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Synthesis of D-Trigalacturonic Acid Methylglycoside and Conformational Comparison with Its Sulfur Analogue

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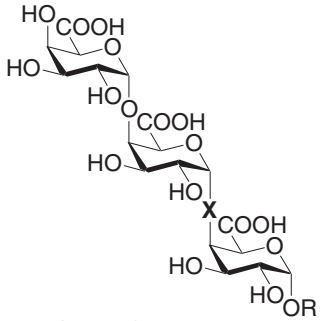
D-Trigalacturonic acid methylglycoside (3) was synthesized to evaluate the previously synthesized sulfur analogue 1 by comparison. The NOE experiments revealed that both 3 and 1 took on a similar conformation around their glycosyl linkage.

Key words: trigalacturonic acid; sulfur-substituted analogue; *endo*-polygalacturonase 1; NOE

Since glycans play a variety of important roles such in-cell recognition, accumulation of energy, and stabilization of the cells, organs and frameworks for living things,[1,2] understanding the reaction mechanisms for glycosidases is very important for their medicinal and industrial applications.[3] Many carbohydrate analogues, so-called glycomimics, have been developed as molecular probes for glycosidases in the last decade.[4] These have mainly focused on *exo*-glycosidases which cleave the terminal glycosidyl linkages. The mechanistic studies of *endo*-glycosidases, which hydrolyze the internal glycoside bonds, lagged behind in comparison with the *exo*-glycosidases, because of the absence of effective molecular probes.

On the other hand, Miyairi, one of authors in this report, has isolated *endo*-polygalacturonase 1 (*endo*-PG 1) from *Stereum purpureum* as the substance responsible for the silver-leaf disease on apple.[5] We expected that this enzyme would be ideal for the mechanistic studies, because *endo*-PG 1 formed a well-developed single crystal to provide the 3D structure with 0.96 Å resolution.[6] However, soaking experiments with trigalacturonic acid gave only a complex not with the trimer, but with two molecules of mono-galacturonic acid. This mono-galacturonic acid occured during the experiment due to the function of *endo*-PG 1 even in the crystal lattice. In the course of our studies on the mechanistic characteristics of *endo*-PG 1, we have designed and synthesized sulfur-substituted trigalacturonic analogue **1** as a stable mimic (Fig. 1).[7] In fact, the complex between **1** and *endo*-PG 1 was found to be 1000 times more stable than that with the natural substrate on the basis of a surface plasmon analysis. However, we met difficulty in a conformational comparison with natural trigalacturonic acid (**2**), because the reducing end of **2** existed as a mixture of anomers under



1: X = S, R = CH_3
2: X = O, R = H
3: X = O, R = CH_3

Fig. 1. Trigalacturonic Acid and Derivatives.

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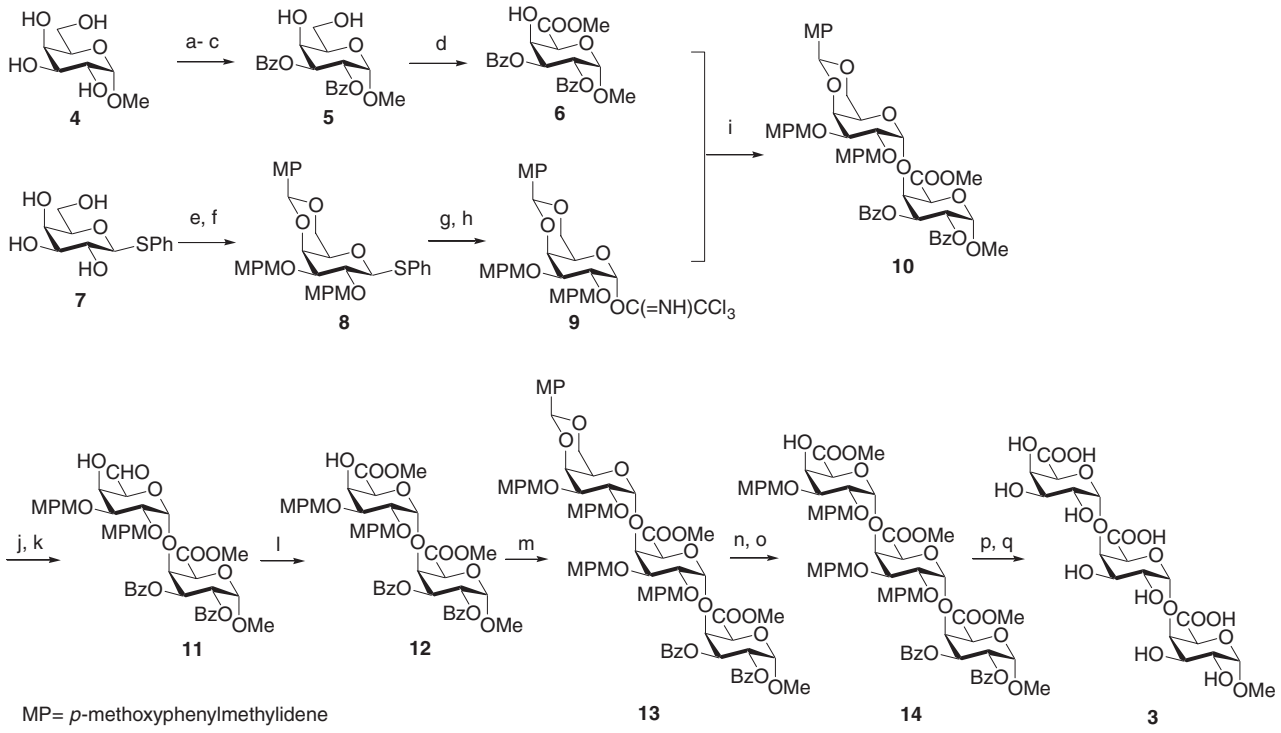
Abbreviations: TEMPO, 2,2,6,6-tetramethyl-1-piperidinyloxyl, free radical; $PhI(OAc)_2$, iodobenzenediacetate; MPMBr, *p*-methoxyphenylmethyl bromide



Scheme 1. Synthesis of D-Trigalacturonic Acid Methylglycoside **3**.

Reagents and conditions: (a) TrCl, Py, 100 °C (73%); (b) BzCl, Py, CH_2Cl_2, 0 °C (95%); (c) AcOH, H_2O, 60 °C (75%); (d) TEMPO, $PhI(OAc)_2$, CH_2Cl_2, H_2O then CH_2N_2, Et_2O (95%, 2 steps); (e) *p*-MeOPhCH(OMe)$_2$, cat. CSA, DMF, 100 °C (72%); (f) NaH, MPMBr, DMF, toluene (96%); (g) NBS, acetone, H_2O, 0 °C (98%); (h) Cl_3CCN, DBU, CH_2Cl_2, −15 °C (89%); (i) TESOTf, CH_2Cl_2, MS4A, −78 °C (73%); (j) AcOH, H_2O, 50 °C (92%); (k) TEMPO, $PhI(OAc)_2$, CH_2Cl_2; (l) $NaClO_2$, NaH_2PO_4, *t*-BuOH, 2-methyl-2-butene then CH_2N_2, Et_2O (80%, 3 steps); (m) **9**, TESOTf, Et_2O, MS4A, 0 °C (99%); (n) AcOH, H_2O, 50 °C (79%); (o) TEMPO, $PhI(OAc)_2$, CH_2Cl_2 then $NaClO_2$, NaH_2PO_4, *t*-BuOH, 2-methyl-2-butene, then CH_2N_2, Et_2O (68%, 3 steps); (p) DDQ, CH_2Cl_2, H_2O (64%); (q) 0.3% NaOH aq, THF, H_2O (98%).

aqueous conditions. We expected that methyl glycoside **3** would reduce this problem, because the introduction of a methyl glycoside to the reducing end should fix the stereochemistry. Our preliminary molecular modeling suggested that the methyl glycoside moiety would not interfere with the complexation with *endo*-PG 1. Unfortunately, the methyl glycoside form of trigalacturonic acid was not known in the literature, so we needed to prepare it by ourselves. In this paper, we describe the synthesis of **3** as well as a preliminary conformational comparison between *S*-glycoside **1** and *O*-glycoside **3**.

Results and Discussion

We initially attempted to prepare **3** from polygalacturonic acid by the enzymatic partial degradation of polygalacturonic acid with *endo*-PG 1 and subsequent methyl glycosylation. However, we failed in this, in spite of many attempts, due to the low yield from enzymatic degradation and the isolation difficulty in the final step. We therefore decided to prepare it by chemical synthesis.

This synthesis is outlined in Scheme 1. Commercial methyl α-D-galactopyranoside (**4**) was converted into 4,6-diol **5** by the sequential reactions of (i) tritylation of the C6 primary alcohol, (ii) benzoylation using two equivalents of benzoyl chloride at low temperature, and (iii) acidic hydrolysis of the trityl ether. The benzoylation reaction proceeded selectively at the sterically less-hindered C2 and C3 hydroxy groups. It was found that a combination of TEMPO and $PhI(OAc)_2$[8,9] took place the regioselective oxidation of **5** to give the corresponding galacturonic acid derivative which was isolated after conversion into methyl ester **6** (95% yield in two steps) by using diazomethane. Glycosyl donor **9** was also synthesized from phenyl 1-thio-β-D-galactopyranoside (**7**).[10] After the C4 and C6 alcohols in **7** had been simultaneously protected in the form of *p*-methoxyphenylmethylidene acetal,[11] the remaining C2 and C3 alcohols were transformed into MPM ethers with MPMBr/NaH to afford **8** in 69% yield in two steps. Treatment of **8** with NBS under the aqueous condition hydrolyzed the phenylthio acetal to provide the corresponding hemiacetal, which was further converted into α-trichloroacetimidate **9** according to Schmidt's protocol.[12]

Since our previous studies had revealed that the carboxylate ester function at the C6 position inhibited the glycosylation reaction,[7] the C6 carboxylic acid group was introduced after glycosylation. As expected, **9** smoothly reacted with acceptor **6** by using catalytic

TESOTf to stereoselectively give α-glycoside **10** in 73% yield. The β-isomer was not found in the ^{1}H-NMR spectrum. After the *p*-methoxyphenylmethylidene acetal was selectively removed under the aqueous acidic condition, C6-OH of the resulting diol was selectively oxidized under the same conditions to those described for the oxidation of **5**. This oxidation did not provide the carboxylic acid, but only aldehyde **11**, so it was further oxidized into carboxylic acid with $NaClO_2$. After treating with CH_2N_2, dimethyl ester **12** was obtained in 80% yield in three steps. Product **12** carried C4-OH, and this function was further glycosylated with **9** to result in triglycoside **13** with α-stereochemistry.

