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Galabiosyl donors; efficient synthesis from 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose

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Abstract

1,2,3,4,6-Penta-*O*-acetyl-β-D-galactopyranose was transformed into phenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-galactopyranoside (**5**) and 4-methoxyphenyl 2,3,6-tri-*O*-benzoyl-β-D-galactopyranoside (**8**) in 73% (two steps) and 58% (three steps) yield, respectively. Glycosylation of the acceptor **8** with donor **5** using *N*-iodosuccinimide–trimethylsilyl trifluoromethanesulfonate as promoter furnished the galabioside **9** (8.8 g) in 95% yield. Further transformations provided in high yields anomerically-activated galabiosides (thioglycoside (**1**), trichloroacetimidate (**2**), and bromosugar (**3**)) suitable for use as glycosyl donors in syntheses of galabiose-containing oligosaccharides. Several of the compounds reported here are crystalline, which greatly simplified purifications.

Keywords: Galabiosyl donor; Globo series; Glycolipids; Protein–oligosaccharide interactions

1. Introduction

In order to facilitate projects aiming at a deepened insight into the molecular recognition between various protein receptors and saccharides of the globo series of glycolipids [1–13], we now report an efficient and high yielding synthetic procedure for the preparation of the galabiosyl donors **1**–**3** (Fig. 1) via several crystalline intermediates. The donors are suitable for glycosylations leading to compounds related to the globo series (Gb3, Gb4, Forssman antigen, P_1 antigen). We used a galabiosyl donor (obtained by reduction of digalacturonic acid from pectin [14]) for early syntheses of Gb3 and P_1-antigen glycoconjugates [15,16], whereas other syntheses were based on α-galactosylation of suitably protected lactosides [11].

2. Results and discussion

1,2,3,4,6-Penta-*O*-acetyl-β-D-galactopyranose was transformed into the phenyl thiogalactoside **4** [17] (Scheme 1) by treatment with thiophenol and $BF_3{\cdot}Et_2O$, followed by extractive removal of residual thiophenol using 2 M aqueous sodium hydroxide, and O-deacetylation with methanolic sodium methanoate. Compound **4** was obtained pure in 81% yield by crystallization from ethanol. Treatment of **4** with benzyl bromide and sodium hydride in DMF, followed by addition of water gave **5** as a precipitate, which was recrystallized from heptane–diethylether to furnish pure donor **5** [18] in 90% yield.

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Treatment of 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranose with 4-methoxyphenol and $BF_3{\cdot}Et_2O$, followed by extractive removal of residual 4-methoxyphenol using 2 M aqueous sodium hydroxide and O-deacetylation with methanolic sodium methanoate gave pure **6** [19] in 75% yield after recrystallization from ethanol.

Attempted regioselective O-benzoylation of **6** (to give **8**) was unsuccessful and a mixture of partially O-benzoylated products were obtained. Instead, treatment of **6** with α,α-dimethoxytoluene and a catalytic amount of 4-toluenesulfonic acid in acetonitrile provided the 4,6-*O*-benzylidene derivative **7** [20] (96%); addition of the reagents to a suspension of **6** in acetonitrile gave rapidly a clear solution, from which pure **7** precipitated.

Treatment of **7** with benzoyl chloride and *N*,*N*-dimethylaminopyridine in pyridine gave the 2,3-di-*O*-benzoate, the 4,6-*O*-benzylidene group of which was removed with aqueous hydrochloric acid in THF. Regioselective 6-O-benzoylation with benzoyl chloride in pyridine

