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Synthesis of the two monomethyl esters of the disaccharide 4-*O*-α-D-galacturonosyl-D-galacturonic acid and of precursors for the preparation of higher oligomers methyl uronated in definite sequences

Didier Magaud [a], Cyrille Grandjean [a], Alain Doutheau [a,*], Daniel Anker [a], Vladimir Shevchik [b], Nicole Cotte-Pattat [b], Janine Robert-Baudouy [b]

[a] *Laboratoire de Chimie Organique, EA 1844, Institut National des Sciences Appliquées, and UMR-CNRS-5622, 20 avenue Albert Einstein, F-69621 Villeurbanne, France*

[b] *Laboratoire de Génétique Moléculaire des Microorganismes et des Interactions Cellulaires, UMR-CNRS-5577, Institut National des Sciences Appliquées, 20 avenue Albert Einstein, F-69621 Villeurbanne, France*

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Abstract

Methyl (α-D-galactopyranosyluronic acid)-(1→4)-D-galactopyranuronate and methyl α-D-galactopyranosyluronate-(1→4)-D-galactopyranuronic acid have been synthesized by coupling methyl (benzyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate (**3**) or benzyl (benzyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate (**4**) with benzyl (phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranosid)uronate and methyl (phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranosid)uronate, respectively, using *N*-iodosuccinimide and trifluoromethanesulphonic acid as promoters, followed by removal of the benzyl groups. The 4′-OH unprotected dimers benzyl (methyl 2,3-di-*O*-benzyl-α-D-galactopyranosyluronate)-(1→4)-(benzyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate and methyl (benzyl 2,3-di-*O*-benzyl-α-D-galactopyranosyluronate)-(1→4)-(benzyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate were prepared from methyl (phenyl 2,3-di-*O*-benzyl-1-thio-4-*O*-trimethylsilyl-β-D-galactopyranosid)uronate and benzyl (phenyl 2,3-di-*O*-benzyl-1-thio-4-*O*-trimethylsilyl-β-D-galactopyranosid)uronate and acceptors **4** or **3**, respectively. These compounds have been designed to serve as precursors for the preparation of higher-membered D-galacturonic acid oligomers methyl esterified in definite positions.

Keywords: Pectins; D-Galacturonic acid esters; Thioglycosides

1. Introduction

Pectins, constituents of plant cell-walls, are mainly composed of a backbone of partially esterified α-(1→4)-linked D-galacturonic acids [1]. Pectins have aroused considerable interest since (a) they possess pronounced gel-forming properties and, thus, are used as thickening agents in the food industry, and (b) their degradation by certain fungi or bacteria causes damage to plants in the field and during storage. It is well recognized that the proportion of methyl galacturonate units in pectins greatly influence both the gel formation [2] and the activity of pectinases produced by phytopathogenic microorganisms [3]. However, no systematic study concerning the im-

* Corresponding author.

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portance of the position of the ester groups for recognition and catalysis by these enzymes has yet been published. Our continuing interest in pectins [4] led us to further investigate this aspect. Consequently, a method was sought that would permit the synthesis of oligomers bearing methyl esters in definite positions for enzyme assays.

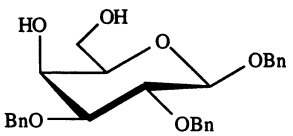
An obvious approach to our target compounds is based on α-(1→4)-glycosylation between two suitably protected and differently esterified galacturonic esters. Nakahara et al. [5] attempted the glycosylation between two D-galacturonic acid methyl esters using Mukaiyama's conditions [6] but did not observe the formation of the expected dimer. The first successful (1→4)-coupling between two D-galacturonic acid esters was reported by Pozsgay using a methyl 1-thioglycoside as the donor [7]. However, no experimental details were published. More recently, Vogel et al. observed the formation of a mixture of three different (1→4)-linked dimers in 45% overall yield [8] from D-galacturonic acid-derived acceptors and donors, using the trityl-cyanoethylidene condensation method [9].

2. Results and discussion

In view of these literature data, we re-examined the coupling between two D-galacturonic acid esters. Attempted condensation of benzyl D-galacturonate derivatives bearing a variety of leaving groups at the anomeric carbon (bromide, trichloroacetimidoyl, pentenyloxy) with acceptor **4** proved to be unsuccessful.

Next we turned our attention to 1-thioglycosides. Since they are sufficiently stable to withstand protecting group manipulations and can readily be activated, 1-thioglycosides have been known for a long time to be powerful glycosyl donors (for a recent review see [10]). We therefore decided to examine the glycosylation between phenyl 1-thioglycoside derivatives of D-galacturonic esters as donors and 4-OH unprotected D-galacturonic esters as acceptors promoted by *N*-iodosuccinimide and trifluoromethanesulfonic acid [11,12]. We now describe the preparation of the two monomethyl esters of α-(1→4)-D-galacturonic acid dimer and the two *O*-protected α-(1→4)-linked dimeric acceptors designed for the further preparation of higher oligomers methyl esterified in definite positions.

Preparation of glycosyl donors and acceptors.—We first focused on the preparation of the two monomethyl esterified D-galacturonic acid dimers. To prepare the required donors and acceptors we decided to use D-galactose as starting material and to carry out the oxidation of the C-6 hydroxyl group into acid later in the sequence[1]. Known methyl (benzyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate (**3**) [14] and the corresponding benzyl uronate **4** were obtained from the sodium salt of benzyl 2,3-di-*O*-benzyl-β-D-galactopyranosiduronic acid (**2**). The latter compound was prepared from β-D-galactose pentaacetate by the nine-step sequence of Turvey and Williams [15] except that we found it easier to perform the oxidation of the intermediate benzyl 2,3-di-*O*-benzyl-β-D-galactopyranoside (**1**) using 4-methoxy-2,2,6,6-tetramethyl-1-piperidinyloxy (4-MeO-TEMPO) [16] according to Anelli's procedure[2] [17].



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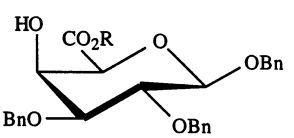


2 R = H
3 R = Me
4 R = Bn

Benzyl (phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranosid)uronate (**11**) and methyl (phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranosid)uronate (**12**) were prepared as follows. Phenyl 1-thio-β-D-galactopyranoside (**5**)[3] was first transformed (TrCl, Pyr., DMAP) into the corresponding 6-*O*-trityl derivative **6** followed by benzylation (NaH, BnBr, DMF) to afford phenyl 2,3,4-tri-*O*-benzyl-1-thio-6-*O*-trityl-β-D-galactopyranoside (**7**). Selective

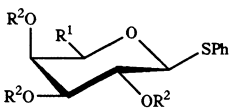
[1] Similar strategies were adopted by several authors. See for example [13].

