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Note

# Fluorination at position 6 of derivatives of methyl α-D-galactopyranoside †

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Our laboratory studies the interaction of the O-specific polysaccharide (O-SP) of *Shigella dysenteriae* type 1 with monoclonal antibodies. Following the identification [2] of the immunodeterminant **I** of the O-SP for a murine anti-*Shigella dysenteriae* type 1 IgM, we wish to explore possible hydrogen bonding interactions of individual hydroxyl groups of that determinant with the antibody. We and others [3] have used deoxy and deoxyfluoro sugars to elucidate the binding pattern of antibody or enzyme subsites to carbohydrate antigens. Our present work requires deoxy and deoxyfluoro analogues of methyl α-D-galactopyranoside (**1**) and of the methyl α-glycoside of **I**. To prepare the 6-deoxy-6-fluoro derivative of the latter (disaccharide **27**), we intend to use methyl 6-deoxy-6-fluoro-3,4-*O*-isopropylidene-α-D-galactopyranoside (**8**) as the glycosyl acceptor (nucleophile) in the condensation reaction. We wish to report our observations on fluorinations that, eventually, lead to nucleophile **8**. Deprotection of **8** gave methyl 6-deoxy-6-fluoro-α-D-galactopyranoside (**2**), also needed for binding studies.

3)-α-L-Rha*p*-(1 → 2)-α-D-Gal*p*-(1 →

**I**

The presence of the axial hydroxyl group at C-4 in D-galactopyranosides causes the displacement of 6-sulfonate groups to be problematic [4–8]. To overcome these difficulties, some investigators [9,10] prepared derivatives of 6-deoxy-6-fluoro-D-galactose from a suitable D-glucopyranose precursor by epimerisation at C-4.

Syntheses of **2** reported to date use the displacement by fluoride ion of a sulfonyloxy group at C-6 of the precursor 1,2:3,4-di-*O*-isopropylidene-α-D-

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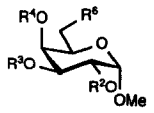
galactopyranose (**12**). Such an approach [6] gave **2** from **13** in a low yield of 23%. In other cases [11–14], fluorination of **12**, to give **13**, was performed in order to study an array of new leaving groups or a set of fluorination reagents. With the aim of improving accessibility to **2**, we started with commercially available **1**. Direct fluorinations of unprotected methyl α-D-glucopyranoside [15,16] (70–88%) or methyl β-D-galactopyranoside [17] (15%) with diethylaminosulfur trifluoride [18] (DAST) have been described. However, direct fluorination of **1** gave a complex mixture [19]. To minimize side-reactions, we treated the known [20] 3,4-*O*-isopropylidene derivative **6** with DAST. Since the selectivity of the fluorination was still not satisfactory [19], we decided on a two-step process of sulfonylation followed by a displacement reaction with fluoride ion.

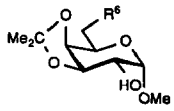
To avoid the formation of 3,6-anhydrides during nucleophilic displacement of a sulfonyloxy group at C-6 of galactopyranosides [8,21–23], we initially adopted the strategy of Sharma et al., who described a successful displacement of a 6-methanesulfonate group in a 3,4-*O*-isopropylidene derivative of *N*-acetyl-D-galactosamine. The *p*-bromobenzenesulfonate group is a better leaving-group in $S_N2$ reactions [24]. And, by analogy to tosylation [25,26], it is expected to be introduced selectively at C-6. Accordingly, we have prepared the isopropylidene derivative **7**. Of the two considered routes to **7**, brosylation at C-6 of **6** was more efficient than initial, selective brosylation of **1** (**1** → **3** → **7**), although methyl 2,6-di-*O*-*p*-bromophenylsulfonyl-3,4-*O*-isopropylidene-α-D-galactopyranoside (**24**) was formed (17%) as a byproduct when **6** was used.

Compound **7** was treated with various fluoride ion donors. The results (Table 1) show that with this substrate elimination is favored over displacement (for an exception see entry 9). Among the significant side reactions observed during these experiments was occasional solvent participation in the displacement (entries 5 and 9), as well as the elimination forming methyl 6-deoxy-3,4-*O*-isopropylidene-β-L-*arabino*-hex-5-enopyranoside (**14**). This occurred under conditions similar to those which had previously led to satisfactory fluorinations with derivatives of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose bearing leaving groups such as 6-trifluoromethanesulfonate [12,13,27] (conditions as in entry 3), 6-(imidazolesulfonate) [11] (conditions as in entry 1), 6-methanesulfonate [6] (conditions as in entries 9 and 10), and 6-*p*-toluenesulfonate [4,28,29] (conditions as in entries 1, 4, and 11). Cesium fluoride (CsF) was completely unreactive with **7** in acetonitrile, whereas it led mainly to the elimination product **14** when DMF was the solvent. In ethylene glycol no reaction occurred below 100°C. Above that temperature the main product was **8**, but also formed was the *exo*-methylene derivative **14**, as well as methyl 6-*O*-(2-hydroxyethyl)-3,4-*O*-isopropylidene-α-D-galactopyranoside (**10**) resulting from solvent participation in the nucleophilic displacement reaction. Similar observations were reported when potassium fluoride in methanol [30] or in ethylene glycol [31] was employed. Perhaps hydroxylic solvents, being uncharged nucleophiles, are not involved in repulsive interactions with the lone pairs of electrons at O-4 and O-5. Thus, they could more favourably compete with the charged fluoride ion present, and substitution by the solvent could occur at C-6. Treatment of **7** with tetraethylammonium fluoride in refluxing acetonitrile for 48 h



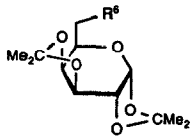
| | $R^2$ | $R^3$ | $R^4$ | $R^6$ |
|---|---|---|---|---|
| 1 | H | H | H | OH |
| 2 | H | H | H | F |
| 3 | H | H | H | OBrs |
| 4 | Ac | Ac | Ac | OBrs |
| 5 | H | H | H | Cl |

Brs = brosyl (*p*-bromophenylsulfonyl)

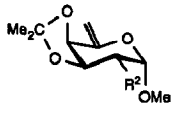


| | $R^6$ |
|---|---|
| 6 | OH |
| 7 | OBrs |
| 8 | F |
| 9 | Cl |
| 10 | $OCH_2CH_2OH$ |
| 11 | OTf |

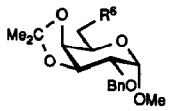
Tf = triflyl (trifluoromethylsulfonyl)



| | $R^6$ |
|---|---|
| 12 | OH |
| 13 | F |



| | $R^2$ |
|---|---|
| 14 | OH |
| 15 | OBn |



| | $R^6$ |
|---|---|
| 16 | OH |
| 17 | OTf |
| 18 | $OCH_2CH_2OH$ |
| 19 | OBrs |
| 20 | F |

afforded mostly **14**. When dichloroethane was the solvent, methyl 6-chloro-6-deoxy-3,4-*O*-isopropylidene-α-D-galactopyranoside (**9**) was formed as the only product. Apparently, the nucleophile responsible for the formation of **9** was the chloride ion, generated from the solvent under the basic reaction conditions applied. The same product **9** was obtained (89%) by treatment (48 h) of **7** with tetraethylammonium chloride. The reaction of **7** with tetraethylammonium fluoride in dichloroethane gave **9** only when carried out in an inert atmosphere. When such conditions were not maintained the known chloro derivative [32] **5** was isolated (**7** → **9** → **5**).