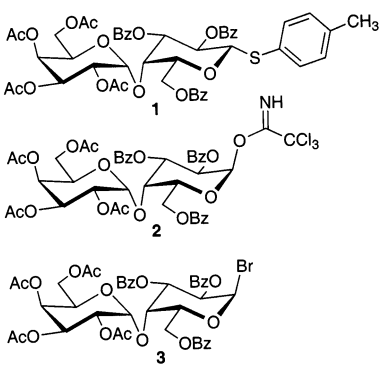
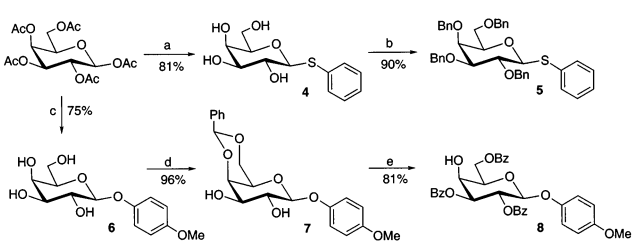
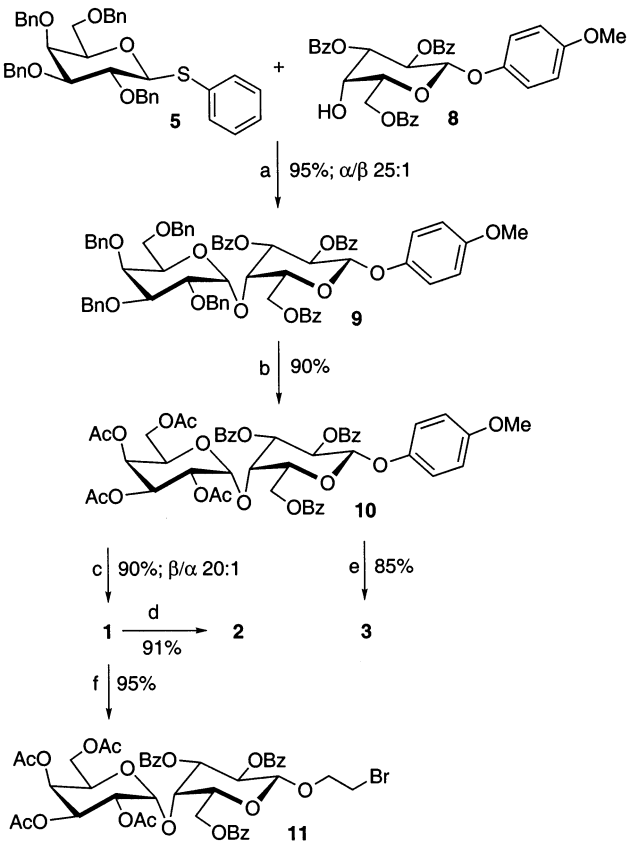


Fig. 1.



Scheme 1. (a) PhSH, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 22 °C, 2 h. (b) $PhCH_2Br$, NaH, DMF, 22 °C, 10 h. (c) MeOPhOH, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 22 °C, 2 h. (d) $(MeO)_2CHPh$, $MePhSO_3H$, MeCN, 22 °C, 30 min. (e) BzCl, pyridine, DMAP, 22 °C, 15 h, then 2 M HCl, THF, 55 °C, 26 h, then BzCl, pyridine, − 10 °C, 60 min, then MeOH.



Scheme 2. (a) NIS, TMSOTf, CH_2Cl_2, Et_2O, − 55 °C, 2 h. (b) H_2, Pd–C, AcOH, 22 °C, 24 h, then Ac_2O, pyridine 22 °C, 19 h. (c) MePhSH, $BF_3{\cdot}Et_2O$, toluene, CH_2Cl_2, 60 °C, 48 h. (d) NBS, Me_2CO, H_2O, then Cl_3CCN, DBU, CH_2Cl_2, 0 °C, 1 h. (e) AcBr, $ZnBr_2$, CH_2Cl_2, 22 °C, 5 h. (f) $BrCH_2CH_2OH$, NIS, TMSOTf, 0 °C, 10 min.

at − 10 °C furnished the acceptor galactoside **8** (81%) as a pure compound after crystallization from heptane–ethyl acetate.

The acceptor **8** was α-galactosylated with the donor **5**, using *N*-iodosuccinimide–trimethylsilyl trifluoromethanesulfonate [21] as promoter in a 1:2 mixture of dichloromethane and diethylether, which furnished the galabioside **9** in 95% yield (α/β > 25:1) (Scheme 2). A number of alternative glycosylation conditions were also investigated: with solvent mixtures containing toluene, lower yields (61–77%) and stereoselectivities (α/β 1:1–20:1) were obtained in reactions that did not go to completion. However, with MeSBr–silver trifluoromethanesulfonate as promoter in dichloromethane, a good yield and stereoselectivity was obtained (93%, α/β 25:1), but the reagents are more expensive than those of the preferred and more convenient procedure described above.