The carboxylic acid function at the non-reducing end was provided by a similar sequence: (i) acidic removal of the *p*-methoxyphenylmethylidene acetal, (ii) TEMPO/PhI(OAc)$_2$ oxidation giving the corresponding C6 aldehyde, (iii) oxidation with $NaClO_2$, and (iv) esterification with CH_2N_2. The last process, methyl ester formation, was required for effective silica gel column chromatographic purification. The MPM groups were then removed by DDQ oxidation, giving the corresponding pentaol in 64% yield. Finally, a basic treatment under aqueous conditions removed all benzoate and methyl esters to achieve the synthesis of **3** after passing the crude mixture through an ion-exchange column (Dowex 50W, H^+ form). Our synthesis afforded a sufficient amount of **3** (25 mg in total) for NMR and subsequent detailed calorimetric experiments.

A preliminary conformational analysis of **1** and **3** was carried out by NMR experiments. NOESY is a powerful tool to investigate distances between two proton atoms.[13] In the carbohydrate research field, this technique has enabled the geometric-relationships of pyranose (or furanose) rings to be deduced in an oligosaccharide.[14–16] The 600-MHz NMR instrument provided the ^{1}H-NMR spectra for **1** and **3**, both with satisfying signal separation, but it gave very poor NOESY spectra. Generally, when the product of correlation time τ and Larmor frequency ω is small, the maximum NOE intensity is positive, while it becomes negative when $\omega\tau_c$ is large. The maximum NOE intensity closes to zero and the number of cross peaks observed in NOESY spectra drastically decreases when $\omega\tau_c$ is around 1.13.[17] Fortunately, in our case, a 920-MHz NMR spectrometer turned these invisible NOEs by the 600-MHz spectrometer into observable as negative NOEs. There was no remarkable difference in the NOE pattern between **1** and **3**. Both compounds **1** and **3** afforded NOE correlations at $1''\leftrightarrow4'$ and $1'\leftrightarrow4$ with similar intensity, suggesting that the glycoside bonds in each compound took on similar conformations (Fig. 2).

This was also supported by molecular modeling calculations. The stable conformers for models **X** (*O*-glycoside) and **Y** (*S*-glycoside) were estimated by structural optimization with Hartree-Fock 6-31G*[18] of the tentatively obtained stable conformers which were

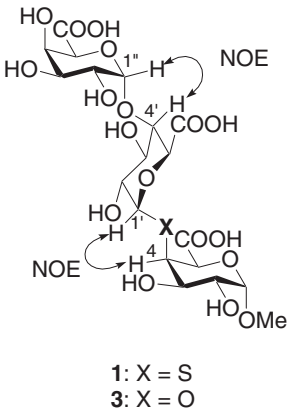


Fig. 2. NOE Correlations Observed around the Glycoside Bond in **1** and **3**.

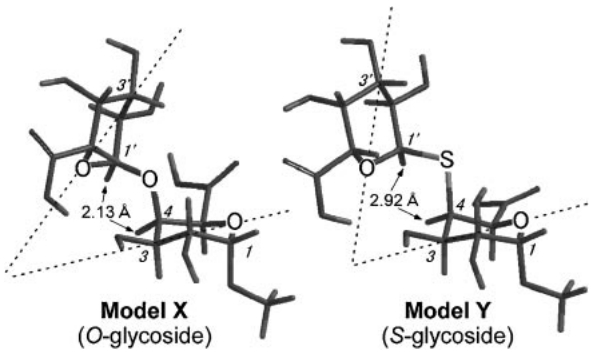


Fig. 3. Stable Conformations of Models **X** (*O*-glycoside) and **Y** (*S*-glycoside) Obtained by Theoretical Calculations.

The additional lines are those penetrating through pyranose oxygens and corresponding C3s.

provided by a conformational search[19] with semiempirical AM1.[20]

As shown in Fig. 3, it was found that the pyranose rings in the stable conformers of models **X** (*O*-glycoside) and **Y** (*S*-glycoside) took on similar orientations. The distances between C4H and C1′H for both models **X** and **Y** were small, showing good accordance with experimental NOEs. However, that for model **Y** (2.92 Å) was larger compared to that for model **X** (2.13 Å), and the geometry of the pyranose rings was slightly different between models **X** and **Y**. Thus, we concluded previously synthesized **1** mimicked **3** with slightly higher steric energy at the glycosyl bond being cleaved by *endo*-PG 1.

As described, we synthesized methyl glycoside **3**. The NOE and modeling experiments suggested that previously synthesized **1** would mimic natural **2**, but with slightly higher steric energy around the glycoside moiety to be cleaved. Since it is known that the enzymes would prefer the substrates taking on a strained conformation, this difference might be an advantage in complexation with an enzyme. Thus, further investigation by calorimetric experiments is underway in our laboratories.

Experimental

General methods. Melting point (mp) data were determined with Yanako MP-J3 micro-melting point apparatus and are uncorrected. Optical rotation values were measured by a HORIBA SEPA300 high-sensitivity polarimeter. ^{1}H- and ^{13}C-NMR spectra were measured by a JEOL ALPHA 400 spectrometer for structural determinations, and a JEOL ECA 920 spectrometer was used for quantitative NOE experiments. In the ^{1}H-NMR spectra, the chemical shifts are expressed in ppm downfield from the signal for trimethylsilane used as an internal standard in the case of $CDCl_3$. When another solvent was employed, the remaining proton signals in deuterosolvent C_6HD_5 (7.15 ppm), CHD_2OD (3.30 ppm), or HDO (4.63 ppm) were used as the internal standards. Splitting patterns are designated as s (*singlet*), d (*doublet*), t (*triplet*), m (*multiplet*), and br (*broad*). In the ^{13}C-NMR spectra, the ^{13}C chemical shifts of the solvents were used as the internal standard ($^{13}CDCl_3$, 77.0 ppm; $^{13}C_6D_6$, 128.0 ppm; or $^{13}CD_3OD$, 49.5 ppm). For the ^{13}C-NMR spectra measured in D_2O, the default offset was employed and we did not perform corrections. Assignments of the signals are according to the numbering based on IUPAC nomenclature. IR spectra were obtained with a Horiba FT-720 Fourier transform infrared spectrometer in a KBr cell. Measurements of field desorption and fast atom bombardment mass spectra (FD-MS and FAB-MS, respectively) were performed with JEOL JMS AX500 or JEOL JMS SX102A spectrometers. Whenever MS spectra were measured in the negative mode, "negative" is mentioned. MS analyses for unstable compounds such as glycosyl imidates were not performed. Analytical and preparative thin-layer chromatography was carried out by using pre-coated Merck silica gel $60F_{254}$ (Art. 1.05715) plates. The silica gel used for column chromatography was Merck silica gel 60 (Art. 1.07734). All reactions were carried out in an N_2 or Ar atmosphere by using dried solvents, except for the aqueous conditions. Dichloromethane and tetrahydrofuran were freshly distilled from diphosphorus pentoxide and benzophenone-ketyl, respectively. Molecular sieves 4A were finely powdered and activated (200 °C *in vacuo* for 1 h) before use.

*Methyl 2,3-di-O-benzoyl-α-D-galactopyranoside (**5**).* Commercial methyl α-D-galactopyranoside (8.48 g, 43.7 mmol) was stirred with chlorotriphenylmethane (14.0 g, 50.2 mmol) in pyridine (50 ml) at 100 °C for 30 min. The mixture was poured into H_2O (200 ml) and extracted with AcOEt (150 ml × 3). The organic layers were washed with brine (100 ml), combined, dried over $MgSO_4$, and then concentrated *in vacuo*. Silica gel column chromatography of the residue (AcOEt 100%) gave the corresponding 6-*O*-triphenylmethyl ether (14.0 g, 73%) as a white solid. Recrystallization from AcOEt:hexane (50:50) gave colorless needles, mp 122–123 °C; $[\alpha]_D^{24}$ +63.3 (*c* 0.94, $CHCl_3$); IR (KBr) cm^{-1}: 3400, 2930, 1490, 1445, 1150, 1075, 1045, 765; ^{1}H-NMR ($CDCl_3$) δ: 2.05 (d, 1H, *J* = 9.5 Hz, C2O*H*), 2.46 (d, 1H, *J* = 2.7 Hz, C4O*H*), 2.58 (d, 1H, *J* = 5.3 Hz, C3O*H*), 3.38 (dd, 1H, *J* = 5.9, 9.4 Hz, C6*H*H), 3.43 (s, 3H, OC*H*$_3$), 3.43 (dd, 1H, *J* = 5.9, 9.4 Hz, C6*H*H), 3.71 (ddd, 1H, *J* = 3.7, 5.3, 9.5 Hz, C3*H*), 3.80 (dt, 1H, *J* = 3.7, 9.5 Hz, C2*H*), 3.82 (brt, 1H, *J* = 5.9 Hz, C5*H*), 4.03 (brdd, 1H, *J* = 2.7, 3.7 Hz, C4*H*), 4.82 (d, 1H, *J* = 3.7 Hz, C1*H*), 7.23 (m, 3H, *aromatic protons*), 7.30 (m, 6H, *aromatic protons*), 7.46 (m, 6H, *aromatic protons*); ^{13}C-NMR ($CDCl_3$) δ: 55.44 (O*C*H$_3$), 63.17 (*C*6), 69.00 (*C*5), 69.60 (*C*4), 69.88 (*C*2), 71.35 (*C*3), 87.05 (O*C*Ph$_3$), 99.36 (*C*1), 127.14, 127.92, 128.61, 143.69 (*aromatic carbons*); negative-FABMS (%, rel. int.) *m/z*: 436 (12, $[M]^-$), 435 (41, $[M-H]^-$), 259 (19, $[Ph_3CO]^-$), 243 (16, $[Ph_3C]^-$), 193 (61, $[M\text{-}Ph_3C]^-$), 148 (100, $[M\text{-}Ph_3COCH_2\text{-}OCH_3]^-$); negative-FAB-HRMS: calcd. for $C_{26}H_{27}O_6$ $[M-H]^-$, 435.1808; found, *m/z* 435.1811.

