Solution Synthesis of Two Orthogonally Protected Lactosides as Tetravalent Disaccharide-Based Scaffolds

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Two tetravalent lactosidic scaffolds have been synthesised in solution from commercial lactose. Careful manipulation of the protecting groups allowed us to orthogonally protect four OH groups for their use as diversity sites for the development of broad screening libraries of sugar mimics. The selective access to each of these hydroxy groups has been demonstrated on scaffold **2** by deprotection and functionalisation with *p*-fluorophenyl isocyanate. Finally, the 6-OH derivative of compound **2** was covalently attached to a polymeric support.

Introduction

The fundamental role played by carbohydrates in many cellular recognition phenomena is now well established.[1] Carbohydrates are primarily involved in inflammatory processes, bacterial and viral invasions, tumour growth and metastasis, and many other crucial biological events. Because of their biological importance and unique chemical features, the synthetic community's interest in these molecules has been raised during last few years: tailor-made sugar-based compounds that are able to interfere in key biological mechanisms would represent a powerful weapons in biomedicine. Therefore, the generation of carbohydrate libraries is a highly attractive goal toward adequately exploiting the broad potential envisioned for saccharide-based drugs. To address this issue, combinatorial chemistry technologies, both in solution and in solid phases,[2−5] should be extremely advantageous, but the application of these techniques to the synthesis of oligosaccharides and glycoconjugates has been hampered largely by the typical challenges associated with classical carbohydrate synthesis,[6] such as laborious protecting group manipulations and the lack of a general method for the stereoselective formation of glycosidic linkages. Although significant developments in solid phase oligosaccharide synthesis have been disclosed recently to allow the preparation of a number of sugar-based libraries,[7] the existing techniques are still inadequate for reproducing the enormous structural and functional diversity of natural carbohydrates. Sugar mimics that are endowed with very similar biological properties, but are structurally and synthetically simpler than their natural counterparts, could offer a valuable alternative. One option that skips the difficulties often related to the stereocontrol of the glycosylation is to generate libraries of carbohydrate mimetics by sequential and regioselective addition of simple sugar analogues to a multifunctionalised, preformed, polymer-bound saccharidic scaffold. The decoration of the scaffold could be addressed by replacing the glycosylation steps with simple and reliable reactions of classical organic synthesis. Moreover, this strategy exploits the advantages of solid phase synthesis in terms of its speed, efficiency, and the elimination of tedious workup and purification steps.

Careful examination of the structures of complex oligosaccharides endowed with biological activity reveals they can often be envisaged as a sequence of blocks assembled in different ways. Examples include both free carbohydrates, such as human milk oligosaccharides, which exhibit antiadhesive properties and inhibitory activity towards many pathogens and protect breast-fed infants against infections during the lactation period,[8,9] and important glycoconjugates, such as glycoproteins and various glycolipids. In these compounds, each block is composed of a disaccharidic *core* with various branches (when present) such as fucose or sialic acid. Typical *core* structures widely occurring in complex oligosaccharides are Galβ(1→4)GlcNAc (lactosamine), Galβ(1→3)GlcNAc and Galβ(1→4)Glc (lactose). In principle, the application of the above strategy can lead to a library of sugar analogues by decorating a scaffold corresponding to one of the disaccharidic *core* structures with

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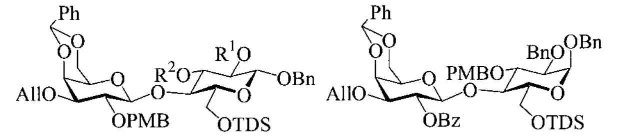
simple blocks mimicking the branches occurring in the natural molecule.

The use of carbohydrates, especially monosaccharides, as molecular scaffolds for the synthesis of combinatorial libraries has already been described.[10–18] Monosaccharides possess a unique set of chemical and structural features that make them particularly attractive for this task. They are readily available in a variety of diastereoisomeric forms, they are chiral and conformationally rigid molecules providing a well-defined three-dimensional spatial arrangement of substituents, and they possess up to five hydroxy groups for chemical modification. Taken together, these features suggest that monosaccharides are privileged platforms with which to design primary screening libraries for drug discovery.[19,20] Additional advantages derive from the ability of disaccharidic scaffolds to mimic or inhibit macromolecular interactions where potential pharmacophoric recognition sites are spatially far apart. To the best of our knowledge, however, very few examples of the syntheses and applications of disaccharidic scaffolds have been reported in the literature.[11,21,22] Lactose, which is available in large quantities as a by-product from dairies, is one of the cheapest disaccharides available on the market and one of the most diffused in nature. Therefore, we selected lactose as a template to generate a disaccharidic scaffold. Herein, we describe the solution synthesis of orthogonally protected tetravalent lactosidic scaffolds **2** and **3** (Figure 1). The regioselective deprotection/functionalisation of template **2** and its covalent attachment to a polymeric support, namely butyl diethylsilane polystyrene (PS-DES) resin, is also reported.



1 $R^1 = Bn, R^2 = Bz$
2 $R^1 = Bz, R^2 = Bn$

3

Figure 1. Structures of lactosidic scaffolds **1**–**3**

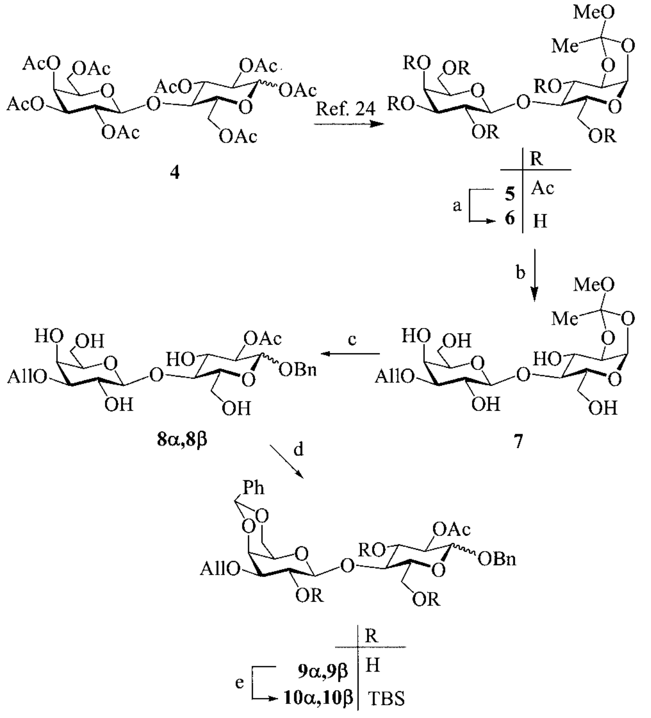
Results and Discussion

The key to developing chemical diversity using carbohydrate scaffolds is to find a strategy that allows chemical differentiation of the hydroxy groups on the sugar nucleus.[5,12,13] To address this issue, our approach towards lactosidic scaffolds required the installation of two distinct sets of protecting groups. A first set of orthogonal protecting groups must be introduced on those hydroxy groups selected as diversification sites to allow their selective deprotection/functionalisation. The second set includes all the other protecting groups that must remain unaffected during the subsequent manipulations of the scaffold and are eventually removed, possibly in a single step. We employed benzoyl ester (Bz) and *p*-methoxybenzyl (PMB), allyl (All) and thexyldimethylsilyl (TDS) ether units as orthogonally cleavable protecting groups and benzyl (Bn) ether and benzylidene acetal moieties as permanent protecting groups.

In the first part of our endeavour, we faced the solution phase synthesis of scaffold **1** (Figure 1), in which the 6-, 3-, 2′- and 3′-OH groups are orthogonally protected. Actually, as we detail below, an unexpected migration led to the alternative scaffold **2** (Figure 1), which contains 6-, 2-, 2′- and 3′-hydroxy groups as diversity sites.

The 6-*O*-TDS group has a twofold role. First, it can be a fourth diversification site for the solution phase synthesis of libraries from scaffold **2**. In addition, it mimics the attachment of the scaffold to the polymeric support through a silyl ethereal linkage, which allows us to validate the suitability of our strategy for its application in solid phase synthesis. Moreover, when using a solid phase protocol, the 6-OH group eventually can be functionalised, once the decorated scaffold has been cleaved from the polymer. Target **2** was obtained according to Schemes 1 and 2.

Peracetylated lactose **4**[23] was first converted into the methyl orthoester **5** in two steps[24] (Scheme 1, 84% overall yield). After Zemplén deacetylation, compound **6** was 3′-*O*-allylated regioselectively by exploiting the stannylene acetal procedure, giving **7** in 87% overall yield. The regioselective opening of the orthoester ring with benzyl alcohol was particularly challenging. After many attempts, the best conditions we found were those in which trifluoromethanesul-



Scheme 1. Synthesis of compounds **10α** and **10β**. Reagents and conditions: a) MeONa, MeOH; b) $Bu_2Sn{=}O$, MeOH reflux, AllBr, TBAI, toluene, 60 °C, 87% from **5**; c) BnOH, TfOH, CH_3CN, 3-Å molecular sieves, 0 °C, 70%; d) $PhCH(OMe)_2$, CSA, CH_3CN; e) TBSOTf, collidine, DMF, 0 °C, 58% from **8** [α/β = 2:5]

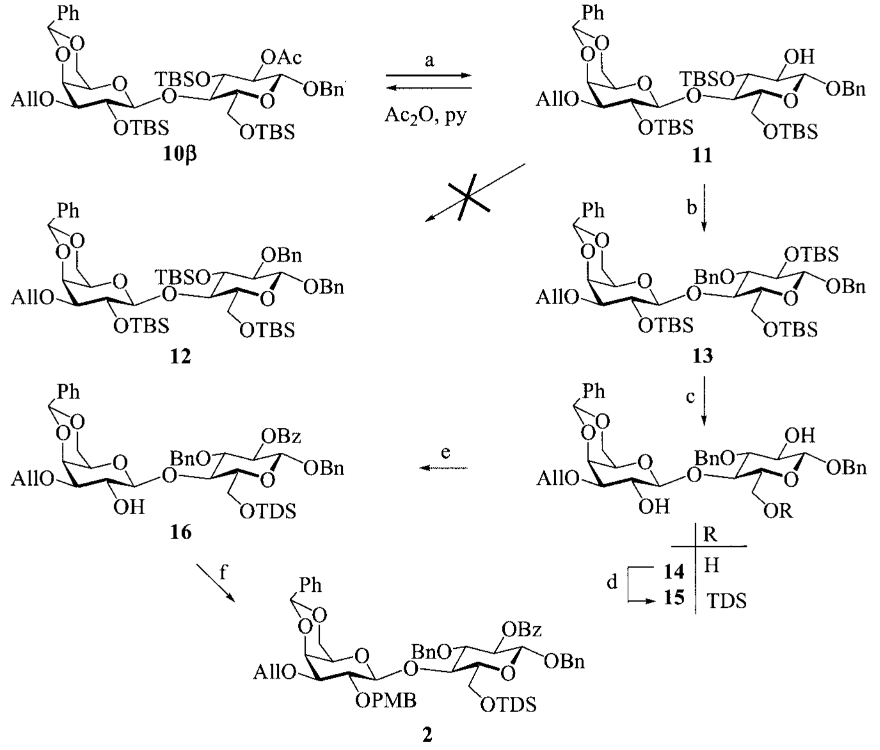
fonic acid (TfOH) was used as an acidic promoter, producing benzyllactoside **8** in 70% yield as a 2:5 α/β mixture, as evidenced by NMR spectroscopy.

