alpha]_D^{25}$ +4° (*c* 0.84, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 4.86 (d, 1 H, *J* 7.6 Hz, H-1′), 4.28 (d, 1 H, *J* 7.7 Hz, H-1), 4.21 (bd, 1 H, *J* 2.8 Hz, H-4), 3.58 (s, 3 H, MeO), 3.30 (dd, 1 H, *J* 8.8 and 7.7 Hz, H-2), 2.10 (dd, 1 H, *J* 11.7 and 5.3 Hz, H-4′*e*), 1.43 (q, 1 H, *J* 11.8 Hz, H-4′*a*).

Anal. Calc. for $C_{55}H_{60}O_{10}$: C, 75.0; H, 6.9. Found: C, 74.6; H, 6.9.

*Methyl 4-O-(4-deoxy-α-*D-xylo-*hexopyranosyl)-β-*D-*galactopyranoside* (**37**). — Debenzylation of **36** (462 mg, 0.52 mmol), as described for **23**, and column chromatography (ethanol–dichloromethane, 2:5) of the product gave, after freeze-drying, amorphous **37** (159 mg, 89%), $[\alpha]_D^{25}$ +92° (*c* 0.74, water). ^{1}H-N.m.r. data (D_2O): δ 4.87 (d, 1 H, *J* 3.8 Hz, H-1′), 4.35 (d, 1 H, *J* 7.8 Hz, H-1), 4.35 (m, 1 H, H-5′), 3.99 (d, 1 H, *J* 2.9 Hz, H-4), 3.97 (ddd, 1 H, *J* 11.2, 10.1, and 4.9 Hz, H-3′), 3.89 (dd, AB-type, 1 H, *J* 11.4 and 7.5 Hz, H-6), 3.82 (dd, AB-type, 1 H, *J* 11.4 and 5.0 Hz, H-6), 3.74 (dd, 1 H, *J* 7.5 and 5.0 Hz, H-5), 3.69 (dd, 1 H, *J* 10.2 and 3.0 Hz, H-3), 3.62 (dd, AB-type, 1 H, *J* 11.9 and 3.7 Hz, H-6′), 3.56 (dd, AB-type, 1 H, *J* 11.9 and 5.2 Hz, H-6′), 3.56 (s, 3 H, MeO), 3.50 (dd, 1 H, *J* 10.2 and 7.7 Hz, H-2), 3.44 (dd, 1 H, *J* 10.0 and 3.8 Hz, H-2′), 1.98 (ddd, 1 H, *J* 12.7, 5.2, and 2.0 Hz, H-4′*e*), 1.46 (q, 1 H, *J* 12.1 Hz, H-4′*a*).

*Methyl 2,3,6-tri-*O*-benzyl-4-O-(3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-*D-*talo-pyranosyl)-β-*D-*galactopyranoside* (**39**). — *N*-Iodosuccinimide (849 mg, 3.77 mmol) was added to a solution of **19**[22] (880 mg, 3.23 mmol) and **21**[19] (1.00 g, 2.16 mmol) in dry acetonitrile (15 mL) at 0° under nitrogen[21]. The mixture was stirred for 24 h at room temperature with protection from light and was then diluted with dichloromethane (100 mL). The solution was washed with aqueous 10% sodium thiosulfate (25 mL) and water (25 mL), dried, and concentrated. Column chromatography (ether–toluene, 1:5) of the residue gave **39** (1.60 g, 86%), isolated as a syrup, $[\alpha]_D^{25}$ +60° (*c* 0.5, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.56 (bs, 1 H, H-1′), 5.38 (m, 1 H, H-4′), 4.91 (dd, 1 H, *J* 5.1 and 3.8 Hz, H-3′), 4.45 (bd, 1 H, *J* 5.1 Hz, H-2′), 4.21 (d, 1 H, *J* 7.7 Hz, H-1), 4.16 (d, 1 H, *J* 3.3 Hz, H-4), 4.11 (dd, 1 H, *J* 10.8 and 8.7 Hz, H-6 or H-6′), 3.52 (s, 3 H, MeO), 3.39 (dd, 1 H, *J* 9.9 and 3.3 Hz, H-3), 2.15, 2.07, 1.87 (3 s, each 3 H, Ac).

Anal. Calc. for $C_{40}H_{47}IO_{13}$: C, 55.7; H, 5.5. Found: C, 56.1; H, 5.7.

