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Facile Synthesis of per-*O*-*tert*-Butyldimethylsilyl-β-D-galactofuranose and Efficient Glycosylation via the Galactofuranosyl Iodide

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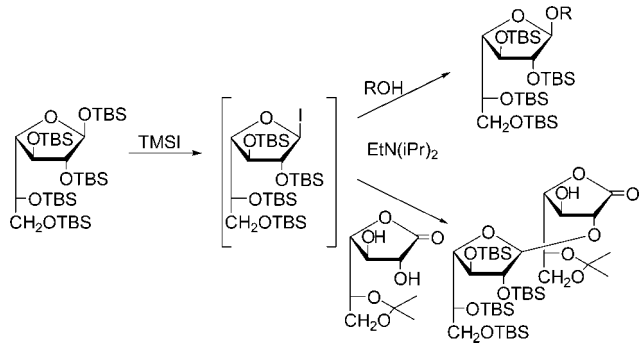

The synthesis of crystalline per-*O*-TBS-β-D-galactofuranose (**4β**) as a new precursor of D-Gal*f* units is described. Anomeric iodination by reaction with TMSI followed by in situ coupling with simple alcohols and a wide variety of glycosyl acceptors, in the absence of a promoter, was employed as a new efficient glycosylation method for the assembly of D-galactofuranosyl moieties with high β-stereoselectivity. Under the mild conditions of this reaction labile protective groups, like acetals, and furanosyl linkages are preserved.

Introduction

Highly immunogenic galactofuranosyl residues are present in glycoconjugates of many pathogenic bacteria, such as *Mycobacterium tuberculosis* and *M. leprae*,[1,2] protozoan parasites, such as *Trypanosoma cruzi* and *Leishmania*,[3−6] and fungi, such as *Paracoccidioides brasilensis*.[7] The fact that D-Gal*f* is essential for the survival or virulence of various pathogenic bacteria,[8,9] but is absent in higher eukaryotes, prompted investigation on its biosynthetic pathways.[9,10] Therefore, the synthesis of oligosaccharides and conjugates containing D-Gal*f* units[11] as tools in glycobiology is an area of active research. Our laboratory has also been largely interested in the glycobiology of galactofuranose.[12] Thus, we have reported the synthesis of derivatives of galactofuranose, which act as substrates[13] or inhibitors[14] of related enzymes, and the preparation of deoxygenated analogues of the natural substrates for the characterization of the carbohydrate−protein interactions.[15] Nevertheless, devising new galactofuranosyl donors and developing new glycosylation methodologies for both the synthesis of galactofuranosyl precursors and glycosylation methods are still required.

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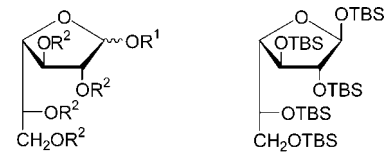
Many efforts have been directed to the development of galactofuranosyl precursors by us[14,15a] and by other teams.[11a,16−19] The peracylated derivatives **1**-**3** (Figure 1) are frequently used as precursors of D-Gal*f* units in oligosaccharides and glycoconjugates.[16,17] They offer the advantage that they may be glycosylated in one pot, without previous activation, affording β-D-galactofuranosides as result of the anchimeric assistance. With the exception of **1**, which was obtained in one step by benzoylation of D-galactose at high temperature and purified from the pyranosic forms by crystallization, the other precursors needed at least three reaction steps and corresponding purifications. On the other hand, successful glycosylation reactions have been optimized for the assembly of D-Gal*f* units for the synthesis of oligosaccharides and glycoconjugates. Glycosyl bromides and chlorides,[20] thioglycosides,[21] trichloacetimidates,[22] pentenylglycosides,[23] and thioimidoyl-type donors[11f] have been used successfully. The synthesis of these donors generally involves more than one step.

Two decades ago, the glycopyranosyl iodides had been considered too reactive, often difficult to handle and isolate, and not suitable as glycosyl donors.[24] However, their efficiency for the synthesis of *O*-, *S*-, and *C*-glycopyranosides and oligosaccharides has been well demonstrated.[25,26] The most convenient procedure for the synthesis of glycopyranosyl iodides is the treatment of per-*O*-acetyl derivatives with TMSI introduced by Thiem and Meyer.[27] Hindsgaul and Uchiyama showed that anomeric TMS derivatives could serve as precursors of in situ formed glycopyranosyl iodides, which react with different acceptors to give the corresponding glycosides.[28] Persilylated derivatives of glycopyranoses have shown to be useful to afford glycoconjugates.[25f,29] By iodonium replacement of the free anomeric hydroxyl groups with a polymer-bound triaryl phosphane−iodine complex and imidazole, several glycopyranosyl and D-mannofuranosyl iodides were prepared.[30] Nevertheless, to the best of our knowledge, the use of galactofuranosyl iodides has not been previously reported.



1 $R^1 = R^2$ = Bz
2 $R^1 = R^2$ =Ac
3 R^1 = Ac, R^2 = Bz

4β

FIGURE 1. Galactofuranosyl precursors.

As continuation of our studies on the development of new methodologies for the synthesis of galactofuranose derivatives, we decided to explore the synthesis of per-*O*-silylated derivatives of D-Gal*f*. In the previous procedure described for the preparation of the anomeric mixture of the TMS derivative of D-Gal*f*, the isolation was performed by GC, and it was useful only for analytical purposes.[31] In contrast, we described here the easy preparation of a new donor of D-galactofuranosyl moieties, per-*O*-silyl derivative **4*β*** (Figure 1), the scope, and the limitations as a glycosyl donor in glycosylations via the galactofuranosyl iodide generated in situ.

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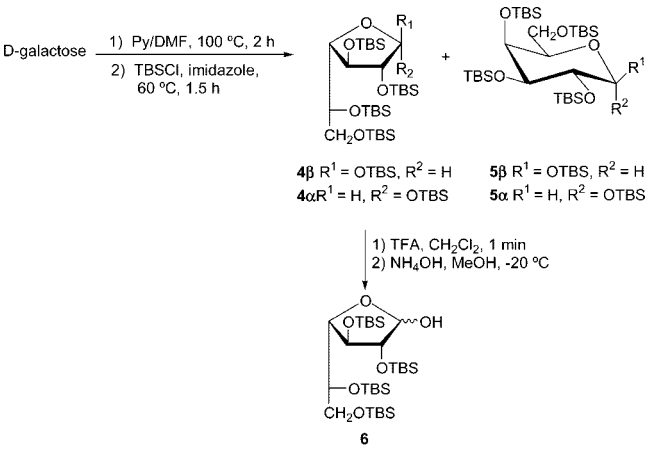
TABLE 1. Reaction Conditions Employed for the Synthesis of per-*O*-Silylated Derivatives of D-Gal*f*

					product distribution (%)			
entry	silylating agent	solvent	temp	time (h)	**4β**	**5β**	**4α**	**5α**
1	TMSCl	DMF	rt	3	–	–	–	100[a]
2	TBSCl	DMF	rt[b]	3	14[a]	32[a]	4[a,c]	
3	TMSCl	1:1 Py-DMF	80 °C	3	55[a,d]	25[a,d]	10[a,d]	10[a,d]
4	TBSCl	1:1 Py-DMF	80 °C	3	48[a]	43[a]	5[a]	4[a]
					45[e]	42[e]	–	–
5	TBSCl	DMF	30 °C	48	100[a]			
					79[e]			

[a] Determined by ^{1}H NMR spectroscopy. [b] 50% of unreacted galactose. [c] Corresponds to the integration of the signals of the **4α** and **5α** glycosides, which were not resolved. [d] Unresolved by preparative chromatography. [e] Isolated pure products after column chromatography.

SCHEME 1. Synthesis of per-*O*-TBS-β-D-galactofuranoside (4β)



Results and Discussion

Silylation of hydroxyl groups is usually conducted in DMF and in the presence of imidazole.[32] Thus, silylation of D-galactose with trimethylsilyl chloride (TMSCl) led to the per-*O*-TMS-α-pyranose derivative (Table 1, entry 1). Under the same conditions, silylation with *tert*-butyldimethylsilyl chloride (TBSCl) afforded a complex mixture of furanosyl and pyranosyl silylated derivatives together with an important proportion of free galactose, as determined by ^{13}C NMR spectroscopy (entry 2).

In order to mimic the conditions employed for the preparation of per-*O*-benzoylated derivative **1**,[17] D-galactose in different proportions of pyridine was refluxed to favor the furanosic configuration, and then the silylating agent and the imidazole were added (Scheme 1). The best results were obtained when 1:1 pyridine/DMF solvent was used. With TMSCl, a chromatographically homogeneous mixture was obtained, which showed by ^{1}H NMR spectroscopy the presence of the β-pyranosic and the β-furanosic forms as main products (Table 1, entry 3). The mixture could not be separated by column chromatography or by fractioned crystallization. Analogous silylation of galactose with TBSCl afforded, according to the ^{1}H NMR spectrum of the crude product, the β-pyranose (δ 4.42, $J_{1,2}$ = 7.9 Hz) and the β-furanose (δ 5.15, $J_{1,2}$ = 2.6 Hz) as main products (table 1, entry 4), and accordingly two spots were detected by TLC (R_f = 0.87 and R_f = 0.75). The faster migrating compound was isolated by crystallization from MeOH (35% yield) and identified as **4β** (Scheme 1). Column chromatography of the mother liquors increased the overall yield to 45%. The lower migrating component was identified as **5β** and isolated in 42% yield after column chromatography (entry 4).