The thiophenyl residue(s) formed in the glycosylation reaction was removed by simple chromatography, the *O*-benzyl groups of the disaccharide were removed by hydrogenolysis, and O-acetylation gave the crystalline per-O-acylated compound **10** in 90% overall yield.

Treatment of **10** with thiocresol and $BF_3{\cdot}Et_2O$ furnished the crystalline cresyl β-thiogalabioside **1** in 90% yield together with a small amount ($<5\%$) of the corresponding α-glycoside. Compound **1** was transformed into the trichloroacetimidate **2** (91%) by treatment with *N*-bromosuccinimide [22] in a mixture of acetone and water (to obtain the corresponding hemiacetal), followed by trichloroacetonitrile–DBU [23]; treatment of **10** with cerium ammonium nitrate [24] gave the hemiacetal in only 48% yield. The bromo sugar **3** was obtained in 85% yield by treatment of **10** with mixture of acetyl bromide and zinc bromide [25].

The cresyl thiogalabioside **1** was transformed into the crystalline 2-bromoethyl glycoside **11** [26] in 95% yield by treatment with 2-bromoethanol and trimethylsilyl trifluoromethanesulfonate in dichloromethane at 0 °C. 2-Bromoethyl glycosides are useful starting materials for the preparation of various spacer–arm glycosides and neoglycolipids, as exemplified by our syntheses of globo series glycoconjugates [27] and a GM3-lactam-BSA conjugate for immunization of mice [28].

3. Experimental

Melting points are uncorrected. NMR spectra were recorded with a 400 MHz instrument. ^{1}H NMR spectral assignments were made by the double resonance technique COSY. Concentrations were made using rotary evaporation with a bath temperature at or below 40 °C. Flash chromatography was performed on Grace Amicon Silica Gel 60 (0.035–0.070 mm) and TLC was performed on Kieselgel 60 F_{254} plates (E. Merck). All non-aqueous reactions were run in septum-capped, oven-dried flasks under Ar (1 atm).

4-Methylphenyl (2,3,4,6-tetra-O-*acetyl*-α-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzoyl-1-thio*-β-D-*galactopyranoside* (**1**).—Compound **10** (3.00 g, 3.28 mmol) and 4-methylthiophenol (1.12 g, 9.85 mmol) were dissolved in a 1:1 mixture of toluene and CH_2Cl_2 (100 mL) at rt and $BF_3{\cdot}Et_2O$ (0.41 mL, 3.28 mmol) was added. The mixture was stirred at 60 °C for 12 h and a second portion of $BF_3{\cdot}Et_2O$ (0.33 mL) was added over 24 h. After 48 h, the mixture was diluted with CH_2Cl_2 (200 mL), washed with satd aq $NaHCO_3$ soln (2 × 50 mL), dried (Na_2SO_4), and concd. The residue was crystallized from Et_2O–heptane (4:1) to give **1** (2.30 g, 77%). Concentration of the mother liquid and flash chromatography (SiO_2, 2:1 heptane–EtOAc) gave additional **1** (total yield 2.70 g, 90%); mp 171–173 °C; $[\alpha]_D^{23}$ +106° (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.09–7.35 (m, 17 H, Ph), 7.18 (d, 2 H, *J* 7.9 Hz, Ph), 5.53 (t, 1 H, *J* 10.1 Hz, H-2), 5.35 (m, 2 H, H-3, 3′), 5.28 (d, 1 H, *J* 3.2 Hz, H-4′), 5.18 (dd, 1 H, *J* 3.6, 11.0 Hz, H-2′), 5.09 (d, 1 H, *J* 3.6 Hz, H-1′), 4.90 (d, 1 H, *J* 9.7 Hz, H-1), 4.77 (dd, 1 H, *J* 7.0, 11.3 Hz, H-6′), 4.56 (dd, 1 H, *J* 5.3, 11.6 Hz, H-6′), 4.37 (d, 1 H, *J* 2.5 Hz, H-4), 4.17 (t, 1 H, *J* 3.7 Hz, H-5′), 3.97 (m, 2 H, H-5, 6), 3.81 (dd, 1 H, *J* 5.2, 10.0 Hz, H-6), 2.39 (s, 3 H, Me), 2.15, 2.09, 2.04, 1.99 (4 s, 3 H each, OAc). ^{13}C NMR ($CDCl_3$): δ 170.9, 170.8, 170.6, 170.1, 166.6, 166.5, 165.3, 139.3, 135.2, 134.0, 133.9, 133.7, 130.4, 130.21, 130.17, 130.1, 129.9, 129.1, 129.0, 128.9, 128.8, 127.2, 99.1, 85.9, 77.7, 77.4, 76.8, 75.3, 68.9, 68.2, 68.0, 67.8, 67.6, 63.7, 61.3, 21.6, 21.3, 21.14, 21.06. HRMS calcd for $C_{48}H_{48}NaO_{17}S$ (M + Na): 951.2533, found: 951.2510.