Since the high polarity of compounds **8α/8β** hampered their efficient chromatographic purification, we postponed the separation of the anomeric mixture to a later stage of the synthesis. The subsequent introduction of the 4′,6′-*O*-benzylidene acetal was therefore carried out on the **8α/8β** mixture to give compound **9** (α/β mixture). Next, silylation of the remaining free hydroxy groups (3, 6 and 2′) furnished the fully protected lactosidic intermediate **10** (α/β mixture) in 58% overall yield from **8**. The separation of the anomers was accomplished on compound **10**, and gave 42% of **10β** together with 16% of **10α**. The complete structure of both isomers was determined by NMR spectroscopy: in particular, **10β** showed H-1 at δ = 5.12 ppm ($J_{1,2}$ = 8.1 Hz), whereas **10α** exhibited H-1 at δ = 5.08 ppm ($J_{1,2}$ = 3.8 Hz). We decided to pursue our synthesis towards scaffold **2** using the major anomer, **10β**. Nevertheless, as we describe below, anomer **10α** turned out to be a useful intermediate for the construction of a second lactosidic scaffold (compound **3**, Figure 1).

Differentiation of the remaining 6-, 2-, 3- and 2′-O atoms units on **10β** was achieved as outlined in Scheme 2. The 2-*O*-acetyl group of **10β** was unaffected under Zemplén conditions, but saponification with 0.15 M NaOH in EtOH gave the alcohol **11**, which was submitted directly to the benzylation step under Williamson conditions. We expected the formation of the 2-*O*-benzylated compound **12**. In contrast, as it became clear a few steps later with compound **16**, only the 3-*O*-benzylated compound **13** was obtained; it derived from a surprisingly clean migration of the TBS group from the 3-OH to the 2-OH group during the benzylation step. Such base-promoted intramolecular migrations of silyl groups have been reported previously.[25–31] Full desilylation of **13** (→ **14**) using tetrabutylammonium fluoride (TBAF) in THF, followed by regioselective 6-*O*-silylation with thexyldimethylsilyl chloride (TDSCl) and imidazole, provided diol **15** (53% from **13**).

Monobenzoylation of **15** was carried out by using a combination of benzoyl cyanide and triethylamine in acetonitrile at −40 °C to afford compound **16**.[32] Careful analysis of the NMR spectra of alcohol **16**, in particular the low-field shift of H-2 (δ = 5.28 ppm), allowed us to unambiguously assign the structure of compound **16** and confirm that migration of the TBS group had occurred. The possibility that such a migration occurred during the preceding saponification step was ruled out by submitting compound **11** to standard acetylation (Ac_2O, py): only intermediate **10β** was obtained (Scheme 2).

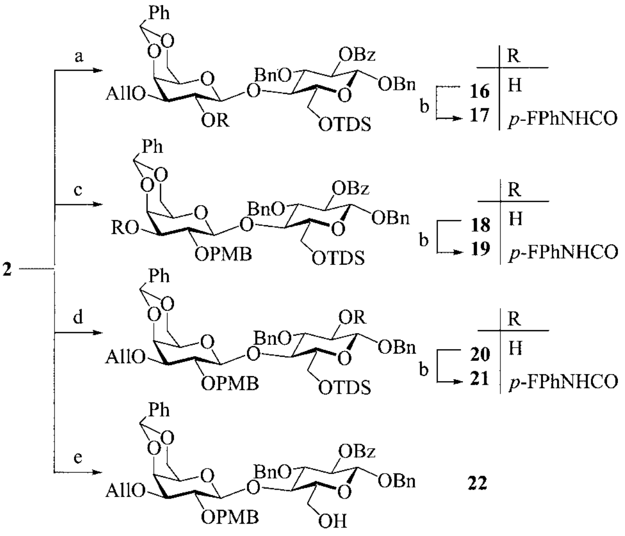
Having proved the correct structure of intermediate **16**, the last free 2′-OH group was alkylated using *p*-methoxybenzyl chloride (PMBCl) in the presence of NaH and KI at −30 °C, providing the fully protected lactosidic scaffold **2** in fair yield (51%). All attempts to improve the yield (e.g., increasing the temperature or extending the reaction time) led to partial decomposition of **16**. Nevertheless, this step did not cause any loss of precious compound, since the unchanged starting material could be recovered and recycled.



Scheme 2. Synthesis of scaffold **2**. Reagents and conditions: a) NaOH, EtOH, 40 °C; b) BnBr, NaH, DMF, 81% from **10β**; c) TBAF, THF, −30 °C; d) TDSCl, imidazole, DMF, 0 °C, 53% from **13**; e) BzCN, Et_3N, CH_3CN, −40 °C, 50%; f) PMBCl, NaH, KI, DMF, −30 °C, 51%

With the protected scaffold **2** in our hands, we wanted to validate our synthetic strategy by demonstrating that selective access to each of the orthogonally protected hydroxy groups is indeed feasible.

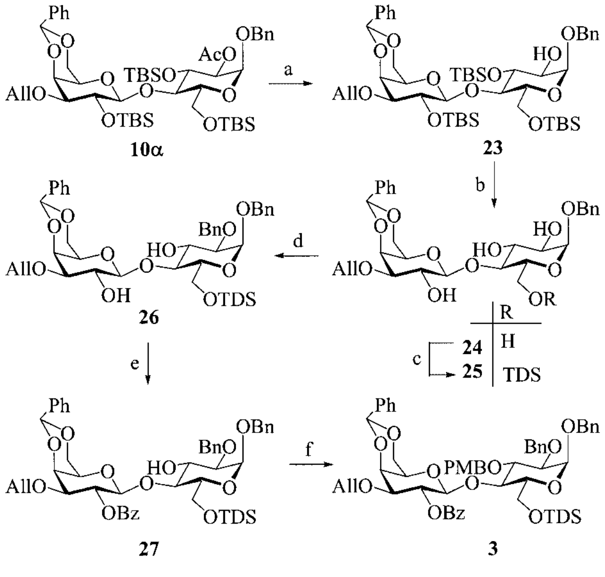
Oxidative removal of the *p*-methoxybenzyl ether from scaffold **2** occurred smoothly by employing 1,2-dichloro-4,5-dicyanobenzoquinone (DDQ) to furnish alcohol **16** (Scheme 3). The newly liberated 2′-OH group was functionalised by a reaction with *p*-fluorophenyl isocyanate in the presence of triethylamine to afford carbamate **17** in an unoptimised yield of 60% from scaffold **2**. Deallylation was achieved by treating **2** with $PdCl_2$ and gave alcohol **18**, which was carbamoylated with *p*-fluorophenyl isocyanate to produce compound **19** in an unoptimised yield of 52% from **2**. Finally, 2-*O*-debenzoylation of **2** using 0.15 M NaOH in EtOH generated alcohol **20** in almost quantitative yield; **20** was converted into the corresponding *p*-fluorophenyl carbamate **21** in an unoptimised yield of 90% from scaffold **2**.



Scheme 3. Selective access to orthogonally protected OH groups. Reagents and conditions: a) DDQ, CH_2Cl_2; H_2O; b) *p*-FPhNCO, Et_3N, CH_2Cl_2: **17** (60%), **19** (52%), **21** (90%) from **2**; c) $PdCl_2$, AcONa, AcOH/H_2O; d) NaOH, EtOH; e) TBAF, THF, −30 °C, 87%

Selective removal of the TDS group was also accomplished to prove the feasibility of an nondestructive cleavage of scaffold **2** from a PS-DES resin featuring silylated linkers. The treatment of lactoside **2** with TBAF in THF afforded compound **22** in 87% yield (Scheme 3).

Synthesis of scaffold **3**, which allows selective access to 6-, 3-, 2′- and 3′-hydroxy groups, is outlined in Scheme 4. Compound **10α** was deacetylated as described previously for **10β** to give alcohol **23**. Desilylation (TBAF, −30 °C to room temp.), followed by regioselective 6-*O*-monosilylation with TDSCl and imidazole, afforded the triol **25** in 57% overall yield.



