JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Two-Step Synthesis of Per-*O*-acetylfuranoses: Optimization and Rationalization

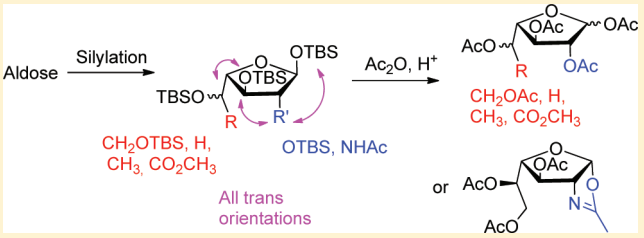
Rémy Dureau,[†,‡] Laurent Legentil,*[,†,‡] Richard Daniellou,[†,‡,§] and Vincent Ferrières*[,†,‡]

[†]Ecole Nationale Supérieure de Chimie de Rennes, CNRS, UMR 6226, Avenue du Général Leclerc, CS 50837, 35708 Rennes Cedex 7, France

[‡]Université Européenne de Bretagne, Rennes, France

Supporting Information

ABSTRACT: A simple two-step procedure yielding peracetylated furanoses directly from free aldoses was implemented. Key steps of the method are (i) highly selective formation of per-*O*-(*tert*-butyldimethylsilyl)furanoses and (ii) their clean conversion into acetyl ones without isomerization. This approach was easily applied to galactose and structurally related carbohydrates such as arabinose, fucose, methyl galacturonate and *N*-acetylgalactosamine to give the corresponding peracetylated targets. The success of this procedure relied on the control of at least three parameters: (i) the tautomeric equilibrium of the starting unprotected oses, (ii) the steric hindrance of both targeted furanoses and silylating agent, and finally, (iii) the reactivity of each soft nucleophile during the protecting group interconversion.



INTRODUCTION

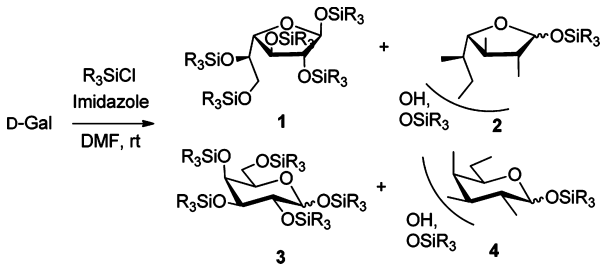
Recent advances in glycobiology have revealed the essential role of furanosyl containing glycoconjugates in crucial biological phenomena such as cell integrity, cell−cell communication, and host−pathogen interactions.[1,2] For example, β-D-galactofuranoside (β-D-Gal*f*), the most abundant form of this family in nature, is a key component of microorganisms like *Mycobacteria*, *Leishmania*, or *Aspergillus* genus. Interestingly, such an entity was proven to be essential for the survival of those pathogenic agents or often responsible for virulence.[3−5] Other structures like arabinofuranosides (Ara*f*) or fucofuranosides (Fuc*f*) were also identified in plants or bacteria, the second one playing a decisive role in host−parasite interactions.[1,2] As opposed to some micro-organisms, mammals do not biosynthesize hexofuranosides making them good candidates for therapeutic developments.[6] Already, uridine 5′-diphospho-D-galactofuranose and its D-fuco- or 6-deoxy-6-fluoro-D-galactofuranose analogues were used to better understand the biological cascade of cell membrane formation, but also as inhibitors of the enzymes involved in their biosynthesis.[7−9] Furthermore, analogues of Gal*f*- or Ara*f*-containing oligosaccharides have proven to be useful detection tools of furanosidases[10] or even new immunomodulators.[11] The majority of these biologically relevant compounds were obtained from the key intermediates per-*O*-ester furanoses. Access to such building blocks is often tricky as it implies to maintain the integrity of the five-membered ring throughout the synthesis. So far, the main protocols that have been reported start from galactose in a direct[12] or three-step[13] strategy. Later, Besra[14] then Baldoni and Marino[15] described an attractive silylation reaction that was only applied to D-Ara and D-Gal, respectively. In this study, we have thoroughly reinvestigated the factors influencing the furanose/pyranose selectivity of the silylation step by performing a screening of chlorosilanes with a wide range of aldoses. Particular attention was given to the initial tautomeric equilibrium, the steric parameters, and the intrinsic reactivity of each protected carbohydrate. On the assumption that silyl ethers are acid-labile groups,[16−20] we were then interested in direct interconversion of such intermediates into per-*O*-acetyl furanoses while maintaining their structural integrity. This strategy relied on a double challenge; (i) the complete silyl ether−acyl protecting group exchange and (ii) the absence of ring expansion.