Trichloroacetimido (2,3,4,6-tetra-O-*acetyl*-α-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzoyl-thio*-β-D-*galactopyranoside* (**2**).—Compound **1** (90 mg, 0.097 mmol) was dissolved in a 9:1 mixture of acetone and water (1.30 mL) and *N*-bromosuccinimide (NBS) (70 mg, 0.386 mmol) was added. After 1 h, the solvent was removed and the residue was dissolved in EtOAc (4 mL), washed with satd aq $NaHCO_3$ (2 mL) and water (2 mL), dried (Na_2SO_4), and concd and the residue was flash chromatographed (SiO_2, 3:1→1:1, heptane: EtOAc gradient). The resulting crude hemiacetal was dissolved in CH_2Cl_2 (1.5 mL), Cl_3CCN (0.35 mL) was added, and the mixture was cooled to 0 °C. (0.022 mL, 0.15

mmol) was added, the reaction mixture was stirred for 1 h, diluted with CH_2Cl_2 (5 mL), washed with ice-cold satd aq $NaHCO_3$ (2 mL), dried (Na_2SO_4), and concd. The residue was flash chromatographed (SiO_2, 2:1:0.01 heptane:EtOAc:Et_3N) to give **2** (85 mg, 91%); $[\alpha]_D^{23}$ +128° (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.64 (s, 1 H, NH), 8.03–7.94 (m, 5 H, Ph), 7.61–7.34 (m, 10 H, Ph), 6.84 (d, 1 H, *J* 3.7 Hz, H-1), 5.95 (dd, 1 H, *J* 3.7, 10.9 Hz, H-2), 5.84 (dd, 1 H, *J* 2.7, 10.9 Hz, H-3), 5.50 (m, 2 H, H-3′, 4′), 5.27 (m, 2 H, H-1′, 2′), 4.67–4.49 (m, 5 H), 3.81 (dd, 1 H, *J* 7.4, 11.1 Hz, H-6), 3.63 (dd, 1 H, *J* 6.4, 11.0 Hz, H-6), 2.19, 2.10, 2.03, 1.80 (4 s, 3 H each, OAc). ^{13}C NMR ($CDCl_3$): δ 170.9, 170.56, 170.55, 170.3, 166.5, 166.4, 165.9, 161.0, 134.2, 134.0, 133.9, 130.3, 130.21, 130.15, 128.7, 129.2, 129.1, 128.93, 128.88, 98.7, 94.2, 91.2, 76.4, 71.6, 70.7, 68.5, 68.2, 67.9, 67.80, 67.77, 63.0, 61.4, 21.3, 21.1, 21.0, 20.9. HRMS calcd for $C_{43}H_{42}Cl_3NNaO_{18}$ (M + Na): 988.1365, found: 988.1366.