A solution of the 6-*O*-triphenylmethyl ether (1.59 g, 3.64 mmol) in CH_2Cl_2 (100 ml) was stirred with benzoyl chloride (1.02 g, 7.26 mmol) and pyridine (576 mg, 7.28 mmol) at 0 °C. After stirring for 5 min, the cooling bath was removed, and the mixture was stirred for 30 min more at room temperature. The mixture was poured into H_2O (100 ml) and extracted with AcOEt (80 ml × 3). The organic layers were washed with brine (80 ml), combined, dried over $MgSO_4$, and then concentrated *in vacuo*. Silica gel column chromatography of the residue (AcOEt:hexane = 10:90) gave methyl 2,3-di-*O*-benzoyl-6-*O*-triphenylmethyl-α-D-galactopyranoside (2.24 g, 95%) as a viscous oil, $[\alpha]_D^{24}$ +93.4 (*c* 0.93, $CHCl_3$); IR (film) cm^{-1}: 3500, 3060, 2935, 1725, 1450, 1280, 1105; ^{1}H-NMR (C_6D_6) δ: 3.11 (s, 3H, OC*H*$_3$), 3.38 (dd, 1H, *J* = 4.1, 9.9 Hz, C6*H*H), 3.56 (dd, 1H, *J* = 5.9, 9.9 Hz, C6*H*H), 3.78 (brdd, 1H, *J* = 4.1, 5.9 Hz, C5*H*), 3.96 (brd, 1H, *J* = 3.0 Hz, C4*H*), 5.29 (d, 1H, *J* = 3.6 Hz, C1*H*), 6.01 (dd, 1H, *J* = 3.0, 10.5 Hz, C3*H*), 6.12 (dd, 1H, *J* = 3.6, 10.5 Hz, C2*H*), 6.83–7.18 (m, 15H, *aromatic protons*), 7.58 (m, 6H, *aromatic protons*), 8.10 (brdd, 2H, *J* = 1.5, 8.1 Hz, *aromatic protons*), 8.14 (brdd, 2H, *J* = 1.5, 8.1 Hz, *aromatic protons*); ^{13}C-NMR (C_6D_6) δ: 54.89 (O*C*H$_3$), 64.56 (*C*6), 69.29 (*C*5), 69.67 (*C*4), 69.79 (*C*2), 71.43 (*C*3), 87.49 (O*C*Ph$_3$), 97.97 (*C*1), 127.35, 128.53, 129.11, 130.05, 130.10, 133.02, 133.04, 144.40 (*aromatic carbons*), 165.85, 166.24 (each Ar*C*=O); FABMS (%, rel. int.) *m/z*: 667 (28, $[M+Na]^+$), 243 (100, $[CPh_3]^+$); FAB-HRMS: calcd. for $C_{26}H_{27}O_6Na$ $[M+Na]^+$, 667.2308; found, *m/z* 667.2280.

A solution of methyl 2,3-di-*O*-benzoyl-6-*O*-triphenylmethyl-α-D-galactopyranoside (2.24 g, 3.48 mmol) was stirred in 60% aqueous acetic acid solution (8.0 ml) at 60 °C for 30 min. After cooling, the mixture was concentrated *in vacuo*. Silica gel column chromatography of the residue (AcOEt:hexane = 60:40) gave **5** (1.05 g, 75%) as an oil, $[\alpha]_D^{23}$ +157 (*c* 1.02, $CHCl_3$); IR

(film) cm^{-1}: 3440, 2935, 1720, 1280, 1105, 1030, 710; ^{1}H-NMR ($CDCl_3$) δ: 2.45 (br, 1H, C6O*H*), 3.07 (br, 1H, C4O*H*), 3.44 (s, 3H, OCH_3), 4.00 (m, 3H, C6H_2, C5*H*), 4.47 (brs, 1H, C4*H*), 5.22 (d, 1H, $J = 1.9$ Hz, C1*H*), 5.70 (m, 2H, C2*H*, C3*H*), 7.36 (m, 4H, *aromatic protons*), 7.50 (m, 2H, *aromatic protons*), 7.98 (m, 4H, *aromatic protons*); ^{13}C-NMR ($CDCl_3$) δ: 55.44 (OCH_3), 62.73 (*C6*), 68.98 (*C2*), 69.09 (*C5*), 69.32 (*C4*), 71.02 (*C3*), 97.55 (*C1*), 128.30, 128.35, 129.23, 129.31, 129.69, 129.76, 133.22, 133.25 (*aromatic carbons*), 165.91, 166.21 (each Ar*C*=*O*); negative-FABMS (%, rel. int.) *m/z*: 402 (3.7, $[M]^-$), 401 (6.0, $[M-H]^-$), 297 (9.3, $[M\text{-}PhCO]^-$), 121 (100, $[PhCOO]^-$); negative-FAB-HRMS: calcd. for $C_{21}H_{21}O_8$ $[M-H]^-$, 401.1236; found, *m/z* 401.1251.

*Methyl (methyl 2,3-di-O-benzoyl-α-D-galactopyranosid)uronate (**6**).* A suspension of **5** (1.05 g, 2.61 mmol) in a mixture of CH_2Cl_2 (10 ml) and H_2O (5.0 ml) was stirred with $PhI(OAc)_2$ (4.33 g, 13.4 mmol) and TEMPO (80.0 mg, 512.0 μmol) at room temperature for 10 min. The mixture was poured into H_2O (70 ml) and extracted with AcOEt (40 ml × 3). The extracts were washed with brine (50 ml), dried over $MgSO_4$, combined, and then concentrated *in vacuo*. After the residue had been diluted with THF (8.0 ml), ethereal diazomethane was added until the yellow color did not disappear. After concentration *in vacuo*, silica gel column chromatography (AcOEt:hexane = 30:70) of the residue gave **6** (1.07 g, 95%) as an oil, $[\alpha]_D^{23}$ +107 (*c* 0.95, $CHCl_3$); IR (film) cm^{-1}: 3940, 2955, 1725, 1450, 1280, 1100, 1025, 915, 710; ^{1}H-NMR ($CDCl_3$) δ: 3.47 (s, 3H, OCH_3), 3.80 (s, 3H, C6OCH_3), 4.65 (brs, 1H, C5*H*), 4.73 (brs, 1H, C4*H*), 5.31 (d, 1H, $J = 2.7$ Hz, C1*H*), 5.71 (dd, 1H, $J = 2.7$, 10.7 Hz, C2*H*), 5.75 (dd, 1H, $J = 1.9$, 10.7 Hz, C3*H*), 7.34 (m, 4H, *aromatic protons*), 7.48 (m, 2H, *aromatic protons*), 7.98 (m, 4H, *aromatic protons*); ^{13}C-NMR ($CDCl_3$) δ: 52.50 (C6OCH_3), 56.06 (OCH_3), 68.23 (*C3*), 68.88 (*C4*), 69.81 (*C5*), 70.16 (*C2*), 97.76 (*C1*), 128.16, 128.24, 128.27, 129.06, 129.64, 129.66, 133.15, 133.23 (*aromatic carbons*), 165.61, 165.83 (each Ar*C*=O), 168.59 (*C6*); FDMS (%, rel. int.) *m/z*: 431 (64, $[M+H]^+$), 398 (100, $[M\text{-}CH_3OH]^+$), 341 (26, $[MH\text{-}(COOCH_3)\text{-}CH_3O]^+$), 308 (42, $[M\text{-}PhCOOH]^+$); FD-HRMS: calcd. for $C_{22}H_{23}O_9$ $[M+H]^+$, 431.1342; found, *m/z* 431.1335.