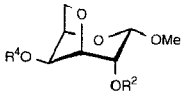
Satisfactory fluorinations at the primary position of benzyl α-D-galactopyranosides [8,33] or methyl β-D-galactopyranoside [34] substituted at C-2 have been reported. Thus, the fluorination of the 2-*O*-benzyl derivative [1] **16** was studied next. Reaction of **16** with DAST gave **20** as the major product but the mixture was complex, the olefin **15** being one of the byproducts. To minimize the side-reac-

Table 1
Products of the reaction of **7** with different fluorinating reagents.

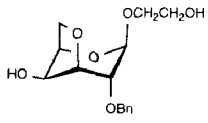
| Entry | Reagent | Solvent | Temperature | Products (% yield) [a] | | |
|---|---|---|---|---|---|---|
| | | | | **8** | **14** | Other |
| 1 | $Bu_4NF$ | DMF/THF | 120°C | 10 | 90 | |
| 2 | TAS-F | $CH_3CN$ | reflux | 10 | 90 | |
| 3 | TAS-F | $CH_2Cl_2$ | RT, reflux | | | [b] |
| 4 | $Et_4NF \cdot 2H_2O$ | $CH_3CN$ | reflux | 18 | 82 | |
| 5 [c] | $Et_4NF \cdot 2H_2O$ | $ClCH_2CH_2Cl$ | reflux | | | **9** (72) |
| 6 | CsF | $CH_3CN$ | reflux | | | [b] |
| 7 | CsF | DMF | reflux | 10 | 90 | |
| 8 | CsF | $HOCH_2CH_2OH$ | 100°C | | | [b] |
| 9 [c] | CsF | $HOCH_2CH_2OH$ | 130°C | 42 | 13 | **10** (30) |
| 10 | Amberlyst A-26 $F^-$ | Benzene | reflux | 30 | 70 | |
| 11 [c] | Amberlyst A-26 $F^-$ | $CH_3CN$ | reflux | 45 | 45 | |

[a] Unless stated otherwise, yields were estimated from $^1H$ NMR spectra.
[b] Complete recovery of the starting material.
[c] Isolated yields are reported.

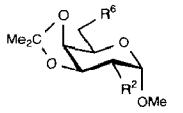
tions, the more reactive trifluoromethanesulfonyl ester **17** was prepared. When **17** was treated with CsF in ethylene glycol (see Experimental), solvent participation was enhanced as compared to the similar reaction of **7** (Table 1, entry 9), and several products were isolated. At 90°C, direct nucleophilic introduction of the 2-hydroxyethyloxy group at C-6, yielding methyl 2-*O*-benzyl-6-*O*-(2-hydroxyethyl)-3,4-*O*-isopropylidene-α-D-galactopyranoside (**18**, 9%), occurred with the concomitant formation of methyl 3,6-anhydro-2-*O*-benzyl-α-D-galactopyranoside (**22**, 57%). In addition, another reaction took place at C-1 giving a compound (5%) to which



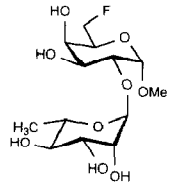

| | $R^2$ | $R^4$ |
|---|---|---|
| **21** | H | H |
| **22** | Bn | H |




**23**




| | $R^2$ | $R^6$ |
|---|---|---|
| **24** | OBrs | OBrs |
| **25** | OTf | OTf |
| **26** | OTf | OH |




**27**

Table 2
Comparison of the reactivity of compounds **7**, **17**, **19**, and **11** towards fluorination.

| Starting material | Reagent/ conditions | Products, ratio [a] | Reagent/ conditions | Products, ratio [a] |
|---|---|---|---|---|
| **7** | TAS-F/$CH_2Cl_2$ reflux, 24 h | complete recovery of the starting material | $Et_4NF \cdot 2H_2O/CH_3CN$ reflux, 3 h | **14**, **8** 80:20 |
| **17** [b] | TAS-F/$CH_2Cl_2$ 25°C | **15**, **20** 15:83 | | |
| **19** | TAS-F/$CH_2Cl_2$ reflux, 24 h | **15**, **20** 70:30 20% conversion | $Et_4NF \cdot 2H_2O/CH_3CN$ reflux, 2.5 h | **15**, **20** 70:30 |
| **11** | TAS-F/$CH_2Cl_2$ 25°C, 16 h | **14**, **8** 15:85 | $Et_4NF \cdot 2H_2O/CH_3CN$ 25°C, 16 h | **14**, **8** 15:85 |

[a] Unless stated otherwise, yields were estimated from $^1H_2$ NMR spectra.
[b] Isolated yields are reported.

structure **23** has been tentatively assigned (see Experimental). Debenzylation of **22** gave the known methyl 3,6-anhydro-α-D-galactopyranoside [23,35] (**21**). The use of higher temperatures [6] did not improve the yield of the desired product **20**. Treatment of **17** with ethylene glycol at 90°C, in the absence of CsF, resulted in the decomposition of the starting material. When CsF in a nonparticipating solvent (DMF) was used, elimination was an important competing reaction, leading to **15** and **20** in a 1:1 ratio.

Treatment of **17** with tris(dimethylamino)sulfur (trimethylsilyl)difluoride [12] (TAS-F) gave **20** in a yield of 83% (based upon **16**), with the olefin **15** as the only byproduct (15%). To further evaluate the influence of the nature of the leaving group, we prepared the fully protected methyl 2-*O*-benzyl-6-*O*-bromophenylsulfonyl-3,4-*O*-isopropylidene-α-D-galactopyranoside (**19**) and methyl 6-*O*-trifluoromethylsulfonyl-3,4-*O*-isopropylidene-α-D-galactopyranoside (**11**). Their attempted fluorination is reported in Table 2. Fluorination of **19** with TAS-F showed only 20% conversion with elimination (→ **15**) predominating. Reaction [19] of **19** with tetraethylammonium fluoride in acetonitrile did not materially improve the substitution (→ **20**) versus elimination (→ **15**) ratio. On the other hand, reaction of the unbenzylated triflate **11** with either TAS-F or tetraethylammonium fluoride afforded the product of substitution, **8**, in good yield (**14**:**8** ~ 1:6.5 $^1H$ NMR).

Thus, to achieve satisfactory fluorination at C-6 the use of trifluoromethanesulfonate as the leaving group is essential. The two routes involving either the fully protected compound **17** (**1** → **16** → **17** → **20** → **8**, 55% overall yield), or the precursor **11** (**1** → **6** → **11** → **8**, 45% overall yield) are especially convenient for the preparation of nucleophile **8**. In addition, the possibility to selectively deprotect the hydroxyl groups of **20** at position 2, or positions 3 and 4, allows further chemical modification at any of these sites.