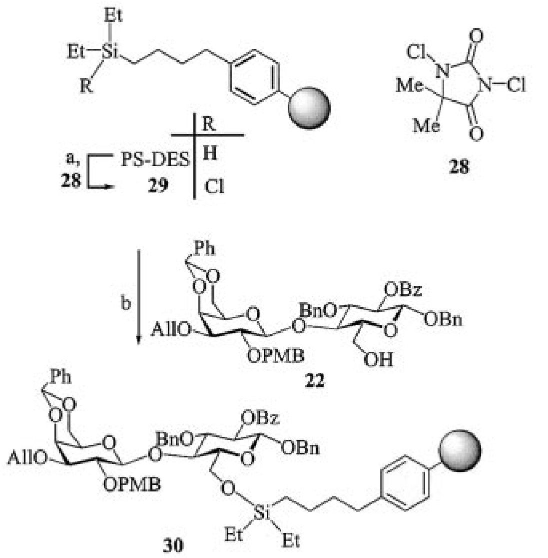
Scheme 4. Synthesis of scaffold **3**. Reagents and conditions: a) NaOH, EtOH, 40 °C; b) TBAF, THF, −30 °C; c) TDSCl, imidazole, DMF, 0 °C, 57% from **10α**; d) $Bu_2Sn{=}O$, MeOH reflux, BnBr, TBAI, toluene, 60 °C, 88%; e) BzCN, Et_3N, CH_3CN, −5 °C, 65%; f) PMBCl, NaH, KI, DMF, −30 °C, 48%

Taking advantage of the stannylene acetal procedure, a benzyl group was installed regioselectively on the 2-OH unit to produce diol **26** in 88% yield. Monobenzoylation of **26** with benzoyl cyanide proceeded smoothly at −5 °C to provide the alcohol **27** in 65% yield. The structure of **27** was readily confirmed from the ^1H NMR spectroscopic data (H-2′: δ = 5.60 ppm). We note that the regioselectivity of the benzoylation on diol **26** changed from that previously described for diol **15**. In the latter case (2,2′-diol), the benzoyl ester was introduced on the 2-OH group, whilst the 3,2′-diol **26** showed a marked preference for 2′-O-acylation, as has reported previously for similar compounds.[32] The synthesis of scaffold **3** was then completed by *p*-methoxybenzylation of the remaining 3-OH group.

As a last stage of our endeavour, the alcohol **22** was anchored to PS-DES resin through its 6-OH group to afford a polymer-bound lactosidic template that is suitable for the solid phase generation of lactose-based libraries for broad screening and for decoration at the 2-, 2′- and 3′-positions.

PS-DES resin required prior activation by treating it with 1,3-dichloro-5,5-dimethylhydantoin (**28**) to convert the Si−H bonds into Si−Cl bonds (Scheme 5).[33]

Next, the activated polymer **29** was reacted with alcohol **22** in CH_2Cl_2 in the presence of imidazole under strictly dry conditions. The resin-bound scaffold **30** was recovered by filtration and washed with DMF, DMF/H_2O (1:1), THF/H_2O (1:1) and THF. Analysis by diffusive reflectance infrared Fourier transform (IR-DRIFT) spectroscopy and magic angle spinning (MAS) ^1H NMR confirmed the attachment of the scaffold to the resin. The loading of 0.64 mmol/g was determined by gravimetry.



Scheme 5. Synthesis of compound **30**. Reagents and conditions: a) 1,3-dichloro-5,5-dimethylhydantoin, CH_2Cl_2; b) **22**, imidazole, CH_2Cl_2

Conclusion

We have described efficient syntheses of lactosidic scaffolds **2** and **3** in solution. Both compounds contain four orthogonally protected OH groups as diversity sites. Selective access to these OH groups has been demonstrated in solution for scaffold **2** through its sequential deprotection and functionalisation using *p*-fluorophenyl isocyanate. The selective deprotection of benzoyl ester and *p*-methoxybenzyl and allyl ether units in the presence of a silyl ethereal bond is particularly noteworthy because it should ensure the applicability of this strategy to solid phase protocols. As a proof of concept, alcohol **22**, derived from scaffold **2**, was eventually anchored to PS-DES resin through a silyl ethereal linkage to obtain a polymer-bound template suitable for the development of lactose-based libraries of sugar mimics. The use of compounds **2** and **3** as molecular scaffolds for the generation of sugar libraries, both in solution and in the solid phase, is currently under investigation in our laboratory.

Experimental Section

General Remarks: ^{1}H NMR and ^{13}C NMR spectra were recorded with Varian Gemini 200, Bruker AC 300 and Bruker Avance 400 spectrometers at 298 K. When required for unambiguous characterization, COSY, TOCSY and HMQC spectra were also recorded. In the description of the ^{13}C NMR spectra, signals corresponding to aromatic carbon atoms are omitted. Solid phase NMR spectra were acquired with a Varian Unity 400 MHz equipped with an HR-MAS Nanoprobe. Optical rotations were measured at room temperature using a Perkin−Elmer 241 polarimeter. TLC was performed on Merck silica gel 60 F_{254} plates (0.25-mm thickness), and spots were visualized by spraying with a solution comprising H_2SO_4 (31 mL), ammonium molybdate (21 g) and $Ce(SO_4)_2$ (1 g) in water (500 mL), followed by heating at 110 °C for 5 min. Column chromatography was performed by the flash procedure using Merck silica gel 60 (230−100.58 mesh). Elemental analyses were performed using a Carlo Erba 1108 elemental analyser. Solvents were dried by standard procedures.

(3-*O*-Allyl-β-D-galactopyranosyl)-(1→4)-[1,2-*O*-(1-methoxyethylidene)]-α-D-glucopyranose (7): 1 M Sodium methoxide in methanol (9.3 mL, 9.3 mmol) was added dropwise under argon to a solution of **5**[24] (21 g, 31 mmol) in dry methanol (120 mL). After 4 h, the mixture was neutralised with Amberlite IR120, filtered and concentrated in vacuo. The crude residue was dissolved in dry methanol (110 mL) and dibutyltin oxide (8.9 g, 35.7 mmol) was added. The reaction was stirred at 60 °C for 15 h, and then the solvent was evaporated under reduced pressure. The solid residue was dissolved in toluene at 60 °C and then tetrabutylammonium iodide (14.3 g, 38.7 mmol) and allyl bromide (26.2 mL, 310 mmol) were added. After stirring the mixture at 60 °C for 17 h, the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography ($CHCl_3/CH_3OH$, 9:1, + 1% triethylamine) to yield **7** (11.84 g, 87% from **5**) as a brown amorphous solid. $[\alpha]_D^{20} = +3.6$ (c = 1, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 1.60 (s, 3 H, CH_3), 3.27 (s, 3 H, OCH_3), 3.51−3.85 (m, 9 H, H-2, H-4, H-5, H-6a, H-3′, H-5′, H-6′a, H-6′b, $CH_2{=}CH{-}CHH$), 4.00 (d, $J_{4',3'}$ = 3.2 Hz, 1 H, H-4′), 4.09−4.30 (m, 4 H, $CH_2{=}CH{-}CH\mathit{H}$, H-3, H-6b, H-2′), 4.38 (d, $J_{1',2'}$ = 7.8 Hz, 1 H, H-1′), 5.12−5.38 (m, 2 H, $C\mathit{H}_2{=}CH{-}CH_2$), 5.69 (d, $J_{1,2}$ = 5.2 Hz, 1 H, H-1), 5.92−6.03 (m, 1 H, $CH_2{=}C\mathit{H}{-}CH_2$) ppm. $C_{18}H_{30}O_{12}$ (438.92): calcd.C 49.31, H 6.90; found C 49.49, H 6.91.

Complete assignment of the ^{1}H NMR spectrum of **7** was hampered by extensive overlapping of signals. Therefore, an analytical sample of **7** (30 mg) was submitted to standard acetylation (Ac_2O, py) and the resulting pentaacetylated product was fully characterised by NMR spectroscopy. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.68 (s, 3 H, CH_3), 1.94−2.16 (m, 15 H, OAc), 3.26 (s, 3 H, OCH_3), 3.47 (dd, $J_{3',4'}$ = 3.7 Hz, 1 H, H-3′), 3.59 (d, $J_{4,5}$ = 9.4 Hz, 1 H, H-4), 3.82−3.93 (m, 3 H, H-5′, H-5, $CH_2{=}CH{-}C\mathit{H}H$), 4.05−4.12 (m, 4 H, H-6a, 2 H-6′, $CH_2{=}CH{-}CH\mathit{H}$), 4.22 (br. dd, $J_{6a,6b}$ = 11.8 Hz, 1 H, H-6b), 4.29 (m, 1 H, H-2), 4.50 (d, $J_{1',2'}$ = 8.0 Hz, 1 H, H-1′), 5.05 (t, $J_{2',3'}$ = 10.0 Hz, 1 H, H-2′), 5.12−5.23 (m, 2 H, $C\mathit{H}_2{=}CH{-}CH_2$), 5.39 (d, 1 H, H-4′), 5.51 (br. s, 1 H, H-3), 5.62 (d, $J_{1,2}$ = 5.2 Hz, 1 H, H-1), 5.68−5.81 (m, 1 H, $CH_2{=}C\mathit{H}{-}CH_2$) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$): δ = 14.3 (CH_3), 21.0, 21.2, 21.3, 21.7, 22.0 (5 OAc), 57.7 (OCH_3), 59.7 ($CH_2{=}CH{-}\mathit{C}H_2$), 62.2, 62.9 (C-6, C-6′), 67.2, 71.6, 71.9, 75.4, 76.9, 76.3, 81.1, 82.3 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 91.2 (C-1′), 106.0 (C-1), 117.2 [*C*(OMe)Me], 117.7 ($CH_2{=}\mathit{C}H{-}CH_2$), 136.8 ($\mathit{C}H_2{=}CH{-}CH_2$), 172.2, 172.7, 180.4 (C=O) ppm.

