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Note

Synthesis of methyl (allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate and methyl (2,3-di-*O*-benzyl-α- and β-D-galactopyranosyl fluoride)uronate*

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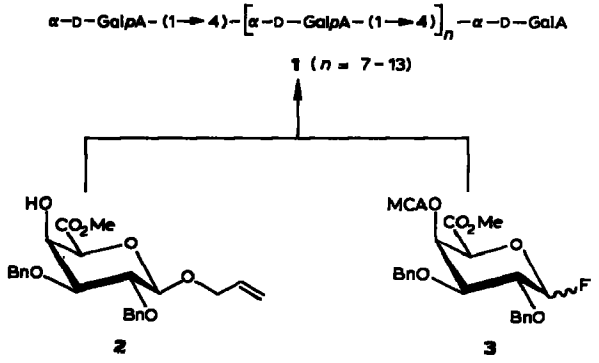
INTRODUCTION

In view of the recently disclosed functions[1] of plant cell wall oligosaccharides as the endogenous elicitor for the defense mechanisms of plant cells against invading biological agents, synthetic investigations of related oligosaccharides should play important roles in providing enough structurally well-defined glycans, which are required to uncover the molecular mechanism of such plant physiological phenomena. The α-(1→4)-linked oligogalacturonides **1**, released from plant cell wall pectin[2] by partial acid hydrolysis or enzymic degradation have been reported[3] to elicit phytoalexin accumulation. An obvious synthetic approach to the glycan **1** may depend on the use of galactopyranosiduronate derivatives, both as a glycosyl acceptor and a donor in the chain elongation sequence. In this connection we are



Scheme 1 (Bn : $CH_2C_6H_5$; MCA : $COCH_2Cl$)

*Part 1 in the series Synthetic Studies on Plant Cell Wall Glycans.

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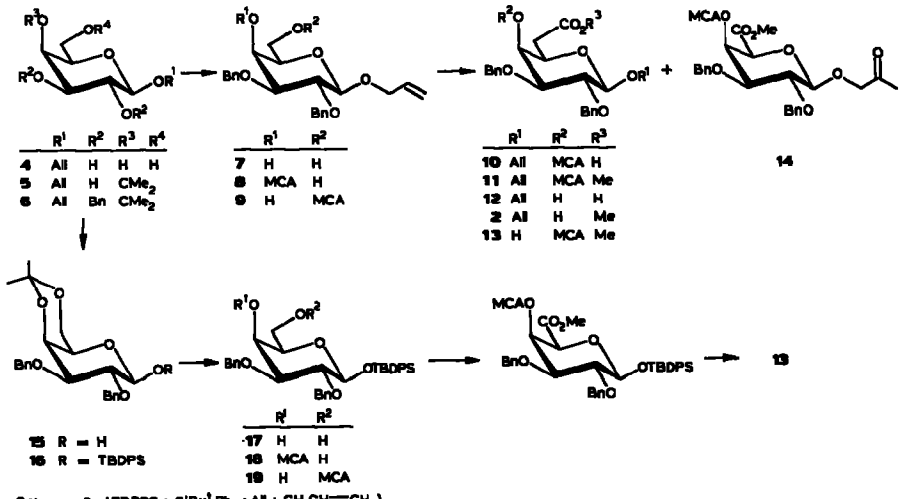
interested in the recent report[4] of the reaction of a protected (galactopyranosyl bromide)uronate with a glycosyl acceptor carrying a free secondary hydroxyl group, ending with the formation of disaccharide in moderate yields (30–60%). Since, to the best of our knowledge, no example has been reported of coupling between monosaccharide donor and acceptor, both derived from glycopyranosyluronates, a properly protected glycosyl acceptor **2** and donor **3** are prepared in order to investigate the feasibility of this approach.

Acetonation of allyl β-D-galactopyranoside **4** (ref. 5) with 2,2-dimethoxypropane and *p*-toluenesulfonic acid in DMF gave a kinetically favored[6] 4,6-*O*-isopropylidene derivative **5** (56%) and its 3,4 isomer (28%)[7]. Benzylation of compound **5** afforded a moderate yield of compound **6**, which was then hydrolyzed to diol **7** (ref. 8). The 4-hydroxyl group was selectively blocked with the chloroacetyl group through 6-*O*-(4,4′-dimethoxy)tritylation, chloroacetylation and then mild acid hydrolysis to give compound **8**.

