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A strategy for chemical synthesis of selectively methyl-esterified oligomers of galacturonic acid

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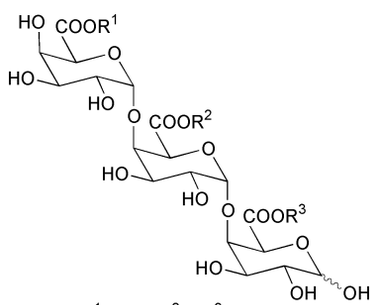
The synthesis of monomethyl-esterified trigalacturonans **1**–**3** is described as part of a general strategy towards pectic oligosaccharides. The necessary monomeric building blocks were all prepared on a large scale from galactose pentaacetate. The glycosylations were carried out between galactose glycosyl donors and acceptors using the *n*-pentenyl glycosylation technique. Yields of the desired α-anomers were in the 50 to 74% range. The trigalactans thus obtained were then subjected to oxidation at C-6. Depending on the protecting group at this position the oxidation either produced the carboxylic acid or the corresponding methyl ester. Hereby, oligomers of galacturonic acid can be prepared with methyl esters introduced in a regiocontrolled fashion.

Introduction

Pectin is one of the main gelling agents used in the food industry and a major polysaccharide in primary plant cell walls.[1] Its main structural feature is a linear chain of α(1→4)-linked D-galacturonic acids, which are partially methyl esterified. Pectin is degraded by a number of pectic enzymes including pectin lyase, polygalacturonase, and pectin esterase.[1] Pectin is an extremely complex polysaccharide and degradation products from pectin are very inhomogeneous. Several analytical techniques have been applied to the analysis of smaller fragments of pectin.[2] However, the vast majority of pectin research so far has concentrated on investigating pectin and pectic enzymes from various sources on a macroscopic level.[1] Owing to the lack of well-defined and homogeneous fragments of pectin few studies have been carried out on a molecular level.[3] A particularly important task is to examine and understand the substrate specificity of pectic enzymes using well-defined galacturonans.[4]

The purpose of our programme is to use chemical synthesis for *de novo* design of well-defined and partially esterified oligomers of galacturonic acid. Previously, a synthetic strategy towards larger oligomers of galacturonic acid was developed, but with no partial esterification of the carboxylic acids.[5] Recently, an interesting method was demonstrated by coupling of protected galacturonic acid glycosyl donors and acceptors.[6] However, these are not very reactive and as a result not well suited for coupling of larger units. Instead, we decided to concentrate on the use of galactose glycosyl donors and acceptors which are significantly more reactive. For our exploratory studies we decided to focus on the synthesis of monomethylated trigalacturonates **1**–**3**. These could be used to demonstrate that methyl ester groups can be introduced at any place in the galacturonic acid oligomer. In addition, compounds **1**–**3** have very recently been used as the first partially methyl esterified galacturonans in the study of pectic enzymes from several fungi and bacteria.[7]



1: R^1 = Me, R^2 = R^3 = H
2: R^2 = Me, R^1 = R^3 = H
3: R^3 = Me, R^1 = R^2 = H

Results and discussion

Retrosynthesis

The strategy requires a protected galactose oligomer to be assembled (Scheme 1). The protecting groups at C-6 in each monomer will then dictate whether these positions are oxidised to the carboxylic acid or to its methyl ester. Acetyl groups and *p*-methoxyphenyl (PMP) groups were chosen for the C-6 protection. These are orthogonal protecting groups which are stable to the strongly acidic conditions used in glycosylation reactions. In addition, they are sterically non-demanding groups and should not provide any significant hindrance for the glycosylation at the 4-position, which was intended to be carried out with pent-4-enyl galactosides. The *n*-pentenyl glycosylation technique[8] was chosen because it provides a minimum of manipulations at the anomeric center, and here, the *n*-pentenyl group serves a dual function. First, it protects the anomeric center during synthesis of the monomeric building blocks, and secondly, at the time of the glycosylation it is also capable of activating the anomeric center in the presence of strong electrophiles. Three different monomeric building blocks are needed: a benzyl galactoside **C** to serve as glycosyl acceptor for the reducing end and two glycosyl donors **A** and **B**, the former for the non-reducing end.

Monomer syntheses

These monomers were all prepared from galactose pentaacetate (Scheme 2). Treatment with pent-4-enyl alcohol and $BF_3 \cdot OEt_2$ followed by deacetylation gave crystalline pent-4-enyl β-galactoside **4**. This can bifurcate to form glycosyl donors **A** and **B**. For preparation of the former, the primary position was first protected with a trityl group to give crystalline **5**. Benzylation followed by subsequent removal of the trityl group gave **6**.

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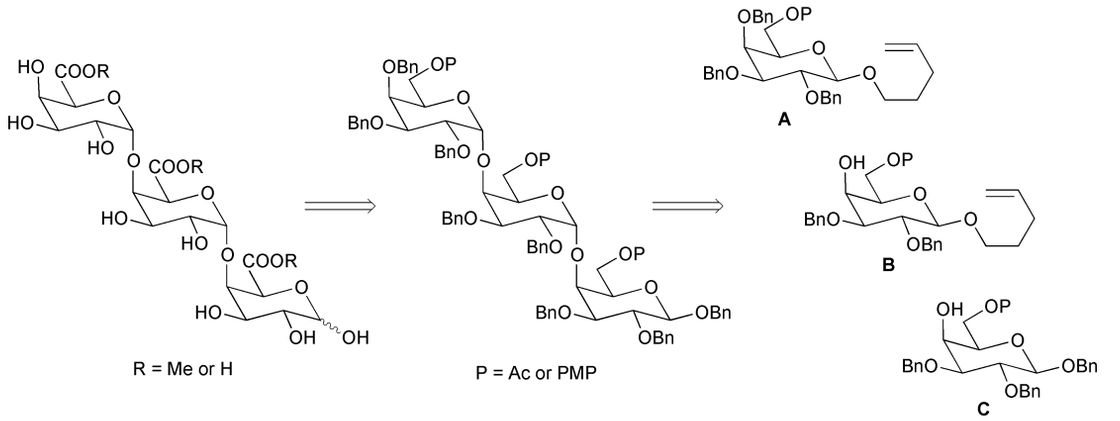
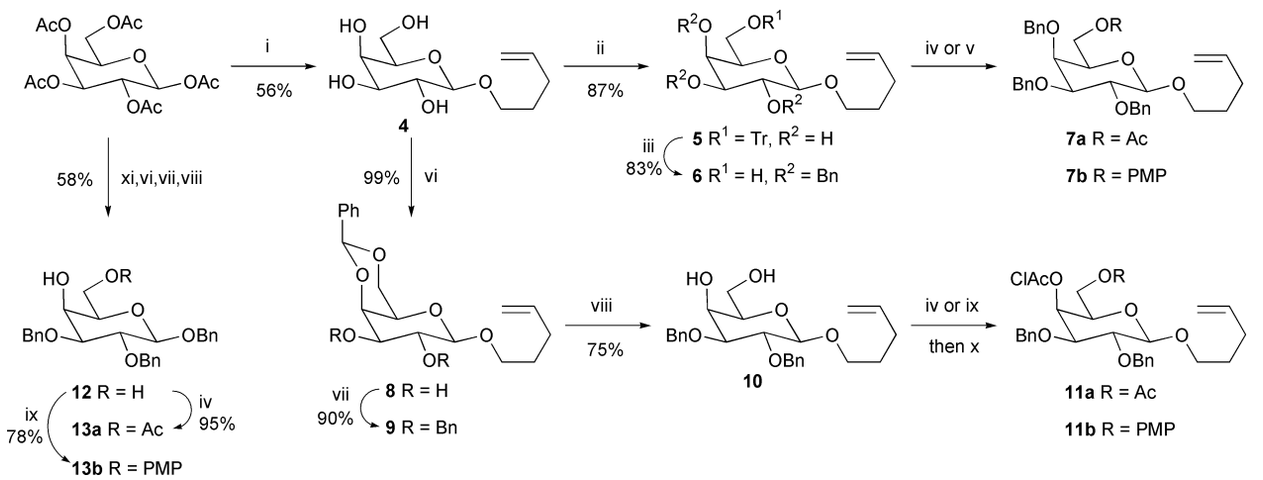


Scheme 1



Scheme 2 *Reagents and conditions*: (i) pent-4–en-1-ol, $BF_3{\cdot}OEt_2$, CH_2Cl_2; then NaOMe, MeOH; (ii) TrCl, pyridine, 90 °C; (iii) BnBr, NaH, Bu_4NI, DMF; then H_2SO_4, MeOH; (iv) Ac_2O, Et_3N, CH_2Cl_2; (v) *p*-methoxyphenol, PPh_3, DEAD, THF; (vi) $PhCH(OMe)_2$, CSA, $CHCl_3$, 60 °C; (vii) BnBr, NaH, Bu_4NI, DMF; (viii) propane-1,3-diol, PTSA, MeOH, CH_2Cl_2; (ix) TsCl, pyridine; then *p*-methoxyphenol, NaH, DMF; (x) $(ClCH_2CO)_2O$, Et_3N, DMAP, CH_2Cl_2; (xi) BnOH, $BF_3{\cdot}OEt_2$, CH_2Cl_2; then NaOMe, MeOH.

This could then be converted into the C-6 acetyl and PMP glycosyl donors **7a** and **7b**.

For synthesis of glycosyl donor **B**, pent-4-enyl galactoside **4** was first temporarily protected with a 4,6-*O*-benzylidene acetal. This was conveniently installed by reflux in chloroform solution[9] and the product **8** isolated by direct crystallisation. Benzylation (to **9**) and removal of the benzylidene acetal then gave diol **10**. Cleavage of the 4,6-benzylidene acetal did not go to completion in acidic methanol alone and required the addition of propane-1,3-diol to further shift the equilibrium. Diol **10** was then selectively acetylated or *p*-methoxyphenylated at the primary position. For protection of the 4-position a chloroacetyl group was chosen to give glycosyl donors **11a** and **11b**. The chloroacetyl group has previously been removed selectively in the presence of acetyl groups.[10]

For synthesis of glycosyl acceptor **C**, galactose pentaacetate was treated with benzyl alcohol followed by deacetylation to give benzyl β-D-galactopyranoside. This was subsequently treated in the same way as the corresponding pent-4-enyl galactoside **4** to provide diol **12**. Selective acetylation or *p*-methoxyphenylation then gave acceptors **13a** and **13b**. It is noteworthy that most of the compounds for these monomer syntheses are crystalline, thus making it easy to perform the syntheses on a large scale.