With the aim of establishing a procedure for easily obtaining a galactofuranose derivative, we studied different conditions. Fortunately, we found that under standard conditions (DMF as solvent, 30 °C) and a longer reaction time (48 h), the **4β** isomer was practically the only product, which was isolated in 79% yield (Table 1, entry 5). Sterically demanding TBS groups require more time than TMS in order to complete the full protection. Long reaction time favors the formation of the β-furanose form, as also observed for the Fisher's glycosylation.[13b]

The ^{1}H NMR spectrum of **4β** showed the H-1 signal as a doublet at δ 5.15 with a small $J_{1,2}$ (2.6 Hz), indicating a *trans* relationship for H-1 and H-2 and hence a β configuration.[33] The ^{13}C NMR spectrum showed the resonances at 102.8 ppm for C-1, and signals at 85.5 and 84.9 ppm for C-4 and C-2, respectively, also characteristic of β anomers of galactofuranosyl derivatives.[34] The chemical shifts for the protons were in good agreement with those reported for the trimethylsilyl analogue, TMS-β-D-Gal*f*,[31] although the $^3J_{H,H}$ values for the ring protons were 0.3−1.9 Hz smaller than in compound **4β**. The presence of adjacent TBS protective groups induces important conformational distortions in pyranose derivatives, which result in the enhancement of their reactivity as glycosyl donors. This is the basis of the "super-armed glycosyl donor concept".[35] In the case of **4β**, the $^3J_{H,H}$ values were similar to those observed for the acylated[14,17] and for other derivatives,[11a] suggesting that no important distortion occurs by the effect of bulky TBS groups in the galactofuranosyl ring.

The arabinose analogue of **4β**, per-*O*-TBS-α,β-D-arabinofuranose, was extensively used for the synthesis of β-D-arabinofuranosyl-1-monophosphorylpolyprenols using different approaches, which involved selective 1-*O*-desilylation using TFA.[36] With the aim of developing a similar chemistry for galactofuranose, the anomeric *O*-desilylation of **4β** was performed, but acid treatment under the controlled conditions described for the arabinose analogue led to a complex mixture of products, as a result of the *O*-desilylation of other positions. Compound **6** was isolated by column chromatography as an anomeric mixture in low yield (10%, Scheme 1).

With compound **4β** in hand, we decided to investigate the glycosylation reaction promoted by TMSI.[28] Thus, compound **4β** was treated with 1.2 equiv of TMSI in anhydrous CH_2Cl_2 at 0 °C for 30 min, when TLC examination showed total consumption of the starting material. Also, the presence of two products was detected, one of R_f = 0.70 attributed to the 1-iodo intermediate **7**, and the other one with the same mobility as compound **6** (R_f = 0.54). Probably, hydrolysis of the galactofuranosyl iodide **7** occurs on the silica gel plate, leading to **6**. Subsequent addition of common alcohols (*n*BuOH, benzyl alcohol, 4-nitrophenol) and EtN(*i*Pr)$_2$ as an acid scavenger afforded glycosides **8**−**10** (Scheme 2, Table 2, entries 1−3).

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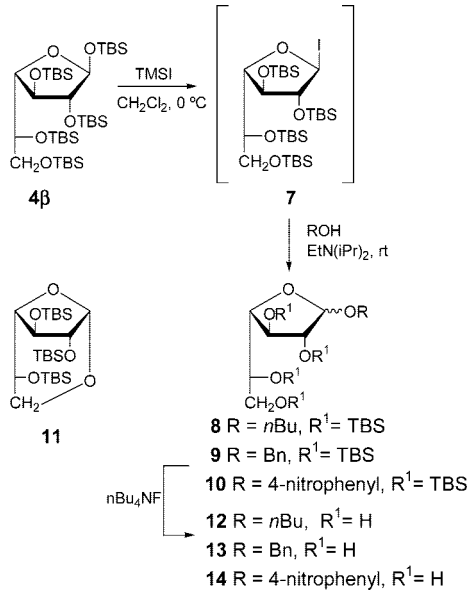
SCHEME 2. Synthesis of Galactofuranosyl Glycosides via in Situ Formed Galactofuranosyl Iodide



Attempts to isolate the intermediate iodide **7**, as described for pyranosyl analogues,[25b,30] were unsuccessful. However, ^{1}H NMR spectrum of the reaction mixture showed at 6.52 ppm the anomeric signal of **7** as a broad singlet ($J_{1,2}$ < 0.5 Hz) indicating the formation of the β-iodide. In the ^{13}C NMR spectrum, the anomeric signal was observed at 89.3 ppm. Both values were in accordance with those observed for the 2,3,4,6-tetra-*O*-benzoyl-β-D-galactofuranosyl bromide described by Varela et al.[20a] Depending on the conditions, a third product was detected by TLC analysis (R_f = 0.62) during the iodide formation. This product remained in the product mixture after the workup, and it was identified as the 1,6-anhydro-α-D-galactofuranose derivative **11** (10−15%, Scheme 2) formed as result of the nucleophilic attack of desilylated HO-6. Its formation was suppressed by strict control of the TMSI amount employed. Several conditions were tested for conducting the reaction. The presence of tetrabutyl ammonium iodide did not change the course of the reaction, in contrast with pyranosyl derivatives, in which halide-ion catalysis was observed.[25a] When diethyl ether was used as a solvent the reaction proceeded slowly, and the insolubility of **4*β*** in DMF or acetonitrile precluded the use of these solvents. The advantage of **4*β*** as galactofuranosyl precursor and this glycosylation method is that the formation of the glycosyl iodide occurs under milder conditions and faster than the formation of the analogous chloride or bromide, which require several hours.[20]

The NMR spectra of **8**−**10** showed that the glycosylation proceeded with moderate diastereoselectivity and with predominance of the β-anomer (Table 2, entries 1−3). This fact suggests a S_N1 mechanism with formation of the anomeric oxonium ion. The attack of the nucleophile to C-1 from the β face could be determined because of the steric effect of the bulky subtituent at C-2 and the lateral chain at C-4.

Removal of the TBS groups from **8**−**10** was accomplished with *n*Bu$_4$NF (TBAF) in THF[32] and afforded glycosides **12**−**14**, having physical and spectral properties identical to those previously reported.[13c,f]

Once the conditions for TMSI-promoted glycosylation of **4*β*** with simple alcohols were optimized, attention was focused on the condensation with different carbohydrate acceptors.

Based on our experience with the glycosyl-aldonolactone approach for the assembly of galactofuranose moieties,[15d,e] we selected as acceptors selectively substituted aldonolactones **15**, **17**, **19**, **21**, and **23** (Table 2, entries 4−8). Also compounds **26**, **28**, and **30** (entries 9−11) were tested as acceptors. D-Gal*f* units have been shown to be present O-glycosidically linked to other D-Gal*f* units by (1→2), (1→3), (1→5), and (1→6) linkages in many natural structures and also attached to D-Man*p*, D-Glc*p*, D-Gal*p* units,[6] so the acceptors chosen would give access to disaccharide precursors of such structures. The condensation of **4*β*** with acceptors having one hydroxyl group free (**15**, **17**, **26**, **28**, and **30**) led to the expected products **16**, **18**, **27**, **29**, and **31** in good isolated yield (Table 2, entries 4, 5, 9−11). The low yield on coupling **4*β*** with **19** to afford **20** (entry 6) could be due to the steric hindrance. In this case, most of **4*β*** was recovered as a result of recombination with the living group TBS. It is noteworthy that labile acceptors like **26**, with a galactofuranose linkage and an isopropylidene protective group, could not be glycosylated using $SnCl_4$ as a promoter; a milder strategy like the trichloroacetimidate method[22] would require several steps to prepare the glycosyl donor. Although $EtN(iPr)_2$ was not essential for the glycosylation, it was necessary in the case of such labile acceptors in order to prevent their decomposition by the iodhydric acid released during the glycosylation.