[2] We used $Ca(OCl)_2$, more stable on storage, instead of NaOCl which is advised by Anelli et al. [17].

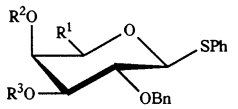
[3] This compound was obtained by Zemplén deacetylation of the corresponding tetraacetate prepared according to Ref. [18].

removal of the trityl group (Amberlyst 15 H^+, MeOH) gave rise to phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranoside (**8**) in 70% overall yield[4]. Using Nilsson's conditions [20] (PDC, *tert*-BuOH, Ac_2O), compound **8** was directly transformed into *tert*-butyl (phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranosid)uronate (**9**) in 70% yield. This compound was then converted (TFA 20%, CH_2Cl_2) into the corresponding acid **10** which was not purified but directly esterified (BnBr, phase transfer conditions) to give **11** in 68% overall yield. The *tert*-butyl ester **9** was also directly transformed (anhyd HCl, MeOH) into the corresponding methyl ester **12** in 96% yield. The use of acidic conditions allowed us to avoid a base-promoted β-elimination resulting in the formation of a double bond between C-4 and C-5.

We thus obtained the two donors required for the preparation of the two monomethyl esterified D-galacturonic acid dimers. To achieve an access to higher oligomers, a phenyl 1-thio-galactopyranosiduronate monomer bearing a selectively removable protecting group at the C-4 position was required. From **5**, we first prepared known phenyl 2-*O*-benzyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside (**13**) using the Fernandez-Mayoralas et al. procedure [21]. Performing the benzylation in dimethylformamide (instead of THF) and using Amberlyst H^+ (instead of CSA) as acidic catalyst for removing the methoxy–isopropyl protective group, with careful monitoring of the reaction by TLC, the yield was improved from 59 to 69%. Compound **13** was then oxidized in 61% yield into *tert*-butyl (phenyl 2-*O*-benzyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranosid)uronate (**14**) in the usual conditions. Treatment of **14** in anhydrous methanolic hydrochloric acid solution gave methyl (phenyl 2-*O*-benzyl-1-thio-β-D-galactopyranosid)uronate (**15**) quantitatively. The selective benzylation of the 3-OH group could be achieved using the dibutyltin oxide activation [22]. As observed by Vogel et al. [23] with closely related galacturonic acid esters, a mixture of methyl (phenyl 2,3-di-*O*-benzyl-1-thio-β-D-galactopyranosid)uronate (**16**) and benzyl (phenyl 2,3-di-*O*-benzyl-1-thio-β-D-galactopyranosid)uronate (**17**) was formed in 38 and 35% yields, respectively. The formation of this mixture was particularly advantageous in our case since the two esters were both needed and proved to be readily separable by silica gel column chromatography. Next, **16** and **17** were quantitatively transformed (TMSOTf, 2,6-lutidine, CH_2Cl_2, −10 °C) into the corresponding 4-*O*-trimethylsilyl derivatives **18** and **19**.



	R^1	R^2
5	CH_2OH	H
6	CH_2OTr	H
7	CH_2OTr	Bn
8	CH_2OH	Bn
9	CO_2Bu^t	Bn
10	CO_2H	Bn
11	CO_2Bn	Bn
12	CO_2Me	Bn



	R^1	R^2	R^3
13	CH_2OH	$-CMe_2-$	
14	CO_2Bu^t	$-CMe_2-$	
15	CO_2Me	H	H
16	CO_2Me	H	Bn
17	CO_2Bn	H	Bn
18	CO_2Me	TMS	Bn
19	CO_2Bn	TMS	Bn

Preparation of dimeric D-*galacturonic acid derivatives.*—The glycosylations were performed at −60 °C using a mixture of diethyl ether and methylene chloride as solvent and *N*-iodosuccinimide and trifluoromethanesulfonic acid as promoters. The results are summarized in Table 1. Reaction of the thioglycoside donors **11** and **12** with the glycosyl acceptors **3** and **4**, respectively, gave rise stereoselectively to the corresponding dimers **20** and **21** in good yields (Table 1, entries 1 and 2). Coupling between **18** and **4** led to dimer **22** after in situ removal of the trimethylsilyl group (entry 3). Similarly, coupling between **19** and **3** gave rise to 4′-OH unprotected dimer **23** (entry 4).

Hydrogenolysis of **20** and **21α** using $Pd(OH)_2/C$ as catalyst [24] afforded the two monomethyl esters of D-galacturonic acid disaccharide **24** and **25** in excellent yields and high purity[5]. The ^1H NMR data of dimer **24**

[4] This compound had been previously obtained by a different route. See Ref. [19].

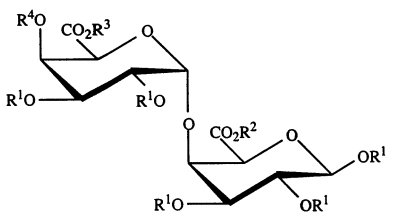
[5] NMR spectra of **24** and **25** exhibited unusually broad lines that could be resolved after treatment with Dowex 50 H^+ as suggested earlier for galacturonic acid containing oligosaccharides [7].

Table 1
Results of glycosylation reactions

Entry	Donor	Acceptor	Time (h)	Product	Yield (%)
1	**11**	**3**	2.5	**20**[a]	88
2	**12**	**4**	2.5	**21** $\alpha/\beta = 97/3$[b]	91
3	**18**	**4**	1.5	**22**[a]	68
4	**19**	**3**	1.5	**23**[a]	70

[a] The β anomer was not detectable either by TLC of the crude glycosylation product or in the NMR spectra of the purified α anomer.

[b] The two anomeric isomers were separated.



	R^1	R^2	R^3	R^4
20	Bn	Me	Bn	Bn
21α	Bn	Bn	Me	Bn
22	Bn	Bn	Me	H
23	Bn	Me	Bn	H
24β	H	Me	H	H
25β	H	H	Me	H

are in full agreement with selected data reported for this compound isolated from pectin degradation [25].

In summary, the direct coupling between two D-galacturonic acid esters was achieved in good yield using phenyl β-1-thioglycosides as donors. This method allowed the two selectively monomethyl esterified α-(1→4)-linked D-galacturonic acid dimers and two 4′-OH unprotected dimeric acceptors to be prepared. The latter compounds would permit the synthesis of trimers and further higher oligomers of D-galacturonic acid methyl esterified in definite positions.