*Phenyl 2,3-bis-O-(4-methoxyphenylmethyl)-4,6-O-(4-methoxyphenylmethylidene)-1-thio-β-D-galactopyranoside (**8**).* A solution of phenyl-1-thio-β-D-galactopyranoside (**7**); (2.62 g, 9.62 mmol) in DMF (20 ml) was stirred with 4-methoxybenzaldehyde dimethylacetal (3.50 g, 19.2 mmol) and camphorsulfonic acid (22.3 mg, 96.0 μmol) at 100 °C for 10 min. After cooling, the mixture was poured into 5% aqueous $NaHCO_3$ solution (100 ml) and extracted with AcOEt (70 ml × 3). The extracts were washed with H_2O (50 ml) and brine (50 ml), combined, dried over $MgSO_4$, and then concentrated *in vacuo* to give a crude solid. Recrystallization from AcOEt:hexane (30:70) gave phenyl 4,6-*O*-(4-methoxyphenylmethylidene)-1-thio-β-D-galactopyranoside (2.74 g, 72%) as colorless needles, mp 151–154 °C; $[\alpha]_D^{23}$ −7.5 (*c* 1.50, $CHCl_3$); IR (KBr) cm^{-1}: 3410, 2910, 1615, 1515, 1250, 1165, 825; ^{1}H-NMR ($CDCl_3$) δ: 2.48 (brd, 1H, $J = 9.0$ Hz, C2O*H*), 2.51 (d, 1H, $J = 1.2$ Hz, C3O*H*), 3.55 (brdd, 1H, $J = 1.4$, 1.7 Hz, C5*H*), 3.69 (m, 2H, C2*H*, C3*H*), 3.82 (s, 3H, OCH_3), 4.02 (dd, 1H, $J = 1.7$, 12.4 Hz, C6*H*H), 4.20 (brd, 1H, $J = 1.9$, C4*H*), 4.37 (dd, 1H, $J = 1.4$, 12.4 Hz, C6*H*H), 4.51 (m, 1H, C1*H*), 5.47 (s, 1H, ArC*H*), 6.86 (brd, 2H, $J = 8.7$ Hz, *aromatic protons*), 7.33 (m, 5H, *aromatic protons*), 7.69 (brdd, 2H, $J = 2.0$, 8.2 Hz, *aromatic protons*); ^{13}C-NMR ($CDCl_3$) δ: 55.33 (OCH_3), 68.86 (*C2*), 69.25 (*C6*), 70.06 (*C5*), 73.82 (*C3*), 75.30 (*C4*), 87.00 (*C1*), 101.29 (Ar*C*$(OR)_2$), 113.57, 127.82, 128.21, 128.93, 130.14, 130.71, 133.76, 160.33 (*aromatic carbons*); negative-FABMS (%, rel. int.) *m/z*: 389 (2.1, $[M-H]^-$), 375 (1.3, $[M\text{-}CH_3]^-$), 148 (100), 109 (91, $[PhS]^-$); negative-FAB-HRMS: calcd. for $C_{20}H_{21}O_8S$ $[M-H]^-$, 389.1059; found, *m/z* 389.1057.

Sodium hydride (washed with hexane, 3.21 g, 8.22 mmol) was slowly added to a DMF solution (20 ml) of the foregoing product (3.21 g, 8.22 mmol) at room temperature. Upon the addition of the substrate, H_2 gas was bubbled. After stirring for 30 min, 50% toluene solution of MPMBr (13.2 g, 32.8 mmol, freshly prepared from anisic alcohol and PBr_3) was added at 0 °C. After 10 min, the cooling bath was removed, and the mixture was stirred at room temperature for 30 min. Methanol (5.0 ml) and triethylamine (5.0 ml) were added to decompose the excess reagent. After stirring for an additional 30 min, the mixture was poured into H_2O (100 ml) and extracted with AcOEt (70 ml × 3). The organic layers were successively washed with H_2O (50 ml), and brine (50 ml), combined, and dried over $MgSO_4$. After concentration, the residue was purified by silica gel column chromatography (AcOEt:hexane = 25:75) to give **8** (4.98 g, 96%) as an oil, $[\alpha]_D^{23}$ +1.7 (*c* 1.25, $CHCl_3$); IR (film) cm^{-1}: 2860, 1610, 1515, 1250, 1170, 1100, 1035, 820; ^{1}H-NMR ($CDCl_3$) δ: 3.37 (brdd, 1H, $J = 1.3$, 1.4 Hz, C5*H*), 3.57 (dd, 1H, $J = 3.3$, 9.2 Hz, C3*H*), 3.79, 3.80, 3.83 (each s, 3H, OCH_3), 3.86 (t, 1H, $J = 9.2$ Hz, C2*H*), 3.95 (dd, 1H, $J = 1.4$, 12.4 Hz, C6*H*H), 4.10 (brd, 1H, $J = 3.3$ Hz, C4*H*), 4.33 (dd, 1H, $J = 1.3$, 12.4 Hz, C6*H*H), 4.58 (d, 1H, $J = 9.2$ Hz, C1*H*), 4.62 (s, 2H, ArCH_2O), 4.63, 4.66 (each d, 1H, $J = 12.3$ Hz, ArC*H*HO), 5.43 (s, 1H, ArC*H*), 6.82 (brd, 2H, $J = 8.7$ Hz, *aromatic protons*), 6.87 (brd, 2H, $J = 8.6$ Hz, *aromatic protons*), 6.91 (brd, 2H, $J = 8.8$ Hz, *aromatic protons*), 7.16–7.27 (m, 5H, *aromatic protons*), 7.33 (brd, 2H, $J = 8.7$ Hz, *aromatic protons*), 7.44 (brd, 2H, $J = 8.6$ Hz, *aromatic protons*), 7.70 (brdd, 2H, $J = 2.1$, 7.8 Hz, *aromatic protons*); ^{13}C-NMR ($CDCl_3$) δ: 55.24, 55.27, 55.34 (each OCH_3), 69.37 (*C6*), 69.84 (*C5*), 71.46 (ArCH_2O), 73.79 (*C4*), 75.05 (ArCH_2O), 75.18 (*C2*), 80.95 (*C3*),

86.59 (*C*1), 101.24 (Ar*C*(OR)$_2$), 113.49, 113.73, 113.76, 127.36, 127.91, 128.82, 129.37, 129.81, 130.23, 130.57, 130.76, 132.67, 132.88, 159.25, 159.27, 160.14 (*aromatic carbons*); FDMS (%, rel. int.) *m/z*: 631 (38, $[M+H]^+$), 630 (100, $[M]^+$); FD-HRMS: calcd. for $C_{36}H_{38}O_8S$ $[M]^+$, 630.2287; found, *m/z* 630.2276.

*2,3-Bis-O-(4-methoxyphenylmethyl)-4,6-O-(4-methoxyphenyl-methylidene)-α-D-galactopyranosyl trichloroacetimidate (**9**).* A solution of **8** (515 mg, 817.0 μmol) in a mixture of acetone (10.0 ml) and H_2O (1.0 ml) was stirred with NBS (356 mg 2.0 mmol) at 0 °C. After 5 min, 10% $Na_2S_2O_3$ (4.0 ml) was added to the mixture. After concentrating *in vacuo*, the residue was diluted with AcOEt (150 ml) and then washed with H_2O (60 ml). The aqueous solution was extracted with AcOEt (50 ml × 2). Each organic layer was washed with brine (50 ml), combined, dried over $MgSO_4$, and then concentrated *in vacuo* to give a white solid. Recrystallization (from AcOEt:hexane = 50:50) gave 2,3-bis-*O*-(4-methoxyphenylmethyl)-4,6-*O*-(4-methoxyphenylmethylidene)-D-galactopyranose as needles (431 mg, 98%), mp 124–130 °C; $[\alpha]_D^{22}$ +39.8 (*c* 0.75, $CHCl_3$); IR (film) cm^{-1}: 3435, 2930, 1610, 1515, 1250, 1195, 1035, 825. The ^{1}H-NMR spectrum indicated that the sample consisted of a mixture of anomers (α:β = 67:33 in $CDCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 2.86 (d, 1H × 0.67, *J* = 1.2 Hz, C1O*H* (α-anomer)), 2.94 (d, 1H × 0.33, *J* = 7.4 Hz, C1O*H* (β-anomer)), 3.37 (brdd, 1H × 0.33, *J* = 1.2, 1.6 Hz, C5*H* (β-anomer)), 3.54 (dd, 1H × 0.33, *J* = 3.6, 9.5 Hz, C3*H* (β-anomer)), 3.73 (dd, 1H × 0.33, *J* = 7.7, 9.5 Hz, C2*H* (β-anomer)), 3.80, 3.80, 3.80 (each s, 3H × 0.33, OC*H*$_3$ (β-anomer)), 3.81, 3.81, 3.81 (each s, 3H × 0.67, OC*H*$_3$ (α-anomer)), 3.81 (1H, m, C5*H* (α-anomer)), 3.91 (dd, 1H × 0.67, *J* = 3.6, 9.7 Hz, C3*H* (α-anomer)), 3.97–4.03 (m, 1H × 0.67, 1H × 0.33, 1H × 0.67, C6*H*H (α-anomer), C6*H*H (β-anomer), C2*H* (α-anomer)), 4.08 (brd, 1H × 0.33, *J* = 3.6 Hz, C4*H* (β-anomer)), 4.15 (brd, 1H × 0.67, *J* = 3.6 Hz, C4*H* (α-anomer)), 4.20 (dd, 1H × 0.67, *J* = 1.6, 12.3 Hz, C6*H*H (α-anomer)), 4.28 (dd, 1H × 0.33, *J* = 1.6, 12.5 Hz, C6*H*H (β-anomer)), 4.62 (d, 1H × 0.33, *J* = 11.2 Hz, ArC*H*HO (β-anomer)), 4.65 (d, 1H × 0.33, *J* = 7.7 Hz, C1*H* (β-anomer)), 4.68 (d, 1H × 0.67, *J* = 12.2 Hz, ArC*H*HO (α-anomer)), 4.69 (s, 2H × 0.67, ArC*H*$_2$O (α-anomer)), 4.72 (d, 1H × 0.67, *J* = 12.2 Hz, ArC*H*HO (α-anomer)), 4.78 (d, 1H × 0.33, *J* = 10.7 Hz, ArC*H*HO (β-anomer)), 4.81 (d, 1H × 0.33, *J* = 11.2 Hz, ArC*H*HO (β-anomer)), 4.82 (d, 1H × 0.33, *J* = 10.7 Hz, ArC*H*HO (β-anomer)), 5.31 (dd, 1H × 0.67, *J* = 1.2, 3.5 Hz, C1*H* (α-anomer)), 5.44 (s, 1H × 0.33, ArC*H* (β-anomer)), 5.45 (s, 1H × 0.67 ArC*H* (α-anomer)), 6.84–7.48 (m, 12H, *aromatic protons*); FABMS (%, rel. int.) *m/z*: 561 (46, $[M+Na]^+$), 417 (61, $[M\text{-}CH_3OPhCH_2]^+$), 121 (100, $[PhCOO]^+$); FAB-HRMS: calcd. for $C_{30}H_{34}O_9Na$ $[M+Na]^+$, 561.2101; found, *m/z* 561.2108.