Several conditions to oxidize **8** to the uronic acid derivative **10** were examined as follows. Jones oxidation of **8** was rather slow and was not completed even by the use of a large excess of the oxidant for 2 h at −5–0°. Chloroacetyl migration (O-4→O-6), forming **9**, occurred to a considerable extent (24%) during the reaction, most probably due to the acidity of the reaction media, and the desired uronic acid **10** was obtained only in a moderate yield (46%). Catalytic oxidation[9] of compound **8** with Pt in water containing sodium bicarbonate gave an acid **12**, which was isolated as the corresponding methyl ester **2** in only 32% yield. About 55% of the diol **7** was recovered from the neutral fraction of the reaction mixture. On the other hand, a two-step procedure involving Swern oxidation[10] and then Jones oxidation converted compound **8** into compound **10** in 72% overall yield. Treatment of the acid **10** with ethereal diazomethane afforded an oily ester **11**. The structure of compound **11** was confirmed by ^{1}H-n.m.r. data which contained signals at δ 3.75 (s, 3



Scheme 2 ; TBDPS : $SiBu^tPh_2$; All : $CH_2CH{=}CH_2$)

H) for OCH_3, 4.10 (s, 2 H) for $COCH_2Cl$, and 5.80 (m, 1 H) for H-4. Deallylation of compound **11** with palladium(II) chloride[11] in aq. acetic acid gave not only a 57% yield of the desired hemiacetal **13** but also an oxidized product **14** in 18% yield which was difficult to separate from compound **13**. Formation of the oxidized product such as **14** during Pd(II) catalyzed deallylation was observed previously[12].

In order to improve the efficiency of the preparation of compound **13**, an alternative approach was also investigated. The allyl group in compound **6** was replaced by a *tert*-butyldiphenylsilyl group *via* sequential treatment with potassium *tert*-butoxide[13] in DMSO at 60°, iodine in aq. THF and pyridine[14], and *tert*-butylchlorodiphenylsilane and imidazole in DMF, to give the β anomer **16** with high stereoselectivity *via* hemiacetal **15**, which was hydrolyzed to diol **17** in 72% overall yield from compound **6**. The hydroxyl group at C-4 of compound **17** was protected in a similar way, as in the case of compound **8**, to give monoester **18**.

Sequential oxidation of compound **18**, as discussed before, and esterification afforded the desired methyl ester **20** in 50% overall yield from the diol **17**. Treatment of compound **20** with 50% hydrogen fluoride–pyridine[15] gave a 93% yield of the desilylated hemiacetal **13** instead of the expected[16] fluoride **3**. The overall conversion of isopropylidene derivative **6** into compound **13** was achieved in 34% yield without formation of inseparable isomers.

The hemiacetal **13** was treated with diethylaminosulfur trifluoride[17] in tetrahydrofuran to give a 1:1 mixture of α- and β-fluorides **3** in 86% yield. The structure of the fluorides **3** was determined by n.m.r. data. Pairs of signals for the protons of OCH_3, $COCH_2Cl$, and H-4 were observed at δ 3.76 and 3.79, 4.05 and 4.10, and 5.82 and 5.94, respectively. Signals for anomeric carbon atoms were observed at δ 105.9 for C-1α and at δ 109.4 for C-1β with $^1J_{CF}$ 230 and 220 Hz, respectively, in agreement with the assigned configurations[18].

Having prepared the key glycosyl donor **3**, the reaction with the glycosyl acceptor **2** was investigated under the condition of Mukaiyama and coworkers[19]. T.l.c. examination of the reaction mixture showed that the reaction did not proceed under the normal condition.

In conclusion, a synthetic route to methyl galactopyranosyluronate derivatives **2** and **3** was developed. The coupling between compounds **2** and **3**, however, did not proceed under the normal condition, or in the presence of a large excess of silver perchlorate.