Benzyl [3-*O*-Allyl-4,6-*O*-benzylidene-2-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl]-(1→4)-2-*O*-acetyl-3,6-di-*O*-(*tert*-butyldimethylsilyl)]-α,β-D-glucopyranoside (10α and 10β): Benzyl alcohol (12.6 mL, 122 mmol) was added under argon to a solution of **7** (5.36 g, 12.2 mmol) in dry CH_3CN (30 mL); 3-Å molecular sieves were added and the mixture was stirred at 0 °C for 30 min. Trifluoromethanesulfonic acid (4.9 mL of a 0.5 M solution in dry CH_3CN), which was cooled to 0 °C for 5 min, was quickly added. After 10 min, the mixture was neutralized with Et_3N, filtered through a pad of Celite, and then the filtrate was evaporated. The crude product was purified by flash column chromatography ($CHCl_3/CH_3OH$, 95:5 + 1% triethylamine) to yield **8** (4.40 g, 70%, α/β mixture) as an amorphous white solid. The anomeric mixture of **8** was not characterised further; rather, it was submitted directly to the next step. A catalytic amount of camphorsulfonic acid was added to a solution of **8** and benzaldehyde dimethyl acetal (2.6 g, 17.1 mmol) in dry CH_3CN (30 mL). After 30 min, the solution was neutralised with Et_3N and concentrated in vacuo to obtain crude **9**. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (6.1 mL, 16.6 mmol) was added dropwise under argon to a cooled (−20 °C) solution of **9** and collidine (5.8 mL, 44 mmol) in dry DMF (25 mL). The mixture was stirred at room temperature overnight. The reaction mixture was washed with H_2O and then the organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 95:5). First elution gave compound **10α** (1.34 g, 16%) as a clear oil. $[\alpha]_D^{20} = -10.4$ (c = 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.00−0.10 (6 s, 18 H, CH_3Si), 0.82−0.93 (3 s, 27 H, CH_3 *t*Bu), 2.05 (s, 3 H, OAc), 3.19−3.23 (m, 2 H, H-5, H-5′), 3.43−3.50 (m, 2 H, H-6a′, H-3′), 3.80 (m, 2 H, H-4, H-2′), 3.91−4.10 (m, 5 H, H-6′b, H-6a, H-3, CH_2=CH−C*H*$_2$), 4.14 (d, $J_{4',3'}$ = 3.6 Hz, 1 H, H-4′), 4.25 (d, $J_{6a',6b'}$ = 12.0 Hz, 1 H, H-6b), 4.49 (d, $J_{1',2'}$ = 7.9 Hz 1 H, H-1′), 4.53−4.64 (m, 2 H, CH*H*Ph, H-2), 5.02 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 5.10−5.30 (m, 2 H, C*H*$_2$=CH−CH_2), 5.44 (s, 1 H, C*H*Ph), 5.85−5.98 (m, 1 H, CH_2=C*H*−CH_2), 7.35−7.51 (m, 10 H, H_{Ar}) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = −4.3, −4.0, 2.1 (CH_3Si), 19.4 (Cq *t*Bu), 26.3 (CH_3 *t*Bu), 61.5 (CH_2=CH−*C*H_2), 69.1, 69.2, 71.8 (*C*H_2Ph, C-6, C-6′), 61.5, 61.5, 74.9, 75.7, 76.2, 76.9, 81.0, 81.8 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 101.8, 102.1, 102.9 (C-1, C-1′, *C*HPh), 117.5 (CH_2=*C*H−CH_2), 135.7 (*C*H_2=CH−CH_2), 169.5 (C=O) ppm. $C_{49}H_{80}O_{12}Si_3$ (945.41): calcd. C 62.25, H 8.53; found C 62.48, H 8.51. Further elution gave compound **10β** (3.35 g, 42%) as a clear oil. $[\alpha]_D^{20} = -17.7$ (c = 1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.02−0.20 (6 s, 18 H, CH_3Si), 0.89−0.94 (3 s, 27 H, CH_3 *t*Bu), 2.10 (s, 1 H, OAc), 3.18−3.30 (m, 3 H, H-3′, H-5, H-5′), 3.64 (t, $J_{3,2} = J_{3,4}$ = 9.0 Hz, 1 H, H-3), 3.84 (t, $J_{2',1'} = J_{2',3'}$ = 8.3 Hz, 1 H, H-2′), 3.86−3.92 (m, 2 H, H-4, H-6a), 3.98 (br. dd, $J_{6'a,6'b}$ = 11.3 Hz, 1 H, H-6′a), 4.06−4.18 (m, 3 H, H-6b, CH_2=CH−C*H*$_2$), 4.19 (d, $J_{4',3'}$ = 3.6 Hz, 1 H, H-4′), 4.30 (br. dd, 1 H, H-6′b), 4.42 (d, $J_{1,2}$ = 8.0 Hz, 1 H, H-1), 4.58 (d, 1 H, H-1′), 4.62 (d, J_{gem} = 12.5 Hz, 1 H, C*H*HPh), 4.86 (d, 1 H, CH*H*Ph), 4.94 (t, 1 H, H-2), 5.16−5.32 (m, 2 H, C*H*$_2$=CH−CH_2), 5.48 (s, 1 H, C*H*Ph), 5.90−6.01 (m, 1 H, CH_2=C*H*−CH_2), 7.25−7.51 (m, 10 H, H_{Ar}) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = −4.4, −4.1, −3.9, −3.0, −2.4 (CH_3Si), 18.2, 18.6, 18.8 (Cq *t*Bu), 21.6 (CH_3Ac), 26.1, 26.3, 26.4 (CH_3 *t*Bu), 61.5 (CH_2=CH−*C*H_2), 69.4, 69.8, 71.0 (CH_2Ph, C-6, C-6′), 67.1, 71.0, 73.7, 74.1, 74.5, 74.7, 77.1, 81.0 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 100.2 (C-1), 101.7, 102.3 (C-1′, *C*HPh), 117.5 (CH_2=*C*H−CH_2), 135.7 (*C*H_2=CH−CH_2), 169.8 (C=O) ppm. $C_{49}H_{80}O_{12}Si_3$ (945.41): calcd. C 62.25, H 8.53; found C 62.04, H 8.54.

Benzyl [3-*O*-Allyl-4,6-*O*-benzylidene-2-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl]-(1→4)-3-*O*-benzyl-2,6-di-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranoside (13): 0.15 M NaOH in ethanol (10.6 mL) was added to a solution of **10β** (750 mg, 0.78 mmol) in EtOH (4 mL). The reaction mixture was stirred overnight at 40 °C and then concentrated in vacuo; the residue was dissolved in dry DMF (5 mL) under argon. Benzyl bromide (0.14 mL, 1.18 mmol) and NaH (56 mg, 2.37 mmol) were added sequentially. When TLC analysis indicated completion of the reaction (5 h), the mixture was quenched with methanol, diluted with CH_2Cl_2 and washed with H_2O; the organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 9:1) to yield **13** (630 mg, 81% from **10β**) as an amorphous white solid. $[\alpha]_D^{20} = -15.6$ (c = 1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = −0.01−0.12 (6 s, 18 H, CH_3Si), 0.86−0.92 (3 s, 27 H, CH_3 *t*Bu), 3.24 (br. d, $J_{5,4}$ = 9.5 Hz, 1 H, H-5), 3.30 (dd, $J_{3',4'}$ = 3.6, $J_{3',2'}$ = 9.3 Hz, 1 H, H-3′), 3.34 (br. s, 1 H, H-5′), 3.44 (t, $J_{3,4}$ = 8.8 Hz, 1 H, H-3), 3.52 (t, $J_{2,3}$ = 7.5 Hz, 1 H, H-2), 3.81 (t, 1 H, H-2′), 3.88 (br. d, $J_{6a,6b}$ = 10.5 Hz, 1 H, H-6a), 4.06 (d, 1 H, H-6′a), 4.08−4.18 (m, 4 H, CH_2=CH−C*H*$_2$, H-4, H-6b), 4.22 (d, 1 H, H-4′), 4.35 (d, $J_{1,2}$ = 7.3 Hz, 1 H, H-1), 4.44 (d, $J_{6'a,6'b}$ = 12.2 Hz, 1 H, H-6′b), 4.53 (d, 1 H, C*H*HPh), 4.61 (d, 1 H, CH*H*Ph), 4.63 (d, $J_{1',2'}$ = 7.3 Hz, 1 H, H-1′), 4.88 (d, J_{gem} = 11.3 Hz, 1 H, CH*H*Ph), 5.18−5.30 (m, 3 H, C*H*$_2$=CH−CH_2, CH*H*Ph), 5.51 (s, 1 H, C*H*Ph), 5.92−6.01 (m, 1 H, CH_2=C*H*−CH_2), 7.10−7.55 (m, 15 H, H_{Ar}) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = −4.4, −4.3, −4.29, −4.20, −3.7 (CH_3Si), 18.20, 18.25 (Cq *t*Bu), 26.0, 26.1 (CH_3 *t*Bu), 61.4 (CH_2=CH−*C*H_2), 70.6, 70.8, 69.1, 75.6 (2 CH_2Ph, C-6, C-6′), 67.0, 71.4, 73.5, 74.9, 75.0, 75.4, 77.6, 83.5 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 101.3, 102.2, 102.6, (C-1, C-1′, *C*HPh), 117.1 (CH_2=*C*H−CH_2), 135.3 (*C*H_2=CH−CH_2) ppm. $C_{54}H_{84}O_{11}Si_3$ (993.49): calcd. C 65.28, H 8.52; found C 65.04, H 8.49.