RESULTS AND DISCUSSION

First, D-galactose (D-Gal), dissolved in dimethylformamide (DMF) in the presence of an excess of imidazole, was submitted to persilylation using electrophiles with increasing hindrance (Table 1). As expected,[15] the smallest trimethylsilyl chloride (TMSCl) exclusively gave the pyranose **3** (entry 1). Remarkably, more or exclusive galactofuranose (Gal*f*) **1** was obtained thanks to the triisopropylsilyl (TIPS) or the *tert*-butyldimethylsilyl (TBS) protecting groups, respectively (entries 2 and 3). It is noteworthy that only the fully protected furanose with the TBS group crystallized out in a pure β-anomeric configuration. Although the total selectivity furanose vs pyranose was maintained, a further increase in the size with bulky *tert*-butyldiphenylsilyl groups (TBDPS, entry 4), however, resulted in a complex mixture of partially silylated

Received: September 16, 2011
Published: December 28, 2011

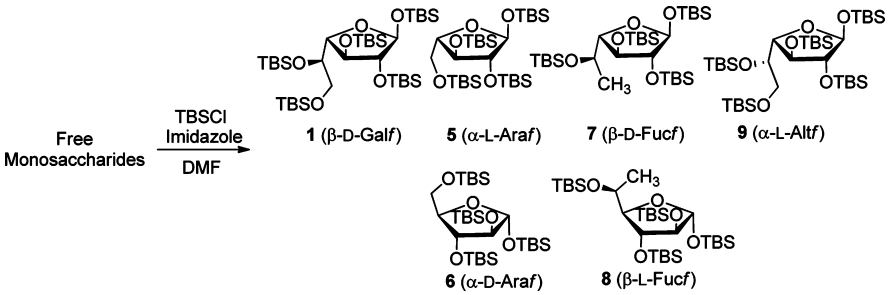
Table 1. Impact of Silylating Reagents



			yield (%)			
entry	silylating agent	time (h)	1	2	3	4
1	TMSCl	3			100	
2[a]	TIPSCl	72	10		50	40
3[b]	TBSCl	48	73			
4[b]	TBDPSCl	72		45[c]		

[a]As determined by ^{1}H NMR. [b]Isolated yield. [c]3-OH/5-OH 3:2.

Table 2. Silylation of Aldoses



						silylated product[b]	
entry	unprotected aldose	temp (°C)	time (h)	conversion[a] (%)	isolated yield (%)	furanose	pyranose
1	D-Xyl	70	2	60		3	2
2	D-Rib	70	2	40		2	3
3	D-Lyx	70	2	10		1	9
4	D-Ara	70	2	70	66	1	0
5	L-Ara	70	2	75	79	1	0
6	D-Gal	20	48	100	73	1	0
7	D-Man	70	2	7		1	14
8	D-Glc	70	2	20		1	4
9	D-All	70	2	0	0	0	1
10	D-Gul	70	2	0	0	0	1
11	D-Fuc	50	2	80	60	1	0
12	L-Fuc	50	2	75	50	1	0
13	L-Alt	70	2	30	17	1	1

[a]Conversion rate of free aldoses into furanoses as determined by ^{1}H NMR. [b]Furanose/pyranose ratio as determined by ^{1}H NMR after workup of the resulting filtrates.

furanoses **2** in 45% yield. The major fraction was elucidated as the 3-OH-1,2,5,6-TBDPS-*β*-furanose and the minor one as an anomeric mixture of 5-OH-1,2,3,6-TBDPS-furanose (see the Supporting Information). Increasing the reaction time or temperature did not allow any isolation of the target. Therefore, steric conflict between bulky TBDPS in adjacent positions should be responsible for the noncompletion of the reaction, and the TBS was the best group to afford the desired per-*O*-silylated Gal*f* intermediate in high yields.