Oligomer assembly

All glycosylation reactions were performed in CH_2Cl_2 at −20 °C using *N*-iodosuccinimide (NIS) and a catalytic amount of triethylsilyl trifluoromethanesulfonate (TESOTf) as the promoter. First, PMP-protected glycosyl donor **11b** and acceptor **13b** were coupled to give disaccharide **14** in 74% yield of the pure α-anomer (Scheme 3). No attempts have been made to isolate and identify a possible β-anomer in these couplings. Subsequent removal of the chloroacetyl group gave alcohol **15**. In a similar manner, disaccharides **21** and **28** were prepared in good yields by coupling of **11a** and **13b** as well as **11b** and **13a**. However, the subsequent dechloroacetylation of **21** and **28** did not proceed very well with thiourea and $NaHCO_3$ in MeOH due to concomitant partial removal of the primary acetates. Instead, we discovered that thiourea in THF could effectively promote the removal of chloroacetate if a catalytic amount of Bu_4NI was added. Hereby, disaccharide alcohols **22** and **29** were obtained in good yields. These were then ready for the next coupling with **7b** to produce trisaccharides **23** and **30**. Both coupling products were isolated as inseparable mixtures of α- and β-anomers which were separated in the next reaction after removal of the primary acetyl group. The last trisaccharide **16** was isolated as the pure α-anomer in 54% yield after coupling of **7a** and **15**. In general, all these glycosylations proceeded well with the desired α-anomers formed in yields ranging from 50 to 74%. The strategy should thus hold great promise for future couplings to larger oligomers. In every coupling the α-configuration at the newly generated stereogenic center has been verified by NMR spectroscopy, and this is most easily done by ^{13}C NMR. For all di- and trigalactans the α-linked anomeric carbons resonate at δ_C 99.5–101.0 while the β-linked anomeric carbon at the reducing end is always found at δ_C 102.5–103.5. This is in accord with literature observations for galactose-containing oligosaccharides.[11]

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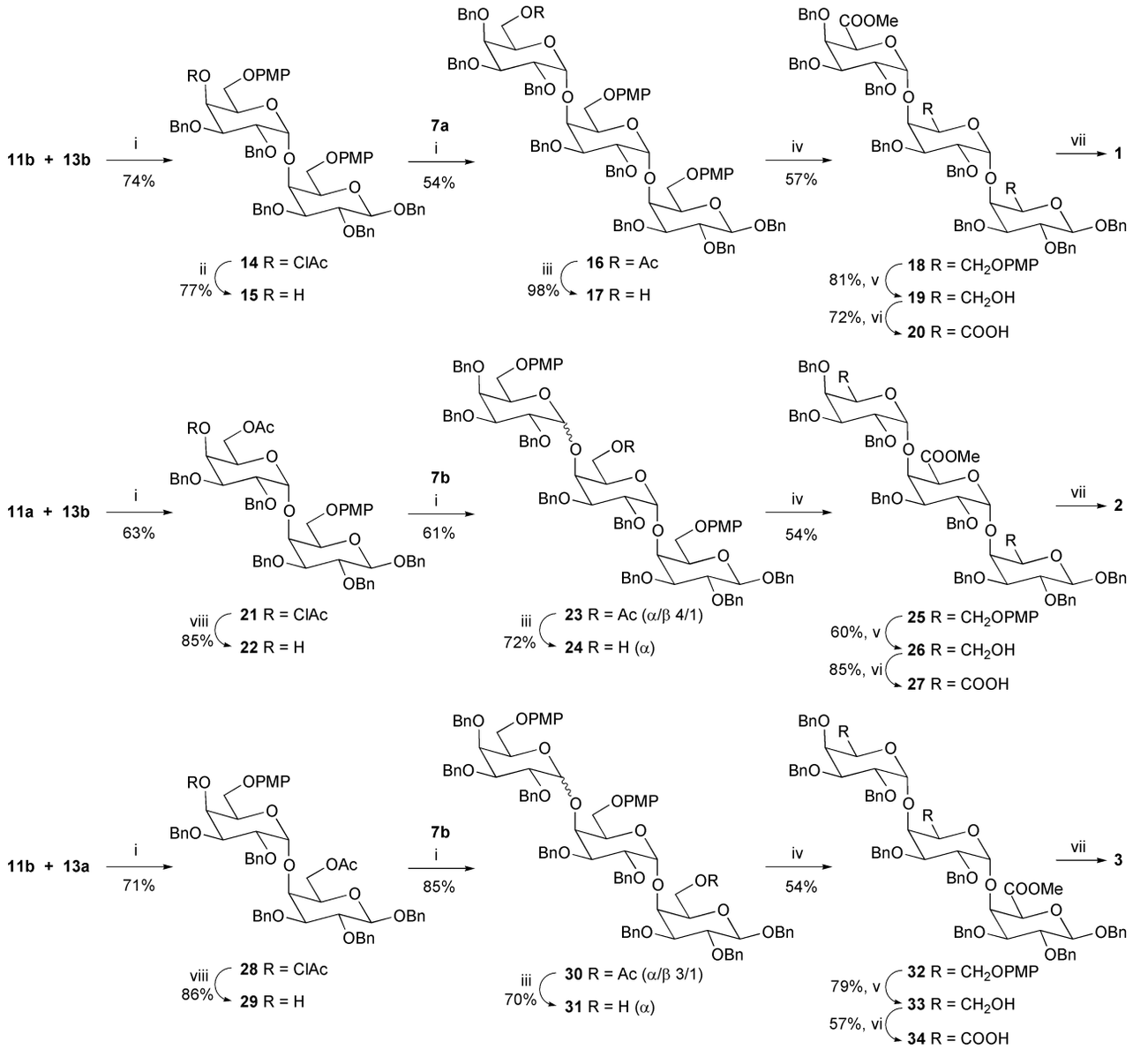

Scheme 3 *Reagents and conditions*: (i) NIS, TESOTf, CH_2Cl_2, −20 °C; (ii) thiourea, $NaHCO_3$, MeOH, CH_2Cl_2; (iii) K_2CO_3, MeOH; (iv) Dess–Martin periodinane, CH_2Cl_2, then $NaClO_2$, NaH_2PO_4, 2-methylbut-2-ene, Bu^{t}OH, aq. THF; then $TMSCHN_2$, MeOH; (v) CAN, aq. MeCN, −10 °C; (vi) Dess–Martin periodinane, CH_2Cl_2; then $NaClO_2$, NaH_2PO_4, 2-methylbut-2-ene, Bu^{t}OH, aq. THF; (vii) Pd/C, H_2, aq. MeOH; (viii) thiourea, $NaHCO_3$, Bu_4NI, THF, 55 °C.

Methyl esters can now be introduced at the positions where acetyl groups are placed. On all three trisaccharides **16**, **23**, and **30** these acetyl groups were removed by transesterification with K_2CO_3 in MeOH. Several procedures were investigated for oxidation of the primary alcohol to the corresponding carboxylic acid methyl ester. The oxidation turned out to be most efficiently carried out by a one-pot three-step procedure. First, the primary alcohols were oxidised to their corresponding aldehydes with the Dess–Martin periodinane.[12] The Swern procedure[13] worked equally well for this oxidation, but for preparative purposes the Dess–Martin protocol was found to be the most convenient. The aldehydes were not purified, but treated directly with $NaClO_2$ in the presence of 2-methylbut-2-ene as scavenger[14] to produce the corresponding carboxylic acids. Severe oxidation of the benzyl groups occurred if the scavenger was not added. These carboxylic acids were then methyl esterified by (trimethylsilyl)diazomethane ($TMSCHN_2$)[15] to produce trisaccharides **18**, **25**, and **32** in satisfactory overall yields from the corresponding alcohols. The remaining PMP-protected C-6 positions were now oxidised to carboxylic acid. The PMP ethers were cleaved with cerium(IV) ammonium nitrate (CAN) to give diols **19**, **26**, and **33**. These were then oxidised in a one-pot two-step procedure using the Dess–Martin periodinane followed by $NaClO_2$ treatment to give diacids **20**, **27**, and **34**. Here, the neutral conditions of the Dess–Martin oxidation turned out to be crucial. If the Swern procedure was used for this oxidation to aldehyde, significant decomposition occurred, presumably due to base-induced β-elimination from the methyl esters. Final removal of the benzyl groups proceeded cleanly *via* catalytic hydrogenation to give selectively methyl-esterified trigalacturonans **1**–**3** with NMR spectra in accordance with literature data.[7]

Conclusions

In conclusion, we have completed the synthesis of monomethyl-esterified trigalacturonans **1**–**3** from D-galactose. The monomer building blocks for the synthesis were easily prepared on a large scale from galactose pentaacetate. The couplings were carried out using pent-4-enyl glycosides to give good yields of the desired α-anomers. Finally, oxidation of the C-6 positions was performed under mild conditions, either to the methyl ester or to the corresponding carboxylic acid. The present strategy is believed to be a viable technique for preparation of larger

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oligomers of selectively methyl-esterified galacturonic acids. Synthesis of these larger units is currently in progress.

Experimental

General

Optical rotations were determined with a Perkin-Elmer 241 polarimeter. $[\alpha]_D$-Values are in units of 10^{-1} deg cm^2 g^{-1}. NMR spectra were recorded on a Varian Mercury 300 spectrometer. Chemical shifts were measured in ppm and coupling constants (J) in Hz. For ^{13}C NMR spectra in $CDCl_3$ ($\delta_C = 76.9$) and CD_3OD ($\delta_C = 49.0$) the solvent was used as internal reference. Mass spectra were obtained at Danisco Biotechnology by MALDI-TOF on a Perseptive Biosystems Voyager-De instrument in positive-ion mode using α-cyano-4-hydroxycinnamic acid as the matrix. TLC was performed on aluminium sheets precoated with silica gel (Merck 1.05554). Compounds were visualised by charring after dipping in a solution of cerium(IV) sulfate (2.5 g) and ammonium molybdate (6.25 g) in 10% aq. H_2SO_4 (250 cm^3). Flash column chromatography was performed using silica gel 60 (Amicon 85040). Microanalyses were performed at the Department of Chemistry at the University of Copenhagen.

Pent-4-enyl β-D-galactopyranoside 4

To a solution of galactose pentaacetate (35 g, 89.7 mmol) and pent-4-en-1-ol (20 cm^3, 194 mmol) in CH_2Cl_2 (250 cm^3) was added $BF_3{\cdot}OEt_2$ (14 cm^3, 110 mmol). The mixture was stirred at rt under an atmosphere of nitrogen for 10 h, and then diluted with CH_2Cl_2 (100 cm^3) and washed with saturated aq. $NaHCO_3$ (350 cm^3). The organic layer was dried and concentrated. The syrupy residue was dissolved in 0.04 M NaOMe in MeOH (300 cm^3) and the solution stirred for 2 h. The mixture was quenched with Amberlite IR-120 (H^+) (15 cm^3) and stirred for an additional 30 min. The resin was filtered off and the filtrate concentrated, and purified by flash chromatography (CH_2Cl_2–MeOH; 6:1) to give 17.5 g of a greasy solid; R_f 0.30. Recrystallisation from EtOAc afforded **4** (12.5 g, 56%) as white crystals; mp 88–90 °C; $[\alpha]_D^{20}$ −10.0 (*c* 1.6, H_2O) [lit.,[16] −9.02 (*c* 1.23, H_2O)]; δ_H (D_2O) 5.82 (m, 1H), 5.01 (d, 1H, *J* 17.4), 4.94 (d, 1H, *J* 10.2), 4.30 (d, 1H, *J* 8.0), 3.84 (m, 2H), 3.72–3.51 (m, 5H), 3.42 (t, 1H, *J* 8.9), 2.07 (m, 2H), 1.65 (m, 2H); δ_C (D_2O) 139.1, 115.0, 103.0, 75.3, 73.1, 71.0, 70.1, 68.9, 61.1, 29.6, 28.3 (Calc. for $C_{11}H_{20}O_6$: C, 53.22; H, 8.12%. Found: C, 53.42; H, 7.98).