2,3,4,6-Tetra-O-*acetyl*-α-D-*galactopyranosyl*-(1→4)-*2,3,6-tri*-O-*benzoyl*-*1-bromo*-α-D-*galactopyranose* (**3**).—Compound **10** (100 mg, 0.109 mmol) was dissolved in CH_2Cl_2 (2.0 mL) and AcBr (0.032 mL, 0.438 mmol) and a catalytic amount of $ZnBr_2$ were added. The reaction was monitored by TLC. The mixture was stirred at ambient temperature for 5 h, then diluted with CH_2Cl_2 (25 mL), washed with satd aq $NaHCO_3$ soln (10 mL) and water (10 mL), dried (Na_2SO_4), and concd. The residue was flash chromatographed (SiO_2, 2:1→1:1 heptane:EtOAc gradient) to give **3** (81 mg, 85%); $[\alpha]_D^{23}$ +162° (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.08–7.97 (m, 5 H, Ph), 7.64–7.37 (m, 10 H, Ph), 6.93 (d, 1 H, *J* 3.9 Hz, H-1), 5.80 (dd, 1 H, *J* 2.6, 10.8 Hz, H-3), 5.65 (dd, 1 H, *J* 4.0, 10.8 Hz, H-2), 5.52–5.45 (m, 2 H, H-3′, 4′), 5.30 (dd, 1 H, *J* 3.6, 10.9 Hz, H-2′), 5.21 (d, 1 H, *J* 3.5 Hz, H-1′), 4.72–4.53 (m, 5 H), 3.82 (m, 1 H, H-6), 3.62 (dd, 1 H, *J* 6.4, 11.1 Hz, H-6), 2.19, 2.10, 2.02, 1.78 (4 s, 3 H each, OAc). ^{13}C NMR ($CDCl_3$): δ 170.8, 170.54, 170.50, 170.4, 166.44, 166.39, 165.8, 134.2, 134.0, 130.4, 130.3, 130.2, 129.6, 129.14, 129.10, 129.02, 129.00, 99.1, 89.3, 76.3, 73.7, 71.3, 68.6, 68.5, 68.1, 67.9, 67.8, 62.6, 61.4, 21.2, 21.1, 21.0, 20.8. HRMS calcd for $C_{41}H_{41}BrNaO_{17}$ (M + Na): 907.1425, found: 907.1420.

Phenyl 1-thio-β-D-*galactopyranoside* (**4**).—1,2,3,4,6-Penta-*O*-acetyl-β-D-galactopyranose (10.0 g, 25.6 mmol) [29] was dissolved in CH_2Cl_2 (50 mL), thiophenol (4.0 mL, 39 mmol) was added, and the mixture was cooled to 0 °C. $BF_3{\cdot}Et_2O$ (4.0 mL, 32 mmol) was added dropwise and the reaction mixture was allowed to reach rt. After 2 h, the mixture was diluted with CH_2Cl_2 (100 mL), washed with 2 M aq NaOH soln (2 × 50 mL) and water (2 × 50 mL), dried ($MgSO_4$) and concd. The residue was dissolved in MeOH (50 mL), 1 M methanolic MeONa (0.25 mL) was added, and the mixture was stirred at rt overnight, then neutralized with Amberlite IR-120 resin, filtered and concd. The residue was crystallized from EtOH to give **4** (5.6 g, 81%); mp 105–107 °C (lit. [17] 98–100 °C). Selected ^1H NMR data (CD_3OD): δ 7.55–7.22 (m, 5 H, Ph), 4.58 (d, 1 H, *J* 9.7 Hz, H-1).

Phenyl 2,3,4,6-tetra-O-*benzyl*-*1-thio*-β-D-*galactopyranoside* (**5**).—To a suspension of NaH (7.5 g, 172 mmol, 55% in mineral oil) in DMF (90 mL) at 0 °C was added dropwise a soln of **4** (9.0 g, 33.0 mmol) in DMF (60 mL) followed by a soln of BzBr (19.6 mL, 165 mmol) in DMF (60 mL) and the mixture was allowed to reach rt. After stirring overnight, water was added until the product precipitated. The precipitate was filtered off, washed with water, dried under reduced pressure, and recrystallized from heptane–Et_2O to give **5** (19.0 g, 90%); mp 89–90 °C (lit. [17] 88–89 °C), $[\alpha]_D^{23}$ +1° (*c* 1.0, $CHCl_3$) (lit. [16] $[\alpha]_D$ +1°). ^1H NMR ($CDCl_3$): δ 7.59–7.16 (m, 25 H, Ph), 4.97 (d, 1 H, *J* 11.7 Hz, H-1), 4.81–3.60 (m, 14 H).