For binding studies with *Shigella dysenteriae* type 1 monoclonal antibodies, the *O*-isopropylidene derivative **8** was deprotected to give **2** in an overall yield of 42%

(**1** → **6** → **11** → **8** → **2**). This compares with the combined yields reported [6,7,11–14,27–29] using the diisopropylidene derivative **12** to ultimately obtain **2** (**12** → **13** → **2** ~20% overall). Thus, the presently reported pathway towards **2**, involving the precursor **11** bearing a free hydroxyl group at C-2, can be used as a practical alternative to previously published approaches [11,12,14,27–29] based on **12**.

## 1. Experimental

*General methods.*—Melting points were determined on a Kofler hot stage. Optical rotations were measured at 25°C with a Perkin–Elmer automatic polarimeter, Model 241 MC. TLC on precoated slides of Silica Gel G F254 (Analtech) was performed with solvent mixtures of appropriately adjusted polarity consisting of *A*, chloroform–methanol; *B*, hexane–EtOAc; *C*, dichloromethane–acetone, *D*, hexane–acetone. Detection was effected by charring with 5% $H_2SO_4$ in EtOH and, when applicable, with UV light. Preparative chromatography was performed by elution from columns of Silica Gel 60 (particle size 0.04–0.063 mm). Unless stated otherwise, the NMR spectra were recorded at 25°C for solutions in $CDCl_3$ on a Varian Gemini-300 spectrometer (300 MHz for $^1H$, 75 MHz for $^{13}C$) and on a Varian XL-300 spectrometer (282.2 MHz for $^{19}F$). Internal references: for solutions in $CDCl_3$, $Me_4Si$ (0.00 ppm for $^1H$), $C_6F_6$ (0.00 ppm for $^{19}F$), and $CDCl_3$ (77.00 ppm for $^{13}C$); for solutions in $D_2O$ or $CD_3OD$, $CD_3OD$ (49.00 ppm for $^{13}C$) and HOD (4.78 ppm for $^1H$); for solutions in benzene-$d_6$, $Me_4Si$ (0.00 ppm for $^1H$). Proton-signal assignments were made by first-order analysis of the spectra, and were supported by homonuclear decoupling experiments. Of the two magnetically nonequivalent geminal protons at C-6, the one resonating at lower field is denoted as Ha and the one at higher field as Hb. The $^{13}C$ NMR assignments were aided by two-dimensional $^{13}C$-$^1H$ correlation spectroscopy (HETCOR). Interchangeable assignments are marked with an asterisk (*). Low resolution mass spectra were obtained by the chemical ionization technique (CIMS), using $NH_3$ as the ionizing gas. Reactions requiring anhydrous conditions were performed under nitrogen or argon. Solutions of products in organic solvents were dried with anhydrous sodium sulfate, and concentrated at 2 kPa/40°C. TAS-F was purchased from Aldrich. Powdered cesium fluoride and Amberlyst A26 ($F^-$ form) were purchased from Fluka. Commercially available tetraethylammonium fluoride was kept at 133 Pa for 5 days at room temperature. The difficulty in removing water from fluoride salts is known, and the presence of residual water cannot be excluded [36]. Chromatographically pure 1,2 : 3,4-di-*O*-isopropylidene-α-D-galactopyranose **12** was obtained by deacetylation of its crystalline 6-acetate [37].

*Methyl 6-O-p-bromophenylsulfonyl-α-D-galactopyranoside* (**3**) *and methyl 2,3,4-tri-O-acetyl-6-O-p-bromophenylsulfonyl-α-D-galactopyranoside* (**4**).—A solution of methyl α-D-galactopyranoside monohydrate (1.06 g, 5 mmol) in dry pyridine (10 mL) was concentrated twice. The residue was dissolved in dry pyridine (25 mL), and a solution of *p*-bromobenzenesulfonyl chloride (1.40 g, 5.5 mmol) in toluene (25 mL) was added dropwise with stirring at −25°C, as described for the similar

O-tosylation [26]. The reaction was kept below 10°C overnight. If necessary, more reagent was added until satisfactory conversion of **1** was achieved (usually 0.3 equiv). When only a little of the starting material remained, MeOH was added (10 mL), and the mixture was stirred for 1 h at room temperature. After conventional workup, chromatography (solvent *A*, 19:1) followed by recrystallisation from EtOAc gave **3** (556 mg, 30%); mp 150–151°C; $[\alpha]_D$ + 84° (*c* 0.7, MeOH); $^1$H NMR ($CD_3OD$): $\delta$ 7.85 (m, 4 H, Ph), 4.62 (d, 1 H, $J_{3,4}$ 2.7 Hz, H-4), 4.24 (d, 1 H, $J_{5,6}$ 6.0 Hz, H-6a, 6b), 3.93 (bt, 1 H, H-5), 3.81 (m, 1 H, H-2), 3.69 (m, 2 H, H-1, 3), and 3.31 (s, 3 H, OMe); $^{13}$C NMR ($CD_3OD$): $\delta$ 101.26 (C-1), 71.85 (C-6), 70.89 (C-3), 70.58 (C-4), 69.75 (C-2), 69.59 (C-5), and 55.75 (OMe); CIMS: *m/z* 430 $[M + NH_4]^+$ and 413 $[M + H]^+$. Anal. Calcd for $C_{13}H_{17}BrO_8S$: C, 37.78; H, 4.15; Br, 19.34; S, 7.76. Found: C, 37.86; H, 4.13; Br, 19.45; S, 7.84.

For further characterisation, **3** (413 mg, 1 mmol) was acetylated with pyridine–acetic anhydride reagent to give, after chromatography (solvent *B*, 2.3:1), **4** in virtually theoretical yield. The analytical sample was crystallised from EtOH; mp 139–140°C; $[\alpha]_D$ + 92° (*c* 1, $CHCl_3$); $^1$H NMR: $\delta$ 7.67 (m, 4 H, Ph), 5.34 (bd, 1 H, H-4), 5.23 (dd, 1 H, $J_{3,4}$ 3.3, $J_{2,3}$ 10.8 Hz, H-3), 5.02 (dd, 1 H, $J_{1,2}$ 3.6 Hz, H-2), 4.87 (d, 1 H, H-1), 4.12 (bt, 1 H, H-5), 3.97 (dd, 1 H, $J_{6a,6b}$ 10.2, $J_{5,6a}$ 6.9 Hz, H-6a), 3.97 (dd, 1 H, $J_{5,6b}$ 5.7 Hz, H-6b), 3.28 (s, 3 H, OMe), 2.00 (s, 6 H, 2 OAc), and 1.90 (s, 3 H, OAc); $^{13}$C NMR: $\delta$ 97.07 (C-1), 67.83 (C-2, C-4), 67.31 (C-6), 67.21 (C-3), 66.07 (C-5), 55.84 (OMe), 20.82, 20.63, and 20.56 (3 OAc); CIMS: *m/z* 556, 558 $[M + NH_4]^+$. Anal. Calcd for $C_{19}H_{23}BrO_{11}S$: C, 42.31; H, 4.30; Br, 14.82; S, 5.94. Found: C, 42.29; H, 4.27; Br, 14.76; S, 6.00.