A solution of the product (489 mg, 908 μmol) in CH_2Cl_2 (8.0 ml) was stirred with CCl_3CN (656 mg, 4.54 mmol) in the presence of DBU (45.6 mg, 6.94 μmol) at −15 °C for 30 min. After concentrating *in vacuo*, the residue was purified by silica gel column chromatography (AcOEt:hexane = 30:70) to give **9** (556 mg, 89%) as an oil. ^{1}H-NMR ($CDCl_3$) δ: 3.80, 3.80 (each s, 3H, OC*H*$_3$), 3.80 (m, 1H, C5*H*), 3.81 (s, 3H, OC*H*$_3$), 3.97 (dd, 1H, *J* = 1.3, 12.6 Hz, C6*H*H), 4.02 (dd, 1H, *J* = 3.3, 10.1 Hz, C3*H*), 4.19 (brd, 1H, *J* = 3.3 Hz, C4*H*), 4.24 (dd, 1H, *J* = 3.4, 10.1 Hz, C2*H*), 4.24 (dd, 1H, *J* = 1.1, 12.6 Hz, C6*H*H), 4.66, 4.70 (each d, 1H, *J* = 11.5 Hz, ArC*H*HO), 4.70, 4.75 (each d, 1H, *J* = 11.8 Hz, ArC*H*HO), 5.45 (s, 1H, ArC*H*), 6.59 (d, 1H, *J* = 3.4 Hz, C1*H*), 6.82–6.90 (m, 6H, *aromatic protons*), 7.25 (brd, 2H, *J* = 8.6 Hz, *aromatic protons*), 7.29 (brd, 2H, *J* = 8.6 Hz, *aromatic protons*), 7.44 (brd, 2H, *J* = 8.7 Hz, *aromatic protons*), 8.55 (s, 1H, C(=N*H*)CCl_3). This sample gradually decomposed, so it was immediately used for the next step.

*Methyl {methyl 2,3-di-O-benzoyl-4-O-[2′,3′-bis-O-(4-methoxyphenylmethyl)-4′,6′-O-(methoxyphenlylmethylidene)-α-D-galactopyranosyl]-α-D-galactopyranosid}uronate (**10**).* Triethylsilyl trifluoromethanesulfonate (1.8 mg, 6.8 μmol) was added to a suspension of **6** (30.1 mg, 69.9 μmol), **9** (138.7 mg, 0.2 mmol), and powdered 4A molecular sieves (43 mg) in CH_2Cl_2 (0.5 ml) at −78 °C. After stirring for 5 min, triethylamine (50 μl) was adding, and the mixture was allowed to warm to room temperature. After filtering through a cotton pad, the filtrate was concentrated *in vacuo*. Purification of the residue by silica gel column chromatography (AcOEt:hexane = 25:75) gave **10** (48.8 mg, 73%) as an oil, $[\alpha]_D^{23}$ +58.4 (*c* 0.60, $CHCl_3$); IR (film) cm^{-1}: 2935, 1730, 1515, 1250, 1100, 1030, 830, 710; ^{1}H-NMR ($CDCl_3$) δ: 3.36, 3.41 (each brd, 1H, *J* = 12.7 Hz, C6′*H*H), 3.49, 3.60, 3.76, 3.78, 3.78 (each s, 3H, OC*H*$_3$), 3.85 (brs, 1H, C5′*H*), 3.96 (dd, 1H, *J* = 3.2, 10.2 Hz, C2′*H*), 4.04 (brd, 1H, *J* = 3.1 Hz, C4′*H*), 4.08 (dd, 1H, *J* = 3.1, 10.2 Hz, C3′*H*), 4.64 (d, 1H, *J* = 11.4 Hz, ArC*H*HO), 4.66 (brs, 1H, C5*H*), 4.66 (s, 2H, ArC*H*$_2$O), 4.71 (d, 1H, *J* = 11.4 Hz, ArC*H*HO), 4.86 (brd, 1H, *J* = 2.5 Hz, C4*H*), 4.96 (d, 1H, *J* = 3.2 Hz, C1′*H*), 5.24 (s, 1H, ArCH), 5.32 (d, 1H, *J* = 3.4 Hz, C1*H*), 5.66 (dd, 1H, *J* = 2.5, 11.0 Hz, C3*H*), 5.72 (dd, 1H, *J* = 3.4, 11.0 Hz, C2*H*), 6.80–6.88 (m, 6H, *aromatic protons*), 7.22–7.40 (m, 10H, *aromatic protons*), 7.48 (m, 2H, *aromatic protons*), 7.89 (brd, 2H, *J* = 7.3 Hz, *aromatic protons*), 7.99 (brd, 2H, *J* = 7.3 Hz, *aromatic protons*); ^{13}C-NMR ($CDCl_3$) δ: 52.39, 55.17, 55.20, 55.25, 56.16, (each O*C*H$_3$), 63.47 (*C*5′), 68.26 (*C*2), 68.94 (*C*6′), 69.73 (*C*5), 70.39 (*C*3), 71.73, 73.19 (each Ar*C*H$_2$O), 74.46 (*C*2′), 74.68 (*C*4′), 75.41 (*C*3′), 76.49 (*C*4), 97.88 (*C*1), 100.40 (*C*1′), 100.60 (Ar*C*(OR)$_2$), 113.35, 113.58, 113.63, 127.61, 127.61, 128.21, 128.45, 128.60, 129.02, 129.23, 129.26, 129.46, 129.73, 129.75, 129.80, 130.60, 130.79, 130.97, 133.38, 133.53, 159.05, 159.05, 159.91

(*aromatic carbons*), 165.82, 166.02 (each Ar*C*=O), 167.90 (*C*6); FABMS (%, rel. int.) *m/z*: 973 (1.9, $[M + Na]^+$), 829 (1.2, $[M\text{-}CH_3OPhCH]^+$), 121 (100, $[PhCOO]^+$); FAB-HRMS: calcd. for $C_{52}H_{54}O_{17}Na$ $[M + Na]^+$, 973.3259; found, *m/z* 973.3230.

*Methyl {methyl 2,3-di-O-benzoyl-4-O-[2′,3′-bis-O-(4-methoxyphenylmethyl)-6′-methyl-α-D-galactopyranuronosyl]-α-D-galactopyranosid}uronate (**12**).* A solution of **10** (348 mg, 366 μmol) in 60% aqueous acetic acid solution (8.0 ml) was stirred at 50 °C for 20 min. After cooling, the mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (AcOEt:hexane = 50:50) to give the corresponding diol (280 mg, 92%) as a viscous oil, $[\alpha]_D^{22}$ +93.7 (*c* 0.52, $CHCl_3$); IR (film) cm^{-1}: 3450, 2935, 1730, 1510, 1250, 1095, 710; ^{1}H-NMR ($CDCl_3$) *δ*: 3.49, 3.62 (each s, 3H, OC*H*$_3$), 3.63 (dd, 1H, *J* = 3.4, 12.0 Hz, C6′*H*H), 3.69, (dd, 1H, *J* = 3.2, 10.0 Hz, C2′*H*), 3.71 (dd, 1H, *J* = 4.5, 12.0 Hz, C6′*H*H), 3.74, 3.80 (each s, 3H, OC*H*$_3$), 3.92 (dd, 1H, *J* = 3.2, 10.0 Hz, C3′*H*), 4.02 (dd, 1H, *J* = 1.1, 3.2 Hz, C4′*H*), 4.16 (ddd, 1H, *J* = 1.1, 3.4, 4.5, Hz, C5′*H*), 4.51, 4.57 (each d, 1H, *J* = 11.7 Hz, ArC*H*$_2$O), 4.61 (d, 1H, *J* = 11.1 Hz, ArC*H*HO), 4.69 (d, 1H, *J* = 1.8 Hz, C5*H*), 4.70 (d, 1H, *J* = 11.1 Hz, ArC*H*HO), 4.71 (brd, 1H, *J* = 1.8 Hz, C4*H*), 4.79 (d, 1H, *J* = 3.2 Hz, C1′*H*), 5.25 (brs, 1H, C1*H*), 5.75 (m, 2H, C2*H*, C3*H*), 6.78 (brd, 2H, *J* = 8.7 Hz, *aromatic protons*), 6.90 (brd, 2H, *J* = 8.7 Hz, *aromatic protons*), 7.22–7.36 (m, 8H, *aromatic protons*), 7.48 (m, 2H, *aromatic protons*), 7.93–7.96 (m, 4H, *aromatic protons*); ^{13}C-NMR ($CDCl_3$) *δ*: 52.43, 55.14, 55.23, 56.19 (each O*C*H$_3$), 62.95 (*C*6′), 68.20 (*C*2 or 3), 69.16 (*C*4′), 69.98 (*C*5), 70.11 (*C*2 or 3), 70.96 (*C*5′), 72.66, 73.17 (each Ar*C*H$_2$O), 75.72 (*C*2′), 76.64 (*C*3′), 76.88 (*C*4), 98.17 (*C*1), 99.98 (*C*1′), 113.73, 113.88, 128.34, 128.49, 128.94, 129.08, 129.62, 129.77, 129.83, 129.87, 130.25, 130.39, 133.34, 133.42, 159.24, 159.36 (*aromatic carbons*), 165.90, 166.98 (each Ar*C*=O), 168.01 (*C*6); FABMS (%, rel. int.) *m/z*: 855 (61, $[M + Na]^+$), 121 (100, $[CH_3OPhCH_2]^+$), 105 (96, $[PhCO]^+$); FAB-HRMS: calcd. for $C_{44}H_{48}O_{16}Na$ $[M + Na]^+$, 855.2840; found, *m/z* 855.2802.