EXPERIMENTAL

General. — Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Optical rotations were determined with a Perkin-Elmer Model 241 MC polarimeter, for solutions in $CHCl_3$ at 25°, unless noted otherwise. Column chromatography was performed on columns of silica gel (Merck 70–230 mesh). T.l.c. and high performance t.l.c. was performed on silica gel 60 F_{254} (Merck, Darmstadt). Molecular sieves were purchased from

Nakarai Chemicals, Ltd. I.r. spectra were recorded with an EPI-G2 Hitachi spectrophotometer, using KBr pellets for the crystalline samples, and films for the liquid samples. ^{1}H-N.m.r. spectra were recorded with either JNM-GX400 or JNM-FX90Q n.m.r. spectrometers. ^{13}C-N.m.r. spectra were recorded with a JNM-FX 90Q n.m.r. spectrometer operated at 22.50 MHz. The values of δ_C and δ_H are expressed in p.p.m. downwards from the signal for internal Me_4Si, for solutions in $CDCl_3$, unless noted otherwise.

Allyl 4,6-O-isopropylidene-β-D-galactopyranoside (**5**). — A mixture of **4** (12 g), 2,2-dimethoxypropane (12 mL) and *p*-TsOH (0.5 g) in dry DMF (250 mL) was stirred for 5 h at room temperature. Et_3N (15 mL) was added to the mixture and most of the DMF was distilled off *in vacuo* (1–2 mmHg). The residue was dissolved in CH_2Cl_2 (500 mL), washed with 1:1 saturated NaCl–saturated $NaHCO_3$ (100 mL), and then dried (Na_2SO_4). After evaporation of the solvent, the crude product was chromatographed on SiO_2 in 1:24 MeOH–$CHCl_3$ to give 3,4-*O*-isopropylidene derivative (4.0 g, 28%) m.p. 95.5–97° (*n*-hexane–EtOAc, needles), $[\alpha]_D^{22}$ +4.3° (*c* 0.3); lit.[8] m.p. 91–92°, $[\alpha]_D^{22}$ +10° (*c* 2); n.m.r.: δ_H 1.35 (s, 3 H, CH_3), 1.52 (s, 3 H, CH_3), 5.20 (m, 1 H, C=CH_2), 5.34 (m, 1 H, C=CH_2), 5.95 (m, 1 H, –CH=CH_2); and secondly **5** (7.9 g, 55.9%), m.p. 91–93° (ether, needles; lit.[7] 88.5–90°); $[\alpha]_D^{22}$ −41.4° (*c* 0.7); ^{1}H-n.m.r.: δ_H 1.46 (s, 6 H, CH_3), 5.20 (m, 1 H, C=CH_2), 5.33 (m, 1 H, *J* 11.7 Hz, C=CH_2), and 5.95 (m, 1 H, –CH=CH_2).

Anal. Calc. for $C_{12}H_{20}O_6$: C, 55.37; H, 7.75. Found: C, 55.36; H, 7.75.

Allyl 2,3-di-O-benzyl-4,6-O-isopropylidene-β-D-galactopyranoside (**6**). — To a suspension of NaH (3.6 g, 60% in mineral oil), washed with *n*-hexane, in dry DMF (5 mL) was added a solution of **5** (7.70 g) in dry DMF (60 mL) at room temperature with stirring. After stirring for 1 h, the mixture was cooled in an ice–water bath and a solution of benzyl bromide (10.5 mL) in dry DMF (10 mL) was added dropwise to the mixture. After stirring for 0.5 h at 0°, the bath was removed, stirring being continued for 2.5 h at room temperature.

MeOH was added to destroy excess NaH before the mixture was poured into water and extracted with ether. The extract was washed with water and saturated NaCl, dried (Na_2SO_4), and finally concentrated *in vacuo*. The residue was chromatographed on SiO_2 in 70:30:1 *n*-hexane–EtOAc–Et_3N to give **6** (7.26 g, 55.7%) as crystals, m.p. 68–69.5°, (prisms, *n*-hexane–ether), $[\alpha]_D^{20}$ −19.6° (*c* 1.33); n.m.r.: δ_H 1.43 (s, 3 H, CH_3), 1.51 (s, 3 H, CH_3), 5.18 (m, 1 H, C=CH_2), 5.32 (m, 1 H, C=CH_2), 5.95 (m, 1 H, –CH=CH_2), 7.33 (m, 10 H, aromatic H); δ_C 18.9 (CH_3), 29.2 (CH_3), 62.9 (C-6), 66.7 (C-4), 98.5 (CMe_2), 102.6 (C-1), 117.0 (=CH_2), and 134.4 (–CH=C).