*Methyl 2,6-di-*O-p-*bromophenylsulfonyl-3,4-*O-*isopropylidene-α-*D-*galactopyranoside* (**24**) *and methyl 6-*O-p-*bromophenylsulfonyl-3,4-*O-*isopropylidene-α-*D-*galactopyranoside* (**7**).—(*a*) A mixture of **6** (ref 20, 1.38 g, 5.9 mmol) and *p*-bromobenzenesulfonyl chloride (1.81 g, 7.08 mmol) in pyridine (6 mL) was stirred at 0°C for 1 h, and then overnight at room temperature. More *p*-bromobenzenesulfonyl chloride (300 mg, 1.18 mmol) was added at 0°C, and stirring was continued for 24 h. Methanol was added and, after 1 h, the mixture was concentrated. Conventional processing and chromatography (solvent *B*, 3:1 → 1.5:1) gave first **24** (698 mg, 17%); mp 125–126°C (EtOH); $[\alpha]_D$ + 108° (*c* 1, $CHCl_3$); $^1$H NMR (benzene-$d_6$): $\delta$ 7.36 (m, 4 H, Ph), 6.86 (m, 4 H, Ph), 4.92 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1), 4.35 (dd, 1 H, $J_{2,3}$ 7.8 Hz, H-2), 4.24 (dd, 1 H, $J_{5,6a}$ 7.9, $J_{6a,6b}$ 10.2 Hz, H-6a), 4.15 (dd, 1 H, $J_{5,6b}$ 4.2 Hz, H-6b), 4.09 (dd, 1 H, $J_{3,4}$ 5.6 Hz, H-3), 3.87 (m, 1 H, H-5), 3.37 (dd, 1 H, $J_{4,5}$ 2.6 Hz, H-4), 2.92 (s, 3 H, OMe), 0.89 and 0.88 (2 s, 6 H, 2 Me); $^{13}$C NMR: $\delta$ 109.93 ($Me_2C$), 97.37 (C-1), 78.72 (C-2*), 73.12 (C-3*), 72.89 (C-4*), 68.94 (C-6), 65.34 (C-5), 55.98 (OMe), 27.37 and 26.12 ($Me_2C$); CIMS: m/z 690 $[M + NH_4]^+$, 673 $[M + H]^+$. Anal. Calcd for $C_{22}H_{24}Br_2O_{10}S_2$: C, 39.30; H, 3.60; Br, 23.77; S, 9.44. Found: C, 39.52; H, 3.64; Br, 23.71; S, 9.44.

Eluted next was **7** (1.5 g, 56%); mp 113–114°C (EtOAc–hexane); $[\alpha]_D$ + 65° (*c* 1.1, $CHCl_3$); $^1$H NMR: $\delta$ 7.78 (d, 2 H, Ph), 7.69 (d, 2 H, Ph), 4.68 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.26 (d, 1 H, $J_{6a,6b}$ 6.2 Hz, H-6a), 4.22 (m, 3 H, H-3, 4, 5), 4.12 (dd, 1 H, $J_{5,6b}$ 1.2 Hz, H-6b), 3.79 (m, 1 H, H-2), 3.40 (s, 3 H, OMe), 2.52 (d, $J_{2,OH}$ 5.6 Hz, 1 H, OH-2), 1.41 and 1.27 (2 s, 6 H, 2 Me); $^{13}$C NMR: $\delta$ 109.89 ($Me_2C$), 97.74

(C-1), 75.44 (C-3), 72.32 (C-4), 69.61 (C-6), 68.47 (C-2*), 66.42 (C-5*), 55.48 (OMe), 27.94 and 26.27 (*Me*$_2$C); $^1$H NMR (benzene-$d_6$): $\delta$ 7.37 (d, 2 H, Ph), 6.89 (d, 2 H, Ph), 4.46 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.29 (dd, 1 H, $J_{5,6a}$ 8.0, $J_{6a,6b}$ 10.3 Hz, H-6a), 4.10 (m, 3 H, H-4, 5, 6b), 3.77 (bq, 1 H, H-2), 3.62 (dd, 1 H, $J_{2,3}$ 6.6, $J_{3,4}$ 2.0 Hz, H-3), 3.01 (s, 3 H, OMe), 1.27 and 1.04 (2 s, 6 H, 2 Me); CIMS: *m/z* 570 $[M + NH_4]^+$, 453 $[M + H]^+$. Anal. Calcd for $C_{16}H_{21}BrO_8S$: C, 42.40; H, 4.67; Br, 17.63; S, 7.07. Found: C, 42.52; H, 4.70; Br, 17.54; S, 7.15.

*Selective trifluoromethanesulfonylation of* **6**.—A solution of trifluoromethanesulfonic anhydride (827 $\mu$L, 4.91 mmol) in dichloromethane (18 mL) was added dropwise, at −60°C over a period of 2.5 h, to a mixture of **6** (1 g, 4.27 mmol) and pyridine (552 $\mu$L, 6.83 mmol) in dichloromethane (42 mL). Stirring was continued at −60°C to −50°C for 1.5 h, when TLC (solvent *D*) showed the presence of one major compound and three minor ones including some unreacted starting material. Ice was added and the organic phase was extracted twice, dried, and concentrated. Chromatography (solvent *D*, 4:1) gave first methyl 2,6-di-*O*-trifluoromethylsulfonyl-3,4-*O*-isopropylidene-α-D-galactopyranoside (**25**) as a colourless oil (439 mg, 20%) which crystallised on standing, $^1$H NMR: $\delta$ 4.93 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.72 (bd, overlapped, 1 H, $J_{6a,6b}$ 10.8 Hz, H-6a), 4.70–4.67 (m, 2 H, $J_{5,6b}$ 2.3 Hz, H-6b, 2), 4.44 (dd, 1 H, $J_{2,3}$ 7.5, $J_{3,4}$ 5.4 Hz, H-3), 4.33-4.26 (m, 2 H, H-4, 5), 3.45 (s, 3 H, OMe), 1.50 and 1.33 (s, 6 H, 2 Me); $^{13}$C NMR: $\delta$ 111.86 ($Me_2C$), 97.62 (C-1), 84.44 (C-2), 74.56 (C-6), 73.76 (C-3*), 73.29 (C-4*), 66.00 (C-5), 56.25 (OMe), 27.50 and 26.09 (*Me*$_2$C); CIMS: *m/z* 516 $[M + NH_4]^+$.