Methyl 4-O-(3,4,6-tri-O-acetyl-2-deoxy-α-D-lyxo-hexopyranosyl)-β-D-galacto-pyranoside (**40**). — Pd/C (10%, 1.15 g) and triethylamine (278 μL, 2.00 mmol) were added to a solution of **39** (1.54 g, 1.78 mmol) in ethyl acetate (20 mL). The mixture was hydrogenated for 7 h, then filtered through Celite and diluted with ethyl acetate (20 mL). The solution was washed with saturated aqueous sodium hydrogencarbonate (15 mL) and water (15 mL), dried, and concentrated. Debenzylation of the crude methyl 2,3,6-tri-*O*-benzyl-4-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*lyxo*-hexopyranosyl)-β-D-galactopyranoside, as described for **23**, and column chromatography (methanol–ethyl acetate, 1:9) of the residue gave **40** (544 mg, 65%), isolated as a syrup, $[\alpha]_D^{25}$ +69° (*c* 0.8, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.35 (bs, 1 H, H-1′), 5.28 (ddd, 1 H, *J* 12.2, 4.8, and 2.9 Hz, H-3′), 5.13 (bd, 1 H, *J* 2.9 Hz, H-4′), 4.60 (t, 1 H, *J* 6.5 Hz, H-5′), 4.20 (d, 1 H, *J* 7.4 Hz, virtually coupled[35] to H-2 and H-3, H-1), 4.10 (dd, AB-type, 1 H, *J* 11.4 and 5.5 Hz, H-6′), 4.07 (dd, AB-type, 1 H, *J* 11.4 and 7.2 Hz, H-6′), 4.01 (d, 1 H, *J* 1.2 Hz, H-4), 3.89 (dd, 1 H, *J* 10.7 and 6.9 Hz, H-6), 3.58 (s, 3 H, MeO), 2.13, 2.09, 1.99 (3 s, each 3 H, Ac).

Anal. Calc. for $C_{19}H_{30}O_{13}$: C, 48.9; H, 6.5. Found: C, 48.6; H, 6.5.

Methyl 4-O-(2-deoxy-α-D-lyxo-hexopyranosyl)-β-D-galactopyranoside (**41**). — Deacetylation of **40** (476 mg, 1.02 mmol), as described for **23**, and column chromatography (methanol–dichloromethane, 1:3) of the product gave, after freeze-drying, amorphous **41** (235 mg, 68%), $[\alpha]_D^{25}$ +82° (*c* 1.1, water). ^{1}H-N.m.r. data (D_2O): δ 5.02 (t, 1 H, *J* 2.4 Hz, H-1′), 4.32 (d, 1 H, *J* 7.7 Hz, H-1), 4.20 (t, 1 H, *J* 6.5 Hz, H-5′), 4.10 (td, 1 H, *J* 8.6 and 2.9 Hz, H-3′), 3.99 (d, 1 H, *J* 3.2 Hz, H-4), 3.88 (bd, 1 H, *J* 2.8 Hz, H-4′), 3.66 (dd, 1 H, *J* 10.2 and 3.2 Hz, H-3), 3.55 (s, 3 H, MeO), 3.48 (dd, 1 H, *J* 10.2 and 7.7 Hz, H-2), 1.92 (m, 2 H, H-2′).

Methyl 2,3,6-tri-O-benzoyl-4-O-(2,3-di-O-benzoyl-4,6-O-benzylidene-α-D-galactopyranosyl)-β-D-galactopyranoside (**43**). — Benzoyl chloride (287 μL, 2.50 mmol) was added to a solution of **42**[11] (630 mg, 0.832 mmol) in dry pyridine (12 mL) at 0°. After 3 h at room temperature, the solution was diluted with dichloromethane (25 mL), washed with saturated aqueous sodium hydrogencarbonate (10 mL), dried, and concentrated. Column chromatography (ethyl acetate–heptane, 2:5) of the residue gave **43** (777 mg, 97%), m.p. 191–193°, $[\alpha]_D^{25}$ +99° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.95 (dd, AB-type, 1 H, *J* 10.9 and 3.0 Hz, H-3′), 5.89 (dd, AB-type, 1 H, *J* 10.9 and 3.2 Hz, H-2′), 5.80 (dd, 1 H, *J* 10.9 and 7.9 Hz, H-2), 5.48 (d, 1 H, *J* 3.2 Hz, H-1′), 5.40 (s, 1 H, PhC*H*), 5.19 (dd, 1 H, *J* 10.9 and 3.1 Hz, H-3), 4.71 (dd, 1 H, *J* 3.0 and 1.3 Hz, H-4′), 4.68 (d, 1 H, *J* 7.9 Hz, H-1), 4.60 (dd, 1 H, *J* 10.8 and 6.1 Hz, H-6), 4.48 (bd, 1 H, *J* 3.1 Hz, H-4), 4.29 (dd, 1 H, *J* 10.8 and 8.5 Hz, H-6), 4.28 (bs, 1 H, H-5′), 4.02 (dd, 1 H, *J* 8.5 and 6.1 Hz, H-5), 3.58 (s, 3 H, MeO), 3.48 (dd, 1 H, *J* 12.9 and 1.6 Hz, H-6′), 3.20 (dd, 1 H, *J* 12.9 and 1.5 Hz, H-6′).

Anal. Calc. for $C_{55}H_{48}O_{16}$: C, 68.5; H, 5.0. Found: C, 68.1; H, 4.9.