In order to further explore the possible parameters likely to influence the outcome of the silylation, we sought to apply the optimized protocol to a wide range of pentoses and hexoses. Some of them are representative of natural furanosyl-containing conjugates[1] and also present structural similarity with D-Gal (L-Ara, D-Fuc) or with their enantiomer (D-Ara, L-Fuc). Other epimers were also screened including D-xylose (D-Xyl), D-ribose (D-Rib), L-lyxose (L-Lyx), D-mannose (D-Man), D-glucose (D-Glc), D-allose (D-All), D-gulose (D-Gul), and L-altrose (L-Alt). The results showed that complex mixtures of partially to fully protected furanose/pyranose compounds were obtained starting from pentoses D-Xyl, D-Rib, L-Lyx, and hexoses D-Man, D-Glc and L-Alt (Table 2, entries 1−3, 7, 8, and 13). For L-Alt, 1,2,4,6-tetra-*O*-TBS-*β*-L-altropyranose in a $^1C_4$ conformation was identified as the major component as confirmed by NOESY-NMR experiments through correlation spot between 3-OH/H-5 and 3-OH/H-1. Pure 1,2-*trans* persilylated furanose

dx.doi.org/10.1021/jo201913f | J. Org. Chem. 2012, 77, 1301−1307

9 was also isolated in 17% yield. Surprisingly, only the pyranose counterparts were identified starting from D-All and D-Gul (entries 9 and 10). Gratifyingly, aldoses D- and L-Ara and D- and L-Fuc afforded exclusively the expected persilylated furanoses in 50−79% yield (entries 4, 5, 11, and 12), and only the corresponding 1,2-*trans* anomers **5**−**8** crystallized, as for the D-Gal*f* **1**.

This set of experiments showed that the silylation reaction using TBSCl strongly depended on the nature of the aldoses. The targeted furanose forms were efficiently synthesized only from carbohydrates that are structurally very close to Gal*f* and that differ only on the C-4 side arm. Indeed, the Gal*f*, Ara*f*, Alt*f* and Fuc*f* isolated derivatives **1**, **5**-**9** share a common spatial arrangement namely 1,2-, 2,3-, and 3,4-*trans*. This feature could obviously not be addressed in any other class of aldoses and also emphasized the importance of the steric factors previously highlighted. Furthermore, minor differences also impacted drastically the outcome of the reaction since the *S*-configuration at C-5 (L-Alt*f*) led to a furanose/pyranose mixture. These observations were corroborated by applying the procedure to 2-deoxy-D-galactose and to D-fructose (increased hindrance on the anomeric center). In both cases, complex mixtures were obtained (data not shown).

In order to understand the observed selectivity, the evolution of the furanose/pyranose ratio for D-Gal and D-Gul, in DMF-d_7 in presence or absence of imidazole was evaluated by NMR. These two sugars behaved quite differently when silylated; the first one gave furanose exclusively (Table 2, entry 6) while the second formed pyranose (Entry 10). So, both sugars were dissolved in DMF and at first only pyranose predominates (T = 0, Table 3, entries 1 and 4). Then imidazole was added and the ratio pyranose/furanose reached within a few minutes 70/30 (Entry 2) and 100/0 (Entry 5) respectively. These values were equal to the ones obtained after 48 h without imidazole (T = 48, entries 3 and 6). Thus, this set of experiments emphasized the role of the nucleophilic base imidazole as an accelerator of the tautomer equilibrium of saccharides in DMF. These effects could partially explain the exclusive formation of **1** and **5**-**8**. Furthermore, regioselective silylation of galactose at OH-6 was performed[21] and the resulting hemiacetal was analyzed by NMR in DMF in presence of 6 equivalents of imidazole. No shift of equilibrium occurred when compared with the unprotected sugar. Consequently, even if the primary 6-OH position was the first to be silylated, it did not thereafter shift equilibrium in favor of the furanose forms.