Next, methyl 6-*O*-trifluoromethylsulfonyl-3,4-*O*-isopropylidene-α-D-galactopyranoside (**11**) was eluted as a colourless oil which crystallised on standing (922 mg, 59%), $^1$H NMR: $\delta$ 4.76 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.65 (dd, overlapped, 1 H, $J_{6a,6b}$ 10.8, $J_{5,6a}$ 4.5 Hz, H-6a), 4.61 (bd, overlapped, 1 H, H-6b), 4.34 (t, 1 H, $J_{2,3}$ 6.0 Hz, H-3), 4.29 (m, 1 H, H-5), 4.18 (dd, 1 H, $J_{3,4}$ 6.5, $J_{4,5}$ 2.2 Hz, H-4), 3.90 (bt, 1 H, H-2), 3.46 (s, 3 H, OMe), 2.58 (bs, 1 H, OH-2), 1.46 and 1.30 (2 s, 6 H, 2 Me); $^{13}$C NMR: $\delta$ 110.52 ($Me_2C$), 97.52 (C-1), 75.38 (C-6), 75.18 (C-3), 72.11 (C-4), 67.83 (C-2*), 66.74 (C-5*), 55.47 (OMe), 26.97 and 25.42 (*Me*$_2$C); CIMS: *m/z* 384 $[M + NH_4]^+$, 367 $[M + H]^+$.

Methyl 2-*O*-trifluoromethylsulfonyl-3,4-*O*-isopropylidene-α-D-galactopyranoside (**26**) was eluted last (78 mg, 5%) as a colourless oil, $^1$H NMR: $\delta$ 4.92 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1), 4.71 (dd, 1 H, $J_{2,3}$ 7.9 Hz, H-2), 4.42 (dd, 1 H, $J_{3,4}$ 5.5 Hz, H-3), 4.31 (dd, 1 H, $J_{4,5}$ 2.6 Hz, H-4), 4.08 (m, 1 H, H-5), 3.95 (dd, 1 H, $J_{6a,6b}$ 12.0, $J_{5,6a}$ 6.7 Hz, H-6a), 3.85 (m, 1 H, H-6b), 3.44 (s, 3 H, OMe), 1.50 and 1.35 (2 s, 6 H, 2 Me); $^{13}$C NMR: $\delta$ 110.77 ($Me_2C$), 97.23 (C-1), 84.80 (C-2), 74.91 (C-3), 72.91 (C-4), 67.41 (C-5), 62.18 (C-6), 55.96 (OMe), 27.65 and 26.16 (*Me*$_2$C).

*Methyl 2-*O*-benzyl-6-*O*-p-bromophenylsulfonyl-3,4-*O*-isopropylidene-α-D-galactopyranoside* (**19**).—*p*-Bromobenzenesulfonyl chloride (1.43 g, 4.57 mmol) was added to a solution of the precursor **16** (ref 1, 1.4 g, 4.3 mmol) in pyridine. The mixture was stirred overnight at room temperature. After concentration the residue was worked up as usual. Chromatography (solvent *D*, 4:1) gave **19** as a colourless oil which crystallised on standing; mp 84–85°C (EtOH); $[\alpha]_D$ +59° (*c* 1.3, $CHCl_3$); $^1$H NMR: $\delta$ 7.75 (d, 2 H, Ph), 7.71 (d, 2 H, Ph), 7.65–7.27 (m, 5 H, Ph), 4.76 (d, 1 H,

$J_{Ha,Hb}$ 12.6 Hz, $OCH_2Ph$), 4.66 (d, 1 H, $OCH_2Ph$), 4.56 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.31 (dd, 1 H, $J_{2,3}$ 7.8, $J_{3,4}$ 5.7 Hz, H-3), 4.25 (dd, 1 H, $J_{5,6a}$ 4.1, $J_{6a,6b}$ 9.8 Hz, H-6a), 4.19 (d, overlapped, 1 H, H-6b), 4.16 (m, overlapped, 1 H, H-5), 4.09 (dd, 1 H, $J_{4,5}$ 2.2 Hz, H-4), 3.42 (dd, 1 H, H-2), 3.31 (s, 3 H, OMe), 1.30 and 1.25 (2 s, 6 H, 2 Me); $^{13}C$ NMR: $\delta$ 109.65 ($Me_2C$), 98.19 (C-1), 75.93 (C-3*), 75.89 (C-2*), 72.93 (C-4), 72.88 ($OCH_2Ph$), 69.62 (C-6), 65.50 (C-5), 55.67 (OMe), 27.90 and 26.32 ($Me_2C$); CIMS: $m/z$ 562 $[M + NH_4]^+$. Anal. Calcd for $C_{18}H_{23}BrO_8S$: C, 50.74; H, 5.18; Br, 14.68; S, 5.89. Found: C, 50.92; H, 5.03; Br, 14.80; S, 6.00.

*Attempted fluorination of* **7** *with tetraethylammonium fluoride.*–A mixture of tetraethylammonium fluoride (1.02 g, 5.5 mmol) and **7** (454 mg, 1 mmol) in acetonitrile (15 mL) was refluxed overnight. The solution was worked up as usual and chromatography (solvent *D*, 4:1) gave first methyl 6-deoxy-3,4-*O*-isopropylidene-β-L-*arabino*-hex-5-enopyranoside (**14**) as a colourless oil (170 mg, 79%); $[\alpha]_D$ +77° (*c* 1.9, $CHCl_3$); $^1H$ NMR: $\delta$ 4.89 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1), 4.70 (s, 1 H, H-6a), 4.65 (d, 1 H, $J_{3,4}$ 6.8 Hz, H-4), 4.57 (s, 1 H, H-6b), 4.25 (bt, 1 H, $J_{2,3}$ 5.9 Hz, H-3), 3.78 (m, 1 H, H-2), 3.48 (s, 3 H, OMe), 2.38 (bd, 1 H, OH-2), 1.48 and 1.35 (2 s, 6 H, 2 Me); $^{13}C$ NMR: $\delta$ 152.28 (C-5), 109.81 ($Me_2C$), 99.29 (C-1), 96.91 (C-6), 76.18 (C-3), 72.93 (C-4), 70.39 (C-2), 56.21 (OMe), 27.44 and 25.37 ($Me_2C$); CIMS: $m/z$ 234 $[M + NH_4]^+$, 217 $[M + H]^+$.

Eluted next was **8** (19 mg, 8%), identical to the material described below.