Anal. Calc. for $C_{26}H_{32}O_6$: C, 70.89; H, 7.32. Found: C, 71.22; H, 7.32.

Allyl 2,3-di-O-benzyl-β-D-galactopyranoside (**7**). — A mixture of **6** (7.26 g) and 80% aq. AcOH (50 mL) was heated for 1 h at 60° and concentrated *in vacuo*. The residue was chromatographed on SiO_2 in 1:1–1:0 EtOAc–*n*-hexane to give **7** (6.08 g, 92.1%) as needles, m.p. 70–70.5° (*n*-hexane–benzene), $[\alpha]_D^{20}$ −3.1° (*c* 1.0); n.m.r.: δ_H 2.35 (br, 2 H, OH), 5.18 (m, 1 H, C=CH_2), 5.31 (m, 1 H, C=CH_2), 5.95 (m, 1 H, –HC=CH_2), and 7.32 (m, 10 H, aromatic H).

Anal. Calc. for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 68.78; H, 7.04.

Allyl 2,3-di-O-benzyl-4-O-chloroacetyl-β-D-galactopyranoside (**8**). — To a solution of **7** (2.0 g) in dry pyridine (20 mL) was added 4,4'-dimethoxytrityl chloride (1.86 g). After the mixture was stirred for 3 h at room temperature, chloroacetic anhydride (1.6 g) was added and stirring was continued for 3.5 h. Most of the pyridine was evaporated *in vacuo*. The residue was extracted with EtOAc. The extract was washed with aqueous $NaHCO_3$, water, and saturated NaCl, dried (Na_2SO_4), and then concentrated *in vacuo*. The residue was co-evaporated with toluene to remove remaining pyridine and dissolved in 7:3 $CHCl_3$–MeOH (15 mL). The solution was stirred with 2% benzenesulfonic acid (7:3 $CHCl_3$–MeOH solution) (15 mL) for 30 min in an ice–water bath. The mixture was diluted with $CHCl_3$, washed with aqueous $NaHCO_3$, water, and saturated NaCl, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was chromatographed on SiO_2 in 3:2 *n*-hexane–EtOAc to give **8** (1.64 g, 68.8%), which slowly crystallized on standing, m.p. 62° (*i*-Pr_2O–*n*-hexane), $[\alpha]_D^{20}$ +25.8° (*c* 0.9); n.m.r.: δ_H 2.42 (br, 1 H), 4.14 (s, 2 H, OCCH_2Cl), 4.5–5.0 (m, 4 H, CH_2Ph), 5.20 (m, 1 H, C=CH_2), 5.35 (m, 1 H, C=CH_2), 5.48 (m, 1 H, H-4), 5.95 (m, 1 H, –C*H*=CH_2), 7.31 (br.s, 10 H, aromatic H); δ_C 40.7 (ClCH_2), 60.9 (C-6), 69.5 (C-4), 102.9 (C-1), 117.4 (=CH_2), 133.9 (–C*H*=CH_2), and 167.7 (*C*=O).

Anal. Calc. for $C_{25}H_{29}O_7Cl$: C, 62.96; H, 6.13; Cl, 7.43. Found: C, 62.98; H, 6.15; Cl, 7.43.

Oxidation of **8**. — *(A) (Jones oxidation):* To a solution of **8** (720 mg) in acetone (20 mL), cooled in an ice–MeOH bath, was added 8N Jones reagent (3 mL). After stirring for 2 h, excess oxidant was destroyed with MeOH. The mixture was diluted with water and concentrated *in vacuo* to remove acetone. The resulting aqueous layer was extracted with ether. The ethereal solution was extracted with saturated Na_2CO_3. The carbonate extract was acidified with dilute HCl and re-extracted with ether. The ethereal extract was washed with water and saturated NaCl, dried (Na_2SO_4), and evaporated *in vacuo* to give a crude crystalline product, which was washed with *i*-Pr_2O–hexane to give *allyl 2,3-di-O-benzyl-4-O-chloroacetyl-β-D-galactopyranosiduronic acid* **10** (351 mg, 46%), m.p. 156–159° (*i*-Pr_2O–$CHCl_3$), $[\alpha]_D^{22}$ +27.3° (*c* 0.8); n.m.r.: δ_H 4.12 (s, 2 H, OCCH_2Cl), 4.5–5.0 (m, 4 H, CH_2Ph), 5.20 (m, 1 H, C=CH_2), 5.35 (m, 1 H, C=CH_2), 5.38 (m, 1 H, H-4), 5.95 (m, 1 H, –C*H*=CH_2), 7.31 (br.s, 10 H, aromatic H), 9.24 (br.s, 1 H, COO*H*); δ_C 40.6 (ClCH_2), 69.6 (C-4), 102.6 (C-1), 117.8 (=CH_2), 133.6 (–C*H*=CH_2), 166.6 (ClCH_2*C*O), and 169.1 (*C*OOH).