Methyl 2,3,6-tri-O-benzoyl-4-O-(2,3-di-O-benzoyl-α-D-galactopyranosyl)-β-D-galactopyranoside (**44**). — Compound **43** (1.32 g, 1.37 mmol) was added to a 1%

(w/v) solution of iodine in methanol–dichloromethane (5:1, 30 mL), and the mixture was boiled under reflux for 3 h after which sodium thiosulfate (500 mg) was added to the resulting clear solution[23]. The mixture was concentrated, the residue was dissolved in ethyl acetate (50 mL), and the solution was washed with water (25 mL). The aqueous phase was extracted with ethyl acetate (25 mL), and the combined organic phases were dried and concentrated. Column chromatography (ethyl acetate–heptane, 1:1) of the residue gave **44** (1.05 g, 87%), isolated as a syrup, $[\alpha]_D^{25}$ +70° (*c* 0.97, chloroform). ^{1}H-N.m.r. data ($CDCl_3$, plus 1 drop of D_2O): δ 5.87 (dd, AB-type, 1 H, *J* 10.8 and 2.9 Hz, H-3′), 5.78 (dd, AB-type, 1 H, *J* 10.8 and 3.6 Hz, H-2′), 5.75 (dd, 1 H, *J* 10.7 and 7.8 Hz, H-2), 5.47 (d, 1 H, *J* 3.6 Hz, H-1′), 5.30 (dd, 1 H, *J* 10.7 and 2.9 Hz, H-3), 4.68 (d, 1 H, *J* 7.8 Hz, H-1), 4.59 (bd, 1 H, *J* 2.9 Hz, H-4′), 4.43 (bd, 1 H, *J* 2.9 Hz, H-4), 4.40 (dd, 1 H, *J* 11.0 and 7.3 Hz, H-6), 4.01 (t, 1 H, *J* 6.6 Hz, H-5), 3.70 (dd, AB-type, 1 H, *J* 12.1 and 4.9 Hz, H-6′), 3.66 (dd, AB-type, 1 H, *J* 12.1 and 3.9 Hz, H-6′), 3.56 (s, 3 H, MeO).

Anal. Calc. for $C_{48}H_{44}O_{16}$: C, 65.8; H, 5.1. Found: C, 65.6; H, 5.0.

Methyl 2,3,6-tri-O-benzoyl-4-O-(2,3-di-O-benzoyl-6-deoxy-6-fluoro-α-D-galactopyranosyl)-β-D-galactopyranoside (**45**). — Diethylaminosulfur trifluoride[17] (DAST, 99 μL, 0.81 mmol) in dichloromethane (1.2 mL) was added to a solution of **44** (677 mg, 0.772 mmol) in dry dichloromethane (30 mL) at −75° under nitrogen. The solution was kept for 16 h at room temperature, then boiled under reflux for 7 h. Ethanol (50 μL) was added at room temperature and, after 30 min, the solution was concentrated. Column chromatography (ether–toluene, 1:15) of the residue gave **45** (480 mg, 71%), isolated as a syrup, $[\alpha]_D^{25}$ +89° (*c* 0.95, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.87 (dd, AB-type, 1 H, *J* 10.8 and 2.9 Hz, H-3′), 5.79 (dd, AB-type, 1 H, *J* 10.8 and 3.4 Hz, H-2′), 5.77 (dd, 1 H, *J* 10.6 and 7.7 Hz, H-2), 5.46 (bd, 1 H, *J* 3.4 Hz, H-1′), 5.36 (dd, 1 H, *J* 10.6 and 2.5 Hz, H-3), 4.73 (dd, 1 H, *J* 11.0 and 6.4 Hz, H-6), 4.68 (d, 1 H, *J* 7.7 Hz, H-1), 4.53 (bs, 1 H, H-4′), 4.44 (d, 1 H, *J* 2.5 Hz, H-4), 4.37 (dd, 1 H, *J* 11.0 and 7.6 Hz, H-6), 4.03 (bt, 1 H, *J* 6.9 Hz, H-5), 3.55 (s, 3 H, MeO). ^{19}F-N.m.r. data ($CDCl_3$): Ø 234 (td, *J* 46.3 and 13.9 Hz, F-6′).

Anal. Calc. for $C_{48}H_{43}FO_{15}$: C, 65.6; H, 4.9. Found: C, 65.6; H, 5.1.

Methyl 4-O-(6-deoxy-6-fluoro-α-D-galactopyranosyl)-β-D-galactopyranoside (**46**). — Debenzoylation of **45** (450 mg, 0.512 mmol), as described for **23**, and column chromatography (ethanol–dichloromethane, 1:3) of the product gave, after freeze-drying, amorphous **46** (154 mg, 84%), $[\alpha]_D^{25}$ +114° (*c* 0.72, water). ^{1}H-N.m.r. data (D_2O): δ 4.96 (d, 1 H, *J* 3.9 Hz, H-1′), 4.35 (d, 1 H, *J* 7.7 Hz, H-1), 4.04 (d, 1 H, *J* 3.1 Hz, H-4′), 4.00 (d, 1 H, *J* 3.1 Hz, H-4), 3.56 (s, 3 H, MeO), 3.50 (dd, 1 H, *J* 10.3 and 7.7 Hz, H-2). ^{19}F-N.m.r. data (D_2O): Ø 231 (td, *J* 45.4 and 18.5 Hz, F-6′).

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