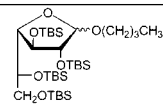
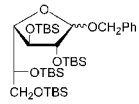
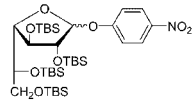
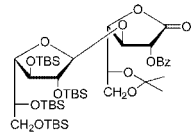
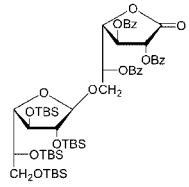
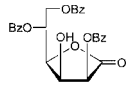
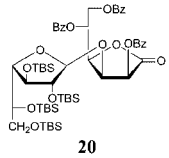
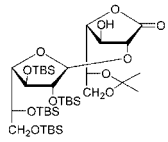
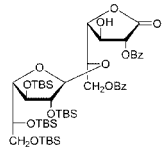
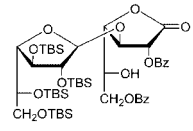
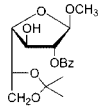
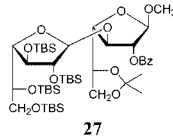
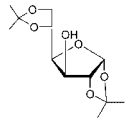
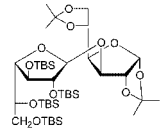
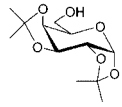
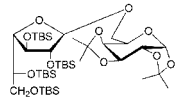
Condensation with acceptors with more than one hydroxyl free was also investigated. Excellent regioselectivity was observed on coupling **4*β*** with 5,6-di-*O*-isopropylidene derivative **21** (Table 2, entry 7) which led to **22**, the glycosylation occurring only at the C-2 hydroxyl group activated by the vicinal lactone function. In the ^{13}C NMR spectrum of **22**, the signal corresponding to C-1 appeared at δ 170, shielded 4 ppm in comparison with the corresponding signal of **21**, as a result of the glycosylation at the vicinal position. For the synthesis of α-D-Gal*f*-(1→2)-D-galactitol, the aldonolactone approach was also used. Although glycosylation of 2,3-diol **21** with 2,3,5,6-tetra-*O*-benzyl-D-galactofuranosyl trichloroacetimidate under conditions favoring 1,2-*cis*-glycosylation occurred mainly at HO-2, the reaction was not completely regioselective, and byproducts resulting from 3-*O*-glycosylation of the lactone were also obtained.[37]

Condensation of **4*β*** with the dibenzoylated lactone **23** was expected to occur at the less hindered exocyclic C-5 hydroxyl group, as previously observed for the $SnCl_4$-promoted glycosylation of **1** with **23**[11n] or in the condensation of the 2,6-di-*O*-pivaloyl-D-galactono-1,4-lactone with **1**, either promoted by $SnCl_4$ or via the trichloroacetimidate.[11b,j] In contrast, two products in this case were formed as deduced by NMR analysis, leading to glycosylation of the aldonolactone at HO-5 (**24**) and HO-3 (**25**) in similar amounts (Table 2, entry 8).

The NMR spectra of the products obtained by reaction of **4*β*** with sugar acceptors (Table 2, entries 4−11) showed in all cases small $J_{1,2}$ values and low-field resonances for the anomeric carbons (>105 ppm) and C-2 and C-4 (>80 ppm), consistent with the β-D-galactofuranoside stereochemistry.[33,34] Thus, the TMSI-promoted glycosylation of **4*β*** with sugar acceptors proceeded in all the cases with complete stereoselectivity, affording the corresponding β-products. The fact that lower stereoselectivity was observed in glycosylations with common alcohols would indicate that steric factors may be responsible for the 1,2-*trans* diastereocontrol.

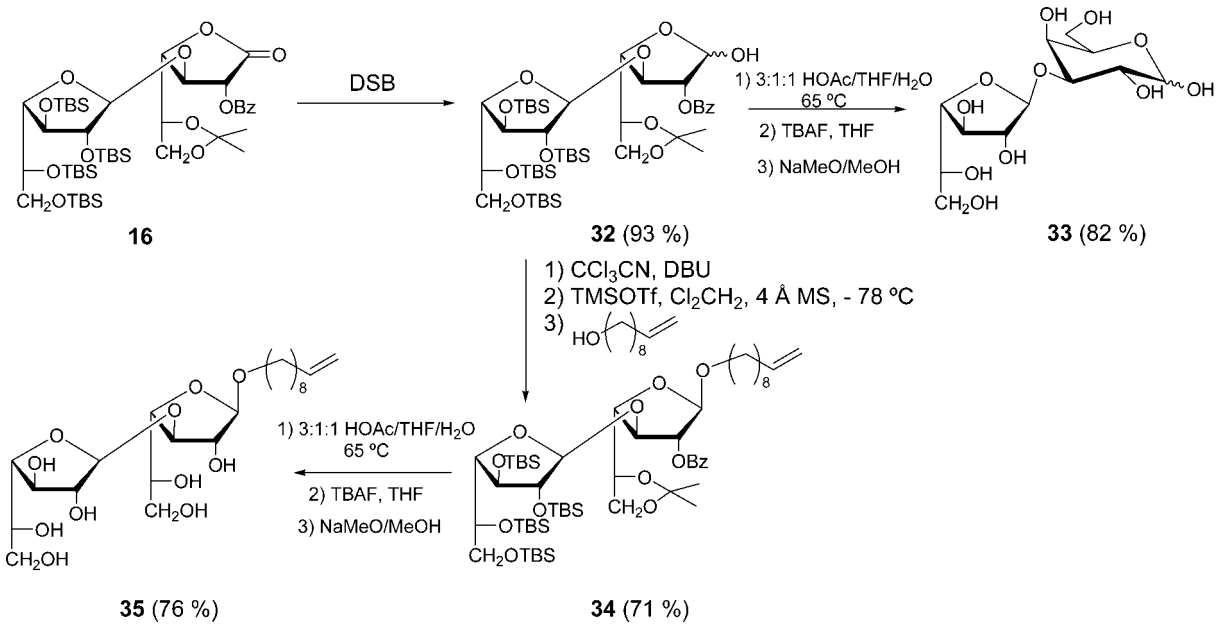
In order to demonstrate the utility of **4*β*,** the TMSI-promoted glycosylation, and the stability of the glycosylated products as

TABLE 2. Glycosylation of 4β via the Galactofuranosyl Iodide Generated in Situ

Entry	Acceptor	Product	time (h)	β:α ratio[a] Yield (%)[b]
1	*n*BuOH	 **8**	1	2:1 (90)
2	$PhCH_2OH$	 **9**	1	6:1 (69)
3	4-nitrophenol	 **10**	1	4:1 (75)
4	 **15**	 **16**	24	only β (75)
5	 **17**	 **18**	24	only β (87)
6	 **19**	 **20**	48	only β (37)
7	 **21**	 **22**	24	only β (83)
8	 **23**	 **24**  **25**	48	only β (87)
9	 **26**	 **27**	24	only β (79)
10	 **28**	 **29**	24	only β (69)
11	 **30**	 **31**	24	only β (80)

[a] Determined from the ^1H NMR spectrum of the crude reaction mixture. [b] Yields refer to isolated pure products after column chromatography.

SCHEME 3. Synthesis of β-D-Gal*f*(1→3)-D-Gal*p* (33) and de-9-enyl β-D-Gal*f*(1→3)-β-D-Gal*f* (35)



intermediates for further reactions, we synthesized β-D-Gal*f*(1→3)-D-Gal*p* (**33**) and 9-decenyl β-D-Gal*f*(1→3)-β-D-Gal*f* (**35**). Disaccharide **33** is the repeating unit of the backbone structure of the *O*-antigenic polysaccharide present in the lipopolysaccharide (LPS) of the genus *Klebsiella.*[38] The motif β-D-Gal*f*(1→3)-D-Gal*p* was recently found in a neutral exopolysaccharide produced by *Lactobacillus delbrueckii* ssp. *bulgaricus* LBB.B26.[39] Compound **33** has been previously synthesized by condensation of 2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl trichloroacetimidate and 1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranose.[40] Although this strategy seems to be very straightforward, the isopropylidene acceptor was obtained only in 50% yield after an improved procedure and the preparation of the trichloroacetimidate donor involved five steps. Methyl β-D-Gal*f*(1→3)-β-D-Gal*f* has been synthesized using as a key step the non-regioselective coupling of 2,3,5,6-tetra-*O*-acetyl-β-D-galactofuranosyl chloride with methyl 5,6-di-*O*-isopropylidene-β-D-galactofuranoside.[41] The synthesis of **33** described here involves the glycosyl-aldonolactone **16** as intermediate, which is obtained by condensation of **4*β*** and **15** in 75% yield (Table 2, entry 4). Reduction of **16** with diisoamylborane[42] led to lactol **32**, as a 0.85:1 α/β anomeric mixture, as indicated by the ^{1}H NMR spectrum. The free disaccharide **33** was obtained in 82% yield by treatment of **32** with HOAc/THF/H_2O for the cleavage of the acetal-protecting group, by removal of the TBS groups with TBAF,[32] and by conventional debenzoylation. The ^{13}C NMR spectrum showed resonances at 109.7 ppm corresponding to C-1′ of both anomers, and signals at 96.9 ppm and 92.8 ppm due to C-1 β- and α-pyranose (1:1 ratio), respectively. The ^{1}H NMR spectrum showed signals characteristic of galactopyranose for the reducing end. The spectroscopical data were in disagreement with those previously reported.[40] The signals observed at 109.0, 105.9, and 96.0 ppm, which were assigned to C-1′, C-1α, and C-1β-furanose, respectively, suggested that upon deprotection the expansion to the galactopyranosyl form did not occur.

On the other hand, **32** was converted into the corresponding trichloroacetimidate by treatment with trichloroacetonitrile and DBU[22] and after purification by column chromatography was coupled with 9-decenol, affording glycoside **34** in good yield. Deprotection of **34** was conducted, as described for **32**, to afford the target **35** in very good yield (Scheme 3). The NMR spectra of **35** showed broad singlets at 5.14 and 4.96 ppm for H-1′ and H-1 and signals at δ 107.5 and 107.2, confirming the β-furanose configuration for both D-Gal units.

In conclusion, we have described the easy preparation of a new precursor of D-galactofuranosyl moieties, the per-*O*-silyl-β-D-Gal*f* derivative **4*β*** obtained as a crystalline product in just one high-yielding step from D-galactose. We also investigated the glycosylation of this donor by in situ activation as galactofuranosyl iodide. This is the first time that this rather unstable intermediate has been employed in glycosylation reactions. We tested the efficiency of the glycosylating method for the introduction of β-D-Gal*f* units at different positions of partially protected sugar acceptors, affording precursors of relevant galactofuranose-containing disaccharides. The advantage of derivative **4*β*** relies on the possibility of introducing a β-D-Gal*f* unit without previous activation under mild conditions that are compatible with labile acceptors. TBS as protective group combines stability under a wide range of conditions, with susceptibility to facile removal by highly specific reagents.