4-Methoxyphenyl β-D-*galactopyranoside* (**6**).—1,2,3,4,6-Penta-*O*-acetyl-β-D-galactopyranose (20.0 g, 53 mmol) [29] was dissolved in CH_2Cl_2 (100 mL), 4-methoxyphenol (8.3 g, 67 mmol) was added, and the mixture was cooled to 0 °C. $BF_3{\cdot}Et_2O$ (8.0 mL, 77 mmol) was added dropwise and the mixture was allowed to reach rt. After 2 h, the mixture was diluted with CH_2Cl_2 (100 mL), washed with 2 M aq NaOH soln (2 × 100 mL) and water (2 × 100 mL), dried ($MgSO_4$), and concd. The residue was dissolved in MeOH (100 mL), methanolic

1 M MeONa (0.50 mL) was added, and the mixture was stirred at rt over night, then neutralized with Amberlite IR-120 resin, filtered and concd. The residue was crystallized from EtOH to give **6** (10.9 g, 75%); mp 159–161 °C (lit. [19] 160–161 °C). Selected ^{1}H NMR data (CD_3OD): δ 7.07 (m, 2 H, Ph), 6.84 (m, 2 H, Ph), 4.78 (d, 1 H, *J* 7.8 Hz, H-1), 3.75 (s, 3 H, OMe).

*4-Methoxyphenyl 4,6-*O*-benzylidene-β-*D*-galactopyranoside* (**7**).—To a suspension of **6** (5.00 g, 17.5 mmol) in MeCN (100 mL) was added α,α-dimethoxytoluene (5.24 mL, 35 mmol) and a catalytic amount of *p*-toluenesulfonic acid, and the mixture was stirred at rt. A clear soln was formed, followed by formation of a precipitate. After 30 min, the mixture was cooled to 0 °C and the precipitated **7** [20] was recovered. The mother liquid was concd and a mixture of heptane–EtOAc was added to give a second crop of **7** (total yield 6.3 g, 96%). Selected ^{1}H NMR data ($CDCl_3$): δ 7.53 (m, 2 H, Ph), 7.39 (m, 3 H, Ph), 5.55 (s, 1 H, C*H*Ph), 4.81 (d, *J* 7.7 Hz, H-1).

*4-Methoxyphenyl 2,3,6-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**8**).—To a mixture of **7** (53 g, 142 mmol) and pyridine (400 mL) at 0 °C was added BzCl (38 mL, 326 mmol) dropwise. A catalytic amount of *N*,*N*-dimethylaminopyridine (DMAP) was added and the resulting mixture was allowed to reach rt. After 15 h, MeOH (50 mL) was added and the mixture was concd. The residue was dissolved in CH_2Cl_2 (1000 mL), washed with satd aq $NaHCO_3$ soln (2 × 300 mL), dried ($MgSO_4$), and concd. To the residue was added THF (1000 mL) and aq 2 M HCl (150 mL) and the mixture was stirred at 55 °C for 26 h. The mixture was diluted with CH_2Cl_2 (500 mL) and washed with satd aq $NaHCO_3$ soln (4 × 300 mL). The aq phases were combined and extracted once with CH_2Cl_2 (200 mL) and the combined organic phases were dried ($MgSO_4$) and concd. To the residue was added pyridine (1200 mL) and the mixture was cooled to −10 °C. Benzoyl chloride (19 mL, 163 mmol) was added dropwise over 30 min and after another 30 min, the reaction was quenched by addition of MeOH (100 mL). The mixture was concd to ca. 200 mL, diluted with CH_2Cl_2 (1200 mL), washed with satd aq $NaHCO_3$ soln (2 × 300 mL) and water (2 × 300 mL), dried ($MgSO_4$) and concd. The residue was crystallized from EtOAc–heptane to give **8** (68.4 g, 81%); mp 187–188 °C, $[\alpha]_D^{23}$ +80° (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.15–7.98 (m, 6 H, Ph), 7.65–7.37 (m, 9 H, Ph), 6.96 (m, 2 H, Ph), 6.68 (m, 2 H, Ph), 6.02 (dd, 1 H, *J* 8.1, 10.4 Hz, H-2), 5.41 (dd, 1 H, *J* 3.3, 10.4 Hz, H-3), 5.15 (d, 1 H, *J* 8.0 Hz, H-1), 4.75 (dd, 1 H, *J* 3.2, 8.9 Hz, H-6), 4.67 (dd, 1 H, *J* 3.6, 11.4 Hz, H-6), 4.49 (m, 1 H, H-4), 4.20 (m, 1 H, H-5), 3.72 (s, 3 H, OMe). ^{13}C NMR ($CDCl_3$): δ 166.8, 166.3, 165.8, 156.1, 151.6, 134.0, 133.8, 133.7, 130.4, 130.24, 130.19, 130.0, 129.8, 129.3, 129.0, 128.9, 128.8, 119.4, 114.8, 101.6, 74.6, 73.1, 69.8, 67.7, 63.4, 56.0.