Table 3. Effect of Imidazole on the Isomerization of D-Gal and D-Gul

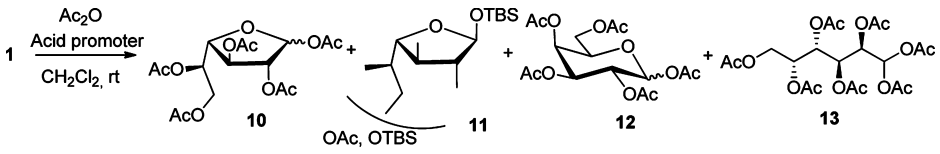
entry	aldose	time[a] (h)	imidazole (equiv)	αp[b] (%)	βp[b] (%)	αf[b] (%)	βf[b] (%)
1	D-Gal	$T = 0$		100			
2	D-Gal	$T = 0$	6	45	24	9	22
3	D-Gal	$T = 48$		30	40	8	22
4	D-Gul	$T = 0$			100		
5	D-Gul	$T = 0$	6	23	77		
6	D-Gul	$T = 48$		20	80		

[a]Equilibrium measured at rt. [b]As determined by ^{13}C NMR.

With this range of persilylated furanoses in hand, a clean one-pot interconversion of all silyl ether groups into acetyl ones without isomerization was sought. Numerous conditions were reported in the literature to selectively transform silyl ether into acetate.[16−20] However, none of them started from silylated hexofuranoses. In this context, different promoters were screened to totally convert **1** into the per-*O*-acetylated galactofuranose **10** (Table 4). Excess sulfuric acid allowed the formation of **10** in moderate 58% yield, but contamination with some peracetylated pyranose **12** and acyclic heptaacetate **13** was observed (entry 1). This linear byproduct was already described in acetylation of diborate galactose mediated by sulfuric acid.[22] Despite shorter reaction times, trifluoromethanesulfonic acid (TfOH) in a catalytic amount gave even more pyranose **12** (entry 2). Gratifyingly, no pyranose formation was observed when the reaction proceeded with an excess of *p*-toluenesulfonic acid (pTSA), and the major products were identified as partially acetylated furanoses **11** (entry 3). Subsequent increased molar ratio of the catalyst and the reaction time led, however, to the desired compound **10** in 83% yield, making these conditions the most suitable so far (entry 4). During the course of this study, a key intermediate was isolated and identified by NMR as the 1,5,6-tri-*O*-acetyl-2,3-di-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranose. The presence of such a structure in the course of the reaction demonstrated the highest nucleophilicity of 1-, 6-, and more importantly, 5-TBS ethers than that observed for 2- and 3-ones. This quick acetylation of position 5 should limit the nucleophilicity of O-5, preventing any isomerization into the pyranose form. Thanks to this two-step procedure, **10** was obtained in 60% yield from D-galactose. This represents a significant improvement compared to previous strategies where **10** was isolated in 49% yield over three steps.[13]

On the assumption of these results, the method was subsequently extended to other per-*O*-TBS furanoses **5**−**9** (Scheme 1). Total conversion of all the silyl groups into the desired acetyl ones was demonstrated for the whole series. As