Pent-4-enyl 6-*O*-trityl-β-D-galactopyranoside 5

A mixture of **4** (10.2 g, 41.1 mmol) and TrCl (12.6 g, 45.2 mmol) in dry pyridine (130 cm^3) was heated at 90 °C for 3 h, and then concentrated and co-concentrated with toluene. The residue was dissolved in CH_2Cl_2 (150 cm^3) and washed with water (150 cm^3). The organic layer was dried and concentrated. The residue was crystallised from Et_2O and recrystallised from EtOAc–hexane to give **5** (17.6 g, 87%); R_f 0.48 (EtOAc); mp 89.0–91.5 °C; $[\alpha]_D^{20}$ −27.6 (*c* 0.7, $CHCl_3$); δ_H ($CDCl_3$) 7.48–7.42 (m, 6H), 7.34–7.21 (m, 9H), 5.83 (m, 1H), 5.02 (dq, 1H, *J* 17.2, 1.7), 4.96 (dq, 1H, *J* 10.2, 1.7), 4.20 (d, 1H, *J* 7.2), 4.02 (t, 1H, *J* 3.3), 3.93 (dt, 1H, *J* 9.7, 6.2), 3.65–3.35 (m, 6H), 2.55 (br d, 1H, *J* 5.9), 2.37 (br s, 1H), 2.28 (d, 1H, *J* 4.3), 2.13 (m, 2H), 1.75 (m, 2H); δ_C ($CDCl_3$) 141.3 (3C), 135.5, 126.1 (6C), 125.3 (6C), 124.5 (3C), 112.4, 100.6, 84.3, 71.2, 71.1, 69.1, 66.8, 66.7, 60.2, 27.5, 26.2; *m*/*z* 513.30 (M + Na^+). Calc. for $C_{30}H_{34}O_6$ + Na^+: *m*/*z*, 513.23.

Pent-4-enyl 2,3,4-tri-*O*-benzyl-β-D-galactopyranoside 6

To a solution of **5** (16.5 g, 33.7 mmol) in DMF (130 cm^3) was added NaH (8 g of ~50% oil dispersion, 167 mmol). The mixture was stirred at rt for 30 min and then cooled to 0 °C followed by addition of BnBr (18 cm^3, 152 mmol) and Bu_4NI (1 g, 2.7 mmol). The mixture was stirred at rt overnight, and then quenched with MeOH, diluted with Et_2O (700 cm^3) and washed with water (700 cm^3). The organic layer was dried, concentrated and the residue was dissolved in 1% H_2SO_4 in MeOH (290 cm^3). After stirring of the mixture at rt for 1 h, solid Na_2CO_3 (15 g) was added and the stirring was continued until neutral pH was attained. The mixture was filtered and the filtrate concentrated to a syrup. This was dissolved in CH_2Cl_2 (300 cm^3), washed with water (200 cm^3), dried, concentrated, and purified by flash chromatography (hexane–EtOAc; 2:1) to give **6** (14.5 g, 83%) as a syrup; R_f 0.31; $[\alpha]_D^{20}$ −23.8 (*c* 0.8, $CHCl_3$); δ_H ($CDCl_3$) 7.41–7.25 (m, 15H), 5.89–5.74 (m, 1H), 5.05–4.92 (m, 4H), 4.85–4.64 (m, 4H), 4.36 (d, 1H, *J* 7.6), 3.95 (dt, 1H, *J* 9.5, 6.4), 3.84 (dd, 1H, *J* 9.7, 7.7), 3.81–3.73 (m, 2H), 3.57–3.46 (m, 3H), 3.37 (t, 1H, *J* 6.2), 2.16 (m, 2H), 1.75 (m, 2H); δ_C ($CDCl_3$) 138.5, 138.3, 138.1, 138.0, 128.6–127.5 (15C), 114.7, 103.9, 82.1, 79.5, 75.1, 74.3, 74.0, 73.3, 72.6, 69.2, 61.9, 30.1, 28.8 (Calc. for $C_{32}H_{38}O_6$: C, 74.11; H, 7.39%. Found: C, 74.14; H, 7.39).

Pent-4-enyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-β-D-galactopyranoside 7a

A solution of **6** (4.0 g, 7.71 mmol), Ac_2O (1.0 cm^3, 10.6 mmol), Et_3N (1.6 cm^3, 11.4 mmol) and 4-(dimethylamino)pyridine (DMAP) (16 mg) in CH_2Cl_2 (75 cm^3) was stirred at rt for 2 h and then concentrated, and purified by flash chromatography (hexane–EtOAc; 3:1) to give **7a** (4.1 g, 95%) as a syrup; R_f 0.35; $[\alpha]_D^{20}$ −22.0 (*c* 1.3, $CHCl_3$); δ_H ($CDCl_3$) 7.40–7.20 (m, 15H), 5.79 (m, 1H), 5.11–4.88 (m, 4H), 4.80–4.62 (m, 4H), 4.33 (d, 1H, *J* 8.0), 4.20 (dd, 1H, *J* 8.0, 11.0), 4.05 (dd, 1H, *J* 8.0, 11.0), 4.08–3.70 (m, 3H), 3.58–3.40 (m, 3H), 2.15 (m, 2H), 1.95 (s, 3H), 1.75 (m, 2H); δ_C ($CDCl_3$) 170.4, 138.6, 138.3, 138.1 (2C), 128.5–127.5 (15C), 114.7, 103.9, 82.2, 79.4, 75.1, 74.2, 73.3, 72.8, 71.9, 69.3, 62.9, 30.1, 28.8, 20.7 (Calc. for $C_{34}H_{40}O_7$: C, 72.83; H, 7.19%. Found: C, 72.25; H, 7.24).

Pent-4-enyl 2,3,4-tri-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galactopyranoside 7b

To a solution of **6** (5.9 g, 11.4 mmol), PPh_3 (6.0 g, 23 mmol), and *p*-methoxyphenol (5.8 g, 47 mmol) in dry THF (45 cm^3) was added diethyl azodicarboxylate (DEAD) (3.6 cm^3, 23 mmol). The mixture was stirred at rt for 2 days during which time additional amounts of PPh_3 (3 g) and DEAD (1.8 cm^3) were added. Concentration and purification by flash chromatography (hexane–EtOAc; 4:1) afforded **7b** (5.2 g, 73%) as a solid; R_f 0.54; mp 77.5–79 °C (from EtOH); $[\alpha]_D^{20}$ −15.3 (*c* 0.8, $CHCl_3$); δ_H ($CDCl_3$) 7.40–7.18 (m, 15H), 6.78 (m, 4H), 5.81 (m, 1H), 5.05–4.91 (m, 4H), 4.80 (d, 1H, *J* 12.0), 4.79 (d, 1H, *J* 11.1), 4.75 (d, 1H, *J* 11.5), 4.62 (d, 1H, *J* 11.5), 4.40 (d, 1H, *J* 7.7), 3.99 (m, 3H), 3.95 (m, 1H), 3.86 (t, 1H, *J* 8.5), 3.78 (s, 3H), 3.69 (t, 1H, *J* 6.2), 3.58 (m, 1H), 3.54 (m, 1H), 2.16 (m, 2H), 1.75 (m, 2H); δ_C ($CDCl_3$) 154.3, 152.8, 139.0, 138.7, 138.6, 138.4, 128.7–127.7 (15C), 115.7, 115.0, 114.8, 104.3, 82.5, 79.8, 75.4, 74.8, 73.5, 73.4, 73.1, 69.6, 67.1, 56.0, 30.5, 29.2 (Calc. for $C_{39}H_{44}O_7$: C, 74.98; H, 7.10%. Found: C, 74.73; H, 7.02).

Pent-4-enyl 4,6-*O*-benzylidene-β-D-galactopyranoside 8

To a solution of $PhCH(OMe)_2$ (33 cm^3, 220 mmol) and camphor-10-sulfonic acid (CSA) (450 mg) in $CHCl_3$ (980 cm^3) was added **4** (38.5 g, 155 mmol). The flask was equipped with a distillation head and the mixture heated at reflux for 1.5 h during which time about 250 cm^3 of a $CHCl_3$–MeOH mixture distilled off. The reaction mixture was quenched with Et_3N (0.7 cm^3) and concentrated to a solid, which was recrystallised from EtOAc to give **8** (51.7 g, 99%); R_f 0.53 (EtOAc); mp 158–160 °C, $[\alpha]_D^{20}$ −36.5 (*c* 1.5, $CHCl_3$); δ_H ($CDCl_3$) 7.49 (m, 2H), 7.35 (m, 3H), 5.81 (m, 1H), 5.54 (s, 1H), 5.04 (dq, 1H, *J* 17.1, 1.7), 4.97 (dq, 1H, *J* 10.4, 1.7), 4.32 (dd, 1H, *J* 12.5, 1.5), 4.26 (d, 1H, *J* 7.3), 4.20 (dd, 1H, *J* 3.6, 1.5), 4.07 (dd, 1H, *J* 12.5, 1.9), 3.98

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(dt, 1H, *J* 9.7, 6.6), 3.74 (dd, 1H, *J* 9.6, 7.3), 3.69 (dd, 1H, *J* 9.6, 3.6), 3.52 (dt, 1H, *J* 9.4, 7.0), 3.46 (m, 1H), 2.24–2.06 (br m, 4H), 1.76 (m, 2H); δ_C ($CDCl_3$) 138.4, 137.8, 129.4, 128.4 (2C), 126.7 (2C), 115.1, 103.1, 101.6, 75.7, 73.0, 72.0, 69.6, 69.4, 66.9, 30.4, 28.9 (Calc. for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19%. Found: C, 64.51; H, 7.23).