*Methyl 6-chloro-6-deoxy-3,4-*O*-isopropylidene-α-*D*-galactopyranoside* (**9**).—Tetraethylammonium fluoride (936 mg, 5 mmol) was added at 0°C to a solution of **7** (228 mg, 0.5 mmol) in dichloroethane (2 mL) and the mixture was kept at this temperature for 15 min, and then stirred with exclusion of moisture at 70°C for 48 h. TLC (solvent *B*) showed complete conversion of the starting material into a less polar major product. The solution was extracted with water, the organic phase was dried and concentrated, and the residue was chromatographed (solvent *B*, 2.3:1) to give **9** (91 mg, 72%); mp 59–61°C (from diisopropyl ether), as a complex with the solvent of crystallisation, as shown by elemental analysis and NMR; $[\alpha]_D$ +119° (*c* 1.1, $CHCl_3$); $^1H$ NMR: $\delta$ 4.78 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 4.30 (t, 1 H, $J_{3,4}$ 6.3 Hz, H-3), 4.27 (dd, 1 H, $J_{4,5}$ 2.0 Hz, H-4), 4.13 (ddd, 1 H, H-5), 3.88 (ddd, 1 H, $J_{2,OH}$ 5.4, $J_{2,3}$ 5.5 Hz, H-2), 3.69 (dd, 1 H, $J_{5,6a}$ 5.7, $J_{6a,6b}$ 11.2 Hz, H-6a), 3.66 (dd, 1 H, $J_{5,6b}$ 7.5 Hz, H-6b), 3.62 (m, 0.3 H, 2 $Me_2CH$), 3.49 (s, 3 H, OMe), 2.53 (bs, 1 H, OH-2), 1.47, 1.33 (2 s, 6 H, 2 Me), 1.12 and 1.10 (2 s, 1.8 H, 2 0.15 $Me_2CH$); $^{13}C$ NMR: $\delta$ 109.36 ($Me_2C$), 98.00 (C-1), 75.58 (C-3), 72.70 (C-4), 69.01 (C-2), 68.57 (C-5), 55.38 (OMe), 42.85 (C-6), 27.94 and 26.27 ($Me_2C$); CIMS: $m/z$ 270 $[M + NH_4]^+$, 253 $[M + H]^+$. Anal. Calcd for $C_{10}H_{17}ClO_5 \cdot 0.15\ C_6H_{14}O$: C, 48.84; H, 7.18; Cl, 13.23. Found: C, 48.82; H, 7.21; Cl, 13.24.

When the above reaction was conducted with **7** (1.6 g, 3.5 mmol) without maintaining inert conditions (e.g., withdrawal of samples for TLC without protecting the reaction mixture from the contact with air), the initially colourless solution rapidly turned into a biphasic dark mixture. Processing as above, and chromatography (solvent *C*, 19:1) of the residue gave methyl 6-chloro-6-deoxy-α-D-galactopyranoside (**5**, 24%); mp 176–177°C (MeOH); $[\alpha]_D$ +178° (*c* 0.7, MeOH) {lit [32] mp 157°C (EtOH), $[\alpha]_D$ +165° (*c* 1.4, MeOH)}; $^1H$ NMR: $\delta$ 4.74 (bs, 1 H, H-1),

3.97 (bt, 1 H, partially overlapped, $J_{5,6}$ 6.5 Hz, H-5), 3.94 (bs, 1 H, overlapped, H-4), 3.72 (bd, 2 H, H-2, 3), 3.65 (dd, 1 H, $J_{5,6a}$ 5.4, $J_{6a,6b}$ 11.6 Hz, H-6a), 3.59 (dd, 1 H, $J_{5,6b}$ 7.8 Hz, H-6b), and 3.33 (s, 3 H, OMe); $^{13}$C NMR: $\delta$ 100.37 (C-1), 71.81 (C-5), 70.26 (C-3, C-4), 68.95 (C-2), 56.04 (OMe), and 43.88 (C-6); CIMS: *m/z* 230 $[M + NH_4]^+$. Anal. Calcd for $C_7H_{13}ClO_5$: C, 39.53; H, 6.16; Cl, 16.67. Found: C, 39.70; H, 6.21; Cl, 16.53.

*Attempted fluorination of* **7** *with cesium fluoride.*—A mixture of **7** (1.02 g, 2.24 mmol) and cesium fluoride in ethylene glycol (40 mL) was heated for 4 h at 160°C. The solution was then partitioned between $CH_2Cl_2$ and $H_2O$, and the organic phase was concentrated. Chromatography of the residue (solvent *D*, 5.7:1 → 2.3:1) gave, in order of elution, oily **14** (33 mg, 7%), **8** (116 mg, 22%, NMR data below) as a white solid, and oily methyl 6-*O*-(2-hydroxyethyl)-3,4-*O*-isopropylidene-α-D-galactopyranoside (**10**) (130 mg, 21%). Spectral data for the hitherto unknown compound **10**: $^1$H NMR (benzene-$d_6$): $\delta$ 4.70 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.32 (t, 1 H, $J_{2,3}$ 6.4 Hz, H-3), 4.20 (ddd, 1 H, H-5), 4.04 (dd, 1 H, $J_{3,4}$ 8.8, $J_{4,5}$ 2.6 Hz, H-4), 3.95 (m, 1 H, H-2), 3.77 (dd, 1 H, $J_{5,6a}$ 7.1, $J_{6a,6b}$ 10.0 Hz, H-6a), 3.72 (dd, 1 H, $J_{5,6b}$ 5.6 Hz, H-6b), 3.58 (m, 2 H, C$H_2$OH), 3.42 (dd, 1 H, partially overlapped, $J_{Ha,Hb}$ 10.6, *J* 4.0 Hz, C$H_2$CH$_2$OH), 3.36 (m, 1 H, partially overlapped, C$H_2$CH$_2$OH), 3.20 (s, 3 H, OMe), 2.98 (d, 1 H, $J_{2,OH}$ 2.3 Hz, OH-2), 2.93 (m, 1 H, OH), 1.48 and 1.24 (2 s, 6 H, 2 Me), $^{13}$C NMR: $\delta$ 109.60 (Me$_2$*C*), 98.43 (C-1), 75.98 (C-3), 73.24 (C-4), 72.44 (*C*H$_2$CH$_2$OH), 70.09 (C-6), 69.36 (C-2), 67.10 (C-5), 61.56 (CH$_2$*C*H$_2$OH), 55.38 (OMe), 27.67 and 25.90 (2 *Me*$_2$C); CIMS: *m/z* 296 $[M + NH_4]^+$.

*Methyl 2-O-benzyl-3,4-O-isopropylidene-6-O-trifluoromethylsulfonyl-α-D-galactopyranoside* (**17**).—Trifluoromethanesulfonic anhydride (2.11 mL, 12.5 mmol) was added dropwise over 30 min to a mixture of **16** (ref. 1, 1.63 g, 5 mmol) and pyridine (1.21 mL, 14.9 mmol) in dichloromethane (40 mL) stirred at −25°C. The mixture was allowed to warm to −10°C. After 1 h at this temperature, ice was added and the mixture was partitioned between ice-cold water and dichloromethane. Chromatography (solvent *B*, 4:1) afforded **17** (2.04 g, 93%) which crystallised upon standing. When kept at room temperature overnight, the compound partially decomposed. Upon recrystallisation from diisopropyl ether–hexane, **17** contained diisopropyl ether of crystallisation and had mp 56–61°C; $[\alpha]_D$ +76° (*c* 1.1, $CHCl_3$); $^1$H NMR: $\delta$ 7.36–7.26 (m, 5 H, Ph), 4.80 (d, 1 H, $J_{Ha,Hb}$ 12.5 Hz, OC$H_2$Ph), 4.69 (m, 4 H, H-1, 6a, 6b, OC$H_2$Ph), 4.39 (dd, 1 H, $J_{2,3}$ 7.3, $J_{3,4}$ 6.0 Hz, H-3), 4.28 (m, 1 H, H-5), 4.18 (dd, 1 H, $J_{4,5}$ 2.5 Hz, H-4), 3.52 (dd, 1 H, $J_{1,2}$ 3.5 Hz, H-2), 3.40 (s, 3 H, OMe), 1.39 and 1.32 (2 s, 6 H, 2 Me); $^{13}$C NMR: $\delta$ 109.95 (Me$_2$*C*), 98.22 (C-1), 75.98 (C-3*), 75.65 (C-2*), 75.09 (C-6), 72.69 (C-4), 72.58 (O*C*H$_2$Ph), 65.59 (C-5), 55.80 (OMe), 26.39 and 27.94 (*Me*$_2$C); CIMS: *m/z* 474 $[M + NH_4]^+$.