Benzyl (3-*O*-Allyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-3-*O*-benzyl-6-*O*-(thexyldimethylsilyl)-β-D-glucopyranoside (15): 1 M Tetrabutylammonium fluoride in dry THF (7.8 mL) was added under argon to a cooled (−30 °C) solution of **13** (2.35 g, 2.36 mmol) in dry THF (20 mL). The mixture was stirred at −30 °C for 1 h, at 0 °C for 12 h and, finally, overnight at room temperature. The mixture was washed with H_2O and then the organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo to yield crude **14**, which was used directly in the next step without purification. Imidazole (265 mg, 3.89 mmol) was added under argon to a cooled (0 °C) solution of **14** (1.2 g, 1.77 mmol) in dry DMF (10 mL) whilst stirring; thexyldimethylsilyl chloride (0.38 mL, 1.95 mmol) was then added dropwise. After 4 h, the reaction mixture was diluted with EtOAc and washed with satd. $NaHCO_3$ and then with H_2O; the organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 9:1) to yield **15** (0.99 g, 53% from **13**) as a clear oil. $[\alpha]_D^{20} = +11.6$ (c = 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.11−0.19 (2 s, 6 H, CH_3Si), 0.83−0.98 (4 s, 12 H, CH_3 thexyl), 1.65 (m, 1 H, CH thexyl), 3.13 (s, 1 H, H-5′), 3.30−3.40 (m, 2 H, H-3, H-5), 3.37 (dd, $J_{3',4'}$ = 3.5, $J_{3',2'}$ = 9.8 Hz, 1 H, H-3′), 3.55 (t, $J_{2,3}$ = 7.2 Hz, 1 H, H-2), 3.60 (d, $J_{6b,6a}$ = 9.0 Hz, 1 H, H-6b), 3.92 (br, 2 H, H-6a, H-6′a), 3.98 (t, $J_{2',3'}$ = 8.3 Hz, 1 H, H-2′), 4.10 (d, 1 H, H-4′), 4.13−4.16 (m, 3 H, H-6′b, CH_2=CH−C*H*$_2$), 4.20 (t, $J_{4,3} = J_{4,5}$ = 6.0 Hz, 1 H, H-4), 4.37 (d, $J_{1,2}$ = 7.3 Hz, 1 H, H-1), 4.59 (d, 1 H, CH*H*Ph), 4.68 (d, $J_{1',2'}$ = 7.7 Hz, 1 H, H-1′), 4.85 (d, 1 H, CH*H*Ph), 4.87 (d, J_{gem} = 11.5 Hz, 1 H, C*H*HPh), 5.08 (d, J_{gem} = 11.3 Hz, 1 H, C*H*HPh), 5.25 (br. dd, 2 H, C*H*$_2$=CH−CH_2), 5.49 (s, 1 H, C*H*Ph), 5.90−6.00 (m, 1 H, CH_2=C*H*−CH_2), 7.20−7.51 (m, 15 H, H_{Ar}) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$): δ = −3.4, −2.9 (CH_3Si), 18.6, 18.7, 20.3, 20.4 (CH_3 thexyl), 29.7 (Cq thexyl), 34.1 (CH thexyl), 61.6 (CH_2=CH−*C*H_2), 69.2, 70.6, 70.9, 75.1 (2 *C*H_2Ph, C-6, C-6′), 63.3, 66.8, 70.9, 73.8, 74.2, 75.6, 76.5, 79.0 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 101.2, 101.4, 103.3 (C-1, C-1′, *C*HPh), 117.5 (*C*H_2=CH−CH_2), 134.9 (CH_2=*C*H−CH_2) ppm. $C_{44}H_{60}O_{11}Si$ (792.39): calcd. C 66.64, H 7.63; found C 66.49, H 7.65.

Benzyl (3-*O*-Allyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2-*O*-benzoyl-3-*O*-benzyl-6-*O*-(thexyldimethylsilyl)-β-D-glucopyranoside (16): Et_3N (2.7 mL, 19.4 mmol) was added under argon to a cooled (−40 °C) solution of **15** (860 mg, 1.08 mmol) in dry CH_3CN (10 mL). Whilst stirring, benzoyl cyanide (3.24 mL of a 0.5 M solution in dry CH_3CN) was added dropwise. After 24 h, the reaction was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$; the organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 7:3) to yield **16** (407 mg, 50%) as a white oil. $[\alpha]_D^{20} = +12.3$ (*c* = 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.13−0.19 (2 s, 6 H, CH_3Si), 0.83−0.90 (4 s, 12 H, CH_3 thexyl), 1.65 (m, 1 H, CH thexyl), 3.12 (br. s, 1 H, H-5′), 3.13−3.39 (m, 2 H, H-5, H-3′), 3.78 (t, $J_{3,2} = J_{3,4} = 9.2$ Hz, 1 H, H-3), 3.86−3.98 (m, 3 H, H-6b, H-2′, H-6′a), 4.09−4.24 (m, 6 H, $CH_2{=}CH{-}CH_2$, H-4, H-6a, H-4′, H-6′b), 4.51 (d, $J_{1,2} = 8.1$ Hz, 1 H, H-1), 4.58 (d, 1 H, CH*H*Ph), 4.68 (d, 1 H, CH*H*Ph), 4.70 (d, $J_{1',2'} = 7.1$ Hz, 1 H, H-1′), 4.81 (d, $J_{gem} = 12.6$ Hz, 1 H, C*H*HPh), 4.97 (d, $J_{gem} = 11.5$ Hz, 1 H, C*H*HPh), 5.28−5.36 (m, 3 H, $CH_2{=}CH{-}CH_2$, H-2), 5.48 (s, 1 H, C*H*Ph), 5.88−6.02 (m, 1 H, $CH_2{=}CH{-}CH_2$), 7.00−7.97 (m, 20 H, H_{Ar}) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$): δ = −3.3, −2.8 (CH_3Si), 18.7, 18.8, 20.3, 20.4 (CH_3 thexyl), 29.7 (Cq thexyl), 34.1 (CH thexyl), 61.4 ($CH_2{=}CH{-}CH_2$), 69.1, 69.6, 73.7 (C-6, C-6′, CH_2Ph), 66.7, 70.9, 73.1, 73.7, 75.6, 79.0, 81.4 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 99.4, 101.1, 103.3 (C-1, C-1′, *C*HPh), 117.6 ($CH_2{=}CH{-}CH_2$), 134.8 ($CH_2{=}CH{-}CH_2$), 165.2 (C = O) ppm. $C_{43}H_{46}O_{12}$ (754.82): calcd. C 68.42, H 6.14; found C 68.54, H 6.12.

Benzyl [3-*O*-Allyl-4,6-*O*-benzylidene-2-*O*-(*p*-methoxybenzyl)-β-D-galactopyranosyl]-(1→4)-2-*O*-benzoyl-3-*O*-benzyl-6-*O*-(thexyldimethylsilyl)-β-D-glucopyranoside (2): *p*-Methoxybenzyl chloride (58 µL, 0.43 mmol), NaH (10 mg, 0.43 mmol) and KI (71 mg, 0.43 mmol) were added under argon to a cooled (−30 °C) solution of **16** (192 mg, 0.21 mmol) in dry DMF (2.5 mL). TLC analysis indicated completion of the reaction after 5 h. The reaction mixture was quenched with methanol, diluted with CH_2Cl_2 and washed with H_2O; the organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash chromatography (toluene/EtOAc, 95:5) to yield **2** (111 mg, 51%) as a yellow oil. $[\alpha]_D^{20} = -10.4$ (*c* = 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.08−0.11 (2 s, 6 H, CH_3Si), 0.82−0.91 (4 s, 12 H, CH_3 thexyl), 1.63 (m, 1 H, CH thexyl), 3.21 (d, 1 H, H-5), 3.29 (br. s, 1 H, H-5′), 3.45 (dd, $J_{3',4'} = 3.4$, $J_{3',2'} = 9.7$ Hz, 1 H, H-3′), 3.69−3.80 (m, 5 H, H-3, H-2′, OCH_3), 3.97 (br. dd, 1 H, H-6′a), 4.16 (t, $J_{4,3} = J_{4,5} = 9.2$ Hz, 1 H, H-4), 4.06−4.22 (m, 5 H, 2 H-6, H-4′, $CH_2{=}CH{-}CH_2$), 4.31 (br. dd, $J_{6'a,6'b} = 12.3$ Hz, 1 H, H-6′b), 4.52 (d, $J_{1,2} = 8.1$ Hz, 1 H, H-1), 4.58 (d, 1 H, C*H*HPh), 4.65−4.77 (m, 4 H, $CH_2C_6H_4$−*p*-OMe, CH*H*Ph, H-1′), 4.80 (d, $J_{gem} = 12.5$ Hz, 1 H, C*H*HPh), 5.05 (d, $J_{gem} = 11.7$ Hz, 1 H, C*H*HPh), 5.15−5.22 (m, 3 H, H-2, $CH_2{=}CH{-}CH_2$), 5.50 (s, 1 H, C*H*Ph), 5.87−6.00 (m, 1 H, $CH_2{=}CH{-}CH_2$), 6.81−7.97 (m, 24 H, H_{Ar}) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$): δ = −3.3, 2.9 (CH_3Si), 18.7, 18.8, 20.3, 20.5 (CH_3 thexyl), 29.7 (Cq thexyl), 34.3 (CH thexyl), 55.3 (OCH_3), 60.9 ($CH_2{=}CH{-}CH_2$), 69.1, 69.5, 71.3 (2 CH_2Ph, $CH_2C_6H_4$−*p*-OMe), 74.6, 74.8 (C-6, C-6′), 66.5, 73.3, 74.1, 76.1, 76.7, 78.8, 79.6, 80.4 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 99.4, 101.4, 102.7 (C-1, C-1′, *C*HPh), 117.1 ($CH_2{=}CH{-}CH_2$), 132.8 ($CH_2{=}CH{-}CH_2$), 165.2 (C=O) ppm. $C_{59}H_{73}O_{13}Si$ (1018.29): calcd. C 69.59, H 7.23; found C 69.54, H 7.21.

Benzyl [3-*O*-Allyl-4,6-*O*-benzylidene-2-*O*-(*p*-fluorophenylcarbamoyl)-β-D-galactopyranosyl]-(1→4)-2-*O*-benzoyl-3-*O*-benzyl-6-*O*-(thexyldimethylsilyl)-β-D-glucopyranoside (17): 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (13 mg, 0.06 mmol) was added to a solution of **2** (50 mg, 0.05 mmol) in CH_2Cl_2 (0.95 mL) and H_2O (0.10 mL). The mixture was stirred for 3 h at room temperature before it was diluted with CH_2Cl_2 and washed with satd. $NaHCO_3$; the organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo to yield crude **16**. *p*-Fluorophenyl isocyanate (18 µL, 0.17 mmol) was added to a solution of **16** (45 mg, 0.05 mmol) in dry CH_2Cl_2 (1 mL). TLC analysis indicated complete disappearance of starting material after 5 h. The reaction mixture was quenched with methanol, diluted with CH_2Cl_2 and washed with H_2O; the organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 8:2) to yield **17** (31 mg, 60% from **2**) as a white amorphous solid. $[\alpha]_D^{20} = -11.4$ (*c* = 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.06−0.10 (2 s, 6 H, CH_3Si), 0.79−0.89 (4 s, 12 H, CH_3 thexyl), 1.59 (m, 1 H, CH thexyl), 3.18−3.28 (m, 3 H, H-3′, H-5′, H-5), 3.39 (br. dd, $J_{6'a,6'b} = 11.4$ Hz, 1 H, H-6′a), 3.71−3.79 (m, 2 H, H-3, H-6′b), 3.96−4.18 (m, 4 H, H-4, H-6a, $CH_2{=}CH{-}CH_2$), 4.25 (d, $J_{4',3'} = 3.0$ Hz, 1 H, H-4′), 4.34 (d, $J_{6a,6b} = 12.5$ Hz, 1 H, H-6b), 4.55 (d, 1 H, H-1), 4.58 (d, 1 H, C*H*HPh), 4.56−4.68 (m, 2 H, C*H*HPh, H-1′), 4.80 (d, $J_{gem} = 12.4$ Hz, 1 H, C*H*HPh), 5.02 (d, $J_{gem} = 11.6$ Hz, 1 H, C*H*HPh), 5.21 (t, $J_{2,1} = J_{2,3} = 9.5$ Hz, 1 H, H-2), 5.25−5.38 (m, 3 H, H-2′, $CH_2{=}CH{-}CH_2$), 5.51 (s, 1 H, C*H*Ph), 5.85−5.95 (m, 1 H, $CH_2{=}CH{-}CH_2$), 6.90−7.90 (m, 24 H, H_{Ar}), 10.82 (s, 1 H, NH) ppm. ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = −3.4, −2.8 (CH_3Si), 18.5, 18.8, 20.2, 20.4 (CH_3 thexyl), 29.6 (Cq thexyl), 34.2 (CH thexyl), 61.0 ($CH_2{=}CH{-}CH_2$), 68.8, 69.6, 70.1, 72.6 (C-6, C-6′, 2 CH_2Ph), 66.7, 72.6, 75.1, 73.9, 75.3, 75.4, 77.4, 79.8, (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 99.1, 101.2 (C-1, C-1′, *C*HPh), 117.8 ($CH_2{=}CH{-}CH_2$), 132.6 ($CH_2{=}CH{-}CH_2$), 161.2, 165.2 (C=O, N−*C*=O) ppm. $C_{58}H_{68}FNO_{13}Si$ (1033.44): calcd. C 67.36, H 6.63, N 1.35; found C 67.13, H 6.62, N 1.35.