Pent-4-enyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galacto-pyranoside 9

A mixture of **8** (51.6 g, 153 mmol) and NaH (28 g of ~50% oil dispersion, 583 mmol) in DMF (500 cm^3) was stirred at rt for 30 min and then cooled to 0 °C. BnBr (55 cm^3, 462 mmol) and Bu_4NI (4 g, 11 mmol) were added and the solution stirred at rt overnight before being quenched with MeOH, diluted with CH_2Cl_2 (750 cm^3) and washed with water (750 cm^3). The organic phase was dried, concentrated, and the residue was crystallised from EtOAc–hexane to afford **9** (71.2 g, 90%); R_f 0.33 (hexane–EtOAc; 3:1); mp 114–117 °C, $[\alpha]_D^{20}$ −27.8 (*c* 1.5, $CHCl_3$); δ_H ($CDCl_3$) 7.55 (m, 2H), 7.41–7.26 (m, 13H), 5.82 (m, 1H), 5.50 (s, 1H), 5.07–4.90 (m, 3H), 4.81–4.72 (m, 3H), 4.39 (d, 1H, *J* 8.0), 4.31 (d, 1H, *J* 12.0), 4.12–3.96 (m, 3H), 3.84 (t, 1H, *J* 8.7), 3.58–3.50 (m, 2H), 3.32 (s, 1H), 2.19 (m, 2H), 1.77 (m, 2H); δ_C ($CDCl_3$) 139.1, 138.7, 138.4, 138.1, 129.1, 128.6 (2C), 128.5 (2C), 128.3 (2C), 128.2 (2C), 128.0 (2C), 127.9, 127.8, 126.8 (2C), 115.1, 103.9, 101.6, 79.4, 78.7, 75.6, 74.2, 72.3, 69.5 (2C), 66.6, 30.5, 29.2 (Calc. for $C_{32}H_{36}O_6$: C, 74.40; H, 7.02%. Found: C, 74.17; H, 6.73).

Pent-4-enyl 2,3-di-*O*-benzyl-β-D-galactopyranoside 10

A solution of **9** (13.0 g, 25.2 mmol), propane-1,3-diol (9.1 cm^3, 126 mmol) and toluene-*p*-sulfonic acid (PTSA) (100 mg, 0.6 mmol) in CH_2Cl_2 (70 cm^3)–MeOH (70 cm^3) was heated at reflux for 96 h. The mixture was cooled, concentrated and purified by flash chromatography (EtOAc–hexane; 1:1) to afford **10** (8.11 g, 75%) as a solid, R_f 0.15; mp 59–63 °C (from EtOAc); $[\alpha]_D^{20}$ −2.5 (*c* 1.6, $CHCl_3$); δ_H ($CDCl_3$) 7.40–7.27 (m, 10H), 5.81 (m, 1H), 5.07–4.90 (m, 3H), 4.77–4.71 (m, 3H), 4.37 (d, 1H, *J* 7.7), 4.01–3.93 (m, 3H), 3.82 (dd, 1H, *J* 11.5, 4.8), 3.69–3.42 (m, 4H), 2.37 (br s, 2H), 2.16 (m, 2H), 1.76 (m, 2H); δ_C ($CDCl_3$) 138.8, 138.2, 138.0, 128.7–127.8 (10C), 115.1, 104.0, 80.7, 79.1, 75.4, 74.2, 72.8, 69.6, 67.7, 62.8, 30.4, 29.2 (Calc. for $C_{25}H_{32}O_6$: C, 70.07; H, 7.53%. Found: C, 69.88; H, 7.56).

Pent-4-enyl 6-*O*-acetyl-2,3-di-*O*-benzyl-4-*O*-chloroacetyl-β-D-galactopyranoside 11a

A solution of **10** (2.0 g, 4.67 mmol), Ac_2O (0.5 cm^3, 5.3 mmol) and Et_3N (1 cm^3, 7.2 mmol) in dry CH_2Cl_2 (25 cm^3) was stirred overnight and then quenched with a drop of MeOH. After stirring of the mixture for an additional 1 h, $(ClCH_2CO)_2O$ (1.2 g, 7.0 mmol), Et_3N (1 cm^3) and DMAP (10 mg) were added. The mixture was stirred for 3 h, and then concentrated, and purified by flash chromatography (hexane–EtOAc; 3:1) to give **11a** (2.4 g, 94%) as a syrup; R_f 0.44; $[\alpha]_D^{20}$ +17.5 (*c* 1.1, $CHCl_3$); δ_H ($CDCl_3$) 7.36–7.27 (m, 10H), 5.81 (m, 1H), 5.53 (m, 1H), 5.06–4.95 (m, 2H), 4.87 (d, 1H, *J* 11.0), 4.74 (d, 1H, *J* 11.0), 4.72 (d, 1H, *J* 11.0), 4.55 (d, 1H, *J* 11.0), 4.38 (m, 1H), 4.21–4.14 (m, 4H), 3.94 (dt, 1H, *J* 9.5, 6.4), 3.80 (dt, 1H, *J* 0.9, 6.8), 3.62–3.52 (m, 3H), 2.16 (m, 2H), 2.07 (s, 3H), 1.76 (m, 2H); δ_C ($CDCl_3$) 170.6, 167.2, 138.6, 138.1, 137.7, 128.6–127.9 (10C), 115.2, 104.0, 79.1, 78.9, 75.6, 72.8, 70.6, 70.0, 68.9, 61.9, 41.1, 30.4, 29.1, 21.0 (Calc. for $C_{29}H_{35}ClO_8$: C, 63.67; H, 6.45%. Found: C, 63.25; H, 6.47).

Pent-4-enyl 2,3-di-*O*-benzyl-4-*O*-chloroacetyl-6-*O*-(4-methoxy-phenyl)-β-D-galactopyranoside 11b

To an ice-cooled solution of **10** (5.0 g, 11.7 mmol) in pyridine (35 cm^3) was added TsCl (3.3 g, 17.3 mmol). The mixture was stirred at rt overnight and then diluted with CH_2Cl_2 (100 cm^3) and washed with 1 M aq. HCl (2 × 75 cm^3). The organic phase was dried and concentrated. To a solution of the residue in DMF (10 cm^3) was added a solution of sodium *p*-methoxy-phenolate in DMF (prepared from 2.5 g of *p*-methoxyphenol and 1.2 g of ~50% NaH oil dispersion in 15 cm^3 of DMF). The mixture was stirred for 2 days and then diluted with Et_2O (100 cm^3) and washed with water (2 × 60 cm^3). The organic layer was dried, concentrated, and purified by flash chromatography (hexane–EtOAc; 4:1) to give 4.43 g of a syrup. This was treated overnight with $(ClCH_2CO)_2O$ (2.2 g), Et_3N (1.8 cm^3), and DMAP (20 mg) in CH_2Cl_2 (50 cm^3) followed by evaporation of the solvent and flash chromatography (hexane–EtOAc; 5:1) to afford **11b** (4.77 g, 67%) as an oil; R_f 0.35; $[\alpha]_D^{20}$ +2.5 (*c* 0.9, $CHCl_3$); δ_H ($CDCl_3$) 7.36–7.27 (m, 10H), 6.87–6.80 (m, 4H), 5.82 (m, 1H), 5.72 (d, 1H, *J* 2.4), 5.00 (m, 2H), 4.88 (d, 1H, *J* 11.0), 4.78 (d, 1H, *J* 11.1), 4.74 (d, 1H, *J* 11.1), 4.57 (d, 1H, *J* 11.5), 4.43 (d, 1H, *J* 7.3), 4.11 (m, 1H), 4.10 (s, 2H), 4.01–3.87 (m, 3H), 3.77 (s, 3H), 3.60 (m, 3H), 2.17 (m, 2H), 1.77 (m, 2H); δ_C ($CDCl_3$) 167.1, 154.6, 152.6, 138.6, 138.1, 137.8, 128.6–127.9 (10C), 116.2, 115.2, 114.9, 104.0, 79.3, 79.0, 75.6, 72.7, 71.6, 70.0, 69.2, 67.1, 55.9, 41.0, 30.4, 29.2 (Calc. for $C_{34}H_{39}ClO_8$: C, 66.82; H, 6.43%. Found: C, 66.75; H, 6.53).

Benzyl 2,3-di-*O*-benzyl-β-D-galactopyranoside 12

A solution of galactose pentaacetate (25 g, 64 mmol), BnOH (12 cm^3, 116 mmol) and $BF_3{\cdot}OEt_2$ (10 cm^3, 79 mmol) in CH_2Cl_2 (200 cm^3) was stirred at rt for 12 h, and then worked up and deacetylated as described above for **4**. Purification by flash chromatography (acetone–EtOAc; 1:1) gave 15.8 g of a solid, which on recrystallisation from MeCN gave 12.4 g of benzyl β-D-galactopyranoside, mp 106–108 °C (lit.,[17] 99–100 °C).

A mixture of this material (10 g, 37 mmol), $PhCH(OMe)_2$ (7.5 cm^3, 50 mmol) and CSA (200 mg) in $CHCl_3$ (175 cm^3) was heated at reflux for 1 h in a flask equipped with a distillation head. About 50 cm^3 of a $CHCl_3$–MeOH mixture distilled off. Benzyl 4,6-*O*-benzylidene-β-D-galactopyranoside crystallised directly, 12.4 g, mp 195–198 °C (lit.,[17] 209–210 °C).

This was benzylated as described above for **8** to give, after direct crystallisation from EtOAc, 16.8 g of benzyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranoside, mp 162–164 °C (lit.,[17] 169.5–170.5 °C).

This was deprotected as described above for **9** to give, after direct crystallisation from EtOAc–hexane, 13.6 g of **12**, mp 113–115 °C (lit.,[17] 116–117 °C).

Benzyl 6-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranoside 13a

A mixture of **12** (3.0 g, 6.7 mmol), Ac_2O (0.7 cm^3, 7.4 mmol) and Et_3N (1.4 cm^3, 10 mmol) in dry CH_2Cl_2 (20 cm^3) was stirred overnight and then quenched with MeOH. The solution was diluted with CH_2Cl_2 (30 cm^3) and washed with water (30 cm^3). The organic phase was dried and concentrated to give a solid, which was recrystallised from EtOAc–hexane to afford **13a** (3.1 g, 95%); R_f 0.31 (hexane–EtOAc; 2:1); mp 99–103 °C; $[\alpha]_D^{20}$ −17.7 (*c* 1.5, $CHCl_3$); δ_H ($CDCl_3$) 7.42–7.25 (m, 15H), 4.96 (d, 1H, *J* 11.0), 4.94 (d, 1H, *J* 11.0), 4.77–4.65 (m, 4H), 4.45 (d, 1H, *J* 7.8), 4.37 (m, 2H), 3.93 (dd, 1H, *J* 3.6, 0.9), 3.72 (dd, 1H, *J* 9.4, 7.8), 3.59 (dt, 1H, *J* 0.9, 6.3), 3.50 (dd, 1H, *J* 9.4, 3.5), 2.10 (s, 3H); δ_C ($CDCl_3$) 171.0, 138.7, 138.0, 137.5, 128.7–127.8 (15C), 102.5, 80.7, 79.0, 75.4, 72.9, 72.1, 71.1, 67.0, 63.3, 21.1 (Calc. for $C_{29}H_{32}O_7$: C, 70.72; H, 6.55%. Found: C, 70.62; H, 6.62).