3. Experimental

General methods.—Aliquat 336 (tricaprylmethylammonium chloride) and TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy, free radical) were supplied by Aldrich Europ. Solvents were dried as follows: MeOH distilled from magnesium methoxide; pyridine and Et_2O from KOH; CH_2Cl_2 from P_2O_5 *tert*-butanol distilled and DMF distilled and stored over 4 Å molecular sieves. Reaction mixtures were magnetically stirred. The reactions were monitored by TLC on Silica Gel 60 F_{254} (E. Merck) and detection was carried out by UV examination and charring with a 5% phosphomolybdic acid solution in EtOH containing 10% of H_2SO_4. Column chromatography was performed on silica gel (Kieselgel 60, 0.04–0.06 mm, E. Merck) using the following solvent systems (v/v): (A_1) 3:1, (A_2) 1:1, and (A_3) 1:2 pentane–Et_2O; (B) Et_2O; (C_1) 4:1, (C_2) 3:1 pentane–acetone; (D) 2:1 pentane–EtOAc; (E) 6:1 CH_2Cl_2–MeOH;(F_1) 60:1, (F_2) 30:1 CH_2Cl_2–Et_2O; (G_1) 10:10:1, (G_2) 10:10:2, (G_3) 10:10:3 CH_2Cl_2–pentane–EtOAc; (H) 5:2:2 2-propanol–H_2O–AcOH. Organic solutions were dried on $MgSO_4$. Melting points were determined with a Kofler hot-stage melting-point apparatus. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. IR spectra were recorded on a Perkin–Elmer 1310 spectrometer, and ^1H NMR and ^{13}C NMR spectra were recorded, in $CDCl_3$ except when otherwise stated, with either a Bruker AM 200 or 300 spectrometer at room temperature. Chemical shifts are given in ppm downfield from internal Me_4Si. Elemental analyses were performed by the 'Service Central de Microanalyses du CNRS' Solaize (France).

*Methyl (benzyl 2,3-di-*O*-benzyl-β-*D*-galactopyranosid)uronate* (**3**).—To a solution of **1** [15] (1 g, 2.2 mmol) in CH_2Cl_2 (2.8 mL) were successively added, at 0 °C, a 0.016 M solution of 4-methoxy TEMPO [17] in CH_2Cl_2 (1.4 mL, 0.022 mmol), then 1.4 mL (0.11 mmol) of

a 0.08 M solution of Aliquat 336 in CH_2Cl_2, and finally 0.45 mL (0.22 mmol) of a 0.5 M aq solution of KBr. To this mixture were then added a cooled (0 °C) solution of calcium hypochlorite (0.796 g, 5.56 mmol) and of $NaHCO_3$ (0.796 g, 9.47 mmol) in 16 mL of water. After 5 min, the reaction was complete (TLC, solvent C_2 and E) whereupon $NaHCO_3$ (1.4 g) was added in order to adjust the pH to 7–8. Solvents were evaporated under reduced pressure and DMF (10 mL) was added to the residue. To this suspension was added 0.62 mL (9.9 mmol) of methyl iodide and the reaction mixture was stirred and heated at 60 °C. The reaction was complete after 2 h (TLC, solvent C_2). Solvent was evaporated under reduced pressure and water (10 mL) and Et_2O (50 mL) were added to the residue. After filtration through celite the organic phase was washed with water (2×10 mL), dried, and concentrated. Column chromatography (solvent C_1) gave **3** (0.640 g, 60%) as a white solid; mp 110–111 °C (EtOH–water), lit. 111–112 °C [14].

Benzyl (benzyl 2,3-di-O-*benzyl-β*-D-*galactopyranosid)uronate* (**4**).—Prepared following the same procedure as for **3** except that methyl iodide was replaced by benzyl bromide (1.18 mL, 9.9 mmol; 60 °C, 2 h), resulting in **4** (0.788 g, 64%) as a white solid; mp 128–129 °C (cyclohexane); $[\alpha]_D^{25} - 23°$ (c 0.7, $CHCl_3$); ^{1}H NMR: δ 7.37–7.25 (m, 20 H, H aromatic); 5.28 (s, 2 H, CH_2Ph); 5.04, 4.91 (2d, 2 H, J 11.0 Hz, CH_2Ph); 4.74–4.64 (m, 4 H, 2 CH_2Ph); 4.46 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1); 4.31 (broad d, 1 H, H-4); 4.07 (broad s, 1 H, H-5); 3.58 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-2), 3.52 (dd, 1 H, $J_{3,4}$ 3.4 Hz, H-3); 2. 56 (s, 1 H, OH); ^{13}C NMR: δ 167.6 (C-6); 138.3, 137.6, 137.2, 135.3, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6 (C aromatic); 102.1 (C-1); 79.8, 78.2, 73.6, 67.9 (C-2,3,4,5); 75.2, 72.5, 71.0, 67.1 (4 CH$_2$Ph). Anal. Calcd for $C_{34}H_{34}O_7$: C, 73.60; H, 6.10. Found: C, 73.78; H, 6.11.

Phenyl 2,3,4-tri-O-*benzyl-1-thio-β*-D-*galactopyranoside* (**8**).—To a solution of **5** [17] (8.48 g, 31.17 mmol) in pyridine (180 mL), were added trityl chloride (14.94 g, 53.60 mmol) and a catalytic amount of 4-dimethylaminopyridine (DMAP). The reaction mixture was stirred at room temperature for 3 days. The reaction mixture was concentrated under reduced pressure and Et_2O (200 mL) was added to the residue. The solution was washed with a saturated aq $NaHCO_3$ solution (2×30 mL), dried and concentrated under reduced pressure to give a solid residue which was dried (P_2O_5) and then dissolved in dry DMF (90 mL). The resulting solution of crude **6** was added to NaH (4.49 g of a 60% suspension in oil, ca. 110 mmol, washed thrice with pentane) in dry DMF (20 mL). A catalytic amount of imidazole was added to the reaction mixture stirred at 20 °C. After the evolution of H_2 ceased, benzyl bromide (13.3 mL, 112.25 mmol) and a catalytic amount of Bu_4NI were added. After 4 h the starting material had disappeared (TLC, solvent A_2). Solvent was evaporated under reduced pressure and Et_2O (200 mL) was added to the residue. Excess NaH was destroyed by careful addition of water (50 mL). The mixture was washed with aq HCl 3 N (2×20 mL) dried, concentrated and the residue was dissolved in 1:1 MeOH–$CHCl_3$ (200 mL). To this solution Amberlyst 15 H^+ (15 g) was added and the reaction mixture was gently stirred (rotatory evaporator) and heated at 60 °C. After 1 h the reaction was complete (TLC, solvent A_2). The resin was removed by filtration and washed with MeOH (3×30 mL). The filtrate was concentrated under reduced pressure in the presence of a small amount of triethylamine at 40 °C giving a residue that was dissolved in Et_2O (100 mL). To this solution water (50 mL) was added and the organic phase was separated, washed with water (3×10 mL) dried and concentrated under reduced pressure. Column chromatography of the crude product (solvent A_2 then solvent A_3) gave **8** (11.8 g, 70% from **5**) as a white solid. An analytical sample was recrystallized from cyclohexane: mp 94–95 °C; lit. 94–95 °C [19].