A suspension of the diol thus obtained (70.6 mg, 84.8 μmol) in CH_2Cl_2 (2.0 ml) was stirred with $PhI(OAc)_2$ (141 mg, 437.8 μmol) and TEMPO (19.9 mg, 127.4 μmol) at room temperature for 10 min. The mixture was poured into H_2O (40 ml) and extracted with AcOEt (30 ml × 3). The organic layers were washed with brine (30 ml), combined, dried over $MgSO_4$, and then concentrated *in vacuo* to give corresponding C6-aldehyde **11** (70.6 mg, 99%). Since this sample gradually decomposed, it was immediately used for the next step. After crude **11** had been dissolved in a mixture of 2-methyl-2-propanol (10 ml) and 2-methyl-2-butene (23.8 mg, 339.4 μmol), sodium dihydrogenphosphate dehydrate (79.4 mg, 508.9 μmol) and sodium chlorite (30.7 mg, 339.5 μmol) were successively added at room temperature. The mixture was stirred for 5 min at room temperature, poured into H_2O (40 ml), and extracted with AcOEt (30 ml × 3). The organic layers were washed with brine (30 ml), combined, dried over $MgSO_4$, and then concentrated *in vacuo*. After diluting with THF (2.0 ml), an ethereal solution of diazomethane was added until the yellow color did not disappear. After concentrating *in vacuo*, silica gel column chromatography (AcOEt:hexane = 40:60) of the residue gave **12** (58.2 mg, 80%) as an oil, $[\alpha]_D^{23}$ +92.7 (*c* 0.74, $CHCl_3$); IR (film) cm^{-1}: 3455, 2935, 1730, 1510, 1250, 1095, 1030, 710; ^{1}H-NMR ($CDCl_3$) *δ*: 3.41, 3.48, 3.64 (each s, 3H, OC*H*$_3$), 3.75 (dd, 1H, *J* = 3.2, 9.9 Hz, C2′*H*), 3.76, 3.80 (each s, 3H, OC*H*$_3$), 4.04 (dd, 1H, *J* = 3.3, 9.9 Hz, C3′*H*), 4.33 (ddd, 1H, *J* = 1.1, 1.6, 3.3 Hz, C4′*H*), 4.58, 4.62 (each d, 1H, *J* = 12.0 Hz, ArC*H*$_2$O), 4.62, 4.68 (each d, 1H, *J* = 10.9 Hz, ArC*H*$_2$O), 4.68 (brs, 1H, C5*H*), 4.73 (dd, 1H, *J* = 1.2, 1.6 Hz, C5′*H*), 4.82 (brd, 1H, *J* = 2.7 Hz, C4*H*), 4.94 (d, 1H, *J* = 3.2 Hz, C1′*H*), 5.33 (d, 1H, *J* = 3.5 Hz, C1*H*), 5.61 (dd, 1H, *J* = 3.5, 10.9 Hz, C2*H*), 5.71 (dd, 1H, *J* = 2.7, 10.9 Hz, C3*H*), 6.80 (brd, 2H, *J* = 8.7 Hz, *aromatic protons*), 6.89 (brd, 2H, *J* = 8.6 Hz, *aromatic protons*), 7.22–7.28 (m, 4H, *aromatic protons*), 7.32–7.37 (m, 4H, *aromatic protons*), 7.49 (m, 2H, *aromatic protons*), 7.93–7.97 (m, 4H, *aromatic protons*); ^{13}C-NMR ($CDCl_3$) *δ*: 49.66, 52.00, 52.44, 55.21, 56.19 (each O*C*H$_3$), 68.44 (*C*2), 68.60 (*C*4′), 69.72 (*C*5), 69.95 (*C*3), 70.82 (*C*5′), 72.49, 73.18 (each Ar*C*H$_2$O), 74.20 (*C*2′), 76.40 (*C*3′), 77.21 (*C*4), 97.85 (*C*1), 99.69 (*C*1′), 113.74, 113.89, 128.38, 128.48, 128.96, 129.20, 129.61, 129.69, 129.76, 129.98, 129.98, 130.25, 133.25, 133.31, 159.24, 159.39 (*aromatic carbons*), 165.88, 166.01 (each Ar*C*=O), 167.92, 168.63 (each *C*=O); FABMS (%, rel. int.) *m/z*: 883 (44, $[M + Na]^+$), 121 (100, $[CH_3OPhCH_2]^+$), 105 (96, $[PhCO]^+$); FAB-HRMS: calcd. for $C_{45}H_{48}O_{17}Na$ $[M + Na]^+$, 883.2789; found, *m/z* 883.2816.

*Methyl {methyl 2,3-di-O-benzoyl-4-O-{2′,3′-bis-O-(4-methoxyphenylmethyl)-4′-O-[2″,3″-bis-O-(4-methoxyphenylmethyl)-4″,6″-O-(methoxyphenlylmethylidene)-α-D-galactopyranosyl]-6′-methyl-α-D-galactopyranuronosyl}-α-D-galactopyranosid}uronate (**13**).* A 0.16 M solution of triethylsilyl trifluoromethanesulfonate in Et_2O (10 μl) was added at 0 °C to a suspension of a mixture of **12** (14.0 mg, 16.3 μmol), **7** (33.3 mg, 48.8 μmol), and powdered 4A molecular sieves (20 mg) in Et_2O (1.0 ml). After stirring for 10 min, triethylamine (10 μl) was added to quench the reaction. The mixture was filtered through a cotton pad, and the filtrate was concentrated *in vacuo*. Purification of the residue by silica gel column chromatography (benzene:AcOEt = 80:20) gave **13** (22.0 mg, 99%) as an oil, $[\alpha]_D^{22}$ +69.7 (*c* 1.15, $CHCl_3$); IR (film) cm^{-1}: 2935, 1730, 1610, 1515, 1250, 1095, 1030, 825, 720; ^{1}H-NMR ($CDCl_3$) *δ*: 2.93 (s, 3H, OC*H*$_3$), 3.40 (dd, 1H, *J* = 1.5, 12.6 Hz, C6″*H*H), 3.49 (s, 3H, OC*H*$_3$), 3.57 (dd, 1H, *J* = 1.7, 12.6 Hz, C6″*H*H), 3.63 (brdd, 1H, *J* = 1.5, 1.7 Hz, C5″*H*), 3.70 (dd, 1H,

$J = 3.3$, 10.2 Hz, C3″*H*), 3.74, 3.75, 3.76, 3.76, 3.76, 3.79 (each s, 3H, OCH_3), 3.83 (dd, 1H, $J = 3.3$, 10.3 Hz, C2′*H*), 3.86 (dd, 1H, $J = 3.2$, 10.2 Hz, C2″*H*), 3.89 (brd, 1H, $J = 3.3$ Hz, C4″*H*), 4.01 (dd, 1H, $J = 2.3$, 10.3 Hz, C3′*H*), 4.37 (brd, 1H, $J = 2.3$ Hz, C4′*H*), 4.50 (d, 1H, $J = 12.0$ Hz, ArC*H*HO), 4.51 (d, 1H, $J = 12.4$ Hz, ArC*H*HO), 4.52 (s, 2H, ArCH_2O), 4.56 (d, 1H, $J = 12.0$ Hz, ArC*H*HO), 4.61 (brs, 1H, C5′*H*), 4.63, 4.67 (each d, 1H, $J = 11.4$ Hz, ArCH_2O), 4.69 (brs, 1H, C5*H*), 4.75 (d, 1H, $J = 12.4$ Hz, ArC*H*HO), 4.90 (d, 1H, $J = 3.2$ Hz, C1″*H*), 4.94 (brd, 1H, $J = 2.4$ Hz, C4*H*), 5.13 (d, 1H, $J = 3.3$ Hz, C1′*H*), 5.24 (s, 1H, ArC*H*), 5.34 (d, 1H, $J = 2.9$ Hz, C1*H*), 5.67 (dd, 1H, $J = 2.9$, 11.0 Hz, C2*H*), 5.71 (dd, 1H, $J = 2.4$, 11.0 Hz, C3*H*), 6.76–6.88 (m, 10H, *aromatic protons*), 7.18 (brd, 2H, $J = 8.7$ Hz, *aromatic protons*), 7.25–7.37 (m, 12H, *aromatic protons*), 7.48 (m, 2H, *aromatic protons*), 7.88 (brdd, 2H, $J = 1.3$, 8.3 Hz, *aromatic protons*), 7.94 (brdd, 2H, $J = 1.4$, 8.6 Hz, *aromatic protons*); ^{13}C-NMR ($CDCl_3$) δ: 51.52, 52.52, 55.13, 55.18, 55.18, 55.21, 55.23, 56.16 (each O*C*H$_3$), 62.85 (*C*5″), 68.35 (*C*3), 69.12 (*C*6″), 69.57 (*C*5), 70.16 (*C*2), 71.23, 71.33, 72.30 (each Ar*C*H$_2$O), 72.63 (*C*5′), 72.78 (Ar*C*H$_2$O), 73.00 (*C*2″), 74.11 (*C*2′), 74.48 (*C*4″), 75.74 (*C*3″), 76.14 (*C*4), 76.20 (*C*3′), 76.33 (*C*4′), 97.80 (*C*1), 98.82 (*C*1′), 99.78 (*C*1″), 100.59 (Ar*C*(OR)$_2$), 113.30, 113.45, 113.51, 113.53, 113.72, 127.61, 128.37, 128.49, 128.96, 129.00, 129.16, 129.16, 129.61, 129.72, 129.80, 129.90, 130.39, 130.40, 130.70, 130.83, 131.05, 133.24, 133.30, 158.86, 159.95, 159.07, 159.09, 159.84 (*aromatic carbons*), 165.87, 165.87 (each Ar*C*=O), 167.88, 168.06 (each *C*=O); FABMS (%, rel. int.) *m/z*: 1403 (4.2, $[M + Na]^+$), 121 (100, $[CH_3OPhCH_2]^+$), 105 (82, $[PhCO]^+$); FAB-HRMS: calcd. for $C_{75}H_{80}O_{25}Na$ $[M + Na]^+$, 1403.4886; found, *m/z* 1403.4907.