*Methyl 2-O-benzyl-6-deoxy-6-fluoro-3,4-O-isopropylidene-α-D-galactopyranoside* (**20**).—TAS-F (4 g, 14.5 mmol) was added portionwise at −30°C to a stirred solution of crude **17** (prepared from 1.63 g, 5 mmol of **16**) in dichloromethane (45 mL). After 30 min, the mixture was allowed to warm to room temperature, and the stirring was continued overnight. Ice was added, and the mixture was partitioned between $CH_2Cl_2$ and water. Chromatography (solvent *B*, 9:1) gave first oily

methyl 2-*O*-benzyl-6-deoxy-3,4-*O*-isopropylidene-β-L-*arabino*-hex-5-enopyranoside (**15**) (150 mg, 15%); $^1$H NMR: δ 7.36–7.29 (m, 5 H, Ph), 4.83 (d, 1 H, $J_{Ha,Hb}$ 12.7 Hz, OC$H_2$Ph), 4.79 (d, 1 H, $J_{1,2}$ 2.6 Hz, H-1), 4.77 (d, 1 H, OC$H_2$Ph), 4.74 (d, 1 H, $J_{3,4}$ 6.4 Hz, H-4), 4.67 (s, 1 H, H-6a), 4.58 (s, 1 H, H-6b), 4.45 (t, 1 H, $J_{2,3}$ 6.6 Hz, H-3), 3.62 (dd, 1 H, H-2), 3.41 (s, 3 H, OMe), 1.46 and 1.37 (2 s, 6 H, 2 Me); $^{13}$C NMR: δ 153.03 (C-5), 110.02 (Me$_2$*C*), 98.97 (C-1), 95.61 (C-6), 77.00 (C-2), 76.24 (C-3), 72.88 (C-4), 72.31 (O*C*H$_2$Ph), 55.97 (OMe), 27.70 and 25.98 (*Me*$_2$C); CIMS: *m/z* 324 $[M + NH_4]^+$, 307 $[M + H]^+$.

Eluted next was **20** (1.07 g, 83%) as a colourless oil; $[\alpha]_D$ +100° (*c* 1.2, $CHCl_3$); $^1$H NMR: δ 7.32 (m, 5 H, Ph), 4.82 (d, 1 H, $J_{Ha,Hb}$ 12.6 Hz, OC$H_2$Ph), 4.73 (d, 1 H, partially overlapped, OC$H_2$Ph), 4.69 (m, 2 H, H-1, 0.5 6a, 0.5 6b), 4.56 (dd, 0.5 H, $J_{6a,6b}$ 9.7, $J_{5,6a}$ 4.3 Hz, 0.5 H-6a), 4.51 (dd, 0.5 H, $J_{5,6b}$ 6.9 Hz, 0.5 H-6b), 4.38 (dd, 1 H, $J_{3,4}$ 5.6, $J_{2,3}$ 7.8 Hz, H-3), 4.24 (m, 1 H, overlapped, H-5), 4.19 (dd, 1 H, partially overlapped, $J_{4,5}$ 2.6 Hz, H-4), 3.52 (dd, 1 H, $J_{1,2}$ 3.4 Hz, H-2), 3.41 (s, 3 H, OMe), 1.38 and 1.33 (2 s, 6 H, 2 Me); $^{13}$C NMR: δ 109.52 (Me$_2$*C*), 98.22 (C-1), 82.56 (d, $J_{C,F}$ 169.1 Hz, C-6), 76.06 (C-2,3), 73.03 (d, $J_{C,F}$ 6.9 Hz, C-4), 72.47 (O*C*H$_2$Ph), 66.25 (d, $J_{C,F}$ 21.3 Hz, C-5), 55.66 (OMe), 28.08 and 26.45 (2 *Me*$_2$C); $^{19}$F NMR: δ −66.07 (dt, 1 F, $J_{F,5}$ 15.6, $J_{F,6}$ 50.7 Hz, F-6); CIMS: *m/z* 344 $[M + NH_4]^+$. Anal. Calcd for $C_{17}H_{23}FO_5$: C, 62.56; H, 7.10; F, 5.82. Found: C, 62.60; H, 7.29; F, 5.47.

*Methyl 6-deoxy-6-fluoro-3,4*-O-*isopropylidene-α*-D-*galactopyranoside* (**8**).—(*a*) A mixture of **20** (1.21 g, 3.7 mmol) and 10% palladium on charcoal catalyst (250 mg) in 1:7 acetone–EtOH (40 mL) was stirred overnight under hydrogen at atmospheric pressure. Conventional processing afforded **8** (847 mg, 97%). Upon deposition from diisopropyl ether, **8** cocrystallised with the solvent as a 7:1 complex, as shown by elemental analysis and $^1$H NMR.

(*b*) To a solution of chromatographically pure **11** (224 mg, 0.61 mmol) in dichloromethane (5 mL) was added TAS-F (900 mg, 3.3 mmol) at −10°C. After 15 min the mixture was allowed to come back to room temperature and stirred overnight. Concentration and chromatography (solvent *B*, 9:1) gave **8** (175 mg, 78%).

(*c*) Compound **6** (1 g, 4.27 mmol) was treated with trifluoromethanesulfonic anhydride as described for the preparation of **11** and processed conventionally. The resulting crude residue was solubilized in dichloromethane (15 mL) and TAS-F (2.9 g, 10.5 mmol) was added dropwise to the mixture at −15°C. After 15 min, the solution was allowed to reach room temperature and was stirred overnight. Concentration and chromatography (solvent *B*, 9:1) afforded **8** (498 mg, 50%); mp 58–75°C (diisopropyl ether); $[\alpha]_D$ +135.6° (*c* 1.1, $CHCl_3$); $^1$H NMR: δ 4.79 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 4.71 (dd, 0.5 H, partially overlapped, $J_{5,6a}$ 5.0, $J_{6a,6b}$ 10.0 Hz, 0.5 H-6a), 4.67 (dd, 0.5 H, partially overlapped, 0.5 H-6b), 4.54 (dd, 0.5 H, partially overlapped, 0.5 H-6a), 4.39 (dd, 0.5 H, partially overlapped, $J_{5,6b}$ 6.9 Hz, 0.5 H-6b), 4.29 (t, 1 H, partially overlapped, $J_{3,4}$ 6.1 $J_{2,3}$ 6.1 Hz, H-3), 4.24 (m, 1 H, overlapped, H-5), 4.21 (dd, 1 H, partially overlapped, $J_{4,5}$ 2.0 Hz, H-4), 3.85 (m, 1 H, H-2), 3.62 (m, 0.3 H, 2 0.15 Me$_2$C*H*), 3.46 (s, 3 H, OMe), 2.40 (bd, 1 H, $J_{2,OH}$ 5.4 Hz, OH), 1.45, 1.32 (2 s, 6 H, 2 Me), 1.12 and 1.10 (2 s, 1.8 H, 2 *Me*$_2$CH);