tert-*Butyl (phenyl 2,3,4-tri*-O-*benzyl-1-thio-β*-D-*galactopyranosid)uronate* (**9**).—To a stirred solution of **8** (1.1 g, 2.03 mmol) in dry CH_2Cl_2 (26 mL) were added pyridinium dichromate (PDC) (1.5 g, 4.1 mmol), acetic anhydride (1.95 mL, 20.6 mmol) and *tert*-butanol (3.8 mL, 40.3 mmol). The starting material had disappeared after 4 h of stirring (TLC

solvent A_2) and the mixture was applied on the top of a silica gel column (200 g) in Et_2O, with a 5-cm layer of Et_2O on the top of the gel. The chromium compounds precipitated in the presence of Et_2O and after 15 min the product was eluted with Et_2O. The crude product obtained after concentration of Et_2O solution was chromatographed on silica gel (solvent A_1) to give **9** (0.870 g, 70%) as a pale yellow oil; $[\alpha]_D^{25}$ +20° (*c* 1.5, $CHCl_3$); ^1H NMR: δ 7.74 – 7.70 (m, 2 H, H aromatic); 7.4 – 7.15 (m, 18 H, H aromatic); 4.96–4.63 (m, 6 H, 3 CH_2Ph); 4.57 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1); 4.29 (broad s, 1 H, H-4); 3.95 (broad s, 1 H, H-5); 3.85 (pt, 1 H, H-2); 3.63 (dd, 1 H, $J_{2,3}$ 9.2, $J_{3,4}$ 2.7 Hz, H-3); 1.46 (s, 9 H, 3 CH_3, *tert*-Bu); ^{13}C NMR: δ 166.9 (C-6); 138.4, 138.2, 138.0, 133.0, 133.1, 128.7, 128.4, 128.0, 127.7, 127.5, 127.3 (C aromatic); 87.0 (C-1); 83.5, 77.3, 76.4, 75.6 (C-2,3,4,5); 82.4 ($C(CH_3)_3$); 75.6, 74.5, 72.7 (3 CH_2Ph); 28.0 (3 CH_3, *tert*-Bu). Anal. Calcd for $C_{37}H_{40}O_6S$: C, 72.55; H, 6.53. Found: C, 72.34; H, 6.34.

Benzyl (phenyl 2,3,4-tri-O-*benzyl-1-thio-β*-D-*galactopyranosid)uronate* (**11**).—To a solution of **9** (6.35 g, 10.37 mmol) in CH_2Cl_2 (19.2 mL) was added trifluoroacetic acid (4.8 mL, 62.8 mmol). After 1 h at ambient temperature, the starting material had disappeared (TLC, solvent A_2) and a more polar product was formed (TLC, solvent *E*). The reaction mixture was concentrated under reduced pressure at 30 °C to give a residue that was dissolved in CH_2Cl_2 (90 mL). To this solution were added successively Aliquat 336 (2.46 g), sat aq $NaHCO_3$ sol (45 mL), a catalytic amount of Bu_4NI and benzyl bromide (1.5 mL, 12.61 mmol). After stirring overnight at room temperature, the intermediate had disappeared (TLC, solvent *E*) and a less polar product was formed (TLC, solvent A_2). The reaction mixture was diluted with CH_2Cl_2 (50 mL) and the organic phase was washed with aq 1 N HCl (2×20 mL), dried, and concentrated under reduced pressure. The crude product was chromatographed (solvent A_1) to give **11** (4.56 g, 68%) as a white solid. An analytical sample was recrystallized from cyclohexane; mp 83–84 °C; $[\alpha]_D^{25}$ +6.7° (*c* 1.07, $CHCl_3$); ^1H NMR: δ 7.68–7.64 (m, 2 H, H aromatic); 7.37–7.11 (m, 23 H, H aromatic); 5.19–4.51 (m, 8 H, 4 CH_2Ph); 4.59 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1); 4.30 (broad d, 1 H, H-4); 4.09 (broad s, 1 H, H-5); 3.92 (pt, 1 H, H-2); 3.63 (dd, 1 H, $J_{2,3}$ 9.2, $J_{3,4}$ 2.7 Hz, H-3). Anal. Calcd for $C_{40}H_{38}O_6S$: C, 74.30; H, 5.88. Found: C, 73.96; H, 5.92.

Methyl (phenyl 2,3,4-tri-O-*benzyl-1-thio-β*-D-*galactopyranosid)uronate* (**12**).—To a stirred solution of **9** (1 g, 1.63 mmol) in dry MeOH (20 mL), cooled to 0 °C, was added dropwise, acetyl chloride (5 mL). After a few minutes, the reaction mixture was allowed to warm to room temperature. After 2.5 h, the reaction was complete (TLC, solvent A_2). The solvent was evaporated under reduced pressure at 40 °C. The white solid obtained was recrystallized from cyclohexane to give **12** (0.89 g, 96%); mp 98–100 °C then solidification; second mp at 110–112 °C; $[\alpha]_D^{25}$ +9.2° (*c* 0.9, $CHCl_3$); ^1H NMR: δ 7.73–7.78 (m, 2 H, H aromatic); 7.47–7.24 (m, 18 H, H aromatic); 4.97–4.78 (m, 6 H, 3CH_2Ph); 4.66 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1); 4.37 (broad s, 1 H, H-4); 4.1 (broad s, 1 H, H-5); 4.0 (pt, 1 H, H-2); 3.74 (s, 3 H, OCH_3); 3.69 (dd, 1 H, $J_{2,3}$ 9.2, $J_{3,4}$ 2.7 Hz, H-3); ^{13}C NMR: δ 168.4 (C-6); 138.3, 138.2, 137.9, 133.5, 132.4, 128.8, 128.5, 128.3, 128.1, 127.8, 127.7, 127.5, (C aromatic); 87.7 (C-1); 83.3, 77.2, 76.6, 75.1 (C-2,3,4,5); 75.6, 74.4, 72.8 (3 CH_2Ph); 52.4 (OCH_3). Anal. Calcd for $C_{34}H_{34}O_6S$: C, 71.58; H, 5.96. Found: C, 71.27; H, 5.86.

tert-*Butyl (phenyl 2*-O-*benzyl-3,4*-O-*isopropylidene-1-thio-β*-D-*galactopyranosid)uronate* (**14**).—To a solution of **13** [22] (6.12 g, 15.2 mmol) in CH_2Cl_2 (15 mL) were successively added acetic anhydride (14.75 mL, 156.3 mmol), *tert*-butanol (21.25 mL, 222.2 mmol) and PDC (11.9 g, 31.15 mmol). The reaction mixture was stirred at room temperature in the dark. After 3 h the reaction was complete (TLC, solvent A_2) and the mixture was applied on the top of a silica gel column (240 g) in EtOAc, with a 5-cm layer of EtOAc on the top of the gel. The chromium compounds precipitated in the presence of EtOAc and after 15 min the product was eluted with EtOAc. After solvent evaporation under reduced pressure at 35 °C the residue was diluted in 3:1 Et_2O–CH_2Cl_2 (500 mL) and the resulting solution washed with saturated aq $NaHCO_3$ (50 mL) then H_2O (50 mL), HCl