Anal. Calc. for $C_{25}H_{27}O_8Cl$: C, 61.16; H, 5.54; Cl, 7.22. Found: C, 61.05; H, 5.57; Cl, 7.29.

From the neutral extract, acyl migrated compound **9** (173 mg, 24%) crystallized out, m.p. 82° (*i*-Pr_2O, needles), $[\alpha]_D^{20}$ +0.9° (*c* 1.1); n.m.r.: δ_H 2.56 (br.s, 1 H, O*H*), 3.90 (m, 1 H, H-4), 4.05 (s, 2 H, OCCH_2Cl), 4.5–5.0 (m, 4 H, CH_2Ph), 5.20 (m, 1 H, C=CH_2), 5.35 (m, 1 H, C=CH_2), 5.95 (m, 1 H, –C*H*=CH_2), 7.31 (br.s, 10 H, aromatic H); δ_C 40.6 (ClCH_2), 64.80 (C-6), 66.80 (C-4), 134.0 (–C*H*=CH_2), and 167.0 (ClCH_2*C*O).

Anal. Calc. for $C_{25}H_{29}O_7Cl$: C, 62.96; H, 6.13; Cl, 7.43. Found: C, 62.86; H, 6.09; Cl, 7.43.

(B) (catalytic oxidation): A suspension of PtO_2 (430 mg) in water (100 mL) was stirred in an atmosphere of hydrogen for 2 h. Then hydrogen was removed by evacuation and to the suspension were added **8** (1.0 g) and 9% aqueous $NaHCO_3$ (4 mL). Oxygen was bubbled into the mixture with vigorous stirring for 5.5 h in an oil bath (60°). After cooling, EtOAc was added to the mixture to dissolve the organic precipitate and the catalyst was filtered off. Na_2CO_3 was added to the filtrate to adjust the pH to 10–11 before extraction with EtOAc to remove the neutral material. From the neutral extract **7** (519 mg) was recovered. The aqueous phase was acidified with HCl (pH 1–2) and extracted with EtOAc. The extract was washed with water and saturated NaCl, dried (Na_2SO_4), and evaporated *in vacuo*. The resulting crude acid **12** was treated with ethereal diazomethane. Evaporation *in vacuo* afforded crude crystals which were recrystallized from *i*-Pr_2O to give methyl (allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate **2** (239 mg, 26.6%). From the mother liquor, additional **2** (48 mg, 5.3%) was obtained by column chromatography on SiO_2 in 3:2 *n*-hexane–EtOAc, m.p. 111–115°, $[\alpha]_D^{20}$ −7.3° (*c* 0.4); n.m.r.: δ_H 2.59 (br.s, 1 H, O*H*), 3.82 (s, 3 H, OCH_3), 4.04 (br.s, 1 H, H-4), 4.5–5.0 (m, 4 H, CH_2Ph), 5.20 (m, 1 H, C=CH_2), 5.35 (m, 1 H, C=CH_2), 5.95 (m, 1 H, –C*H*=CH_2), 7.32 (br.s, 10 H, aromatic H); δ_C 52.5 (OCH_3), 68.1 (C-4), 102.4 (C-1), 117.4 (=CH_2), 133.9 (–*C*H=CH_2), and 168.4 (C=O).

Anal. Calc. for $C_{24}H_{28}O_7$: C, 67.27; H, 6.59. Found: C, 67.21; H, 6.61.