*Methyl {methyl 2,3-di-O-benzoyl-4-O-{2′,3′-bis-O-(4-methoxyphenylmethyl)-4′-O-[2″,3″-bis-O-(4-methoxyphenylmethyl)-6″-methyl-α-D-galactopyranuronosyl]-6′-methyl-α-D-galactopyranuronosyl}-α-D-galactopyranosid}uronate (**14**).* A solution of **13** (21.1 mg, 15.4 mmol) in 90% aqueous acetic acid solution (1.0 ml) was stirred at 50 °C for 20 min. After cooling, the mixture was concentrated *in vacuo*. Silica gel column chromatography of the residue (AcOEt:hexane = 70:30) gave the corresponding diol (15.4 mg, 79%) as an oil, $[\alpha]_D^{23}$ +75.0 (*c* 0.84, $CHCl_3$); IR (film) cm^{-1}: 3450, 2935, 1730, 1510, 1250, 1095, 1030, 710; ^{1}H-NMR ($CDCl_3$) δ: 2.33 (brd, 1H, $J = 8.9$ Hz, C6″O*H*), 2.51 (brs, 1H, C4″O*H*), 3.04 (s, 3H, OCH_3), 3.48 (m, 1H, C6″*H*H), 3.49 (s, 3H, OCH_3), 3.57–3.65 (m, 3H, C6″*H*H, C2″*H*, C3″*H*), 3.70, 3.73, 3.75, 3.76, 3.79 (each s, 3H, OCH_3), 3.83 (dd, 1H, $J = 3.3$, 10.3 Hz, C2′*H*), 3.87–3.90 (m, 2H, C4″*H*, C5″*H*), 4.03 (dd, 1H, $J = 2.5$, 10.3 Hz, C3′*H*), 4.27 (dd, 1H, $J = 0.9$, 2.5 Hz, C4′*H*), 4.43 (d, 1H, $J = 12.1$ Hz, ArC*H*HO), 4.45 (d, 1H, $J = 10.6$ Hz, ArC*H*HO), 4.51 (d, 1H, $J = 12.1$ Hz, ArC*H*HO), 4.53 (d, 1H, $J = 10.6$ Hz, ArC*H*HO), 4.59 (d, 1H, $J = 12.1$ Hz, ArC*H*HO), 4.65 (d, 1H, $J = 0.9$ Hz, C5′*H*), 4.65, 4.68 (each d, 1H, $J = 12.1$ Hz, ArCH_2O), 4.68 (brs, 1H, C5*H*), 4.70 (d, 1H, $J = 12.1$ Hz, ArC*H*HO), 4.81 (brs, 1H, C1″*H*), 4.91 (brd, 1H, $J = 2.1$ Hz, C4*H*), 5.06 (d, 1H, $J = 3.3$ Hz, C1′*H*), 5.35 (d, 1H, $J = 2.8$ Hz, C1*H*), 5.66 (dd, 1H, $J = 2.8$, 10.9 Hz, C2*H*), 5.70 (dd, 1H, $J = 2.1$, 10.9 Hz, C3*H*), 6.78–6.81 (m, 4H, *aromatic protons*), 6.81–6.89 (m, 4H, *aromatic protons*), 7.18–7.21 (m, 4H, *aromatic protons*), 7.26–7.36 (m, 8H, *aromatic protons*), 7.48 (m, 2H, *aromatic protons*), 7.88 (brdd, 2H, $J = 1.3$, 8.3 Hz, *aromatic protons*), 7.95 (brdd, 2H, $J = 1.3$, 8.3 Hz, *aromatic protons*); ^{13}C-NMR ($CDCl_3$) δ: 51.68, 52.54, 55.12, 55.21, 55.21, 55.25, 56.19 (each O*C*H$_3$), 62.96 (*C*6″), 68.39 (*C*3), 69.09 (*C*4″), 69.61 (*C*5), 69.70 (*C*5″), 70.23 (*C*2), 71.37 (*C*5′), 72.20, 72.57, 72.63, 73.01 (each Ar*C*H$_2$O) 73.79 (*C*2′), 74.82 (*C*2″ or 3″), 76.18 (*C*3′), 76.53 (*C*4), 77.20 (*C*2″ or 3″), 77.81 (*C*4′), 97.82 (*C*1), 99.21 (*C*1″), 99.25 (*C*1′), 113.61, 113.61, 113.79, 113.82, 128.38, 128.46, 129.00, 129.20, 129.36, 129.56, 129.69, 129.69, 129.74, 129.88, 130.13, 130.28, 130.56, 130.59, 133.22, 133.31, 159.07, 159.09, 159.25, 159.28 (*aromatic carbons*), 165.86, 165.94 (each Ar*C*=O), 167.99, 168.02 (each *C*=O); FABMS (%, rel. int.) *m/z*: 1285 (0.6, $[M + Na]^+$), 121 (100, $[CH_3OPhCH_2]^+$); FAB-HRMS: calcd. for $C_{67}H_{74}O_{24}Na$ $[M + Na]^+$, 1285.4468; found, *m/z* 1285.4490.

A suspension of the product (20.0 mg, 15.8 μmol) in CH_2Cl_2 (1.0 ml) was stirred with PhI(OAc)$_2$ (26.2 mg, 81.3 μmol) and TEMPO (1.2 mg, 7.7 μmol) at room temperature for 30 min. The mixture was poured into H_2O (20 ml) and extracted with AcOEt (15 ml × 3). The organic layers were washed with brine (15 ml), combined, dried over $MgSO_4$, and then concentrated *in vacuo*. After diluting with a mixture of 2-methyl-2-propanol (0.5 ml) and 2-methyl-2-butene (4.4 mg, 63.0 μmol), sodium dihydrogenphosphate dehydrate (14.8 mg, 94.9 μmol) and sodium chlorite (5.7 mg, 63.0 μmol) were successively added at room temperature. After stirring for 30 min, the mixture was poured into H_2O (20 ml) and extracted with AcOEt (15 ml × 3). The organic layers were washed with brine (15 ml), combined, dried over $MgSO_4$, and then concentrated *in vacuo*. After diluting with THF (1.0 ml), an ethereal solution of diazomethane was added until the yellow color did not disappear. After concentrating *in vacuo*, silica gel column chromatography (AcOEt:hexane = 40:60) of the residue gave **14** (14.0 mg, 68%) as an oil, $[\alpha]_D^{23}$ +67.2 (*c* 0.75, $CHCl_3$); IR (film) cm^{-1}: 3450, 2935, 1730, 1510, 1250, 1100, 1030, 820, 715; ^{1}H-NMR ($CDCl_3$) δ: 2.92, 3.49 (each s, 3H, OCH_3), 3.54 (dd, 1H, $J = 3.2$, 10.0 Hz, C3″*H*), 3.59 (s, 3H, OCH_3), 3.62 (d, 1H, $J = 3.0$, 10.0 Hz, C2″*H*), 3.70, 3.74, 3.74, 3.79, 3.80 (each s, 3H, OCH_3), 3.28 (dd, 1H, $J = 3.3$, 10.5 Hz, C2′*H*), 4.03 (dd, 1H, $J = 2.2$, 10.5 Hz, C3′*H*), 4.23 (brd, 1H, $J = 3.2$ Hz, C4″*H*), 4.25 (brd, 1H, $J = 2.2$ Hz, C4′*H*), 4.39 (d, 1H, $J = 12.3$ Hz, ArCH_2O), 4.43 (s, 2H, ArCH_2O), 4.52 (d, 1H, $J = 12.3$ Hz, ArCH_2O), 4.55