Experimental Section

1,2,3,5,6-Penta-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranose (4*β*) and 1,2,3,5,6-Penta-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranose (5*β*). Method A. A solution of D-galactose (0.5 g, 2.77 mmol) in dry pyridine (7 mL) and DMF (7 mL) was heated at 100 °C for 2 h. Then, imidazole (2.74 g, 18.25 mmol) and TBSCl (3.0 g, 20.08 mmol) were added, and the reaction mixture was stirred at 80 °C for 3 h. The solution was poured into ice/water

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(39) Sánchez-Medina, I.; Gerwig, G. J.; Urshev, Z. L.; Kamerling, J. P. *Carbohydr. Res.* **2007**, *342*, 2430–2439.
(40) Wang, H.; Zhang, G.; Ning, J. *Carbohydr. Res.* **2003**, *338*, 1033–1037.
(41) Veeneman, G.; Notermans, S.; Liskamp, R. M. J.; van der Marel, G. M.; van Boom, J. H. *Recl. Trav. Chim. Pays-Bas* **1989**, *108*, 344–350.
(42) Lerner, L. M. *Methods Carbohydr. Chem.* **1972**, *6*, 131–134.

and was diluted with CH_2Cl_2. The organic layer was washed with HCl (5%), water, $NaHCO_3$ (ss), and water, dried (Na_2SO_4), and concentrated. TLC analysis of the syrup showed two products of $R_f = 0.87$ and $R_f = 0.75$ (10:1 hexane/EtOAc). Addition of MeOH (5 mL) to the syrup afforded crystalline compound **4*β*** (0.72 g, 35%). Purification by column chromatography (100:1 hexane/EtOAc) of the mother liquors afforded a second crop of crystals of **4*β*** (0.21 g, 10%, $R_f = 0.87$). Recrystallized from MeOH, compound **4*β*** gave mp 109−111 °C, $[\alpha]_D$ −24 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.15 (d, $J = 2.6$ Hz, 1H, H-1), 4.09 (dd, $J = 2.9$, 4.7 Hz, 1H, H-3), 4.00 (dd, $J = 3.5$, 4.7 Hz, 1H, H-4), 3.92 (apparent t, $J = 2.9$ Hz, 1H, H-2), 3.74 (m, 1H, H-5), 3.67 (dd, $J = 5.1$, 10.1 Hz, 1H, H-6a), 3.55 (dd, $J = 5.8$, 10.1 Hz, 1H, H-6b), 0.90, 0.89, 0.883, 0.881, 0.86 (5 s, $SiC(CH_3)_3$, 45 H), 0.10, 0.09, 0.086, 0.082, 0.07 × 2, 0.069, 0.060, 0.043, 0.041 (9 s, $Si(CH_3)_2$, 30H). ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 102.8, 85.8, 84.4, 79.5, 74.0, 64.7, 25.9−24.7 ($SiC(CH_3)_3$), 17.9−17.8 ($SiC(CH_3)_3$), −4.3−(−5.5) ($Si(CH_3)_2$). Anal. calcd for $C_{36}H_{82}O_6Si_5$ C 57.54, H 11.00. Found C 57.70, H 11.20.

The second fraction from the column $R_f = 0.75$ was identified as **5*β*** (0.87 g, 42%), $[\alpha]_D$ −2 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.41 (d, $J = 7.1$ Hz, 1H, H-1), 3.57 (m, 2H, H-2, 3), 4.00 (d, $J = 2.3$ Hz, 1H, H-4), 3.38 (ddd, $J = 9.3$, 5.4, 2.9 Hz, 1H, H-5), 3.85 (dd, $J = 10.0$, 5.8, 2.9 Hz, 1H, H-6), 3.71 (dd, $J = 10.0$, 5.8 Hz, 1H, H-6′), 0.93, 0.91, 0.905, 0.90, 0.89, 0.88, 0.87 ($SiC(CH_3)_3$, 45H), 0.14, 0.12, 0.116, 0.110, 0.099, 0.095, 0.088, 0.080, 0.068, 0.060, 0.05, 0.04 (30H, $Si(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 98.7, 76.2, 75.2, 74.1, 69.2, 61.6, 26.29, 26.25, 26.22, 26.1, 26.0, 25.9, 25.88, 25.84, 25.79, 25.74, 18.49, 18.40, 18.25, 18.23, 18.1, 18.0, −3.2, −3.54, −3.56, −3.58, −3.75, −3.77, −4.1, −4.42, −4.45.

Method B. To a solution of D-galactose (0.5 g, 2.77 mmol) in dry DMF (14 mL), imidazole (2.74 g, 18.25 mmol) and TBSCl (3.0 g, 20.08 mmol) were added, and the reaction mixture was stirred at room temperature. After 48 h TLC monitoring showed total consumption of the starting material. The reaction solution was treated as described in method A, and the ^{1}H NMR spectrum of the crude showed that **4*β*** was the only product. Addition of MeOH (5 mL) to the syrup gave crystalline **4*β*** (1.29 g, 62%). Column chromatography (100:1 hexane/EtOAc) of the mother liquors afforded a second fraction of **4*β*** (0.36 g, overall yield 79%).

1,2,3,5,6-Penta-*O*-trimethylsilyl-α-D-galactopyranose. Treatment of D-galactose (0.5 g, 2.77 mmol) with TMSCl (3.0 mL, 23.56 mmol), according to method A, afforded a crude product chromatographically homogeneous $R_f = 0.79$ (10:1 hexane/EtOAc), which showed in the ^{1}H NMR ($CDCl_3$, 200 MHz) spectrum anomeric signals with the following integration: δ 5.13 (d, $J = 2.5$ Hz, 0.10H, H-1 α-pyranosic), 5.10 (d, $J = 4.2$ Hz, 0.10H, H-1 α-furanosic), 5.06 (br s, 0.55H, H-1 *β*-furanosic), 4.40 (d, $J = 7.9$ Hz, 0.25H, H-1 *β*-pyranosic). ^{13}C NMR ($CDCl_3$, 50.3 MHz) anomeric region δ 102.4, 98.3, 95.5, 94.5.

Silylation of D-Gal under the conditions of method B (3 h of reaction) gave 1,2,3,5,6-penta-*O*-trimethylsilyl-α-D-galactopyranose (1.38 g, 92%). ^{1}H NMR ($CDCl_3$, 200 MHz) anomeric region δ 5.06 (bs, 1H, H-1). ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 94.5, 72.3, 71.1, 70.5, 69.9, 61.2, in agreement with reported data.[43]

2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-α,*β*-D-galactofuranose (6). To a solution of **4*β*** (0.40 g, 0.53 mmol) in CH_2Cl_2 (15 mL) TFA (2.0 mL) was added, and the mixture was stirred 1 min and immediately poured into a stirred solution of NH_4OH (5.0 mL) in MeOH (40 mL) at −20 °C.[36] The mixture was allowed to reach room temperature and then was partitionated with CH_2Cl_2/H_2O. The organic phase was washed with NaCl (ss), dried (Na_2SO_4), concentrated, and purified by column chromatography (99:1→98:2 hexane/EtOAc). Fractions of $R_f = 0.35$ (10:1 hexane/EtOAc) afforded compound **6** (0.027 g, 8%), as a 0.6:1 α/*β* mixture $[\alpha]_D$ −4.6 (*c* 1.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.07 (d, $J =$ 11.4 Hz, 1H, H-1 *β*-anomer), 5.05 (d, $J = 4.7$, 11.6 Hz, 0.6H, H-1 α-anomer), 4.20−4.18 (m, 1.6H, H-3 α,*β*-anomers), 4.09 (dd, $J = 1.1$, 8.1 Hz, 1H, H-4 *β*-anomer), 4.03−4.00 (m, 1.2H, H-2,4 α-anomer), 3.96 (d, $J = 1.2$ Hz, 1H, H-2 *β*-anomer), 3.86 (d, $J = 11.6$ Hz, 0.6H, OH α-anomer), 3.77 (ddd, $J = 5.3$, 5.3, 8.1 Hz, 1H, H-5 *β*-anomer), 3.73−3.64 (m, 2.2H, H-5, 6 α-anomer, H-6 *β*-anomer), 3.59 (dd, $J = 4.5$, 10.75 Hz, 1H, H-6′ *β*-anomer), 3.57−3.55 (m, 0.6H, H-6′ α-anomer), 3.53 (d, $J = 11.4$ Hz, 1H, HO *β*-anomer), 0.96−0.83 ($SiC(CH_3)_3$), 0.20−0.01 ($Si(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 103.4, 97.2, 90.0, 84.0, 81.9, 81.6, 78.2, 77.6, 73.8, 73.5, 66.2, 63.8, 25.9−25.1 ($SiC(CH_3)_3$), 17.8−17.7 ($SiC(CH_3)_3$), −4.3−(−5.5) ($Si(CH_3)_2$). HRMS (ESI/APCI) calcd for $C_{30}H_{68}O_6Si_4$ $[M + NH_4]^+$ 654.4437, found 654.4459.