(C) (two-step oxidation): To a solution of oxalyl chloride (1 mL) in dry CH_2Cl_2 (25 mL) was added a solution of DMSO (1.7 mL) in dry CH_2Cl_2 (5 mL) in a dry ice–acetone bath. The mixture was stirred for 2 min and a solution of **8** (2.49 g) in dry CH_2Cl_2 (10 mL) was added. After stirring for 15 min, Et_3N (6.6 mL) was added to the mixture. Stirring was continued for 5 min at −78° and then for 15 min at room temperature. The mixture was diluted with CH_2Cl_2, washed with water and saturated NaCl, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was treated with 8N Jones reagent (3.9 mL) in acetone (80 mL) for 1.5 h at 0°. A similar work-up procedure as described above (*A*) provided **10** (1.84 g, 71.8%).

*Methyl (allyl 2,3-di-*O*-benzyl-4-*O*-chloroacetyl-β-*D*-galactopyranosid)uronate* (**11**). — An ethereal solution of **10** was treated with ethereal diazomethane to give **11** as an oil quantitatively, $[\alpha]_D^{20}$ +31.0° (*c* 1.2); n.m.r.: δ_H 3.75 (s, 3 H, OCH_3), 4.10 (s, 2 H, OCCH_2Cl), 4.5–5.0 (m, 4 H, CH_2Ph), 5.20 (m, 1 H, C=CH_2), 5.35 (m, 1 H, C=CH_2), 5.80 (m, 1 H, H-4), 5.95 (m, 1 H, –C*H*=CH_2), 7.30 (br.s, 10 H, aromatic H); δ_C 40.5 (ClCH_2), 52.6 (OCH_3), 69.8 (C-4), 102.5 (C-1), 117.5 (=CH_2), 133.7 (–CH=CH_2), 166.6 (*C*=O), and 166.9 (*C*=O).

Anal. Calc. for $C_{26}H_{29}O_8Cl$: C, 61.84; H, 5.79; Cl, 7.02. Found: C, 61.62; H, 5.74; Cl, 6.93.

*Methyl (allyl 2,3-di-*O*-benzyl-β-*D*-galactopyranosid)uronate* (**2**). — A mixture of **11** (49 mg) and thiourea (15 mg) in ethanol (1.5 mL) was heated under reflux for 4 h. After cooling, the mixture was evaporated *in vacuo*. The residue was dissolved

in $CHCl_3$, and the insoluble material was filtered off. The filtrate was concentrated *in vacuo* and the residue was chromatographed on SiO_2 in 3:2 *n*-hexane–EtOAc to give **2** (29 mg, 69.7%) which was identified with the sample already described.

Deallylation of compound **11**. — A mixture of **11** (333 mg), $PdCl_2$ (584 mg), and NaOAc (540 mg) in 90% aqueous AcOH (44 mL) was sonicated overnight under Ar at 30–35° in a ultrasonic bath (27 KHz, 48 W). The insoluble material was filtered off and the filtrate was concentrated *in vacuo*. The residue was extracted with EtOAc. The extract was washed with water, saturated $NaHCO_3$, and saturated NaCl, and dried (Na_2SO_4). After evaporation, the residue was chromatographed on SiO_2 in 9:11 *n*-hexane–EtOAc to give a 3:1 mixture (231 mg) of *methyl 2,3-di-O-benzyl-4-O-chloroacetyl-D-galactopyranuronate* **13** and compound **14**. N.m.r. data of the mixture contained characteristic signals for compound **14**: δ_H 2.17 (s, CH_2COCH_3); δ_C 205.7 (CH_2COCH_3), 102.7 (C-1), and 26.4 (CH_2COCH_3).

2,3-Di-O-benzyl-4,6-O-isopropylidene-D-galactopyranose (**15**). — A mixture of **6** (3.63 g) and *t*-BuOK (16.3 g) in dry DMSO (70 mL) was stirred for 3 h at 60° under Ar. After cooling, the mixture was diluted with water and extracted with ether. The extract was washed with water and saturated NaCl, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was dissolved in 80% aqueous THF (80 mL) and treated with I_2 (4.3 g) followed by pyridine (2.9 mL) for 30 min at room temperature. The mixture was diluted with water and extracted with $CHCl_3$. The extract was washed with aqueous $Na_2S_2O_3$, saturated $NaHCO_3$, and saturated NaCl, dried (Na_2SO_4), and evaporated *in vacuo*. The crude product was chromatographed on SiO_2 in 70:30:1 EtOAc–*n*-hexane–Et_3N to give **15** (3.0 g, 90.9%) as an oil, n.m.r.: δ_H 1.41 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 4.5–5.0 (m, 4 H, CH_2Ph), 5.31 (H-1β), 7.34 (m, 10 H, aromatic H); δ_C 18.4 and 18.6 (CH_3), 29.4 and 29.0 (CH_3), 92.3 and 97.3 (C-1), 98.8 (CMe_2).