(brs, 1H, C5′*H*), 4.57 (d, 1H, $J = 11.8$ Hz, ArCH_2O), 4.62 (d, 1H, $J = 12.7$ Hz, ArCH_2O), 4.68 (brs, 1H, C5*H*), 4.73 (d, 1H, $J = 11.8$ Hz, ArCH_2O), 4.80 (d, 1H, $J = 12.7$ Hz, ArCH_2O), 4.85 (brs, 1H, C5″*H*), 4.88 (d, 1H, $J = 3.3$ Hz, C1″*H*), 4.91 (brd, 1H, $J = 2.3$ Hz, C4*H*), 5.05 (d, 1H, $J = 3.3$ Hz, C1′*H*), 5.35 (d, 1H, $J = 3.0$ Hz, C1*H*), 5.67 (dd, 1H, $J = 3.0$, 11.0 Hz, C2*H*), 5.71 (dd, 1H, $J = 2.3$, 11.0 Hz, C3*H*), 6.72 (brd, 2H, $J = 8.4$ Hz, *aromatic protons*), 6.83–6.90 (m, 6H, *aromatic protons*), 7.11 (brd, 2H, $J = 8.5$ Hz, *aromatic protons*), 7.19 (brd, 2H, $J = 8.5$ Hz, *aromatic protons*), 7.24–7.38 (m, 8H, *aromatic protons*), 7.48 (m, 2H, *aromatic protons*), 7.81 (brd, 2H, $J = 7.5$ Hz, *aromatic protons*), 7.94 (brd, 2H, $J = 7.5$ Hz, *aromatic protons*); ^{13}C-NMR ($CDCl_3$) δ: 51.49, 52.08, 52.59, 55.07, 55.17, 55.20, 55.24, 56.19 (each O*C*H$_3$), 68.27 (*C*4″), 68.36 (*C*3), 69.47 (*C*5), 70.08 (*C*2), 70.42 (*C*5″), 71.08 (*C*5′), 71.82 (*C*2′), 71.94, 72.16, 72.61, 72.63 (each Ar*C*H$_2$O), 72.96 (*C*2″), 75.74 (*C*4), 75.87 (*C*3′), 77.21 (*C*3″), 77.21 (*C*4′), 97.79 (*C*1), 98.64 (*C*1′), 99.20 (*C*1″), 113.58, 113.68, 113.70, 113.79, 128.39, 128.52, 128.95, 129.18, 129.35, 129.47, 129.54, 129.69, 129.72, 129.87, 130.03, 130.14, 130.26, 130.34, 133.27, 133.31, 159.01, 159.01, 159.15, 159.29 (*aromatic carbons*), 165.75, 165.82 (each Ar*C*=O), 167.76, 168.09, 168.47 (each *C*=O); FABMS (%, rel. int.) *m/z*: 1313 (8.4, $[M + Na]^+$), 121 (100, $[CH_3OPhCH_2]^+$), 105 (76, $[PhCO]^+$); FAB-HRMS: calcd. for $C_{68}H_{74}O_{25}Na$ $[M + Na]^+$, 1313.4417; found, *m/z* 1313.4409.

*Methyl O-(α-D-galactopyranuronosyl)-(1′→4)-O-(α-D-galactopyranuronosyl)-(1″→4′)-α-D-galactopyranosiduronic acid (**3**).* A suspension of **14** (26.4 mg, 20.4 μmol) in a mixture of CH_2Cl_2 (1.0 ml) and H_2O (0.1 ml) was vigorously stirred with DDQ (23.2 mg, 102.2 μmol) at room temperature for 6 h. After concentrating, silica gel column chromatography (acetone:CH_2Cl_2 = 80:20) of the residue gave the MPM deprotected pentaol (14.9 mg, 90%) as an oil, $[\alpha]_D^{23}$ +32.4 (*c* 0.59, CH_3OH); IR (film) cm^{-1}: 3420, 2925, 1730, 1580, 1450, 1275, 1105, 1020, 715; ^{1}H-NMR (CD_3OD) δ: 3.12, 3.50 (each s, 3H, OC*H*$_3$), 3.59 (dd, 1H, $J = 3.8$, 10.3 Hz, C2″*H*), 3.66 (dd, 1H, $J = 3.8$, 10.7 Hz, C2′*H*), 3.68 (dd, 1H, $J = 3.4$, 10.3 Hz, C3″*H*), 3.73, 3.84 (each s, 3H, OC*H*$_3$), 4.02 (dd, 1H, $J = 2.9$, 10.7 Hz, C3′*H*), 4.15 (dd, 1H, $J = 1.4$, 3.4 Hz, C4″*H*), 4.32 (brd, 1H, $J = 2.9$ Hz, C4′*H*), 4.74 (d, 1H, $J = 3.8$ Hz, C1″*H*), 4.76 (brs, 1H, C5′*H*), 4.84 (brs, 1H, C5*H*), 4.91 (brd, 1H, $J = 3.0$ Hz, C4*H*), 5.02 (d, 1H, $J = 3.8$, C1′*H*), 5.05 (d, 1H, $J = 1.4$ Hz, C5″*H*), 5.27 (d, 1H, $J = 3.5$ Hz, C1*H*), 5.58 (dd, 1H, $J = 3.0$, 11.0 Hz, C3*H*), 5.68 (dd, 1H, $J = 3.5$, 11.0 Hz, C2*H*), 7.34 (m, 4H, *aromatic protons*), 7.52 (m, 2H, *aromatic protons*), 7.84 (brd, 2H, $J = 7.4$ Hz, *aromatic protons*), 7.90 (brd, 2H, $J = 7.1$ Hz, *aromatic protons*); ^{13}C-NMR (CD_3OD) δ: 52.47, 52.59, 53.19, 56.55 (each O*C*H$_3$), 69.33 (*C*2′), 69.40 (*C*2), 69.40 (*C*3′), 69.62 (*C*2″), 70.70 (*C*3″), 70.97 (*C*5), 71.81 (*C*4″), 71.91 (*C*3), 72.48 (*C*5′), 72.81 (*C*5″), 79.00 (*C*4), 80.50 (*C*4′), 99.20 (*C*1), 102.18 (*C*1″), 102.92 (*C*1′), 129.63, 129.81, 130.35, 130.48, 130.65, 130.79, 134.65, 134.71 (*aromatic carbons*), 167.32, 167.40 (each Ar*C*=O), 169.84, 170.02, 171.67 (each *C*=O); FABMS (%, rel. int.) *m/z*: 833 (50, $[M + Na]^+$), 121 (86, $[PhCOO]^+$), 105 (100, $[PhCO]^+$); FAB-HRMS: calcd. for $C_{36}H_{42}O_{21}Na$ $[M + Na]^+$, 833.2038; found, *m/z* 833.2101. The product (10.3 mg, 12.7 μmol) was stirred in a mixture of THF (1.0 ml) and a 0.3% NaOH aqueous solution (1.5 ml) at room temperature for 30 min. The mixture was passed through an ion-exchange column (DOWEX 50W, H^+ form). Lyophilization of the eluent gave **3** (7.0 mg, 98%) as an amorphous powder, $[\alpha]_D^{24}$ +107.7 (*c* 1.25, H_2O); ^{1}H-NMR (D_2O) δ: 3.25 (s, 3H, OC*H*$_3$), 3.56 (dd, 1H, $J = 3.9$, 10.3 Hz, C2″*H*), 3.60 (dd, 1H, $J = 3.9$, 10.7 Hz, C2′*H*), 3.67 (dd, 1H, $J = 3.8$, 10.6 Hz, C2*H*), 3.76 (dd, 1H, $J = 3.4$, 10.3 Hz, C3″*H*), 3.82 (dd, 1H, $J = 3.1$, 10.6 Hz, C3*H*) 3.87 (dd, 1H, $J = 3.0$, 10.7 Hz, C3′*H*), 4.16 (dd, 1H, $J = 1.4$, 3.4 Hz, C4″*H*), 4.29 (brd, 1H, $J = 3.0$ Hz, C4′*H*), 4.30 (dd, 1H, $J = 0.7$, 3.1 Hz, C4*H*), 4.47 (d, 1H, $J = 0.7$ Hz, C5*H*), 4.77 (d, 1H, $J = 3.8$ Hz, C1*H*), 4.88 (d, 1H, $J = 3.9$ Hz, C1″*H*), 4.91 (d, 1H, $J = 1.4$ Hz, C5″*H*), 4.93 (brs, 1H, C5′*H*), 4.94 (d, 1H, $J = 3.9$ Hz, C1′*H*); ^{13}C-NMR (D_2O) δ: 58.22 (O*C*H$_3$), 70.15 (*C*2), 70.35 (*C*2″), 70.37 (*C*2′), 70.57 (*C*3′), 70.63 (*C*3), 71.24 (*C*3″), 72.03 (*C*5), 72.48 (*C*4″), 72.72 (*C*5′), 73.45 (*C*5″), 80.69 (*C*4), 80.96 (*C*4′), 102.12 (*C*1), 102.46 (*C*1″), 102.59 (*C*1′), 174.51, 174.72, 175.35 (each *C*=O); negative-FABMS (%, rel. int.) *m/z*: 599 (4.5, $[M - H]^-$), 148 (100, $[C_5H_8O_5]^-$); negative-FAB-HRMS: calcd. for $C_{19}H_{27}O_{19}$ $[M - H]^-$, 559.1147; found, *m/z* 559.1169.

920-MHz NMR measurements. Sample solutions for NMR measurements were prepared by dissolving in 99.9% D_2O, the sample pH not being adjusted. Shigemi NMR sample tubes matched with D_2O were used. 920-MHz NMR spectra were measured by a JEOL spectrometer at Institute for Molecular Science, Okazaki, Japan. The sample was not spun, and the spectra were recorded at a temperature of 298 K. The water signal was suppressed by DANTE (Delay Alternating with Nutation for Tailored Exitation) method.[21] One-dimensional ^{1}H-NMR experiments were performed with a spectral width of 11,510.12891 Hz, 64 K data points and 8 scans. Both the two-dimensional ROESY[14,15] and NOESY[16] spectra were recorded in the phase-sensitive mode, with a mixing time of 300 msec. and with 2048 × 512 data points, and were zero-filled to yield 2048 × 2048 data matrices. The two-dimensional {^{13}C}-^{1}H HSQC[22] spectrum was recorded without ^{13}C decoupling during the acquisition period and with 2048 × 128 data points. The number of scans for all spectra was 8. Time domain data in both dimensions were multiplied by a sine bell squared function. All 2D NMR spectra were processed by NMRPipe software,[23] and the signals were assigned by Sparky 3 (Goddard, T., and Kneller, D. G., *SPARKY 3*, University of California, San Francisco, CA, USA) run under Windows XP.

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