$^{13}$C NMR: δ 109.94 ($Me_2C$), 97.99 (C-1), 82.62 (d, $J_{C,F}$ 168.9 Hz, C-6), 75.74 (C-3), 72.47 (d, $J_{C,F}$ 7.2 Hz, C-4), 68.91 (C-2), 67.19 (d, $J_{C,F}$ 21.6 Hz, C-5), 55.52 (OMe), 27.52, 25.87 ($Me_2C$); $^{19}$F NMR: δ 67.08 (dt, 1 F, $J_{F,5}$ 5.8, $J_{F,6}$ 48.9 Hz, F-6); CIMS: $m/z$ 254 $[M + NH_4]^+$. Anal. Calcd for $C_{10}H_{17}FO_5 \cdot 0.15\ C_6H_{14}O$: C, 52.04; H, 7.65; F, 7.55. Found: C, 52.23; H, 7.92; F, 7.48.

*Methyl 6-deoxy-6-fluoro-α-*D*-galactopyranoside* (**2**).—Compound **8** (200 mg, 0.85 mmol) in 10:1 acetic acid–water (4 mL) was heated at 90°C for 4 h. Concentration followed by chromatography (solvent *C*, 19:1) gave **2** (155 mg, 93%); mp 145–146°C (acetone–MeOH); $[\alpha]_D$ +195° (*c* 0.8, MeOH), {lit. [6] mp 139°C (acetone–$Et_2O$), $[\alpha]_D$ +194° (*c* 0.1, $H_2O$)}.

*Methyl 2-O-benzyl-6-O-(2-hydroxyethyl)-3,4-O-isopropylidene-α-*D*-galactopyranoside* (**18**).—Crude **17**, prepared from **16** (1.4 g, 4.3 mmol), was dissolved in $CH_2Cl_2$ (5 mL) and added to a warm suspension of CsF (6.8 g, 45 mmol) in ethylene glycol (40 mL). The mixture was heated at 80°C for 5.5 h, cooled to room temperature, and partitioned between $CH_2Cl_2$ and water. After concentration, chromatography (solvent *D*, 1.8:1 → 1:1) of the residue gave first methyl 3,6-anhydro-2-*O*-benzyl-α-D-galactopyranoside (**22**) (660 mg, 57%); $^1$H NMR: δ 7.32–7.24 (m, 5 H, Ph), 4.85 (d, 1 H, $J_{Ha,Hb}$ 12.3 Hz, OC$H_2$Ph), 4.71 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1), 4.58 (dd, 1 H, $J_{4,OH}$ 4.6, $J_{4,5}$ 1.9 Hz, H-4), 4.52 (d, 1 H, OC$H_2$Ph), 4.27 (bs, 1 H, H-5), 4.13 (d, 1 H, $J_{2,3}$ 5.4 Hz, H-3), 4.02 (d, 1 H, $J_{6a,6b}$ 10.1 Hz, H-6a), 3.98 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 3.69 (dd, 1 H, H-2), and 3.51 (s, 3 H, OMe); $^{13}$C NMR: δ 98.67 (C-1), 80.58 (C-3), 77.26 (C-2*), 76.57 (C-4*), 73.89 (O$CH_2$Ph), 71.11 (C-5), 69.10 (C-6), and 57.57 (OMe); CIMS: $m/z$ 284 $[M + NH_4]^+$.

Hydrogenolysis with 10% palladium on charcoal catalyst of a portion of **22** (500 mg, 1.9 mmol) in ethanol (10 mL) gave the known methyl 3,6-anhydro-α-D-galactopyranoside [23,35] (**21**); mp 142–143°C (acetone–MeOH); $[\alpha]_D$ +80.0° (*c* 0.5, $H_2O$), {lit. [23] mp 140°C, $[\alpha]_D$ +82° (*c* 1, $H_2O$)}.

Eluted next was **18** (150 mg, 9.5%); $[\alpha]_D$ +79° (*c* 1, $CHCl_3$); $^1$H NMR: δ 7.36–7.28 (m, 5 H, Ph), 4.82 (d, 1 H, $J_{Ha,Hb}$ 12.5 Hz, OC$H_2$Ph), 4.71 (d, 1 H, OC$H_2$Ph), 4.67 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), 4.36 (dd, 1 H, $J_{3,2}$ 7.8, $J_{3,4}$ 5.5 Hz, H-3), 4.21 (dd, 1 H, $J_{4,5}$ 2.5 Hz, H-4), 4.14 (m, 1 H, H-5), 3.78 (m, 6 H, H-6a, 6b, 2 C$H_2$), 3.51 (dd, 1 H, H-2), 3.40 (s, 3 H, OMe), 1.39 and 1.34 (2 s, 6 H, 2 Me); $^{13}$C NMR: δ 109.23 ($Me_2C$), 98.29 (C-1), 76.18 (C-3*), 76.06 (C-2*), 73.79 (C-4), 72.43 (O$CH_2$Ph, $CH_2$O), 70.12 (C-6), 66.30 (C-5), 61.10 ($CH_2$OH), 55.60 (OMe), 28.11 and 26.42 ($Me_2C$); CIMS: $m/z$ 386 $[M + NH_4]^+$. Anal. Calcd for $C_{19}H_{28}O_7$: C, 61.94; H, 7.66. Found: C, 61.72; H, 7.61.

Further elution gave 62 mg (5%) of a compound to which, based on spectral data, structure **23** (2-hydroxyethyl 3,6-anhydro-2-*O*-benzyl-β-D-galactopyranoside) has been tentatively assigned; CIMS: $m/z$ 314 $[M + NH_4]^+$, 297 $[M + H]^+$; $^1$H NMR: δ 7.38–7.28 (m, 5 H, Ph), 5.10 (d, 1 H, $J_{1,2}$ 6.3 Hz, H-1), 4.92 (d, 1 H, $J_{Ha,Hb}$ 11.1 Hz, OC$H_2$Ph), 4.64 (d, 1 H, OC$H_2$Ph), 4.65–3.80 (m, 11 H, H-3, 4, 5, 6a, 6b, OC$H_2$Ph, C$H_2$C$H_2$OH), 3.48 (dd, 1 H, $J_{2,3}$ 2.3 Hz, H-2), and 2.46 (d, 1 H, *J* 3.3 Hz, OH); $^{13}$C NMR: δ 104.13 (C-1), 85.65 (C-3), 79.38 (C-4*), 78.16 (C-2), 77.52 (C-5), 74.35 ($CH_2O$), 73.77 (O$CH_2$Ph), 65.27 (C-6*), and 64.76 ($CH_2$OH*).

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