3 N (50 mL), H_2O (50 mL), saturated aq $NaHCO_3$ (50 mL), dried and concentrated. The colourless solid thus obtained was washed with pentane (10 mL) and dried (P_2O_5) to give **14** (4.37 g, 61%); mp 132–133 °C (cyclohexane/pentane); $[\alpha]_D^{25}$ −40.2° (*c* 1.2, $CHCl_3$); ^1H NMR: δ 7.67–7.60 (m, 2 H, H aromatic); 7.43–7.25 (m, 8 H, H aromatic); 4.78, 4.64 (2d, 2 H, *J* 11.3 Hz, 2 CH_2Ph); 4.63 (d, 1 H, $J_{1,2}$ 8.7 Hz, H-1); 4.48 (dd, 1 H, $J_{3,4}$ 5.8, $J_{4,5}$ 2.4 Hz, H-4); 4.30 (pt, 1 H, $J_{2,3}$ 6.0, H-3); 4.24 (d, 1 H, H-5); 3.58 (broad dd, 1 H, H-2); 1.50 (s, 9 H, 3 CH_3, *tert*-Bu); 1.39, 1.34 (2 s, 2 × 3 H, 2 CH_3). Anal. Calcd for $C_{26}H_{32}O_6S$: C, 66.10 H; 6.78; S, 6.78. Found: C, 65.90; H, 6.65; S, 6.66.

*Methyl (phenyl 2-*O*-benzyl-1-thio-β-*D*-galactopyranosid)uronate* (**15**).—To a stirred solution of **14** (3.34 g, 7.08 mmol) in dry MeOH (67 mL) at 0 °C was added, dropwise, acetyl chloride (16.7 mL, 234 mmol). The reaction mixture was then allowed to reach ambient temperature. After 2.5 h the reaction was complete (TLC, solvent *B*) and the volatiles were evaporated under reduced pressure. Crystallization of the residue from cyclohexane afforded **15** (2.7 g, 98%) as a white solid; mp 137–138 °C; $[\alpha]_D^{25}$ −24.5° (*c* 1.06, $CHCl_3$); ^1H NMR ($CDCl_3 + D_2O$): δ 7.77–7.72 (m, 2 H, H aromatic); 7.52–7.37 (m, 8 H, H aromatic); 4.96, 4.70 (2d, 2 H, *J* 11.3 Hz, 2 CH_2Ph); 4.61 (d, 1 H, $J_{1,2}$ 9.2 Hz, H-1); 4.30 (dd, 1 H, $J_{3,4}$ 3.0, $J_{4,5}$ 1.2 Hz, H-4); 4.10 (d, 1 H, H-5); 3.83 (s, 3 H, OCH_3); 3.71 (dd, 1 H, $J_{2,3}$ 8.7 Hz, H-3); 3.63 (pt, 1 H, H-2). Anal. Calcd for $C_{20}H_{22}O_6S$: C, 61.52; H, 5.68; S, 8.21. Found: C, 61.56; H, 5.67; S, 8.42.

*Methyl (phenyl 2,3-di-*O*-benzyl-1-thio-β-*D*-galactopyranosid)uronate* (**16**) *and benzyl (phenyl 2,3-di-*O*-benzyl-1-thio-β-*D*-galactopyranosid)uronate* (**17**).—A mixture of **15** (1.6 g, 4.1 mmol), Bu_2SnO (1.18 g, 4.74 mmol), and toluene (40 mL) was stirred under reflux using a Dean–Stark separator between the reaction flask and the condenser. When about the stoichiometric amount of water had been distilled, 4 Å beads molecular sieves were added in the receptor of the Dean–Stark separator and heating was continued for 1 h. The reaction mixture was cooled to 60 °C and treated with Bu_4NI (1.75 g, 4.74 mmol) and benzyl bromide (3.35 mL, 28.20 mmol). The mixture had been stirred at this temperature for an additional period of 3 h. The methyl ester was first formed (R_f 0.31) and then, gradually, the benzyl ester (R_f 0.66) (solvent A_3). The reaction mixture was concentrated under reduced pressure at 40 °C. A solution of the residue in CH_2Cl_2 (100 mL) was sequentially extracted with water (20 mL), an aq solution of sodium metabisulfite (20 mL) and water (20 mL). The organic phase was dried, concentrated and the residue chromatographed (solvent G_1 then G_2 then G_3). Compound **17** (0.8 g, 35%) was first eluted and then **16** (0.75 g, 38%) which were both crystallized in cyclohexane. Compound **17**; mp 154–155 °C; $[\alpha]_D^{25}$ −18.8° (*c* 1.45, $CHCl_3$); ^1H NMR ($CDCl_3 + D_2O$): δ 7.67–7.62 (m, 2 H, H aromatic); 7.37–7.23 (m, 18 H, H aromatic); 5.26 (s, 2 H, CH_2Ph); 4.87–4.63 (m, 4 H, 2CH_2Ph); 4.57 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1); 4.39 (broad d, 1 H, H-4); 4.07 (broad s, 1 H, H-5); 3.74 (pt, 1 H, H-2); 3.61 (dd, 1 H, $J_{2,3}$ 8.9, $J_{3,4}$ 3.0 Hz, H-3). Anal. Calcd for $C_{33}H_{32}O_6S$: C, 71.22; H, 5.76; S, 5.76. Found: C, 70.93; H, 5.80; S, 5.55. Compound **16**; mp 128–130 °C; $[\alpha]_D^{25}$ −14.8° (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3 + D_2O$): δ 7.66–7.61 (m, 2 H, H aromatic); 7.38–7.25 (m, 13 H, H aromatic); 4.87–4.64 (m, 4 H, 2 CH_2Ph); 4.59 (d, 1 H, $J_{1,2}$ 9.4 Hz, H-1); 4.39 (broad t, 1 H, H-4); 4.07 (d, 1 H, $J_{4,5}$ 1.1 Hz, H-5); 3.83 (s, 3 H, OCH_3); 3.75 (pst, 1 H, H-2); 3.63 (dd, 1 H, $J_{2,3}$ 8.9, $J_{3,4}$ 3.1 Hz, H-3). Anal. Calcd for $C_{27}H_{28}O_6S$: C, 65.50; H, 5.83; S, 6.67. Found: C, 66.95; H, 6.02; S, 6.92.