Benzyl [4,6-*O*-Benzylidene-3-*O*-(*p*-fluorophenylcarbamoyl)-2-*O*-(*p*-methoxybenzyl)-β-D-galactopyranosyl]-(1→4)-2-*O*-benzoyl-3-*O*-benzyl-6-*O*-(thexyldimethylsilyl)-β-D-glucopyranoside (19): Palladium(II) chloride (36 mg, 0.2 mmol) and NaOAc (62 mg, 0.46 mmol) were added to a solution of **2** (186 mg, 0.18 mmol) in aqueous acetic acid (3 mL, solution 0.5 M). After 24 h, TLC analysis indicated the complete disappearance of starting material. The reaction mixture was diluted with CH_2Cl_2, filtered through a Celite pad and washed with satd. $NaHCO_3$ until it became neutral; the organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo to yield crude **18**. *p*-Fluorophenyl isocyanate (53 µL, 0.39 mmol) was added to a solution of **18** in dry CH_2Cl_2 (3.5 mL). After 5 h, the reaction mixture was quenched with methanol, diluted with CH_2Cl_2 and washed with H_2O; the organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 8:2) to yield **19** (104 mg, 52% from **2**) as a white amorphous solid. $[\alpha]_D^{20} = -12.2$ (*c* = 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.09−0.12 (2 s, 6 H, CH_3Si), 0.84−0.90 (4 s, 12 H, CH_3 thexyl), 1.64 (m, 1 H, CH thexyl), 3.26 (m, 1 H, H-5), 3.41 (br. s, 1 H, H-5′), 3.72 (s, 3 H, OCH_3), 3.73−3.88 (m, 3 H, H-3, H-6a, H-2′), 3.97 (br. dd, 1 H, H-6′a), 4.06 (dd, $J_{6a,6b} = 11.6$, $J_{5,6} = 2.6$ Hz, 1 H, H-6b), 4.19 (t, $J_{4,3} = J_{4,5} = 9.1$ Hz, 1 H, H-4), 4.31 (br. dd, $J_{6'a,6'b} = 12.6$ Hz, 1 H, H-6′b), 4.37 (d, $J_{4',3'} = 3.5$ Hz, 1 H, H-4′), 4.53 (d, $J_{1,2} = 8.3$ Hz, 1 H, H-1), 4.55−4.67 (m, 2 H, 2 C*H*HPh), 4.69−4.89 (m, 5 H, H-3′, H-1′, 2 CH*H*Ph, C*H*HC_6H_4-*p*-OMe), 5.27 (t, $J_{2,3} = 8.2$ Hz, 1 H, H-2), 5.07 (d, $J_{gem} = 11.5$ Hz, 1 H, CH*H*C_6H_4−*p*-OMe), 5.49 (s, 1 H, C*H*Ph), 6.75−8.00 (m, 28 H, H_{Ar}), 10.61 (s, 1 H, NH) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$): δ = −3.3, 2.9 (CH_3Si), 18.6, 18.7, 20.3, 20.4 (CH_3 thexyl), 27.4 (Cq thexyl), 34.2 (CH thexyl), 55.2 (OCH_3), 60.9, 68.8, 69.5, 74.5, 74.7 (C6, C-6′, 2 CH_2Ph, $CH_2C_6H_4$−*p*-OMe), 66.1, 73.3, 74.2, 76.2, 76.5, 80.5 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 99.2, 101.1, 102.7 (C-1, C-1′, *C*HPh), 160.5, 162.5 (C=O, N−C=O) ppm. $C_{63}H_{72}FNO_{14}Si$ (1113.47): calcd. C 67.90, H 6.51, N 1.26; found C 68.04, H 6.52, N 1.26.

Benzyl (3-*O*-Allyl-4,6-*O*-benzylidene-2-*O*-(*p*-methoxybenzyl)-β-D-galactopyranosyl)-(1→4)-3-*O*-benzyl-2-*O*-(*p*-fluorophenylcarbamoyl)-6-*O*-(thexyldimethylsilyl)-β-D-glucopyranoside (21): 0.15 M Sodium hydroxide in EtOH (1.64 mL) was added to a solution of **2** (146 mg, 0.12 mmol) in EtOH (1.5 mL) and then stirred for 36 h. The reaction mixture was diluted with $\mathrm{CH_2Cl_2}$ and washed with $\mathrm{H_2O}$ until it became neutral; the organic layer was dried ($\mathrm{Na_2SO_4}$), filtered and concentrated in vacuo to yield **20**. *p*-Fluorophenyl isocyanate (51 µL, 0.37 mmol) was added to a solution of **20** in dry $\mathrm{CH_2Cl_2}$ (3 mL). After 6 h, the reaction mixture was quenched with methanol, diluted with $\mathrm{CH_2Cl_2}$ and washed with $\mathrm{H_2O}$; the organic layer was dried ($\mathrm{Na_2SO_4}$), filtered and concentrated in vacuo. The residue was purified by flash chromatography (toluene/EtOAc, 95:5) to yield **21** (117 mg, 90% from **2**) as a yellow oil. $[\alpha]_{\mathrm{D}}^{20} = -11.4$ (c = 1, $\mathrm{CHCl_3}$). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): δ = 0.13−0.19 (2 s, 6 H, $\mathrm{CH_3Si}$), 0.78−0.89 (4 s, 12 H, $\mathrm{CH_3}$ thexyl), 1.60 (m, 1 H, CH thexyl), 3.05 (br. d, $J_{5,4}$ = 9.6 Hz, 1 H, H-5), 3.28 (br. s, 1 H, H-5′), 3.34 (t, $J_{3,2} = J_{3,4}$ = 9.3 Hz, 1 H, H-3), 3.44 (dd, $J_{3',4'}$ = 3.6, $J_{3',2'}$ = 9.7 Hz, 1 H, H-3′), 3.68−3.73 (m, 2 H, H-2′, H-6a), 3.75 (s, 3 H, $\mathrm{OCH_3}$), 3.96 (br. d, 1 H, H-6′a), 4.04 (br. d, 1 H, H-6b), 4.08 (t, 1 H, H-4), 4.16−4.23 (m, 4 H, H-1, H-4′, $\mathrm{CH_2{=}CH{-}C}\mathit{H}_2$), 4.27 (d, $J_{6'a,6'b}$ = 12.1 Hz, 1 H, H-6′b), 4.49 (d, J_{gem} = 11.7 Hz, 1 H, $\mathrm{C}\mathit{H}\mathrm{HC_6H_4}$-*p*-OMe), 4.52 (d, 1 H, C*H*HPh), 4.61 (d, 1 H, C*H*HPh), 4.67 (d, $J_{1',2'}$ = 7.1 Hz, 1 H, H-1′), 4.69 (d, J_{gem} = 10.5 Hz, 1 H, CH*H*Ph), 4.80 (d, J_{gem} = 12.3 Hz, 1 H, CH*H*Ph), 4.90 (t, $J_{2,1}$ = 9.1 Hz, 1 H, H-2), 5.15−5.32 (m, 3 H, $\mathrm{C}\mathit{H}_2\mathrm{{=}CH{-}CH_2}$, $\mathrm{CH}\mathit{H}\mathrm{C_6H_4}$−*p*-OMe), 5.50 (s, 1 H, C*H*Ph), 5.86−6.00 (m, 1 H, $\mathrm{CH_2{=}C}\mathit{H}\mathrm{{-}CH_2}$), 6.72−7.40 (m, 23 H, $\mathrm{H_{Ar}}$), 10.84 (s, 1 H, NH) ppm. ^{13}C NMR (75.43 MHz, $\mathrm{CDCl_3}$): δ = −3.4, −3.0 ($\mathrm{CH_3Si}$), 18.5, 18.7, 20.2, 20.4 ($\mathrm{CH_3}$ thexyl), 29.6 (Cq thexyl), 34.1 (CH thexyl), 52.4 ($\mathrm{OCH_3}$), 60.4 ($\mathrm{CH_2{=}CH{-}}\mathit{C}\mathrm{H_2}$), 68.8, 70.0, 71.4, 75.0, 75.1 (2 $\mathit{C}\mathrm{H_2Ph}$, $\mathit{C}\mathrm{H_2C_6H_4}$−*p*-OMe, C-6, C-6′), 67.4, 74.1, 75.7, 76.0, 76.2 78.8, 79.2, 80.8 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 98.1, 101.5, 102.5 (C-1, C-1′, *C*HPh), 117.4 ($\mathrm{CH_2{=}}\mathit{C}\mathrm{H{-}CH_2}$), 133.9 ($\mathit{C}\mathrm{H_2{=}CH{-}CH_2}$), 160.5 (N−C=O) ppm. $\mathrm{C_{59}H_{72}FNO_{13}Si}$ (1050.29): calcd. C 67.47, H 6.91, N 1.33; found C 67.32, H 6.90, N 1.33.