Benzyl 2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galacto-pyranoside 13b

To an ice-cooled solution of **12** (3.5 g, 7.77 mmol) in dry pyridine (10 cm^3) was added TsCl (2.08 g, 10.9 mmol). The mixture was stirred at rt for 6 h and then diluted with CH_2Cl_2 (60 cm^3) and washed with 1 M aq. HCl (3 × 50 cm^3). The

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organic phase was dried and concentrated. To a solution of the residue in DMF (15 cm^3) was added a solution of sodium *p*-methoxyphenolate in DMF (prepared from 1.4 g of *p*-methoxyphenol and 0.54 g of ~50% NaH oil dispersion in 5 cm^3 of DMF). The mixture was stirred for 16 h and then diluted with Et_2O (70 cm^3) and washed with water (2 × 50 cm^3). The organic layer was dried, concentrated, and purified by flash chromatography (hexane–EtOAc; 3 : 1) to give **13b** (3.37 g, 78%) as an oil, which crystallised from EtOH to give 3.12 g of title compound; R_f 0.31; mp 87–87.5 °C; $[\alpha]_D^{20}$ −34.4 (*c* 1.0, $CHCl_3$); δ_H ($CDCl_3$) 7.41–7.28 (m, 15H), 6.88 (m, 4H), 4.96 (d, 1H, *J* 12.2), 4.95 (d, 1H, *J* 11.0), 4.75 (m, 3H), 4.69 (d, 1H, *J* 11.8), 4.51 (d, 1H, *J* 7.7), 4.31–4.18 (m, 2H), 4.11 (d, 1H, *J* 3.3), 3.79 (s, 3H), 3.74 (m, 2H), 3.56 (dd, 1H, *J* 9.7, 3.5), 2.09 (br s, 1H); δ_C ($CDCl_3$) 154.4, 153.0, 138.7, 138.0, 137.6, 128.7–127.8 (15C), 116.1, 114.9, 102.7, 80.9, 79.2, 75.5, 73.0, 72.9, 71.1, 67.7, 66.9, 56.0 (Calc. for $C_{34}H_{36}O_7$: C, 73.36; H, 6.52%. Found: C, 73.47; H, 6.55).

General procedure for glycosylation reactions

A mixture of the donor (1 mmol) and the acceptor (0.77 mmol) was dried azeotropically with toluene, and then subjected to high vacuum for 2 h. The mixture was dissolved in dry CH_2Cl_2 (10 cm^3), cooled to −20 °C, and treated with NIS (230 mg, 1.02 mmol) and TESOTf (0.03 cm^3, 0.13 mmol). The reaction mixture was stirred at −20 °C until TLC revealed full conversion of the donor (15–45 min). The solution was diluted with CH_2Cl_2 (15 cm^3) and washed successively with 10% aq. $Na_2S_2O_3$ (15 cm^3) and saturated aq. $NaHCO_3$ (15 cm^3). The organic phase was dried and concentrated and the residue purified by flash chromatography.

Benzyl *O*-[2,3-di-*O*-benzyl-4-*O*-chloroacetyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galactopyranoside 14

Syrup; R_f 0.54 (hexane–EtOAc; 2 : 1); $[\alpha]_D^{20}$ +18.5 (*c* 3.3, $CHCl_3$); δ_H ($CDCl_3$) 7.47–7.09 (m, 25H), 6.83–6.49 (m, 8H), 5.81 (d, 1H, *J* 2.0), 5.05–4.44 (m, 13H), 4.19 (m, 1H), 4.12 (d, 1H, *J* 7.0), 4.08–3.96 (m, 2H), 3.95 (s, 2H), 3.83–3.45 (m, 12H); δ_C ($CDCl_3$) 166.5, 153.9 (2C), 152.2 (2C), 138.3–137.3 (5C), 128.3–127.2 (25C), 115.5 (2C), 115.2 (2C), 114.5 (2C), 114.3 (2C), 102.9, 100.5, 80.6, 78.5, 76.2, 75.3, 74.9, 74.8, 73.3, 73.0, 72.8, 71.9, 71.0, 69.9, 67.0, 65.9, 65.2, 55.5 (2C), 40.7 (Calc. for $C_{63}H_{65}ClO_{14}$: C, 69.96; H, 6.06%. Found: C, 69.57; H, 6.14).

Benzyl *O*-[2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galactopyranoside 15

A mixture of **14** (1.81 g, 1.67 mmol), thiourea (1.3 g, 17 mmol) and $NaHCO_3$ (0.7 g, 8.3 mmol) in MeOH (25 cm^3)–CH_2Cl_2 (25 cm^3) was heated at 50 °C overnight and then diluted with CH_2Cl_2 (150 cm^3) and washed with saturated aq. $NaHCO_3$ (150 cm^3). The organic phase was dried, concentrated and purified by flash chromatography (hexane–EtOAc; 3 : 1) to give **15** (1.29 g, 77%) as a foam; R_f 0.32; $[\alpha]_D^{20}$ +21.6 (*c* 2.6, $CHCl_3$); δ_H ($CDCl_3$) 7.44–7.13 (m, 25H), 6.76–6.57 (m, 8H), 5.07–4.40 (m, 14H), 4.26 (m, 1H), 4.18 (d, 1H, *J* 3.0), 4.12–3.42 (m, 14H), 2.05 (br s, 1H); δ_C ($CDCl_3$) 153.8 (2C), 152.6, 152.6, 138.4–137.4 (5C), 128.3–127.2 (25C), 115.3 (4C), 114.5 (2C), 114.3 (2C), 102.8, 100.3, 80.7, 78.7, 77.7, 75.6, 75.0 (2C), 73.3, 72.9, 72.6, 72.0, 71.0, 68.0, 66.8, 66.6, 65.6, 55.6 (2C) (Calc. for $C_{61}H_{64}O_{13}$: C, 72.89; H, 6.42%. Found: C, 72.43; H, 6.28).

Benzyl *O*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-*O*-[2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galactopyranoside 16

Syrup; R_f 0.49 (hexane–EtOAc; 2 : 1); $[\alpha]_D^{20}$ +36.1 (*c* 1.1, $CHCl_3$); δ_H ($CDCl_3$) 7.44–7.11 (m, 40H), 6.78 (s, 4H), 6.65–6.44 (m, 4H), 5.07 (m, 2H), 5.00–4.81 (m, 5H), 4.81–4.36 (m, 15H), 4.29–4.17 (m, 3H), 4.14–3.79 (m, 8H), 3.78–3.63 (m, 3H), 3.76 (s, 3H), 3.67 (s, 3H), 3.49 (dd, 1H, *J* 9.9, 2.8), 1.78 (s, 3H); δ_C ($CDCl_3$) 170.0, 154.2, 154.0, 152.7, 152.5, 139.0–137.8 (8C), 128.6–127.3 (40C), 115.6 (4C), 114.9 (2C), 114.7 (2C), 103.2, 100.6, 99.6, 81.2, 79.5, 79.0, 77.5, 77.3, 76.1, 75.3 (2C), 75.0 (2C), 74.7, 74.3, 73.7, 73.2, 73.0 (2C), 72.6, 71.2, 69.7, 68.5, 65.8, 64.9, 62.5, 56.0, 55.9, 20.9; *m*/*z* 1502.91 ($M + Na^+$). Calc. for $C_{90}H_{94}O_{19} + Na^+$: *m*/*z*, 1501.63.

Benzyl *O*-(2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-*O*-[2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galactopyranoside 17

A mixture of **16** (530 mg, 0.358 mmol) and K_2CO_3 (150 mg) in MeOH (15 cm^3) was stirred overnight and then filtered and concentrated. The residue was purified by flash chromatography (hexane–EtOAc; 2 : 1) to afford **17** (507 mg, 98%) as a foam; R_f 0.45; $[\alpha]_D^{20}$ +31.9 (*c* 2.3, $CHCl_3$); δ_H ($CDCl_3$) 7.44–7.12 (m, 40H), 6.76 (s, 4H), 6.65–6.46 (m, 4H), 5.08 (d, 1H, *J* 13.5), 5.07 (d, 1H, *J* 13.5), 4.98 (d, 1H, *J* 11.9), 4.91–4.83 (m, 4H), 4.79–4.44 (m, 14H), 4.30–4.21 (m, 3H), 4.11–4.02 (m, 3H), 3.98–3.90 (m, 3H), 3.87–3.62 (m, 4H), 3.76 (s, 3H), 3.67 (s, 3H), 3.50 (m, 1H), 3.33 (m, 2H), 0.9 (br s, 1H); δ_C ($CDCl_3$) 154.2, 153.9, 152.7, 152.6, 138.9–137.8 (8C), 128.6–127.4 (40C), 115.6 (2C), 115.5 (2C), 114.9 (2C), 114.7 (2C), 103.2, 100.5, 99.9, 81.1, 79.4, 79.0, 77.5, 76.2, 75.9 (2C), 75.5, 75.3, 75.1, 74.7, 73.7, 73.2, 73.1, 73.0 (2C), 72.9, 71.2, 70.8, 69.8, 65.9, 65.0, 62.5, 56.0, 55.9; *m*/*z* 1460.49 ($M + Na^+$). Calc. for $C_{88}H_{92}O_{18} + Na^+$: *m*/*z*, 1459.62.