*4-Methoxyphenyl (2,3,4,6-tetra-*O*-benzyl-α-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**9**).—To a mixture of **8** (5.0 g, 8.35 mmol), **5** (6.3 g, 10.0 mmol) and *N*-iodosuccinimide (NIS) (2.25 g, 10.0 mmol) was added CH_2Cl_2 (87.5 mL) and Et_2O (175 mL) and the soln was cooled to −55 °C. Trimethylsilyl trifluoromethanesulfonate (TMSOTf) (0.302 mL, 1.67 mmol) was added and the mixture was stirred for 1 h. Triethylamine (5 mL) was added and the mixture was stirred for 1 h at −55 °C. The mixture was allowed to obtain rt, diluted with CH_2Cl_2 (250 mL), washed with 10% aq $Na_2S_2O_3$ soln (75 mL) and satd aq $NaHCO_3$ soln (100 mL), dried ($MgSO_4$), and concd. The residue was flash chromatographed (SiO_2, 3:1 heptane–EtOAc) to give **9** (8.8 g, 95%); $[\alpha]_D^{23}$ +74° (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.10–7.20 (m, 35 H, Ph), 6.99 (d, 2 H, *J* 9.0 Hz, Ph), 6.69 (d, 2 H, *J* 9.1 Hz, Ph), 6.03 (dd, 1 H, *J* 7.7, 10.5 Hz, H-2), 5.30 (dd, 1 H, *J* 2.8, 10.4 Hz, H-3), 5.16 (d, 1 H, *J* 7.8 Hz, H-1), 4.95–4.72 (m, 8 H), 4.52 (d, 1 H, *J* 9.1 Hz, H-1), 4.49 (d, 1 H, *J* 2.5 Hz, H-4), 4.41 (dd, 1 H, *J* 4.7, 9.3 Hz), 4.25–4.03 (m, 6 H), 3.73 (s, 3 H, OMe), 3.44 (t, 1 H, *J* 9.0 Hz), 3.01 (dd, 1 H, *J* 4.9, 8.4 Hz). ^{13}C NMR ($CDCl_3$): δ 166.9, 166.5, 165.8, 155.9, 151.7, 139.3, 138.8, 133.8, 133.7, 133.6, 130.4, 130.3, 130.2, 130.1, 130.0, 129.5, 128.93, 128.90, 128.84, 128.78, 128.72, 128.71, 128.54, 128.45, 128.01, 127.98, 127.94, 127.87, 127.82, 127.79, 119.2, 114.8, 101.7, 101.5, 79.4, 77.7, 76.0, 75.5, 75.1, 74.6, 74.5, 73.5, 73.4, 73.0, 70.3, 70.0, 67.9, 63.2,