*Methyl (phenyl 2,3-di-*O*-benzyl-1-thio-4-*O*-trimethylsilyl-β-*D*-galactopyranosid)uronate* (**18**).—A stirred solution of **16** (0.5 g, 1.04 mmol) in dry CH_2Cl_2 (1 mL), was treated at −10 °C with trimethylsilyl triflate (280 μL, 1.82 mmol) and 2,6-lutidine (305 μL, 2.6 mmol). After 5 min the reaction was complete (TLC, solvent A_3). The reaction mixture was diluted with Et_2O (10 mL) washed with aq $NaHCO_3$ (2 mL) dried and concentrated to give **18** as a syrup (0.574 g, 100%); $[\alpha]_D^{25}$ −3.3° (*c* 0.8, $CHCl_3$); ^1H NMR: δ 7.72–7.68 (m, 2 H, H aromatic); 7.42–7.28 (m, 13 H, H aromatic); 4.81–4.71 (m, 4 H, 2 CH_2Ph); 4.62 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1); 4.49 (broad d, 1 H, H-4); 4.08 (broad s, 1 H, H-5); 3.85 (broad

pst, 1 H, H-2); 3.82 (s, 3 H, OCH_3); 3.51 (dd, 1 H, $J_{2,3}$ 9.2, $J_{3,4}$ 2.6 Hz, H-3); 0.10 (s, 9 H, 3 CH_3Si). The compound was not stable enough to obtain satisfactory elemental analysis.

Benzyl (phenyl 2,3-di-O-*benzyl-1-thio-4*-O-*trimethylsilyl-β*-D-*galactopyranosid)uronate* (**19**).—A stirred solution of **17** (0.5 g, 0.89 mmol) in dry CH_2Cl_2 (1 mL) was treated at −10 °C with trimethylsilyl triflate (245 μL, 1.57 mmol) and 2,6-lutidine (262 μL, 2.26 mmol). After 10 min the reaction was complete (TLC, solvent A_3). The reaction mixture was diluted with Et_2O (10 mL) washed with aq saturated $NaHCO_3$ (2 mL), dried and concentrated giving **19** as a syrup (0.564 g, 100%); $[\alpha]_D^{25}$ −1.6° (*c* 0.9, $CHCl_3$); ^{1}H NMR: δ 7.72–7.68 (m, 2 H, H aromatic); 7.40–7.20 (m, 18 H, H aromatic); 5.24 (s, 2 H, C*H*$_2$Ph ester); 4.83–4.67 (m, 4 H, 2 C*H*$_2$Ph); 4.60 (d, 1 H, $J_{1,2}$ 9.5 Hz, H-1); 4.49 (broad d, 1 H, H-4); 4.09 (broad s, 1 H, H-5); 3.81 (pst, 1 H, H-2); 3.51 (dd, 1 H, $J_{2,3}$ 9.2, $J_{3,4}$ 2.6 Hz, H-3); 0.03 (s, 9 H, 3 CH_3Si). The compound was not stable enough to obtain satisfactory elemental analysis.

Methyl (benzyl 2,3,4-tri-O-*benzyl-α*-D-*galactopyranosyluronate)-(1→4)-(benzyl 2,3-di*-O-*benzyl-β*-D-*galactopyranosid)uronate* (**20**).—Compounds **11** (0.387 g, 0.6 mmol) and **3** (0.239 g, 0.5 mmol) were dried (vacuum dessicator; P_2O_5; 0.1 mmHg) for 24 h and then dissolved freshly distilled (P_2O_5) CH_2Cl_2 (4 mL). Under dry nitrogen, to this solution were added *N*-iodosuccinimide (NIS) (0.15 g, 0.66 mmol) (crystallized from dioxane–CCl_4 and dried with P_2O_5) and dried (300 °C, 1 h, 0.1 mmHg) 4 Å powder molecular sieves (0.9 g) and the reaction mixture was diluted with freshly distilled ($LiAlH_4$) Et_2O (8 mL). To this cooled (−60 °C) stirred solution was added (syringe) 200 μL (0.06 mmol) of a solution of 0.03 mL of TfOH in of CH_2Cl_2 (1 mL). The temperature of the solution was maintained below −55 °C. After 2.5 h, the donor had disappeared (TLC, solvent F_2), and the reaction mixture was poured into a saturated aq $NaHCO_3$ solution (50 mL) and Et_2O (100 mL). A small amount of $Na_2S_2O_5$ was added until decoloration. After extraction with Et_2O (3 × 50 mL), the organic layers were pooled and dried. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (solvent F_1 then F_2) to give **20** (0.448 g, 88%) as a white solid: mp 100 °C (MeOH); $[\alpha]_D^{25}$ +26.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR: δ 7.42–7.12 (m, 35 H, H aromatic); 5.23 (d, 1 H, $J_{1',2'}$ 3 Hz, H-1′); 5.09–4.40 (m, 14 H, 7C*H*$_2$Ph); 4.97 (d, 1 H, $J_{4',5'}$ 1.1 Hz, H-5′); 4.50 (broad s, 1 H, H-4); 4.44 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1); 4.30 (broad pst, 1 H, H4′); 4.10 (dd, 1 H, $J_{2',3'}$ 9.9 Hz, H-2′); 4.04 (dd, 1 H, $J_{3',4'}$ 2.6 Hz, H-3′); 3.94 (broad s, 1 H, H-5); 3.70 (dd, 1 H, $J_{2,3}$ 9.9 Hz, H-2); 3.55 (s, 3 H, OCH_3); 3.55 (dd, 1 H, $J_{3,4}$ 2.6 Hz, H-3); ^{13}C NMR: δ 168.9 (C-6); 168.2 (C-6′); 138.7, 138.6, 138.5, 138.0, 137.5, 135.3, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 127.5, 127.4, 127.3 (C aromatic); 102.8 (C-1); 99.8 (C-1′); 79.6, 78.3, 77.9, 76.5, 75.3, 74.7, 73.6, 71.6 (C-2,3,4,5,2′,3′,4′,5′); 75.0, 74.5, 73.0, 72.8, 72.1, 71.3, 66.7 (7 *C*H$_2$Ph); 52.3 (OCH_3). Anal. Calcd for $C_{62}H_{62}O_{13}$ (0.5 H_2O): C, 72.72; H, 6.15. Found: C, 72.70; H, 6.16.