Anal. Calc. for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 69.09; H, 7.12.

tert-*Butyldiphenylsilyl 2,3-di-O-benzyl-4,6-O-isopropylidene-β-D-galactopyranoside* (**16**). — A mixture of **15** (2.2 g), *t*-$BuPh_2SiCl$ (4.5 mL), and imidazole (2.5 g) in dry DMF (60 mL) was heated for 7 h at 60° with stirring. After cooling, the mixture was diluted with ether, washed with water and saturated NaCl, and dried (Na_2SO_4). Evaporation *in vacuo* gave crude **16**. A small amount of the pure sample **16** was obtained by chromatography on an SiO_2 column in 85:15:1 *n*-hexane–EtOAc–Et_3N, $[\alpha]_D^{17}$ +25.0° (*c* 0.7); n.m.r.: δ_H 1.13 [s, 9 H, $C(CH_3)_3$], 1.36 [s, 3 H, $C(CH_3)_2$], 1.51 [s, 3 H, $C(CH_3)_2$], 4.56 (d, 1 H, *J* 7.6 Hz, H-1), 7.30 (m, 16 H, aromatic H), 7.74 (m, 4 H, aromatic H); δ_C 19.1 [$C(CH_3)_2$ and CMe_3], 27.0 [$C(CH_3)_3$], 28.8 [$C(CH_3)_2$], 62.3 (C-6), 97.6 (C-1, $^1J_{CH}$ 161.1 Hz), 98.6 (CMe_2).

Anal. Calc. for $C_{39}H_{46}O_6Si$: C, 73.32; H, 7.26. Found: C, 73.13; H, 7.24.

Deisopropylidenation of compound **16**. — The crude **16**, obtained above, was stirred in a mixture of 80% AcOH (40 mL) and THF (4 mL) overnight at room temperature. The mixture was concentrated *in vacuo* and the residue was chromatographed on SiO_2 in 3:2 toluene–EtOAc to give tert-*butyldiphenylsilyl 2,3-di-O-benzyl-β-D-galactopyranoside* **17** (2.6 g, 79.3%) as an oil, $[\alpha]_D^{17}$ +54.9° (*c* 0.8);

n.m.r.: δ_H 1.11 [s, 9 H, –C(CH_3)$_3$], 2.60 (br.s, 2 H, OH), 4.66 (s, 2 H, CH_2Ph), 4.70 (d, 1 H, J 7.6 Hz, H-1), 4.86 (d, 1 H, J 10.8 Hz, CH_2Ph), 5.06 (d, 1 H, J 10.8 Hz, CH_2Ph), 7.29 (m, 16 H, aromatic H), 7.74 (m, 4 H, aromatic H); δ_C 19.1 (*C*Me$_3$), 27.0 [C(*C*H$_3$)$_3$], 62.3 (C-6) and 98.3 (C-1).

*Methyl (*tert*-butyldiphenylsilyl 2,3-di-O-benzyl-4-O-chloroacetyl-β-D-galacto-pyranosid)uronate* (**20**). — Diol **17** (593 mg) was treated with 4,4'-dimethoxytrityl chloride (370 mg) and then with chloroacetic anhydride (330 mg) in dry pyridine (4.5 mL). A similar work-up procedure including hydrolysis catalyzed by benzenesulfonic acid as described above afforded crude product which was chromatographed over SiO_2 (once washed with 70:30:1 hexane–EtOAc–pyridine) in 7:3 *n*-hexane–EtOAc to give *tert*-butyldiphenylsilyl 2,3-di-*O*-benzyl-4-*O*-chloroacetyl β-D-galactopyranoside **18** (554 mg) which was used for the next step without further purification, R_F 0.25 (9:1 toluene–EtOAc); n.m.r.: δ_H 1.12 [s, 9 H, C(CH_3)$_3$], 4.11 (s, 2 H, OCCH_2Cl), 5.33 (br.d, 1 H, J 2.7 Hz, H-4), 7.31 (m, 16 H, aromatic H), 7.73 (m, 4 H, aromatic H); δ_C 19.1 (*C*Me$_3$), 27.0 [C(*C*H$_3$)$_3$], 40.7 (ClCH$_2$), 61.1 (C-6), 98.2 (C-1), and 167.4 (*C*=O).