Benzyl *O*-(methyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl-uronate)-(1→4)-*O*-[2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galactopyranoside 18

To a suspension of the Dess–Martin periodinane (259 mg, 0.611 mmol) in CH_2Cl_2 (10 cm^3) was added a solution of **17** (585 mg, 0.407 mmol) in CH_2Cl_2 (7 cm^3). The mixture was stirred for 20 min and then quenched by addition of Et_2O (12 cm^3) and saturated aq. $NaHCO_3$ containing 3 g of $Na_2S_2O_3$ (12 cm^3). After being stirred for an additional 2 h the solution was diluted with Et_2O (10 cm^3) and washed successively with saturated aq. $NaHCO_3$ (10 cm^3) and water (10 cm^3). The organic phase was dried and concentrated. To a solution of the residue in Bu′OH (7 cm^3), THF (3 cm^3), and 2-methylbut-2-ene (2.2 cm^3) were added $NaClO_2$ (368 mg, 4.07 mmol) and $NaH_2PO_4 \cdot H_2O$ (0.4 g) in water (3 cm^3). The mixture was stirred overnight and then quenched with 1 M aq. HCl (10 cm^3) and extracted with EtOAc (2 × 20 cm^3). The organic extracts were dried and concentrated. To a solution of the residue in MeOH (30 cm^3) was added a 2 M solution of $TMSCHN_2$ in hexanes (3.2 cm^3, 6.4 mmol). After being stirred overnight the solution was concentrated, and purified by flash chromatography (hexane–EtOAc; 3 : 1) to give **18** (339 mg, 57%) as a foam; R_f 0.14; $[\alpha]_D^{20}$ +3.5 (*c* 2.4, $CHCl_3$); δ_H ($CDCl_3$) 7.41–7.04 (m, 40H), 6.78 (s, 4H), 6.65–6.47 (m, 4H), 5.18 (d, 1H, *J* 3.8), 5.07 (d, 1H, *J* 3.4), 4.99–4.81 (m, 6H), 4.76–4.41 (m, 13H), 4.35 (br d, 1H, *J* 1.7), 4.24–4.17 (m, 3H), 4.09–4.04 (m, 2H), 3.97 (dd, 1H, *J* 10.7, 3.4), 3.88 (dd, 1H, *J* 10.7, 3.4), 3.80 (dd, 1H, *J* 10.3, 3.4), 3.76 (s, 3H), 3.75–3.62 (m, 4H), 3.67 (s, 3H), 3.48 (dd, 1H, *J* 10.0, 2.8), 3.22 (s, 3H); δ_C ($CDCl_3$) 169.5, 154.0, 153.8, 152.5, 152.2, 138.6–137.6 (8C), 128.3–126.9 (40C), 115.3 (4C), 114.7 (2C), 114.5 (2C), 102.9, 100.5, 99.4, 81.0, 78.6 (2C), 77.9, 76.7, 74.9 (3C), 74.5, 74.4, 74.3, 73.6, 73.0, 72.8, 72.7 (2C), 71.8, 71.5, 71.0, 69.1, 65.4, 64.2, 55.7, 55.6, 51.7; *m*/*z* 1487.29 ($M + Na^+$). Calc. for $C_{89}H_{92}O_{19} + Na^+$: *m*/*z*, 1487.61.

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Benzyl *O*-(methyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl-uronate)-(1→4)-*O*-(2,3-di-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-2,3-di-*O*-benzyl-β-D-galactopyranoside 19

To a solution of **18** (303 mg, 0.207 mmol) in MeCN (7 cm^3) at −10 °C was added aq. CAN (1.2 g, 2.2 mmol in 2 cm^3). The mixture was stirred at −10 °C for 30 min and then diluted with $CHCl_3$ (20 cm^3) and washed with water (2 × 15 cm^3). The organic phase was dried, concentrated and purified by flash chromatography (hexane–EtOAc; 3:2) to give **19** (210 mg, 81%) as a foam; R_f 0.12; $[\alpha]_D^{20}$ +48.3 (*c* 0.8, $CHCl_3$); δ_H ($CDCl_3$) 7.42–7.22 (m, 40H), 5.01 (d, 1H, *J* 3.4), 4.98 (d, 1H, *J* 3.4), 4.93 (d, 1H, *J* 7.3), 4.91–4.55 (m, 16H), 4.41 (d, 1H, *J* 7.7), 4.34 (t, 1H, *J* 2.1), 4.14 (dd, 1H, *J* 10.2, 3.4), 4.08 (d, 1H, *J* 2.9), 4.04 (t, 1H, *J* 6.2), 4.00–3.95 (m, 3H), 3.88 (dd, 1H, *J* 10.7, 3.2), 3.72–3.62 (m, 4H), 3.59 (dd, 1H, *J* 11.1, 6.0), 3.48–3.37 (m, 2H), 3.43 (s, 3H), 1.73 (br s, 2H); δ_C ($CDCl_3$) 169.7, 138.9–137.8 (8C), 128.9–127.4 (40C), 103.3, 100.5, 100.3, 80.8, 79.4, 78.9, 77.6, 77.1, 76.8, 76.4, 76.2, 75.7, 75.4, 75.0, 74.7, 74.6, 74.3, 73.1 (2C), 72.0 (3C), 71.5, 61.6, 60.5, 52.3; *m/z* 1276.27 (M + Na^+). Calc. for $C_{75}H_{80}O_{17}$ + Na^+: *m/z*, 1275.53.

Benzyl *O*-(methyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl-uronate)-(1→4)-*O*-(2,3-di-*O*-benzyl-α-D-galactopyranosyluronic acid)-(1→4)-2,3-di-*O*-benzyl-β-D-galactopyranosyluronic acid 20

Diol **19** (192 mg, 0.153 mmol) was oxidised with the Dess–Martin periodinane (195 mg, 0.460 mmol) and then with $NaClO_2$ (278 mg, 3.07 mmol) as described above for **17** to give **20** (141 mg, 72%) after purification by flash chromatography (EtOAc–hexane; 2:1 + 3% AcOH); R_f 0.15; $[\alpha]_D^{20}$ +72.6 (*c* 0.6, $CHCl_3$); δ_H ($CDCl_3$) 7.52–7.08 (m, 40H), 5.38 (br s, 1H), 5.23 (d, 1H, *J* 3.3), 5.05 (d, 1H, *J* 11.7), 4.94–4.39 (m, 20H), 4.18–4.11 (m, 3H), 3.90 (s, 3H), 3.86 (m, 1H), 3.69–3.52 (m, 4H); δ_C (CD_3OD) 170.8, 170.4, 170.0, 138.9–137.9 (8C), 128.6–127.2 (40C), 102.8, 98.3, 97.7, 79.7, 77.8, 77.6, 76.6, 76.1, 76.0, 75.1, 74.6 (2C), 74.5, 73.2, 73.1, 73.0, 72.4 (2C), 72.2, 71.5, 71.3, 71.2, 70.8, 51.2; *m/z* 1304.46 (M + Na^+). Calc. for $C_{75}H_{76}O_{19}$ + Na^+: *m/z*, 1303.49.

***O*-(Methyl α-D-galactopyranosyluronate)-(1→4)-*O*-(α-D-galactopyranosyluronic acid)-(1→4)-D-galactopyranuronic acid 1**

A solution of **20** (280 mg, 0.219 mmol) in MeOH (40 cm^3)–water (10 cm^3) was hydrogenated over 10% Pd/C (200 mg) at 1 atm H_2 pressure for 7 h. The catalyst was removed by filtration through Celite and rinsed successively with MeOH and water. The filtrate was concentrated to give **1** (107 mg, 87%) as a foam, which was pure by NMR; R_f 0.43 (MeOH–H_2O; 2:1 + 3% AcOH); δ_H (D_2O) 5.26 (d, 0.4H, *J* 3.7, $H^{1\alpha}$), 5.07 (m, 2H), 5.03 (d, 1H, *J* 3.8, $H^{1'}$), 4.76 (d, 0.4H, *J* 0.8), 4.71 (s, 1H), 4.68–4.63 (signals hidden under HDO peak), 4.55 (d, 0.6H, *J* 8.0, $H^{1\beta}$), 4.40–4.32 (m, 2.6H), 4.27 (m, 1H), 4.01–3.92 (m, 2H), 3.87 (dd, 1H, *J* 10.3, 3.4), 3.77 (m, 0.6H), 3.74 (s, 3H), 3.72–3.68 (m, 1.6H), 3.67 (dd, 1H, *J* 10.0, 3.8), 3.44 (dd, 0.6H, *J* 9.5, 8.0); δ_C (D_2O) 175.4, 174.6, 171.7, 99.6, 99.3, 99.1, 96.4, 92.4, 78.8, 78.2, 77.3, 74.4, 72.5, 71.7, 71.6, 71.4, 70.8, 70.3, 69.0 (2C), 68.4, 68.2, 53.0.

Benzyl *O*-(6-*O*-acetyl-2,3-di-*O*-benzyl-4-*O*-chloroacetyl-α-D-galactopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galactopyranoside 21

Syrup; R_f 0.37 (hexane–EtOAc; 3:1); $[\alpha]_D^{20}$ +43.9 (*c* 0.9, $CHCl_3$); δ_H ($CDCl_3$) 7.45–7.16 (m, 25H), 6.72 (m, 4H), 5.61 (m, 1H), 4.99 (m, 3H), 4.88–4.43 (m, 11H), 4.20–4.09 (m, 4H), 4.05–3.97 (m, 4H), 3.81–3.63 (m, 2H), 3.75 (s, 3H), 3.50 (dd, 1H, *J* 10.9, 2.9), 1.95 (s, 3H); δ_C ($CDCl_3$) 170.3, 167.1, 154.3, 152.5, 138.8, 138.6, 138.4, 138.0, 137.7, 128.7–127.6 (25C), 115.7 (2C), 114.9 (2C), 103.2, 100.3, 80.4, 79.0, 76.2, 75.2 (3C), 73.7, 73.3, 73.2, 72.3, 71.4, 70.0, 66.7, 65.7, 61.4, 56.0, 41.0, 20.9 (Calc. for $C_{58}H_{61}ClO_{14}$: C, 68.46; H, 6.04%. Found: C, 68.08; H, 5.94).

Benzyl *O*-(6-*O*-acetyl-2,3-di-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galactopyranoside 22

To a solution of **21** (1.0 g, 0.98 mmol) in THF (12 cm^3) were added thiourea (150 mg, 2.0 mmol), $NaHCO_3$ (180 mg, 2.1 mmol) and Bu_4NI (18 mg, 0.05 mmol). The mixture was heated at 55 °C overnight and then diluted with CH_2Cl_2 (50 cm^3) and washed with water (50 cm^3). The organic layer was dried, concentrated, and purified by flash chromatography (hexane–EtOAc; 3:1) to afford **22** (790 mg, 85%) as a foam; R_f 0.25; $[\alpha]_D^{20}$ +32.7 (*c* 0.8, $CHCl_3$); δ_H ($CDCl_3$) 7.46–7.25 (m, 25H), 6.78–6.68 (m, 4H), 5.05 (d, 1H, *J* 3.5), 4.99 (d, 1H, *J* 11.4), 4.98 (d, 1H, *J* 11.4), 4.97 (s, 1H), 4.86 (d, 1H, *J* 12.6), 4.85 (d, 1H, *J* 10.9), 4.80–4.67 (m, 5H), 4.59 (d, 1H, *J* 12), 4.57 (d, 1H, *J* 7.5), 4.45 (m, 2H), 4.48–4.02 (m, 6H), 3.89–3.67 (m, 3H), 3.76 (s, 3H), 3.51 (dd, 1H, *J* 9.8, 2.9), 1.94 (s, 3H); δ_C ($CDCl_3$) 170.7, 154.2, 152.6 (2C), 138.9, 138.6, 138.3, 137.7, 128.7–127.6 (25C), 115.8 (2C), 114.9 (2C), 103.1, 100.2, 80.4, 79.2, 77.8, 76.1, 75.2 (2C), 73.7, 73.3, 72.7, 72.5, 71.3, 68.0, 67.4, 66.3, 63.0, 56.0, 21.1 (Calc. for $C_{56}H_{60}O_{13}$: C, 71.47; H, 6.43%. Found: C, 71.02; H, 6.47).