General Procedure for the Glycosylation of 4*β* Promoted by Iodotrimethylsilane. A solution of **4*β*** (0.20 g, 0.26 mmol) in anhydrous CH_2Cl_2 (10.0 mL) containing dry 4 Å powdered molecular sieves was cooled to 0 °C and stirred for 10 min under Ar. Then, iodotrimethylsilane (1.2 equiv, 0.042 mL, 0.32 mmol) was added, and the solution was stirred at 0 °C until TLC monitoring showed complete transformation of **4*β*** in two products $R_f = 0.70$ and $R_f = 0.54$ (10:1 hexane/EtOAc). Then, $EtN(iPr)_2$ (0.054 mL, 0.32 mmol) and a solution of the acceptor (1.3 equiv, 0.34 mmol) in CH_2Cl_2 (5.0 mL) were added by syringe, and the stirring was continued until consumption of the components of $R_f = 0.70$ and $R_f = 0.54$. The solution was diluted with CH_2Cl_2, washed with $NaHCO_3$ (ss) and water, dried (Na_2SO_4), and concentrated. The syrup obtained was purified by column chromatography, as indicated in each individual case.

***n*-Butyl 2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-α,*β*-D-galactofuranoside (8).** Compound **8** was obtained according to the general procedure, using *n*-butanol (0.023 g, 27 μL, 0.31 mmol) as acceptor. After purification by column chromatography (99:1 hexane/EtOAc) syrupy compound **10** (0.16 g, 90%) was obtained as an inseparable *β*/α mixture in a 2:1 ratio, which gave $R_f = 0.80$ (10:1 hexane/EtOAc). For the major product (*β*-anomer): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.79 (d, $J = 2.6$ Hz, 1H, H-1), 4.12 (dd, $J = 3.5$, 6.2 Hz, 1H, H-3), 3.98 (dd, $J = 2.5$, 3.5 Hz, 1H, H-2), 3.94 (dd, $J = 2.5$, 6.2 Hz, 1H, H-4), 3.76 (m, 1H, H-5), 3.67(m, 2H, H-6, OCH_2 butyl), 3.57 (dd, $J = 5.8$, 9.9 Hz, 1H, H-6′), 1.54 (m, 2H, CH_2 butyl), 1.37 (m, 2H, CH_2 butyl), 0.91−0.80 (m, 38H, CH_2 butyl and $SiC(CH_3)_3$), 0.10−0.04 (m, 27H, CH_3 butyl and $Si(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 107.9, 84.6, 83.1, 79.7, 73.2, 67.6, 64.5, 31.8, 26.0, 25.9, 25.8, 25.76, 25.72, 19.3, 17.9−17.8 ($SiC(CH_3)_3$), 13.9, 13.8, −3.5, −3.8, −4.0, −4.1, −4.3, −4.5, −4.6, −4.8, −5.2, −5.3, −5.4. For α-anomer, anomeric region: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.84 (d, $J = 3.85$ Hz). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 102.10. Anal. calcd for $C_{34}H_{76}O_5Si_4$, C 60.29, H 11.31. Found C 60.10, H 11.14.

Benzyl 2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-α,*β*-D-galactofuranoside (9). Compound **9** was obtained according to the general procedure using benzyl alcohol (0.033 g, 32 μL, 0.31 mmol) as acceptor. After purification by column chromatography (99:1 hexane/EtOAc) syrupy compound **9** (0.134 g, 69%) was obtained as an inseparable anomeric mixture (*β*/α 6:1), $R_f = 0.73$ (10:1 hexane/EtOAc). For the major product (*β*-anomer): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.36−7.27 (m, aromatic), 4.91 (d, $J = 2.2$ Hz, 1H, H-1), 4.76, 4.46 (2 d, $J = 11.9$ Hz, 2H, CH_2Ph), 4.16 (dd, $J = 3.2$, 6.1 Hz, 1H, H-3), 4.09 (dd, $J = 2.2$, 3.2 Hz, 1H, H-2), 4.02 (dd, $J = 2.9$, 6.1 Hz, 1H, H-4), 3.80 (m, 1H, H-5), 3.72 (dd, $J = 7.6$, 9.8 Hz, 1H, H-6), 3.60 (dd, $J = 5.9$, 9.9 Hz, 1H, H-6′), 0.889, 0.882, 0.87, 0.86 ($SiC(CH_3)_3$), 0.12, 0.10, 0.09, 0.08 ($Si(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 138.1, 128.2, 127.92, 127.89, 127.4, 127.1, 107.3, 84.8, 83.8, 79.7, 73.2, 69.1, 64.6, 26.05, 26.03, 26.00, 25.9, 25.8, 25.77, 25.73, 18.35, 18.32, 18.08, 17.88, 17.85, −3.5, −3.7, −3.95, −3.99, −4.1, −4.4. For the minor product (α-anomer), selected signals: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.90 (partially overlapped with H-1*β*, 1H, H-1), 4.33 (apparent t, $J = 5.5$ Hz, 1H, H-3), 3.98 (dd, $J = 4.0$, 6.1 Hz, 1H, H-2), 3.85 (dd, $J = 3.9$, 5.6 Hz, 1H, H-4). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ

(43) Bhat, A. S.; Gervay-Hague, J. *Org. Lett.* **2002**, *3*, 2081–2084.

100.5, 83.2, 78.9, 76.1, 73.0, 69.1, 64.9. Anal. calcd for $C_{37}H_{74}O_6Si_4$ C 61.10, H 10.26. Found C 61.18, H 10.16.

4-Nitrophenyl 2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranoside (10β). It was prepared according to the general procedure, using 4-nitrophenol (0.05 g, 0.35 mmol) as acceptor. Crude compound **10** was obtained as an anomeric mixture in a 4:1 β/α ratio, as observed by ^{1}H NMR spectroscopy. A fraction enriched in the major β-isomer (**10β**) was isolated by column chromatography (2:1 hexane/chloroform) as a syrup (0.15 g, 75%), $R_f = 0.72$ (10:1 hexane/EtOAc). For the major product (β-anomer): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.18 (d, $J = 7.0$ Hz, 2H, aromatic), 7.08 (d, $J = 7.0$ Hz, 2H, aromatic), 5.52 (d, $J = 3.1$ Hz, 1H, H-1), 4.32 (t, $J = 3.2$ Hz, 1H, H-2), 4.27 (dd, $J = 3.2$, 4.8 Hz, 1H, H-3), 4.12 (dd, $J = 3.4$, 4.8 Hz, 1H, H-4), 3.79 (ddd, $J = 3.3$, 5.5, 7.1 Hz, 1H, H-5), 3.63 (dd, $J = 7.1$, 9.9 Hz, 1H, H-6), 3.58 (dd, $J = 5.5$, 9.9 Hz, 1H, H-6′), 0.95−0.82 (SiC(CH_3)$_3$), 0.10−0.02 (Si(CH_3)$_2$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.2, 142.2, 125.7 × 2, 116.2 × 2 (6C, aromatic), 105.89 (C-1), 85.6 (C-4), 84.00 (C-2), 78.57 (C-3), 73.37 (C-5), 64.23 (C-6), 25.88, 25.81, 25.68, 25.62, 18.2, 18.1, 17.8, 17.7, −3.7, −4.2, −4.3, −4.4, −4.5, −4.7, −5.4, −5.5. Selected signals for the α-anomer: ^{1}H NMR ($CDCl_3$, 500 MHz,) δ 5.43 (d, $J = 4.5$ Hz, 1H, H-1), 4.45 (t, $J = 6.7$, 1H, H-3), 4.22 (dd, $J = 4.5$, 6.7 Hz, 1H, H-2), 4.04 (dd, $J = 2.7$, 6.7 Hz, 1H, H-4), 3.72 (m, 1H, H-5), 3.53 (m, 2H, H-6,6′). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 99.7, 83.2, 78.7, 75.7, 71.4, 63.7. Anal. calcd for $C_{36}H_{71}NO_8Si_4$ C 57.02, H 9.44. Found C 57.34, H 9.46.

2,3,5-Tri-*O*-*tert*-butyldimethylsilyl-1,6-anhydro-α-D-galactofuranose (11). It was isolated by column chromatography (98.6:1.4 hexane/EtOAc) from the crude mixture of glycosides **8**−**10**, yield 8−15%, syrupy compound **11** gave $R_f = 0.52$ (10:1 hexane/EtOAc), $[\alpha]_D$ +42 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.05 (d, $J = 4.5$ Hz, 1H, H-1), 4.20 (d, $J = 1.8$ Hz, 1H, H-3), 4.15 (dd, $J = 1.8$, 4.5 Hz, 1H, H-2), 3.97 (ddd, $J = 4.3$, 6.3, 10.5 Hz, 1H, H-5), 3.91 (br d, $J = 4.0$ Hz, 1H, H-4), 3.72 (ddd, $J = 1.5$, 6.2, 10.5 Hz, 1H, H-6), 3.60 (apparent t, $J = 10.7$ Hz, 1H, H-6′), 0.94−0.86 (SiC(CH_3)$_3$), 0.12−0.04 (Si(CH_3)$_2$). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 98.4, 85.3, 83.2, 77.6, 65.9, 64.2, 25.84, 25.89, 25.6, 17.9, −4.49, −4.57, −4.64, −4.68, −4.93, −5.02. Anal. calcd for $C_{24}H_{52}O_5Si_3$ C 57.09, H 10.38. Found C 56.90, H 10.52.