Benzyl (methyl 2,3,4-tri-O-*benzyl-α*-D-*galactopyranosyluronate)-(1→4)-(benzyl 2,3-di*-O-*benzyl-β*-D-*galactopyranosid)uronate* (**21α**) *and benzyl (methyl 2,3,4-tri*-O-*benzyl-β*-D-*galactopyranosyluronate)-(1→4)-(benzyl 2,3-di*-O-*benzyl-β*-D-*galactopyranosid)uronate* (**21β**).—These compounds were prepared following the same procedure as for **20** from donor **12** (0.561 g, 0.984 mmol) and acceptor **4** (0.544 g, 0.982 mmol) using 0.272 g (1.21 mmol) of NIS, 6 mL of CH_2Cl_2, 12 mL of Et_2O, 1.3 g of 4 Å powder molecular sieves and 0.3 mL (0.1 mmol) of a solution of 0.03 mL of TfOH in CH_2Cl_2 (1 mL). The reaction was complete after 2.5 h. The crude reaction mixture was purified by two silica gel chromatographies (solvent F_2 then A_2). During the second chromatography, we first eluted **21α** (0.884 g, 88%) as a syrup and then **21β** (0.030 g, 3%) as a syrup. **21α**; $[\alpha]_D^{25}$ +36.2° (*c* 0.8, $CHCl_3$); ^{1}H NMR: δ 7.40–7.14 (m, 35 H, H aromatic); 5.25 (d, 1 H, $J_{1',2'}$ 3 Hz, H-1′); 5.05–4.50 (m, 14 H, 7 C*H*$_2$Ph); 4.92 (d, 1 H, $J_{4',5'}$ 1.5 Hz, H-5′); 4.48 (broad s, 1 H, H-4); 4.43 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1); 4.28 (broad pt, 1 H, H-4′); 4.12 (dd, 1 H, $J_{2',3'}$ 10.2 Hz, H-2′); 4.06 (dd, 1 H, $J_{3',4'}$ 2.4 Hz, H-3′); 3.94 (broad s, 1 H, H-5); 3.72 (dd, 1 H, $J_{2,3}$ 9.9 Hz, H-2);

3.42 (dd, 1 H, $J_{3,4}$ 3 Hz, H-3); 3.35 (s, 3 H, OCH_3); ^{13}C NMR: δ 169.3 (C-6); 167.1 (C-6′); 138.5, 138.4, 138.3, 137.9, 137.2, 135.1; 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.4, 127.3, 127.2 (C aromatic); 102.5 (C-1); 99.6 (C-1′); 79.9, 77.9, 77.8, 76.3, 75.2, 74.9, 73.4, 71.5 (C-2,3,4,5,2′,3′,4′,5′); 74.9, 74.5, 72.9, 72.7, 72.2, 71.1, 66.8 (7 CH_2Ph); 51.7 (OCH_3). Anal. Calcd for $C_{62}H_{62}O_{13}$: C, 73.37; H, 6.11. Found: C, 73.03; H, 6.24. **21β**; ^1H NMR: δ 7.48–7.09 (m, 35 H, H aromatic); 5.33–4.44 (m, 14 H, 7 CH_2Ph); 4.97 (d, 1 H, $J_{1',2'}$ 7.6, H-1′); 4.86 (broad dd, 1 H, $J_{3,4}$ 2.9, $J_{4,5}$ 1.2 Hz, H-4); 4.5 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1); 4.17 (broad dd, 1 H, $J_{3',4'}$ 3.1, $J_{4',5'}$ 1.2 Hz, H-4′); 4.13 (broad d, 1 H, H-5); 3.86 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-2); 3.80 (dd, 1 H, $J_{2',3'}$ 9.8 Hz, H-2′); 3.74 (broad d, 1 H, H-5′); 3.6 (s, 3 H, OCH_3); 3.59 (dd, 1 H, H-3); 3.48 (dd, 1 H, H-3′).

*Benzyl (methyl 2,3-di-*O*-benzyl-α-*D*-galactopyranosyluronate)-(1→4)-(benzyl 2,3-di-*O*-benzyl-β-*D*-galactopyranosid)uronate* (**22**).—This compound was prepared as described for **20** from donor **18** (0.55 g, 0.996 mmol) and acceptor **4** (0.46 g, 0.830 mmol) using 0.237 g (1.05 mmol) of NIS, 6 mL of CH_2Cl_2, 12 mL of Et_2O, 1.3 g of 4 Å powder molecular sieves and 0.335 mL (0.11 mmol) of a solution of 0.03 mL of TfOH in 1 mL of CH_2Cl_2. The reaction was complete after 1.5 h (1:1 pentane–Et_2O). After the usual treatment, the crude product was dissolved in MeOH (30 mL) and the resulting solution was occasionally stirred with Amberlyst 15 H^+ resin (0.5 g). After 15 min the cleavage of the trimethylsilyl group was complete (TLC, solvent A_2). The resin was filtered off and washed with methanol (3 × 30 mL). The filtrate was concentrated and the residue was chromatographed (solvent *D*) to give 0.527 g (68%) of **22** as a syrup; $[\alpha]_D^{25}$ +38.2° (*c* 1.0, $CHCl_3$); ^1H NMR: δ 7.40–7.18 (m, 30 H, H aromatic); 5.23 (d, 1 H, $J_{1',2'}$ 3.4 Hz, H-1′); 5.04–4.56 (m, 12 H, 6 CH_2Ph); 4.96 (broad s, 1 H, H-5′); 4.48 (broad d, 1 H, $J_{3,4}$ 2.5 Hz, H-4); 4.43 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1); 4.37 (broad s, 1 H, H-4′); 4.02 (dd, 1 H, $J_{2',3'}$ 10, $J_{3',4'}$ 3.3 Hz, H-3′); 3.95 (s, 1 H, H-5); 3.85 (dd, 1 H, H-2′); 3.72 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2); 3.53 (s, 3 H, OCH_3); 3.43 (dd, 1 H, H-3); ^{13}C NMR: δ 169.4, 164.3 (C-6,6′); 138.4, 138.3, 137.9, 137.3, 137.2, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 127.5, 127.4, (C aromatic); 102.7 (C-1); 99.5 (C-1′); 80.0, 77.8, 76.9, 75.5, 74.3, 73.5, 70.5, 68.4 (C-2,3,4,5,2′,3′,4′,5′); 75.0, 73.0, 72.5, 72.4, 71.2, 66.9 (6 CH_2Ph); 52.1 (OCH_3). Anal. Calcd for $C_{55}H_{56}O_{13}$: C, 71.43; H, 6.06. Found: C, 71.25; H, 6.16.