When crude **18** was chromatographed over SiO_2 in 19:1–9:1 toluene–EtOAc, a 7:3 mixture of **18** and **19** resulted. The presence of the second component, **19**, presumably an isomeric product formed through acyl migration, was deduced from n.m.r. data of the mixture. Compound **19**, R_F 0.31 (9:1 toluene–EtOAc); δ_H 3.80 (s, COCH_2Cl); δ_C 40.5 (CO*C*H$_2$Cl), 98.0 (C-1), and 163 (*C*=O).

Compound **18** (199 mg) was oxidized according to the two step procedure (*C*) described in the case of compound **8**. The intermediate crude aldehyde was purified through a short column (SiO_2) and then treated with Jones reagent in acetone. The oxidation product was taken up into EtOAc and then esterified with ethereal diazomethane. The crude ester was chromatographed on SiO_2 in 19:1 toluene–EtOAc to give **20** (103 mg, 49.7%), $[\alpha]_D^{22}$ +40.2° (*c* 0.5); n.m.r.: δ_H 1.12 [s, 9 H, C(CH_3)$_3$], 3.70 (s, 3 H, OCH_3), 4.14 (s, 2 H, OCCH_2Cl), 5.77 (m, 1 H, H-4), 7.30 (m, 16 H, aromatic H), 7.74 (m, 4 H, aromatic H); δ_C 19.2 (*C*Me$_3$), 27.0 [C(*C*H$_3$)$_3$], 40.7 (ClCH$_2$), 52.3 (O*C*H$_3$), 97.9 (C-1), and 166.6 (*C*=O).

Anal. Calc. for $C_{39}H_{43}O_8SiCl$: C, 66.60; H, 6.16. Found: C, 66.65; H, 6.14.

Desilylation of compound **20**. — In a polyethylene vessel, **20** (70 mg) was stirred with 50% HF-pyridine (0.7 mL) for 1 day at room temperature. The mixture was poured into saturated $NaHCO_3$ solution (10 mL) and extracted with ether–EtOAc (1:1). The extract was washed with saturated $NaHCO_3$ and saturated NaCl, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was chromatographed on SiO_2 in 1:1 toluene–EtOAc to give **13** (43 mg, 93%), n.m.r.: δ_H 3.73 (s, 3 H, OCH_3), 4.05 (s, 2 H, OCCH_2Cl), 5.37 (br.s, 1 H, H-1), 5.88 (m, 1 H, H-4), 7.29 (m, 10 H, aromatic H); δ_C 40.5 (ClCH$_2$), 52.6 (O*C*H$_3$), 92.0 (C-1α), 97.4 (C-1β), 166.5 (*C*=O), and 168.0 (*C*=O).

Conversion of compound **13** *into fluoride* **3**. — To a solution of **13** (43 mg) in dry THF (0.25 mL) was added diethylaminosulfur trifluoride (DAST, 16 μL) with stirring in a dry ice–CCl_4 bath. Then the bath was removed and stirring was con-

tinued for 30 min at room temperature. MeOH (0.2 mL) was added to the mixture, which was then evaporated *in vacuo*. The residue was dissolved in $CHCl_3$, washed with water and saturated NaCl, and dried (Na_2SO_4). After evaporation, the residue was chromatographed on SiO_2 in 13:7 *n*-hexane–EtOAc to give *methyl (2,3-di-O-benzyl-4-O-chloroacetyl-D-galactopyranosyl fluoride)uronate* **3** (37 mg, 85.7%) as a (1:1) mixture of α- and β-anomers, n.m.r.: δ_H 3.76, 3.79 (2 s, total 3 H, OCH_3), 4.05, 4.10 (2 s, total 2 H, $OCCH_2Cl$), 5.82, 5.94 (2 m, total 1 H, H-4), and 7.31 (m, 10 H, aromatic H); δ_C 40.5 ($ClCH_2$), 52.8, 52.9 (2 OCH_3), 105.9 ($^1J_{CF}$ 229.5 Hz, C-1α), and 109.4 ($^1J_{CF}$ 219.7 Hz, C-1β).

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