Benzyl [3-*O*-Allyl-4,6-*O*-benzylidene-2-*O*-(*p*-methoxybenzyl)-β-D-galactopyranosyl]-(1→4)-2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranoside (22): 1 M Tetrabutylammonium fluoride in dry THF (47 µL) was added under argon to a cooled (−30 °C) solution of **2** (40 mg, 0.03 mmol) in dry THF (1 mL). The mixture was stirred at −30 °C for 3 h then at 0 °C for 5 h. The reaction mixture was diluted with EtOAc and washed with $\mathrm{H_2O}$; the organic layer was dried ($\mathrm{Na_2SO_4}$), filtered and concentrated in vacuo. The residue was purified by flash chromatography (toluene/EtOAc, 7:3) to yield **22** (22 mg, 87%) as a clear oil. $[\alpha]_{\mathrm{D}}^{20} = -11.1$ (c = 1, $\mathrm{CHCl_3}$). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): δ = 3.27 (br. s, 1 H, H-5′), 3.45 (br. d, 1 H, H-5), 3.51 (dd, $J_{3',2'}$ = 9.7, $J_{3',4'}$ = 3.4 Hz, 1 H, H-3′), 3.69−3.88 (m, 7 H, H-3, H-2′, H-6a, H-6b, $\mathrm{OCH_3}$), 4.00 (d, 1 H, H-6′a), 4.17 (t, $J_{4,3} = J_{4,5}$ = 9.2 Hz, 1 H, H-4), 4.18−4.29 (m, 3 H, $\mathrm{CH_2{=}CH{-}C}\mathit{H}_2$, H-4′), 4.31 (d, $J_{6'a,6'b}$ = 12.3 Hz, 1 H, H-6′b), 4.52 (d, $J_{1,2}$ = 8.1 Hz, 1 H, H-1), 4.58 (d, 1 H, C*H*HPh), 4.70−4.78 (m, 4 H, H-1′, $\mathrm{C}\mathit{H}\mathrm{HC_6H_4}$−*p*-OMe, $\mathrm{C}\mathit{H}_2\mathrm{Ph}$), 4.80 (d, J_{gem} = 12.6 Hz, 1 H, CH*H*Ph), 5.07 (d, J_{gem} = 11.7 Hz, 1 H, $\mathrm{CH}\mathit{H}\mathrm{C_6H_4}$−*p*-OMe), 5.26 (t, $J_{2,3}$ = 9.1 Hz, 1 H, H-2), 5.18−5.40 (m, 2 H, $\mathrm{C}\mathit{H}_2\mathrm{{=}CH{-}CH_2}$), 5.52 (s, 1 H, C*H*Ph), 5.89−6.10 (m, 1 H, $\mathrm{CH_2{=}C}\mathit{H}\mathrm{{-}CH_2}$), 6.98−8.05 (m, 24 H, $\mathrm{H_{Ar}}$) ppm. ^{13}C NMR (75.43 MHz, $\mathrm{CDCl_3}$): δ = 55.3 ($\mathrm{OCH_3}$), 61.0 ($\mathrm{CH_2{=}CH{-}}\mathit{C}\mathrm{H_2}$), 69.1, 70.5, 71.3, 74.6, 75.1 (2 $\mathit{C}\mathrm{H_2Ph}$, $\mathit{C}\mathrm{H_2C_6H_4}$−*p*-OMe, C-6, C-6′), 66.4, 73.3, 73.9, 75.7, 77.7, 78.6, 79.7, 80.3 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 99.7, 101.3, 101.4 (C-1, C-1′, *C*HPh), 117.2 ($\mathit{C}\mathrm{H_2{=}CH{-}CH_2}$), 132.9 ($\mathit{C}\mathrm{H_2{=}CH{-}CH_2}$), 165.1 (C=O) ppm. $\mathrm{C_{51}H_{54}O_{13}}$ (874.97): calcd. C 70.01, H 6.22; found C 70.19, H 6.23.

Benzyl (3-*O*-Allyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-6-*O*-(thexyldimethylsilyl)-α-D-glucopyranoside (25): 0.15 M NaOH in ethanol (5.9 mL) was added to a solution of **10α** (0.42 g, 0.44 mmol) in EtOH (2 mL); the mixture was stirred overnight at 40 °C then concentrated in vacuo. Crude alcohol **23** was dissolved under argon in dry THF (4.0 mL) and then cooled to −30 °C. 1 M Tetrabutylammonium fluoride (1.45 mL) was added under argon; the mixture was stirred at −30 °C for 1 h and then overnight at room temperature. The mixture was washed with $\mathrm{H_2O}$, and the organic layer was dried ($\mathrm{Na_2SO_4}$), filtered and concentrated in vacuo to yield crude **24**, which was used directly in next step without purification. Imidazole (54 mg, 0.79 mmol) was added under argon to a cooled (0 °C) solution of **24** in dry DMF (5 mL) whilst stirring; thexyldimethylsilyl chloride (0.08 mL, 0.40 mmol) was added dropwise. After 4 h, the reaction mixture was diluted with EtOAc and washed with satd. $\mathrm{NaHCO_3}$ and then with $\mathrm{H_2O}$; the organic layer was dried ($\mathrm{Na_2SO_4}$), filtered and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 9:1) to yield **25** (176 mg, 57% from **10α**) as a clear oil. $[\alpha]_{\mathrm{D}}^{20} = -10.7$ (c = 1, $\mathrm{CHCl_3}$). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): δ = 0.07−0.13 (2 s, 6 H, $\mathrm{CH_3Si}$), 0.89−0.91 (4 s, 12 H, $\mathrm{CH_3}$ thexyl), 1.62 (m, 1 H, CH thexyl), 3.39 (dd, $J_{3',4'}$ = 3.7, $J_{3',2'}$ = 9.6 Hz, 1 H, H-3′), 3.44 (s, 1 H, H-5′), 3.51−3.58 (m, 2 H, H-2, H-5), 3.71−3.95 (m, 5 H, H-3, H-4, H-6a, H-6b, H-2′), 4.04 (d, $J_{6'a,6'b}$ = 12.6, $J_{6',5'}$ = 1.3 Hz, 1 H, H-6′a), 4.15−4.23 (m, 3 H, H-4′, $\mathrm{CH_2{=}CH{-}C}\mathit{H}_2$), 4.29 (d, 1 H, H-6′b), 4.41 (d, $J_{1',2'}$ = 7.8 Hz, 1 H, H-1′), 4.52 (d, 1 H, C*H*HPh), 4.72 (d, J_{gem} = 11.9 Hz, 1 H, C*H*HPh), 4.94 (dd, $J_{1,2}$ = 3.9 Hz, 1 H, H-1), 5.18−5.36 (m, 2 H, $\mathrm{C}\mathit{H}_2\mathrm{{=}CH{-}CH_2}$), 5.49 (s, 1 H, C*H*Ph), 5.89−6.01 (m, 1 H, $\mathrm{CH_2{=}C}\mathit{H}\mathrm{{-}CH_2}$), 7.22−7.50 (m, 10 H, $\mathrm{H_{Ar}}$) ppm. ^{13}C NMR (75.43 MHz, $\mathrm{CDCl_3}$): δ = −3.3, −3.2 ($\mathrm{CH_3Si}$), 18.6, 18.7, 20.3, 20.4 ($\mathrm{CH_3}$ thexyl), 25.2 (Cq thexyl), 34.1 (CH thexyl), 61.9 ($\mathrm{CH_2{=}CH{-}}\mathit{C}\mathrm{H_2}$), 69.0, 69.5, 70.6 (C-6, C-6′, $\mathrm{CH_2Ph}$), 66.9, 69.8, 70.7, 70.9, 72.5, 72.6, 78.9, 80.8 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 97.4, 101.1, 103.7 (C-1, C-1′, *C*HPh), 117.9 ($\mathrm{CH_2{=}}\mathit{C}\mathrm{H{-}CH_2}$), 134.6 ($\mathit{C}\mathrm{H_2{=}CH{-}CH_2}$) ppm. $\mathrm{C_{37}H_{54}O_{11}Si}$ (702.90) Calcd. C 63.22, H 7.74; found C 63.25, H 7.89.

Benzyl (3-*O*-Allyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2-*O*-benzyl-6-*O*-(thexyldimethylsilyl)-α-D-glucopyranoside (26): Dibutyltin oxide (240 mg, 0.96 mmol) was added to a solution of **25** (580 mg, 0.84 mmol) in dry methanol (5 mL). The reaction mixture was stirred at 60 °C for 15 h and then the solvent was evaporated under reduced pressure. The solid residue was dissolved in toluene (15 mL) at 60 °C and then tetrabutylammonium iodide (380 mg, 1.04 mmol) and benzyl bromide (1.0 mL, 8.4 mmol) were added. After stirring the mixture at 60 °C for 17 h, the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography ($\mathrm{CHCl_3/CH_3OH}$, 9:1, + 1% triethylamine) to yield **26** (570 mg, 88%) as an amorphous brown solid. $[\alpha]_{\mathrm{D}}^{20} = +15.5$ (c = 1, $\mathrm{CHCl_3}$). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): δ = 0.06−0.13 (2 s, 6 H, $\mathrm{CH_3Si}$), 0.82−0.96 (4 s, 12 H, $\mathrm{CH_3}$ thexyl), 1.62 (m, 1 H, CH thexyl), 3.33−3.44 (m, 2 H, H-5, H-5′), 3.45−3.62 (m, 4 H, H-3, H-4, H-6a, H-6′a), 3.66 (dd, $J_{3',4'}$ = 3.5, $J_{3',2'}$ = 9.6 Hz, 1 H, H-3′), 3.95−4.20 (m, 5 H, $\mathrm{CH_2{=}CH{-}C}\mathit{H}_2$, H-2, H-6b, H-6′b), 4.30 (d, 1 H, H-4′), 4.36−4.45 (m, 2 H, H-1, C*H*HPh), 4.58 (br. d, 2 H, 2 C*H*HPh), 4.71−4.85 (m, 2 H, H-1′, CH*H*Ph), 5.05−5.22 (m, 2 H, $\mathrm{C}\mathit{H}_2\mathrm{{=}CH{-}CH_2}$) 5.54 (s, 1 H, C*H*Ph), 5.61 (t, $J_{1',2'}$ = 9.6 Hz, 1 H, H-2′), 5.63−5.82 (m, 1 H, $\mathrm{CH_2{=}C}\mathit{H}\mathrm{{-}CH_2}$), 7.10−8.10 (m, 15 H, $\mathrm{H_{Ar}}$) ppm. ^{13}C NMR (75.43 MHz, $\mathrm{CDCl_3}$): δ = −3.3, −3.2 ($\mathrm{CH_3Si}$), 18.6, 18.7, 20.4, 20.5 ($\mathrm{CH_3}$ thexyl), 25.2 (Cq thexyl), 34.2