2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranosyl-(1→3)-2-*O*-benzoyl-5,6-diisopropylidene-D-galactono-1,4-lactone (16). Compound **16** was obtained according to the general procedure, using 2-*O*-benzoyl-5,6-diisopropylidene-D-galactono-1,4-lactone[11j] (**15**, 0.10 g, 0.31 mmol) as acceptor. After purification by column chromatography (49:1→49:3 hexane/EtOAc), fractions of $R_f = 0.31$ (10:1 hexane/EtOAc) afforded compound **16** as a foam (0.18 g, 75%), $[\alpha]_D$ −59 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.07−7.58 (5H, aromatic), 5.86 (d, $J = 7.3$ Hz, 1H, H-2), 4.98 (d, $J = 1.6$ Hz, 1H, H-1′), 4.73 (apparent t, $J = 7.0$ Hz, 1H, H-3), 4.50 (m, 1H, H-5), 4.34 (dd, $J = 2.9$, 6.6 Hz, 1H, H-4), 4.11−4.07 (m, 2H, H-3′,6a), 4.02−4.00 (m, 2H, H-2′,6b), 3.96 (apparent t, $J = 4.6$ Hz, 1H, H-4′), 3.70 (m, 1H, H-5′), 3.58 (m, 2H, H-6′a,b), 0.93−0.86 (SiC(CH_3)$_3$), 0.09−0.04 (Si(CH_3)$_2$). ^{13}C NMR ($CDCl_3$,125.8 MHz) δ 169.2, 164.9, 133.7, 130.1 × 2, 128.6, 128.4 × 2, 110.2, 108.1, 86.6, 83.8, 80.0, 78.8, 76.6, 74.2, 74.0, 73.4, 65.2, 64.7, 26.0, 25.9, 25.7, 25.6, 25.5, 18.3, 18.2, 17.8, 17.3, −3.9, −4.2, −4.4, −4.5, −4.6, −4.9, −5.23, −5.25. Anal. calcd for $C_{46}H_{84}O_{12}Si_4$ C 58.68, H 8.99. Found C 59.11, H 9.04.

2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzoyl-D-galactono-1,4-lactone (18). Compound **18** was obtained according to the general procedure, using 2,3,5-tri-*O*-benzoyl-D-galactono-1,4-lactone[11o] (**17**, 0.156 g, 0.32 mmol) as acceptor. After purification by column chromatography (98:2→95:5 hexane/EtOAc) fractions of $R_f = 0.26$ (10:1 hexane/EtOAc) afforded compound **18** as a foam (0.25 g, 87%), $[\alpha]_D$ −28 (*c* 1.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.15−7.27 (15H, aromatic), 6.07 (d, $J = 5.9$ Hz, 1H, H-2), 5.79 (apparent t, $J = 5.6$ Hz, 1H, H-3), 5.73, (apparent t, $J = 7.1$ Hz, 1H, H-5), 5.04 (apparent d, $J = 5.6$ Hz, 1H, H-4), 4.86 (d, $J = 1.4$ Hz, 1H, H-1′), 4.11 (dd, $J = 2.6$, 5.3 Hz, 1H, H-3′), 4.05 (t, $J = 8.8$ Hz, 1H, H-6a), 3.97 (br s, 1H, H-2′), 3.94 (apparent t, $J = 3.8$ Hz, 1H, H-4′), 3.76 (m, 2H, H-5′, 6b), 3.69 (dd, $J = 5.7$, 10.1 Hz, 1H, H-6′a), 3.57 (dd, $J = 6.0$, 10.1 Hz, 1H, H-6′b), 1.57 (s, 1H), 0.89, 0.88, 0.86, 0.85, 0.84, 0.83 (SiC(CH_3)$_3$), 0.10, 0.09, 0.06, 0.05, −0.001, −0.016 (SiC(CH_3)$_2$). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 168.9, 165.3, 165.2, 164.9, 133.8−128.0 (C-aromatic), 108.0, 105.0, 85.2, 84.1, 79.2, 79.0, 74.0, 73.6, 72.4, 70.6, 64.9, 63.8, 26.04, 26.00, 25.7, 25.6, 18.36, 18.35, 17.8, 17.7, −3.74, −4.1, −4.40, −4.47, −4.5, −4.9. HRMS (ESI/APCI) calcd for $C_{57}H_{88}O_{14}Si_4$ [M + NH_4]$^+$ 1126.5595, found 1126.5560.

2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranosyl-(1→3)-2,5,6-tri-*O*-benzoyl-D-mannono-1,4-lactone (20). Compound **20** was obtained according to the general procedure, using 2,5,6-tri-*O*-benzoyl-D-mannono-1,4-lactone[15e] (**19**, 0.156 g, 0.32 mmol) as acceptor. After purification by column chromatography (95:5 toluene/EtOAc) fractions of $R_f = 0.22$ (10:1 hexane/EtOAc) afforded syrupy compound **20** (0.11 g, 37%), $[\alpha]_D$ −59 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.08−7.32 (15H, aromatic), 6.09 (dd, $J = 3.3$, 4.5 Hz, 1H, H-3), 5.71 (m, 1H, H-5), 5.36 (s, $J < 0.5$ Hz, 1H, H-1′), 4.99 (dd, $J = 2.9$, 9.3 Hz, 1H, H-4), 4.93 (dd, $J = 2.3$, 12.6 Hz, 1H, H-6a), 4.61 (dd, $J = 4.3$, 12.6 Hz, 1H, H-6b), 4.10 (dd, $J = 2.6$, 6.4 Hz, 1H, H-3′), 3.92 (d, $J = 1.5$ Hz, 1H, H-2′), 3.84 (dd, $J = 2.4$, 6.4 Hz, 1H, H-4′), 3.73 (m, 1H, H-5′), 3.66 (dd, $J = 5.6$, 10.2 Hz, 1H, H-6′a), 3.59 (dd, $J = 6.6$, 10.2 Hz, 1H, H-6′b), 0.95−0.81 (SiC(CH_3)$_3$), 0.10−(−0.1) (Si(CH_3)$_2$). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 171.6, 165.9, 164.8, 164.4, 133.3−128.3 (C-aromatic), 107.3, 84.9, 84.8, 79.9, 75.2, 72.8, 71.9, 70.4, 65.2, 62.8, 26.01, 26.00, 25.9, 25.8, 25.71, 25.69, 25.60, 25.5, 18.4, 18.3, 18.2, 17.8, 17.7, 17.6, −3.5, −4.2, −4.4, −4.5, −4.7, −5.1, −5.2, −5.3. Anal. calcd for $C_{57}H_{88}O_{14}Si_4$ C 61.70, H 7.99. Found C 61.47, H 7.92.

2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranosyl-(1→2)-5,6-diisopropylidene-D-galactono-1,4-lactone (22). Compound **22** was obtained according to the general procedure, using 5,6-*O*-isopropylidene-D-galactono-1,4-lactone[44] (**21**, 0.07 g, 0.32 mmol) as acceptor. After purification by column chromatography (4:1 hexane/EtOAc) fractions of $R_f = 0.29$ (3:1 hexane/EtOAc) afforded syrupy compound **22** (0.18 g, 83%) which gave $[\alpha]_D$ −46 (*c* 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.17 (d, $J = 1.3$ Hz, 1H, H-1′), 4.63 (d, $J = 9.2$ Hz, 1H, H-2), 4.56 (apparent t, $J = 8.8$ Hz, 1H, H-3), 4.30 (m, 1H, H-5), 4.17 (m, 2H, H-4′,3′), 4.14 (bs, 1H, H-2′), 4.08 (dd, $J = 6.7$, 8.6 Hz, 1H, H-6a), 4.03 (dd, $J = 4.5$, 8.3 Hz, 1H, H-4), 3.98 (dd, $J = 6.9$, 8.6 Hz, 1H, H-6b), 3.80 (m, 1H, H-5′), 3.65 (m, 2H, H-6′a,b), 1.39 (2s, 6H, C(CH_3)$_2$), 0.91−0.86 (SiC(CH_3)$_3$), 0.10−0.04 (Si(CH_3)$_2$). ^{13}C NMR ($CDCl_3$, 125.8 MHz), δ 170.2, 110.1, 107.2, 85.1, 84.1, 79.1, 78.7, 77.9, 74.6, 72.9, 71.7, 65.0, 64.8, 26.1, 25.96, 25.90, 25.7, 25.6, 25.5, 18.4, 18.2, 17.83, 17.81, −3.7, −4.1, −4.4, −4.5, −4.6, −4.9, −5.2, −5.3. Anal. calcd for $C_{39}H_{80}O_{11}Si_4$ C 55.94, H 9.63. Found C 56.09, H 9.50.