*Methyl (benzyl 2,3-di-*O*-benzyl-α-*D*-galactopyranosyluronate)-(1→4)-(benzyl 2,3-di-*O*-benzyl-β-*D*-galactopyranosid)uronate* (**23**).—This compound was prepared, as described for **22**, from donor **19** (0.254 g, 0.4 mmol) and acceptor **3** (0.162 g, 0.337 mmol) using 0.111 g (0.49 mmol) of NIS, 0.6 g of 4 Å powder molecular sieves, 2.5 mL of CH_2Cl_2, 5 mL of Et_2O, and 0.135 mL of a solution of 0.03 mL of TfOH in CH_2Cl_2 (1 mL). The reaction was complete in 1.5 h (TLC, solvent A_2). After cleavage of the trimethylsilyl group as for **22** the residue was chromatographed (solvent A_3) to give **23** as a syrup (0.220 g, 70%): $[\alpha]_D^{25}$ +28.2° (*c* 1.15, $CHCl_3$); ^1H NMR: δ 7.43–7.20 (m, 30 H, H aromatic); 5.22 (d, 1 H, $J_{1',2'}$ 3.3 Hz, H-1′); 5.12–4.50 (m, 12 H, 6 CH_2Ph); 5.01 (broad s, 1 H, H-5′); 4.46 (broad d, 1 H, H-4); 4.45 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1); 4.39 (broad s, 1 H, H-4′); 4.00 (dd, 1 H, $J_{2',3'}$ 9.9, $J_{3',4'}$ 3.3 Hz, H-3′); 3.95 (s, 1 H, H-5); 3.87 (dd, 1 H, H-2′); 3.70 (dd, 1 H, $J_{2,3}$ 9.9 Hz, H-2); 3.57 (s, 3 H, OCH_3); 3.43 (dd, 1 H, $J_{3,4}$ 2.6 Hz, H-3); ^{13}C NMR: δ 168.9, 168.2 (C-6,6′); 138.5, 138.4, 138.0, 137.9, 137.4, 135.5, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.6, (C aromatic); 102.8 (C-1); 99.7 (C-1′); 79.6, 77.8, 77.1, 75.6, 74.1, 73.6, 70.6, 68.5 (C-2,3,4,5,2′,3′,4′,5′); 75.0, 73.0, 72.5, 72.2, 71.4, 66.8 (6 CH_2Ph); 52.4 (OCH_3). Anal. Calcd for $C_{55}H_{56}O_{13}$: C 71.43; H 6.06. Found: C 71.03; H 6.06.

*Methyl (α-*D*-galactopyranosyluronic acid)-(1→4)-α,β-*D*-galactopyranuronate* (**24**).—To a solution of dimer **20** (0.2 g, 0.19 mmol) in EtOAc (5 mL) were added 3:1:1 2-propanol–water–acetic acid (34 mL) and $Pd(OH)_2/C$ (20%, 0.2 g). The reaction mixture was stirred under hydrogen (10^5 Pa) until TLC analysis (solvent *H*) showed one spot (8 h). The catalyst was removed by filtration and washed with water. The combined filtrates were con-

centrated under reduced pressure to give crude **24** (72 mg, 95%) as a colorless solid. In order to get correctly resolved NMR spectra, a solution of **24** in water was treated with Dowex 50 H^+ (0.2 g) for 10 min. Then the resin was filtered off and washed with water. After concentration the residue was thrice dissolved in D_2O (2 mL) and the resulting solution was concentrated under reduced pressure before recording the NMR spectra. $[\alpha]_D^{25}$ +135° (*c* 0.83, water); ^{1}H NMR (D_2O): δ 5.35 (d, 0.4 H, $J_{1,2}$ 3.7 Hz, α H-1); 5.04 (s, 0.4 H, α H-5′); 5.03 (s, 0.6 H, β H-5′); 4.94 (broad d, 1 H, H-1′); 4.82 (broad s, 0.4 H, α H-5); 4.66 (d, 0.6 H, $J_{1,2}$ 7.8 Hz, β H-1); 4.49 (s, 0.6 H, β H-5); 4.44 (broad d, 0.4 H, α H-4); 4.38 (broad d, 0.6 H, β H-4); 4.33–4.32 (m, 1 H, H-4′); 4.02 (dd, 0.4 H, $J_{2,3}$ 10.6, $J_{3,4}$ 3.1 Hz, α H-3); 3.95–3.88 (m, 1 H, H-3′); 3.81, 3.80 (2s, 3 H, CH_3O); 3.80–3.75 (m, 1 H, α H-2, β H-3); 3.71–3.70 (m, 1 H, H-2′); 3.48 (dd, 0.6 H, $J_{2,3}$ 10.1 Hz, β H-2); ^{13}C NMR (D_2O): δ 173.3, 171.2, 170.3 (C-6,6′); 100.9 (C-1′); 96.9 (β C-1); 92.9 (α C-1); 79.5, 78.6, 73.7, 71.8, 71.5, 71.4, 70.4, 70.3, 69.2, 68.3, 68.2, 68.1 (C-2,3,4,5,2′,3′,4′,5′); 53.5, 53.4 (CH_3O). Satisfactory elemental analysis for this very hygroscopic compound was not possible. ^{1}H NMR data of this dimer are in full agreement with selected reported values [25].

Methyl α-D-*galactopyranosyluronate-(1→4)-*α,β-D-*galactopyranuronic acid* (**25**).—This compound was obtained from **21** (0.1 g), as described for **24**, as a colorless solid (0.034 g, 90%); $[\alpha]_D^{25}$ +113° (*c* 0.43, water); ^{1}H NMR (D_2O): δ 5.35 (d, 0.4 H, $J_{1',2'}$ 3.8 Hz, α H-1); 5.13 (broad s, 1 H, H-5′); 5.06 (broad d, 1 H, H-1′); 4.76 (broad s, 0.4 H, α H-5); 4.66 (d, 0.6 H, $J_{1,2}$ 7.8 Hz, β H-1); 4.45 (broad d, 0.4 H, α H-4); 4.42 (s, 0.6 H, β H-5); 4.39 (broad d, 0.6 H, β H-4); 4.33–4.34 (m, 1 H, H-4′); 4.03 (dd, 0.4 H, $J_{2,3}$ 10.5, $J_{3,4}$ 3.1 Hz, α H-3); 3.98-3.90 (m, 1H, H-3′); 3.84–3.78 (m, 1 H, α H-2, β H-3); 3.80 (s, 3 H, OCH_3); 3.73 (dd, 0.6 H, $J_{1',2'}$ 3.9, $J_{2',3'}$ 10.6 Hz, β H-2′); 3.72 (dd, 0.4 H, $J_{1',2'}$ 3.9, $J_{2',3'}$ 10.5 Hz, α H-2′); 3.49 (dd, 0.6 H, $J_{2,3}$ 10.2 Hz, β H-2); ^{13}C NMR (D_2O): δ 172.5, 171.9, 171.6 (C-6,6′); 100.6 (C-1′); 96.8 (β C-1); 92.8 (α C-1); 79.0, 78.2, 73.3, 72.0, 71.7, 71.5, 70.5, 69.8, 69.1, 69.0, 68.3, 68.2 (C-2,3,4,5,2′,3′,4′,5′); 53.3 (CH_3O). Satisfactory elemental analysis for this very hygroscopic compound was not obtained.

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