(CH thexyl), 62.0 ($CH_2{=}CH{-}CH_2$), 68.9, 70.5, 72.8 (C-6, C-6′, 2 CH_2Ph), 67.0, 69.0, 69.7, 71.6, 73.0, 79.0, 79.2, 81.0 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 95.7, 101.1, 103.6 (C-1, C-1′, *C*HPh), 117.7 ($CH_2{=}CH{-}CH_2$), 134.8 ($CH_2{=}CH{-}CH_2$) ppm. $C_{43}H_{58}O_{11}Si$ (779.00) Calcd. C 66.30, H 7.50; found C 66.13, H 7.48.

Benzyl (3-*O*-Allyl-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2-*O*-benzyl-6-*O*-(thexyldimethylsilyl)-α-D-glucopyranoside (27): Et_3N (1.37 mL, 9.9 mmol) was added under argon to a cooled (−5 °C) solution of **26** (430 mg, 0.54 mmol) in dry CH_3CN (5 mL). Benzoyl cyanide (1.62 mL of a 0.5 M solution in dry CH_3CN) was added dropwise whilst stirring. After 24 h the reaction mixture was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$; the organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/EtOAc, 7:3) to yield **27** (310 mg, 65%) as a clear oil. $[\alpha]_D^{20} = +29.6$ ($c = 1$, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.08{-}0.12$ (2 s, 6 H, CH_3Si), 0.80−0.91 (4 s, 12 H, CH_3 thexyl), 1.63 (m, 1 H, CH thexyl), 3.28−3.39 (m, 2 H, H-5, H-2), 3.49−3.61 (m, 4 H, H-6a, H-6b, H-4, H-5′), 3.66 (dd, $J_{3',4'} = 3.1$, $J_{3',2'} = 10.3$ Hz, 1 H, H-3′), 3.99−4.17 (m, 5 H, $CH_2{=}CH{-}CH_2$, H-3, H-6′a, H-6′b), 4.30 (br. s, 1 H, H-4′), 4.38 (d, $J_{1,2} = 3.9$ Hz, 1 H, H-1), 4.42 (d, 1 H, CH*H*Ph), 4.61 (d, $J_{gem} = 12.2$ Hz, 1 H, C*H*HPh), 4.74 (m, 2 H, H-1′, C*H*HPh), 4.80 (d, $J_{gem} = 11.9$ Hz, 1 H, CH*H*Ph), 5.12 (br. dd, 2 H, $CH_2{=}CH{-}CH_2$), 5.54 (s, 1 H, C*H*Ph), 5.61 (t, $J_{2',1'} = 9.5$ Hz, 1 H, H-2′) 5.68−5.80 (m, 1 H, $CH_2{=}CH{-}CH_2$), 7.10−7.60 (m, 20 H, H_{Ar}) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$): $\delta = 1.7$, 2.1 (CH_3Si), 14.9, 15.0, 20.6, 22.9 (CH_3 thexyl), 30.0 (Cq thexyl), 61.4 ($CH_2{=}CH{-}CH_2$), 69.1, 69.7, 70.6, 74.8 (C-6, C-6′, 2 CH_2Ph), 66.8, 70.8, 73.2, 73.6, 75.6, 76.9, 79.0, 81.4 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 99.4, 101.1, 103.3 (C-1, C-1′, *C*HPh), 117.6 ($CH_2{=}CH{-}CH_2$), 134.7 ($CH_2{=}CH{-}CH_2$), 165.2 (C=O) ppm. $C_{50}H_{62}O_{12}Si$ (883.11) Calcd. C 68.00, H 7.08; found C 67.92, H 7.06.

Benzyl (3-*O*-Allyl-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2-*O*-benzyl-3-*O*-(*p*-methoxybenzyl)-6-*O*-(thexyldimethylsilyl)-α-D-glucopyranoside (3): *p*-Methoxybenzyl chloride (90 µL, 0.67 mmol), NaH (16 mg, 0.67 mmol) and KI (110 mg, 0.67 mmol) were added under argon to a cooled (−30 °C) solution of **27** (300 mg, 0.33 mmol) in dry DMF (3 mL). After 5 h, the reaction mixture was quenched with methanol, diluted with CH_2Cl_2 and washed with H_2O; the organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash chromatography (toluene/EtOAc, 95:5) to yield **3** (161 mg, 48%) as a yellow oil. $[\alpha]_D^{20} = -56.5$ ($c = 1$, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.08{-}0.10$ (2 s, 6 H, CH_3Si), 0.78−0.89 (4 s, 12 H, CH_3 thexyl), 1.65 (m, 1 H, CH thexyl), 3.27 (br. dd, $J_{2,3} = 10.2$ Hz, 1 H, H-2), 3.33 (br. d, $J_{5,4} = 9.5$ Hz, 1 H, H-5), 3.45−3.85 (m, 9 H, H-4, 2 H-6, H-3′, H-5′, OCH_3, $CH_2{=}CH{-}CHH$), 3.91 (br. dd, 1 H, $CH_2{=}CH{-}CHH$), 4.01−4.18 (m, 3 H, H-3, 2 H-6′), 4.30 (br. s, 1 H, H-4′), 4.35−4.65 (m, 5 H, 3 C*H*HPh, $CH_2C_6H_4$-*p*-OMe), 4.74 (br. d, 1 H, H-1′), 4.78 (br. d, $J_{1,2} = 3.8$ Hz, 1 H, H-1), 4,79 (d, $J_{gem} = 12.3$ Hz, 1 H, CH*H*Ph), 5.07−5.30 (m, 2 H, $CH_2{=}CH{-}CH_2$), 5.55 (s, 1 H, C*H*Ph), 5.61 (t, $J_{2',1'} = J_{2',3'} = 9.6$ Hz, 1 H, H-2′), 5.67−5.78 (m, 1 H, $CH_2{=}CH{-}CH_2$), 7.00−8.10 (m, 24 H, H_{Ar}) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$): $\delta = -4.0$, −2.3 (CH_3Si), 18.8, 18.9, 20.1, 20.2 (CH_3 thexyl), 29.6 (Cq thexyl), 34.0 (CH thexyl), 55.5 (OCH_3), 61.1 ($CH_2{=}CH{-}CH_2$), 69.0, 69.5, 71.4, 75.0, 75.2 (2 CH_2Ph, C-6, C-6′, $CH_2C_6H_4$-*p*-OMe), 66.0, 73.1, 74.8, 74.2, 76.4, 79.2, 79.8, 80.0 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 99.5, 101.3, 103.0 (C-1, C-1′, *C*HPh), 117.8 ($CH_2{=}CH{-}CH_2$), 132.5 ($CH_2{=}CH{-}CH_2$), 165.6 (C=O) ppm. $C_{59}H_{73}O_{13}Si$ (1018.29) Calcd. C 69.59, H 7.23, found C 69.74, H 7.24.

Loading 22 onto PS-DES Resin (30): PS-DES gel-type polystyrene silane resin (300 mg, 0.29 mmol) was suspended in dry CH_2Cl_2 (2.9 mL) and then 1,3-dichloro-5,5-dimethylhydantoin (**28**) (170 mg, 0.86 mmol) was added (to ensure complete chlorination of the silane linker, the concentration of the chlorinating agent should be approximately 0.3 M). After 1.5 h, the polymer was filtered off and washed with CH_2Cl_2 (3 × 9 mL) and THF (2 × 9 mL). The product was transferred to a glass tray and dried in vacuo for 12 h to give activated resin **29**. The conversion of Si−H units into Si−Cl bonds was ascertained using IR spectroscopic analysis (DRIFT), monitoring the disappearance of the typical stretch Si−H at 2100 cm^{-1}. The anchoring of the scaffold was performed by treating resin **29** (250 mg) with a solution of scaffold **22** (610 mg, 0.7 mmol) and imidazole (55 mg, 0.8 mmol) in dry CH_2Cl_2 (5 mL) under argon. After 24 h, the polymer was filtered off and washed with CH_2Cl_2 (2 × 15 mL), DMF/H_2O (1:1, 2 × 15 mL), THF/H_2O (1:1, 2 × 15 mL) and finally THF (2 × 15 mL) to yield **30** (390 mg). ^1H NMR HR-MAS (400 MHz, CD_2Cl_2, selected data): $\delta = 3.31$ (br. s, 2 H, H-5, H-5′), 3.47 (br. dd, 1 H, H-3′), 3.60−3.80 (m, 5 H, H-2′, H-3, OCH_3), 3.96 (br. d, 1 H, H-6′), 4.02−4.32 (m, 6 H, H-6′, H-4′, H-4, H-6, $CH_2{=}CH{-}CH_2$), 4.52−4.86 (m, 7 H, 2 CH_2Ph, C*H*HPh, H-1, H-1′), 5.11 (t, 1 H, H-2′), 5.18−5.30 (3 H, $CH_2{=}CH{-}CH_2$, CH*H*Ph), 5.51 (s, 1 H, C*H*Ph), 5.86−6.00 (m, 1 H, $CH_2{=}CH{-}CH_2$) ppm. IR (DRIFT): $\tilde{\nu}_{max.} = 1745$, 1240 cm^{-1}.

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