2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranosyl-(1→5)-2,6-di-*O*-benzoyl-D-galactono-1,4-lactone (24) and 2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranosyl-(1→3)-2,6-di-*O*-benzoyl-D-galactono-1,4-lactone (25). 2,6-Di-*O*-benzoyl-D-galactono-1,4-lactone[11n] (**23**, 0.10 g, 0.54 mmol) previously dissolved in anhydrous acetonitrile (6.0 mL) was coupled with **4β** according to the general procedure. After the usual workup, the excess of **23** was removed by treatment of the syrup with ether. Compound **23** was suspended and filtered off, and the soluble material was purified by column chromatography (19:1 toluene/EtOAc). Fractions of $R_f = 0.42$ (19:1 toluene/EtOAc) were evaporated (0.23 g, 87%), and NMR analysis showed the presence of two regioisomers (1:1 ratio). ^{1}H NMR ($CDCl_3$, 500 MHz) selected signals δ 5.92 (d, $J = 2.8$ Hz, 1H, H-2 **25**), 5.91 (d, $J = 3.6$ Hz, 1H, H-2 **24**), 5.11 (d, $J = 1.4$ Hz, 1H, H-1′ **24** or **25**), 5.01 (t, $J = 8.0$ Hz, 1H, H-3 **25**), 4.99 (d, $J = 1.9$ Hz, 1H, H-1′ **24** or

(44) Fleet, G. W. J.; Son, J. C. *Tetrahedron* **1988**, *44*, 2637–2647.

25), 4.88 (dt, J = 5.3, 9.0 Hz, 1H, H-3 **24**). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 168.9, 168.8 (C-1 **24** and **25**), 166.0, 165.0, 165.4, 133.7, 133.6, 133.27, 133.24, 130.2, 130.1, 129.9, 129.79, 129.72, 129.61, 128.47, 128.45, 128.41, 128.3, 108.2, 108.0, 85.7, 84.4, 84.1, 83.9, 79.9, 79.5, 79.1, 78.8, 75.2, 74.7, 73.9, 72.9, 71.5, 70.7, 69.2, 66.5, 65.2, 64.4, 64.1, 62.9, 25.9, 25.87, 25.85, 25.83, 25., 25.64, 25.63, 25.5, 18.3, 18.2, 18.1, 17.8, 17.75, 17.73, 17.71, −3.4, −3.8, −4.1, −4.25, −4.26, −4.27, −4.44, −4.47, −4.6, −4.8, −5.0, −5.2, −5.3, −5.4. Anal. calcd for $C_{50}H_{84}O_{13}Si_4$ C 59.72, H 8.42. Found C 59.87, H 8.53.

Methyl 2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranosyl-(1→3)-2-*O*-benzoyl-5,6-*O*-isopropylidene-β-D-galactofuranoside (27). Methyl 2-*O*-benzoyl-5,6-*O*-isopropylidene-β-D-galactofuranoside (**26**) was obtained by 5,6-*O*-isopropylidenation of methyl β-D-Galf[13b] and further benzoylation with 1.0 equiv of BzCl. Compound **27** was obtained according to the general procedure using **26** (0.11 g, 0.32 mmol) as acceptor. After purification by column chromatography (98:2 toluene/EtOAc) fractions of R_f = 0.21 (10:1 hexane/EtOAc) afforded syrupy compound **27** (0.2 g, 79%), $[\alpha]_D$ −42.2 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.04−7.42 (aromatic), 5.20 (dd, J = 0.9, 4.6 Hz, 1H, H-2), 5.07 (d, J = 1.2 Hz, 1H, H-1′), 5.05 (d, J = 0.9 Hz, 1H, H-1), 4.37 (dd, J = 6.5, 13.2 Hz, 1H, H-5), 4.20 (m, 2H, H-4, 3), 4.11 (dd, J = 2.5, 5.3 Hz, 1H, H-3′), 4.06 (dd, J = 6.8, 8.6 Hz, 1H, H-6a), 4.03 (dd, J = 1.2, 2.5 Hz, 1H, H-2′), 3.93 (dd, J = 3.9, 5.3 Hz, 1H, H-4′), 3.89 (dd, J = 6.3, 8.6 Hz, 1H, H-6b), 3.74 (m, 1H, H-5′), 3.64 (dd, J = 6.1, 10.1 Hz, 1H, H-6′a), 3.56 (dd, J = 5.9, 10.1 Hz, 1H, H-6′b), 3.40 (s, 3H, OCH_3), 1.43, 1.37 (2s, 6H, $C(CH_3)_2$), 0.88, 0.87, 0.86 ($SiC(CH_3)_3$), 0.11, 0.10, 0.08, 0.07, 0.05, 0.045, 0.041 ($Si(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 165.7, 133.3, 129.8, 129.5, 128.3, 108.3, 107.7, 85.2, 84.7, 84.4, 83.0, 79.4, 77.9, 75.9, 73.3, 65.6, 64.8, 54.9, 26.5, 25.98, 25.97, 25.7, 25.6, 25.2, 18.31, 18.30, 17.8, −3.7, −4.1, −4.3, −4.4, −4.5, −4.8, −5.1, −5.2, −5.3. Anal. calcd for $C_{47}H_{88}O_{12}Si_4$ C 58.95, H 9.26. Found C 58.71, H 9.40.

2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranosyl-(1→3)-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (29). Compound **29** was obtained according to the general procedure using 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[45] (**28**, 0.083 g, 0.32 mmol) as acceptor. After purification by column chromatography (49:1→4:1 hexane/EtOAc containing a trace of Et_3N) compound **29** was obtained as a syrup (0.16 g, 69%), which gave R_f = 0.30 (10:1 hexane/EtOAc), $[\alpha]_D$ −39 (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.86 (d, J = 3.7 Hz, 1H, H-1), 4.93 (br s, 1H, H-1′), 4.43 (d, J = 3.7 Hz, 1H, H-2), 4.35−4.28 (m, 3H, H-3, 4, 5), 4.14 (dd, J = 2.0, 6.3 Hz, 1H, H-3′), 4.06 (dd, J = 6.4, 8.5 Hz, 1H, H-6a), 4.01 (dd, J = 5.8, 8.5 Hz, 1H, H-6b), 3.95 (m, 1H, H-4′), 3.94 (m, 1H, H-2′), 3.78 (m, 1H, H-5′), 3.65 (dd, J = 5.3, 10.3 Hz, 1H, H-6′a), 3.61(dd, J = 6.5, 10.3 Hz, 1H, H-6′b), 1.60, 1.49, 1.31, 1.39 (4s, 12H, $C(CH_3)_2$), 0.90−0.87 ($SiC(CH_3)_3$), 0.11−0.05 ($Si(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 111.9, 108.5, 105.4, 105.2, 85.5, 84.9, 81.8, 80.7, 79.9, 76.4, 73.4, 73.0, 66.2, 65.3, 26.8, 26.6, 26.2, 26.1, 26.0, 25.7, 25.6, 25.4, 18.4, 18.3, 17.86, 17.81, −3.6, −4.1, −4.2, −4.4, −4.6, −4.7, −5.23, −5.28. Anal. calcd for $C_{42}H_{86}O_{11}Si_4$ C 57.36, H 9.86. Found C 57.03, H 10.06.

2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (31). Compound **31** was obtained according to the general procedure using 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[46] (**30**, 0.083 g, 0.32 mmol) as acceptor. After purification by column chromatography (49:1→31:1 hexane/EtOAc) compound **31** was obtained as a syrup (0.18 g, 80%), which gave R_f = 0.36 (10:1 hexane/EtOAc), $[\alpha]_D$ −62 (*c* 1.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz), δ 5.51 (d, J = 5.0 Hz, 1H, H-1), 4.86 (d, J = 2.5 Hz, 1H, H-1′), 4.57 (dd, J = 2.3, 7.9 Hz, 1H, H-3), 4.29−4.26 (m, 2H, H-2,4), 4.12 (dd, J = 3.2, 5.5 Hz, 1H, H-3′), 4.01 (dd, J = 2.5, 3.2 Hz, 1H, H-2′), 3.96−3.93 (m, 2H, H-5, 4′), 3.89 (dd, J = 6.2, 10.0 Hz, 1H, H-6a), 3.75 (dt, J = 3.1, 6.1 Hz, 1H, H-5′), 3.67 (dd, J = 6.1, 10.0 Hz, 1H, H-6′a), 3.59−3.52 (m, 2H, H-6b,6′b), 1.61, 1.52, 1.43, 1.33 (4s, 12H, $C(CH_3)_2$), 0.90−0.86 ($SiC(CH_3)_3$), 0.10−0.04 ($Si(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 109.1, 108.4, 108.2, 96.3, 84.2, 84.0, 79.5, 73.6, 71.0, 70.7, 70.6, 67.0, 66.1, 64.7, 26.1, 26.0, 25.9, 25.8, 25.7, 24.9, 24.4, 18.35, 18.31, 17.9, 17.8, −3.7, −4.0, −4.3, −4.4, −4.6, −4.8, −5.2, −5.3. Anal. calcd for $C_{42}H_{86}O_{11}Si_4$ C 57.36, H 9.86. Found C 57.20, H 10.16.