Benzyl *O*-[2,3,4-tri-*O*-benzyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-*O*-(6-*O*-acetyl-2,3-di-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galactopyranoside 23

Syrup; R_f 0.15 (hexane–EtOAc; 3:1); $[\alpha]_D^{20}$ +14.7 (*c* 0.9, $CHCl_3$); δ_H ($CDCl_3$) 7.46–7.12 (m, 40H), 6.82–6.54 (m, 8H), 5.11 (d, 1H, *J* 3.3), 5.05–3.54 (m, 35H), 3.78 (s, 3H), 3.77 (s, 3H), 3.49 (dd, 1H, *J* 9.8, 2.9), 1.93 (s, 3H); δ_C ($CDCl_3$) 170.1, 154.0 (2C), 152.8, 152.7, 139.1–137.9 (8C), 128.9–127.5 (40C), 115.7 (2C), 115.5 (2C), 114.9 (2C), 114.7 (2C), 103.1, 100.6, 100.3, 79.9, 79.7, 79.3, 77.9, 76.5, 75.9, 75.2, 75.0, 74.8, 74.5, 74.2, 73.6, 73.3, 73.2, 72.9, 72.8, 72.5, 71.3, 69.5, 69.4, 66.1, 65.7, 62.1, 56.0, 55.9, 21.2 (Calc. for $C_{90}H_{94}O_{19}$: C, 73.05; H, 6.40%. Found: C, 72.99; H, 6.56).

Benzyl *O*-[2,3,4-tri-*O*-benzyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-*O*-(2,3-di-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galactopyranoside 24

Deacetylation of **23** as described above for **16** gave **24** as a foam; R_f 0.50 (hexane–EtOAc; 2:1); $[\alpha]_D^{20}$ +20.0 (*c* 0.8, $CHCl_3$); δ_H ($CDCl_3$) 7.48–7.17 (m, 40H), 6.87–6.55 (m, 4H), 6.78 (s, 4H), 5.09–4.52 (m, 19H), 4.38 (m, 1H), 4.29–3.45 (m, 23H), 3.24 (br s, 1H); δ_C ($CDCl_3$) 154.2, 154.1, 152.8, 152.7, 139.0–137.9 (8C), 128.9–127.2 (40C), 115.7 (2C), 115.5 (2C), 114.9 (2C), 114.8 (2C), 103.2, 101.0, 100.7, 80.4, 79.6, 79.1 (2C), 78.1, 76.7, 75.6, 75.3 (2C), 75.0, 74.7 (2C), 73.5, 73.3, 72.9, 72.8, 72.7, 71.3, 71.0, 69.8, 65.9 (2C), 61.3, 56.0 (2C) (Calc. for $C_{88}H_{92}O_{18}$: C, 73.52; H, 6.45%. Found: C, 72.99; H, 6.38).

Benzyl *O*-[2,3,4-tri-*O*-benzyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-*O*-(methyl 2,3-di-*O*-benzyl-α-D-galactopyranosyluronate)-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-β-D-galactopyranoside 25

Oxidation and methyl esterification of **24** as described above for **17** gave **25** as a syrup; R_f 0.42 (hexane–EtOAc; 3:1); $[\alpha]_D^{20}$ +21.9 (*c* 1.3, $CHCl_3$); δ_H ($CDCl_3$) 7.36–7.03 (m, 40H), 6.75–6.40 (m, 4H), 6.69 (s, 4H), 5.11 (d, 1H, *J* 3.1), 4.95–4.36 (m, 20H), 4.29 (dd, 1H, *J* 8.3, 5.2), 4.21 (d, 1H, *J* 3.3), 4.08–3.34 (m, 12H), 3.67 (s, 3H), 3.66 (s, 3H), 3.17 (s, 3H); δ_C ($CDCl_3$) 169.5, 154.3, 154.0, 152.9, 152.5, 139.2–137.8 (8C), 128.7–127.3 (40C), 115.6 (4C), 115.0 (2C), 114.7 (2C), 103.3, 100.3, 100.1, 80.4, 79.5, 78.6, 77.9, 77.6, 76.0, 75.2 (2C), 75.0, 74.9, 74.3, 74.0, 73.5 (2C), 73.1, 72.9, 72.2, 71.6, 71.4, 69.8, 66.2, 65.0, 56.0, 55.9, 52.1 (Calc. for $C_{89}H_{92}O_{19}$: C, 72.93; H, 6.33%. Found: C, 72.67; H, 6.50).

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Benzyl *O*-(2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-*O*-(methyl 2,3-di-*O*-benzyl-α-D-galactopyranosyluronate)-(1→4)-2,3-di-*O*-benzyl-β-D-galactopyranoside 26

Deprotection of **25** as described above for **18** gave **26** as a foam; R_f 0.12 (EtOAc–hexane; 3:2); $[\alpha]_D^{20}$ +39.0 (*c* 0.9, $CHCl_3$); δ_H ($CDCl_3$) 7.41–7.23 (m, 40H), 5.13 (s, 1H), 5.02 (d, 1H, *J* 3.0), 4.95 (d, 1H, *J* 8.9), 4.93–4.86 (m, 3H), 4.84–4.53 (m, 13H), 4.47 (s, 1H), 4.43 (d, 1H, *J* 7.5), 4.06–3.89 (m, 6H), 3.85 (s, 1H), 3.79 (m, 2H), 3.69–3.54 (m, 2H), 3.44–3.31 (m, 3H), 3.37 (s, 3H), 2.12 (br s, 2H); δ_C ($CDCl_3$) 169.1, 138.7–138.1 (8C), 128.7–127.6 (40C), 103.2, 100.1, 99.7, 80.2, 79.3, 79.0, 77.8, 77.4, 76.8, 76.0, 75.8, 75.7, 75.2, 74.7, 74.5, 74.4, 73.6 (2C), 73.1, 72.4, 71.9, 71.5 (2C), 62.8, 60.9, 52.2 (Calc. for $C_{75}H_{80}O_{17}$: C, 71.87; H, 6.43%. Found: C, 71.45; H, 6.41).

Benzyl *O*-(2,3,4-tri-*O*-benzyl-α-D-galactopyranosyluronic acid)-(1→4)-*O*-(methyl 2,3-di-*O*-benzyl-α-D-galactopyranosyl-uronate)-(1→4)-2,3-di-*O*-benzyl-β-D-galactopyranosyluronic acid 27

Oxidation of **26** as described above for **19** gave **27** as a foam; R_f 0.11 (EtOAc–hexane; 2:1 + 3% AcOH); $[\alpha]_D^{20}$ +65.2 (*c* 0.6, $CHCl_3$); δ_H (CD_3OD) 7.51–7.20 (m, 40H), 5.30 (d, 1H, *J* 2.8), 5.10 (d, 1H, *J* 11.5), 4.98 (d, 1H, *J* 3.3), 4.90–4.78 (6H, hidden under HDO signal), 4.75–4.50 (m, 13H), 4.34–4.21 (m, 3H), 3.95–3.81 (m, 3H), 3.69–3.54 (m, 3H), 3.19 (s, 3H); δ_C ($CDCl_3$) 172.0, 169.5, 169.0, 138.7–137.4 (8C), 128.9–127.4 (40C), 103.1, 99.8, 99.1, 79.3, 78.6, 77.7, 77.6, 76.3, 75.4, 75.2 (2C), 74.6 (2C), 73.7 (2C), 73.3, 73.0, 72.9, 72.6, 72.4, 72.2, 71.6, 71.4, 52.1; *m*/*z* 1304.54 ($M + Na^+$). Calc. for $C_{75}H_{76}O_{19} + Na^+$: *m*/*z*, 1303.49.

***O*-(α-D-Galactopyranosyluronic acid)-(1→4)-*O*-(methyl α-D-galactopyranosyluronate)-(1→4)-D-galactopyranuronic acid 2**

Hydrogenation of **27** gave **2** as a foam; R_f 0.51 (MeOH–water; 2:1 + 3% AcOH); δ_H (D_2O) 5.29 (d, 0.4H, *J* 4.1, $H^{1\alpha}$), 5.09 (s, 1H), 5.06 (d, 1H, *J* 3.9, $H^{1'}$), 4.94 (br s, 1H), 4.88 (d, 1H, *J* 3.9, $H^{1''}$), 4.70–4.63 (signals hidden under HDO-peak), 4.59 (d, 0.6H, *J* 7.7, $H^{1\beta}$), 4.42–4.39 (m, 1.6H), 4.35 (d, 0.6H, *J* 2.8), 4.27 (m, 1.6H), 4.00 (dd, 1H, *J* 10.5, 3.3), 3.85 (dd, 1H, *J* 10.3, 3.3), 3.76 (s, 3H), 3.74 (dd, 1H, *J* 10.0, 3.2), 3.70 (m, 1H), 3.67 (dd, 1H, *J* 10.7, 4.0), 3.43 (dd, 0.6H, *J* 10.1, 7.7); δ_C (D_2O) 175.9, 175.6, 174.8, 173.5, 103.1, 102.7, 99.0, 95.1, 81.5 (2C), 80.7, 76.0, 74.5, 74.0, 73.4, 72.9, 72.5, 71.6, 70.7 (2C), 70.6, 55.7.

Benzyl *O*-[2,3-di-*O*-benzyl-4-*O*-chloroacetyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-6-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranoside 28

Foam; R_f 0.10 (hexane–EtOAc; 3:1); $[\alpha]_D^{20}$ +21.9 (*c* 0.6, $CHCl_3$); δ_H ($CDCl_3$) 7.35–7.09 (m, 25H), 6.65–6.45 (m, 4H), 5.72 (br d, 1H, *J* 2), 5.19 (s, 1H), 4.93–4.47 (m, 11H), 4.38 (m, 3H), 4.05 (m, 1H), 3.91 (s, 2H), 3.84 (d, 1H, *J* 2.9), 3.73 (dd, 1H, *J* 10.3, 3.5), 3.65 (m, 1H), 3.61 (s, 3H), 3.59–3.42 (m, 3H), 3.33 (dd, 1H, *J* 9.9, 2.7), 1.98 (s, 3H); δ_C ($CDCl_3$) 170.7, 166.8, 154.2, 152.5, 138.5–137.6 (5C), 128.7–127.9 (25C), 115.9 (2C), 114.7 (2C), 103.0, 101.0, 80.8, 78.7, 76.6, 76.5, 75.3 (2C), 74.2, 73.5, 72.5, 72.3, 71.4, 70.2, 67.5, 66.3, 62.4, 55.9, 41.1, 21.2; *m*/*z* 1060.98 ($M - H^+ + 2Na^+$). Calc. for $C_{58}H_{60}ClO_{14} + 2Na^+$: *m*/*z*, 1061.35.