56.0. HRMS calcd for $C_{68}H_{64}NaO_{15}$ (M + Na): 1143.4143, found: 1143.4159.

*4-Methoxyphenyl (2,3,4,6-tetra-*O*-acetyl-α-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**10**).—Compound **9** (174 mg, 0.155 mmol) was dissolved in AcOH (4 mL) and hydrogenolyzed (H_2, 10% Pd–C, 50 mg) for 24 h. The mixture was filtered through Celite and concd. The residue was dissolved in pyridine (2.0 mL), Ac_2O (2.0 mL) was added, and the mixture was stirred overnight, then concd and flash chromatographed (SiO_2, 1:1, heptane–EtOAc) to give **10** (130 mg, 90%). Recrystallization from 10:1 EtOAc–Et_2O gave an analytical sample; mp 205–207 °C; $[\alpha]_D^{23}$ +104° (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.07–7.95 (m, 6 H, Ph), 7.65–7.36 (m, 9 H, Ph), 7.00 (d, 2 H, *J* 9.1 Hz, Ph), 6.72 (d, 2 H, *J* 9.1 Hz, Ph), 5.96 (dd, 1 H, *J* 7.7, 10.6 Hz, H-2), 5.50 (m, 2 H, H-3′, 4′), 4.39 (dd, 1 H, *J* 3.0, 10.6 Hz, H-3), 5.26 (m, 1 H, H-2′), 5.22 (d, 1 H, *J* 3.0 Hz, H-1′), 5.20 (d, 1 H, *J* 7.8 Hz, H-1), 4.79 (dd, 1 H, *J* 7.7, 11.4 Hz, H-6), 4.62 (m, 2 H, H-6, 5′), 4.48 (d, 1 H, *J* 2.5 Hz, H-4), 4.37 (m, 1 H, H-5), 3.90 (dd, 1 H, *J* 7.7, 10.9 Hz, H-6′), 3.75 (s, 3 H, OMe), 3.72 (dd, 1 H, *J* 6.1, 11.0 Hz, H-6′), 2.17, 2.10, 2.01, 1.92 (4 s, 3 H each, OAc). ^{13}C NMR ($CDCl_3$): δ 171.0, 170.8, 170.6, 170.2, 166.6, 166.5, 165.6, 156.1, 151.5, 134.2, 133.9, 133.7, 130.4, 130.2, 130.1, 129.8, 129.7, 129.1, 129.0, 128.9, 119.3, 114.9, 101.4, 99.0, 76.2, 73.9, 73.3, 69.7, 68.8, 68.2, 67.9, 67.8, 63.2, 61.3, 56.0, 21.3, 21.10, 21.05, 21.0. HRMS calcd for $C_{48}H_{48}NaO_{19}$ (M + Na): 951.2687, found: 951.2669.

*2-Bromoethyl (2,3,4,6-tetra-*O*-acetyl-α-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**11**).—To a soln of **1** (2.42 g, 2.65 mmol) and *N*-iodosuccinimide (715 mg, 3.19 mmol) in CH_2Cl_2 (100 mL) at 0 °C was added 2-bromoethanol (0.38 mL, 5.30 mmol) and trimethylsilyl trifluoromethanesulfonate (0.052 mL, 0.27 mmol). The mixture was stirred for 10 min at 0 °C, diluted with CH_2Cl_2 (200 mL), washed with 10% aq $Na_2S_2O_3$ (50 mL) and satd aq $NaHCO_3$ (2 × 25 mL), dried (Na_2SO_4), and concd. The residue was flash chromatographed (SiO_2, 4:1 → 1:1 heptane–EtOAc gradient) to give **11** (2.31 g, 95%). Recrystallization from MeOH gave an analytical sample; mp 163–164 °C (lit. [26] 150–151 °C). ^{1}H NMR ($CDCl_3$): δ 8.15–7.95 (m, 6 H, Ph), 7.65–7.35 (m, 9 H, Ph), 5.73 (dd, 1 H, *J* 7.7, 10.6 Hz, H-2), 5.50 (ABq, 2 H, *J* 9.2, 11.9 Hz, H-3′, 4′), 5.34 (dd, 1 H, *J* 3.0, 10.7 Hz, H-3), 5.24 (m, 2 H, H-1′, 2′), 4.84 (d, 1 H, *J* 3.9 Hz, H-1), 4.75 (dd, 1 H, *J* 7.2, 11.4 Hz, H-6), 4.60 (t, 1 H, *J* 7.2 Hz, H-5′), 4.54 (dd, 1 H, *J* 6.2, 11.5 Hz, H-6), 4.43 (d, 1 H, *J* 2.1 Hz, H-4), 4.20 (ddd, 1 H, *J* 5.1, 6.9, 4.4 Hz, OCH_2CH_2Br), 4.13 (m, 1 H, H-5), 3.90 (m, 2 H, H-6′, OCH_2CH_2Br), 3.65 (dd, 1 H, *J* 6.2, 11.0 Hz, H-6′), 3.50 (m, 2 H, OCH_2CH_2Br), 2.09, 2.06, 2.01, 1.88 (4 s, 3 H each, OAc).

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