2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranosyl-(1→3)-2-*O*-benzoyl-5,6-diisopropylidene-D-galactofuranose (32). To a solution of bis(2-butyl-3-methyl)borane (4.38 mmol) in anhyd THF (3.0 mL) cooled to 0 °C under argon atmosphere was added a solution of compound **16** (0.41 g, 0.43 mmol) in THF (2.0 mL). The resulting solution was stirred at room temperature for 16 h and then processed as previously described.[42] The organic layer was washed with water, dried (Na_2SO_4), and concentrated. Boric acid was eliminated by coevaporations with MeOH. The syrup obtained was purified by column chromatography (9:1:0.05→6:4:0.05 hexane/EtOAc/Et_3N) to give syrupy compound **32** (0.37 g, 93%), as a 0.85:1 α/β anomeric mixture, R_f = 0.50 (3:1 hexane/EtOAc), $[\alpha]_D$ −14 (*c* 1.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz), only the assigned δ are listed: 5.55 (dd, J = 10.0, 4.5 Hz, 0.46H, H-1α), 5.50 (d, J = 5.3 Hz, 0.54H, H-1β), 5.27 (d, J = 2.0 Hz, 0.54H, H-2β), 5.16 (ddd, J = 0.6, 4.3, 7.2 Hz, 0.46H, H-2α), 5.08 (d, J = 1.5 Hz, 0.54H, H-1′β), 5.02 (d, J = 2.3 Hz, 0.46H, H-1′α), 4.55 (dd, J = 5.6, 7.1 Hz, 0.46H, H-3α), 3.76 (d, J = 10.0 Hz, 0.46H, HO), 3.02 (d, J = 5.3 Hz, 0.54H, HO). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 165.8, 133.4, 133.2, 129.9, 129.8, 129.3, 129.2, 128.3, 128.2, 109.8, 108.9, 107.6, 101.1, 94.4, 87.0, 84.5, 84.2, 83.82, 83.80, 82.2, 80.5, 80.0, 79.8, 79.5, 79.0, 78.9, 76.3, 75.1, 73.9, 72.9, 65.74, 65.71, 65.0, 64.4, 26.4, 26.0, 25.96, 25.92, 25.76, 25.71, 25.66, 25.62, 25.61, 25.5, 18.27, 18.25, 17.8, 17.7, −3.6, −4.1, −4.2, −4.3, −4.4, −4.46, −4.49, −4.8, −4.9, −5.21, −5.23, −5.24, −5.29. Anal. calcd. for $C_{46}H_{86}O_{12}Si_4$ C 58.56, H 9.19. Found C 58.10, H 9.21.

β-D-Galactofuranosyl-3-*O*-α,β-D-galactopyranose (33). A solution of compound **32** (0.10 g, 0.10 mmol) in 3:1:1 HOAc/THF/H_2O (6 mL) was heated at 65 °C for 3 h. After evaporation of the solvent and several co-evaporations with water and toluene, the product was desilylated by treatment with (nBu)$_4$NF (0.34 g, 1.3 mmol)[32] and without purification was debenzoylated with 3 mL of 0.1 M NaOMe at 0 °C. The solution was deionized by elution with MeOH through a column of ion exchange mixed resin. The eluate was evaporated, and the residue was dissolved in water and purified through a RP18 cartridge. Lyophilization of the solution gave compound **33** (0.03 g, 82%) as a 1:1 anomeric mixture, R_f = 0.25 (7:1:2 nPrOH/NH_3/H_2O), $[\alpha]_D$ −32 (*c* 1.3, MeOH). ^{1}H NMR (D_2O, 500 MHz) anomeric region δ 5.25 (d, J = 3.2 Hz, 1H, H-1α), 5.19 (d, J = 1.6 Hz, 1H, H-1′α), 5.18 (d, J = 1.7 Hz, 1H, H-1′β), 4.61 (d, J = 3.2 Hz, 1H, H-1β). ^{13}C NMR (D_2O,125.8 MHz) δ 109.7 (C-1′ α and β anomers), 96.9 (C-1 β anomer), 92.8 (C-1 α anomer), 83.3, 82.0, 81.1, 77.8, 77.4, 77.3, 75.6, 71.6, 71.3, 71.2, 70.9, 69.9, 69.3, 68.0, 63.3, 61.7, 61.5. HRMS (ESI/APCI) calcd for $C_{12}H_{22}O_{11}$ $[M + NH_4]^+$ 360.1506, found 360.1482.

9-Decenyl 2,3,5,6-Tetra-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranosyl-(1→3)-2-*O*-benzoyl-5,6-diisopropylidene-β-D-galactofuranoside (34). To a stirred solution of **32** (0.37 g, 0.39 mmol) and trichloroacetonitrile (0.65 mL, 6.54 mmol) in CH_2Cl_2 (8 mL) cooled to 0 °C was slowly added DBU (63 μL, 0.43 mmol). After 1 h, the solution was carefully concentrated under reduced pressure at room temperature, and the residue was purified by column chromatography (5:2 hexane/EtOAc) to give 356 mg (84%) of the trichloroacetimidate of **32** as a syrup, R_f = 0.75 (5:2 hexane/EtOAc). A stirred suspension of the trichloroacetimidate of **32** (356 mg, 0.33 mmol), 9-decen-1-ol (0.086 mL, 0.49 mmol), and 4 Å powdered molecular sieves (0.5 g) in anhyd CH_2Cl_2 (8 mL) was cooled to −78 °C, and TMSOTf (18 μL, 0.099 mmol) was slowly

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added. After 48 h of stirring at 5 °C, the mixture was quenched by addition of saturated aq $NaHCO_3$ (10 mL) and then extracted with CH_2Cl_2. After purification by column chromatography (5:1 hexane/EtOAc) compound **34** was obtained as a syrup (0.25 g, 71%), R_f = 0.83 (5:2 hexane/EtOAc); $[\alpha]_D$ −49.7 (*c* 0.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.02, 7.56, 7.43 (3H, aromatic), 5.80 (m, 1H, C*H*=CH_2), 5.27 (d, *J* = 1.3 Hz, 1H, H-2), 5.12 (br s, 1H, H-1), 5.08 (d, *J* = 1.5 Hz, 1H, H-1′), 4.98 (m, 1H, CH=CH_aH), 4.92 (m, 1H, CH=CHH_b), 4.27 (dd, *J* = 6.85, 13.7 Hz, 1H, H-5), 4.10 (m, 2H, H-3, 3′), 4.03 (m, 3H, H-6a, 4, 2′), 3.90 (m, 2H, H-6b, 4′), 3.73 (m, 2H, H-5′, CH_aHO), 3.59 (m, 2H, H-6′a, 6′b), 3.45 (m, 1H, CHH_bO). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 165.1, 139.2, 133.2, 129.8, 129.5, 128.3, 114.0, 109.6, 106.8, 105.9, 86.4, 83.9, 83.1, 82.0, 80.6, 79.1, 76.5, 73.9, 67.4, 65.7, 65.0, 63.3, 62.7, 33.7, 32.8, 32.7, 29.6, 29.48, 29.43, 29.3, 29.1, 29.0, 28.93, 28.90, 26.5, 26.03, 26.00, 25.97, 25.91, 25.77, 25.72, 25.6, 18.3, 18.2, 17.8, −3.9, −4.3, −4.47, −4.49, −4.8, −5.25, −5.27, −5.3. Anal. calcd for $C_{56}H_{104}O_{12}Si_4$ C 62.18, H 9.69. Found C 62.54, H 9.79.

9-Decenyl β-D-Galactofuranosyl-3-*O*-β-D-galactofuranoside (35). A solution of compound **34** (0.10 g, 0.093 mmol) in 3:1:1 HOAc/THF/H_2O (6 mL) was heated at 50 °C for 13 h. After evaporation of the solvent and several co-evaporations with water and toluene, the product was desilylated with TBAF in THF[32] and purified by column chromatography (99:1 EtOAc/MeOH). Fractions of R_f = 0.49 (9:1 EtOAc/MeOH) were treated with 3 mL of 0.1 M NaOMe/MeOH at 0 °C, and after 1 h the solution was deionized by elution with MeOH through a column of strongly acidic cation exchange resin (H^+). The syrup obtained was purified by silica gel column chromatography (95:5:0.3 EtOAc/MeOH/TEA) to afford 34 mg (76%) of compound **35**, R_f = 0.62 (7:1:2 *n*PrOH/NH_3/H_2O); $[\alpha]_D$ −134 (*c* 0.7, MeOH). ^{1}H NMR (D_2O, 500 MHz) δ 5.80 (ddt, 1 H, *J* = 17.2, 10.8, 6.8 Hz, 1H, C*H*=CH_2), 5.14 (d, *J* = 1.3 Hz, 1H, H-1′), 4.98 (dd, 1H, *J* = 17.2, 1.4 Hz, CH=CH_aH), 4.96 (br s, 1H, H-1), 4.92 (m, 1H, CH=CHH_b), 4.17−4.15 (m, 2H, H-2, 3), 4.10−4.06 (m, 2H, H-2′, 3′), 4.00−3.99 (m, 1H, H-4), 3.93−3.90 (m, 2H, H-4′, 5), 3.83 (m, 1H, H-5), 3.71−3.64 (m, 5H, H-6a, 6b, 6′a, 6′b, CH_aHO), 3.47 (m, 1H, CH_bHO), 2.04 (dd, *J* = 13.7, 7.2 Hz, 2H, CH_2), 1.6 (m, 2H, CH_2), 1.41−1.32 (m, 10H, CH_2). ^{13}C NMR (D_2O, 125.8 MHz) δ 139.1, 114.2, 107.5, 107.2, 82.8, 82.7, 81.7, 81.5, 79.9, 76.7, 70.6, 70.5, 68.0, 63.3, 62.9. HRMS (ESI/APCI) calcd for $C_{22}H_{40}O_{11}$ $[M + NH_4]^+$ 498.2914, found 498.2905.

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Supporting Information Available: Details on the desilylation, data for the products not included above, ^{1}H NMR and ^{13}C NMR spectra for new compounds are included. This material is available free of charge via the Internet at http://pubs.acs.org.

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