Benzyl *O*-[2,3-di-*O*-benzyl-6-*O*-(4-methoxyphenyl)-α-D-galacto-pyranosyl]-(1→4)-6-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galacto-pyranoside 29

Dechloroacetylation of **28** as described above for **21** gave **29** as a foam, which was crystallised from EtOH; R_f 0.08 (hexane–EtOAc; 3:1); mp 103–104 °C; $[\alpha]_D^{20}$ +22.3 (*c* 0.8, $CHCl_3$); δ_H ($CDCl_3$) 7.43–7.18 (m, 25H), 6.74–6.61 (m, 4H), 5.02–4.61 (m, 11H), 4.52–4.43 (m, 4H), 4.25 (m, 1H), 4.08–3.91 (m, 4H), 3.77–3.72 (m, 2H), 3.70 (s, 3H), 3.54 (t, 1H, *J* 6.5), 3.42 (dd, 1H, *J* 9.9, 2.9), 2.05 (s, 3H), 1.70 (br s, 1H); δ_C ($CDCl_3$) 170.4, 153.7, 152.6, 138.3–137.3 (5C), 128.3–127.5 (25C), 115.3 (2C), 114.3 (2C), 102.6, 100.6, 80.5, 78.5, 76.3, 75.9, 75.6, 74.9, 73.7, 72.8, 72.2, 72.1, 71.0, 68.1, 66.8, 66.6, 52.3, 55.5, 20.8 (Calc. for $C_{56}H_{60}O_{13}$: C, 71.47; H, 6.43%. Found: C, 71.35; H, 6.37).

Benzyl *O*-[2,3,4-tri-*O*-benzyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-*O*-[2,3-di-*O*-benzyl-6-*O*-(4-methoxy-phenyl)-α-D-galactopyranosyl]-(1→4)-6-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranoside 30

Foam; R_f 0.13 (hexane–EtOAc; 3:1); $[\alpha]_D^{20}$ +15.9 (*c* 1.1, $CHCl_3$); δ_H ($CDCl_3$) 7.42–7.08 (m, 40H), 6.75–6.58 (m, 4H), 6.55–6.48 (m, 4H), 5.30 (m, 1H), 5.08–3.36 (m, 36H), 3.74 (s, 3H), 3.64 (s, 3H), 2.10 (s, 3H); δ_C ($CDCl_3$) 170.7, 153.9 (2C), 152.8, 152.6, 139.0–137.7 (8C), 128.5–127.4 (40C), 115.5 (2C), 115.4 (2C), 114.7 (4C), 102.9, 101.1, 100.3, 80.9, 79.7, 78.9, 78.3, 76.1, 76.0, 75.7, 75.2 (2C), 75.0, 74.5, 73.7, 73.5, 73.0, 72.9, 72.7, 72.6, 71.2, 69.8, 69.2, 65.6, 64.9, 62.7, 56.0, 55.9, 22.9 (Calc. for $C_{90}H_{94}O_{19}$: C, 73.05; H, 6.40%. Found: C, 72.51; H, 6.46).

Benzyl *O*-[2,3,4-tri-*O*-benzyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-*O*-[2,3-di-*O*-benzyl-6-*O*-(4-methoxy-phenyl)-α-D-galactopyranosyl]-(1→4)-2,3-di-*O*-benzyl-β-D-galactopyranoside 31

Deacetylation of **30** as described above for **16** gave **31** as a foam; R_f 0.10 (hexane–EtOAc; 2:1); $[\alpha]_D^{20}$ +22.5 (*c* 0.8, $CHCl_3$); δ_H ($CDCl_3$) 7.42–7.15 (m, 40H), 6.76–6.55 (m, 8H), 5.14 (d, 1H, *J* 2.9), 5.07 (d, 1H, *J* 3.0), 4.96–4.50 (m, 16H), 4.45 (d, 1H, *J* 7.5), 4.37–4.30 (m, 3H), 4.21 (br s, 1H), 4.11–3.97 (m, 5H), 3.91 (t, 1H, *J* 8.8), 3.83–3.62 (m, 5H), 3.75 (s, 3H), 3.66 (s, 3H), 3.53–3.42 (m, 3H), 3.33 (br s, 1H); δ_C ($CDCl_3$) 154.0 (2C), 152.8 (2C), 139.0–137.8 (8C), 128.8–127.5 (40C), 115.6 (2C), 115.5 (2C), 114.8 (2C), 114.7 (2C), 103.2, 100.6, 100.5, 81.2, 79.5, 79.3, 78.1, 76.4 (2C), 76.0, 75.8, 75.2 (2C), 74.6 (2C), 74.4, 73.8, 73.1, 72.8, 72.5, 71.4, 70.2, 69.5, 65.9, 65.5, 60.5, 56.0, 55.9 (Calc. for $C_{88}H_{92}O_{18}$: C, 73.52; H, 6.45%. Found: C, 73.22; H, 6.26).

Benzyl *O*-[2,3,4-tri-*O*-benzyl-6-*O*-(4-methoxyphenyl)-α-D-galactopyranosyl]-(1→4)-*O*-[2,3-di-*O*-benzyl-6-*O*-(4-methoxy-phenyl)-α-D-galactopyranosyl]-(1→4)-(methyl 2,3-di-*O*-benzyl-β-D-galactopyranosyluronate) 32

Oxidation and methyl esterification of **31** as described above for **17** gave **32** as a foam; R_f 0.11 (hexane–EtOAc; 3:1); $[\alpha]_D^{20}$ +15.0 (*c* 0.9, $CHCl_3$); δ_H ($CDCl_3$) 7.48–7.07 (m, 40H), 6.68 (m, 4H), 6.53 (m, 4H), 5.19 (d, 1H, *J* 3.1), 5.04 (m, 2H), 4.92–4.37 (m, 19H), 4.29 (m, 2H), 4.15 (s, 1H), 4.06–3.92 (m, 4H), 3.91–3.73 (m, 4H), 3.77 (s, 3H), 3.67 (s, 3H), 3.65 (s, 3H), 3.50 (m, 2H); δ_C ($CDCl_3$) 168.7, 153.9 (2C), 152.8 (2C), 139.1–137.7 (8C), 128.6–127.4 (40C), 115.6 (2C), 115.4 (2C), 114.7 (4C), 103.0, 100.2, 99.7, 80.7, 79.6, 78.5, 78.0, 77.5, 76.2, 75.9, 75.7, 75.3, 75.1, 74.9, 74.5, 74.0, 73.7, 72.9, 72.8, 72.7, 71.4, 70.1, 69.2, 65.5, 65.4, 56.0, 55.9, 52.6 (Calc. for $C_{89}H_{92}O_{19}$: C, 72.93; H, 6.33%. Found: C, 72.57; H, 6.42).

Benzyl *O*-(2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-*O*-(2,3-di-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-(methyl 2,3-di-*O*-benzyl-β-D-galactopyranosyluronate) 33

Deprotection of **32** as described above for **18** gave **33** as a foam; R_f 0.09 (hexane–EtOAc; 2:1); $[\alpha]_D^{20}$ +34.3 (*c* 0.8, $CHCl_3$); δ_H ($CDCl_3$) 7.45–7.23 (m, 40H), 5.14–5.05 (m, 2H), 4.96–4.87 (m, 4H), 4.83–4.60 (m, 12H), 4.48 (d, 1H, *J* 7.6), 4.41 (d, 1H, *J* 2.2), 4.15 (t, 1H, *J* 6.0), 4.08 (dd, 1H, *J* 10.2, 3.5), 4.02–3.91 (m, 5H), 3.87 (m, 1H), 3.84–3.73 (m, 2H), 3.66–3.50 (m, 3H), 3.54 (s, 3H), 3.47 (dd, 1H, *J* 9.7, 2.6), 3.30 (dd, 1H, *J* 11.2, 4.1), 2.3 (br s, 2H); δ_C ($CDCl_3$) 168.5, 139.2–137.7 (8C), 128.8–127.6 (40C), 103.0, 100.8, 99.1, 80.2, 79.7, 79.4, 78.7, 77.3, 77.1, 76.4, 75.7,

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75.4, 75.2, 74.8, 74.7, 73.9, 73.2, 73.2, 73.1, 72.9, 72.3, 71.5, 71.0, 62.9, 61.4, 52.5 (Calc. for $C_{75}H_{80}O_{17}$: C, 71.87; H, 6.43%. Found: C, 71.53; H, 6.32).

Benzyl *O*-(2,3,4-tri-*O*-benzyl-α-D-galactopyranosyluronic acid)-(1→4)-*O*-(2,3-di-*O*-benzyl-α-D-galactopyranosyluronic acid)-(1→4)-(methyl 2,3-di-*O*-benzyl-β-D-galactopyranosyluronate) 34

Oxidation of **33** as described above for **19** gave **34** as a foam; R_f 0.10 (EtOAc–hexane; 2:1 + 3% AcOH); $[\alpha]_D^{20}$ +80.6 (*c* 0.9, $CHCl_3$); δ_H ($CDCl_3$) 7.50–7.18 (m, 40H), 5.31–5.07 (m, 3H), 4.95–4.41 (m, 20H), 4.28 (s, 1H), 4.05–3.60 (m, 6H), 3.69 (s, 3H), 3.47 (m, 1H); δ_C ($CDCl_3$) 177.2, 170.3, 168.5, 138.7–137.5 (8C), 128.8–127.5 (40C), 102.9, 99.5, 99.0, 79.1, 78.4, 78.1, 76.4, 76.3, 76.2, 75.6, 75.3 (2C), 75.1, 73.7 (3C), 73.1 (3C), 72.8, 71.5 (2C), 71.1, 52.7; *m*/*z* 1304.60 ($M + Na^+$). Calc. for $C_{75}H_{76}O_{19} + Na^+$: *m*/*z*, 1303.49.

***O*-(α-D-Galactopyranosyluronic acid)-(1→4)-*O*-(α-D-galactopyranosyluronic acid)-(1→4)-(methyl D-galactopyranuronate) 3**

Hydrogenation of **34** gave **3** as a foam; R_f 0.28 (MeOH–water; 3:1 + 3% AcOH); δ_H (D_2O) 5.30 (d, 0.4H, *J* 3.8, $H^{1\alpha}$), 5.01–4.97 (m, 3H), 4.92 (d, 1H, *J* 3.5, $H^{1''}$), 4.79–4.53 (signals hidden under HDO peak), 4.45–4.34 (m, 2.6H), 4.26 (d, 1H, *J* 2.2), 3.98 (m, 0.4H), 3.95 (m, 1H), 3.86 (dd, 1H, *J* 10.5, 3.4), 3.77–3.64 (m, 3.4H), 3.75 (s, 1.8H), 3.75 (s, 1.2H), 3.42 (dd, 0.6H, *J* 10.0, 7.7); δ_C (D_2O) 172.9, 172.2, 170.9, 170.0, 100.6, 100.1, 96.6, 92.6, 79.2, 78.4, 73.4, 71.5, 71.3, 71.1, 70.4, 70.1 (2C), 70.0, 68.9, 68.2, 68.0 (2C), 67.8, 53.2, 53.1.

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