Table 4. Acetylation of Persilylated Furanoses

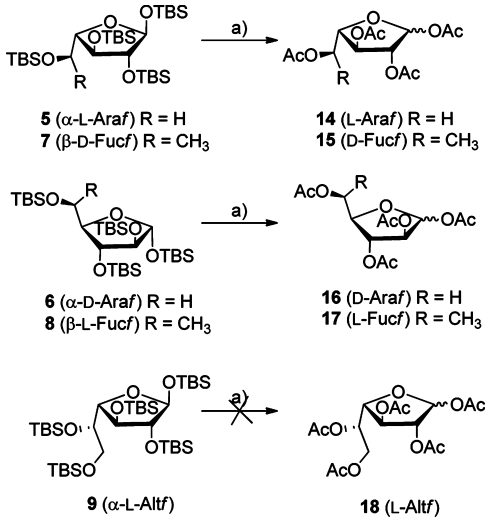


entry	substrate	acid promoter (equiv)	time (h)	products (%)			
1	**1**	H_2SO_4 (10)	1	**10** (58)	**11** (0)	**12** (8, β/α = 4:1[a])	**13** (8)
2	**1**	TfOH (0.1)	0.5	**10** (43)	**11** (0)	**12** (23, β/α = 6:1[a])	**13** (8)
3	**1**	*p*TSA (10)	12	**10** (0)	**11** (70 tetraSi/triSi = 3:2)	**12** (0)	**13** (0)
4	**1**	*p*TSA (20)	72	**10** (83)	**11** (0)	**12** (0)	**13** (0)

[a]Ratio determined by ^1H NMR.

dx.doi.org/10.1021/jo201913f | J. Org. Chem. 2012, 77, 1301−1307

Scheme 1[a]



[a]Conditions: (a) *p*TSA, Ac_2O, CH_2Cl_2, rt, 48 h for **14** and **16**; 24 h for **15** and **17** (61% for **14**; 80% for **15**; 57% for **16**; 84% for **17**).

required, for L- and D-Ara*f*, no trace of pyranose counterparts was found, even after 48 h of reaction. For D- and L-Fuc*f*, the reaction was stopped after only 24 h, and yields reached 80% (**15**) and 84% (**17**), respectively. However, a complex mixture of mainly pyranoses was identified starting from L-Alt **9**. It confirmed the crucial role of hydroxyl at the C-5 position.

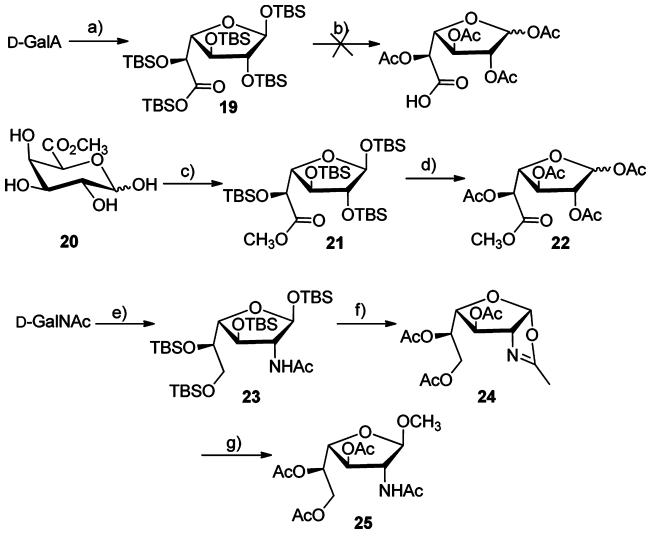
To demonstrate the efficiency and reliability of this methodology, rare oses, namely D-galacturonic acid (GalA) and *N*-acetyl-D-galactosamine (GalNAc), were screened. Galacturonic acid derivatives are the major constituent of pectins,[23] and their furanose counterparts have been proposed as surfactants[10] or substrates for furanosidases.[24] On the other hand, *N*-acetamidogalactofuranose (Gal*f*NAc) was recently found as part of the *O*-specific polysaccharide of *Proteus penneri* strain 22[25] or in capsular polysaccharide from *Campilobacter jejuni* 11168, a Gram-negative bacteria responsible for serious gastroenteritis.[26] Again, selective synthesis of both per-*O*-acetylated furanose remains a challenging task, in particular for Gal*f*NAc, as the only published procedure generated a mixture of Gal*f*NAc and Gal*p*NAc.[27] Thus, the silylation/acetylation procedure was applied to D-GalA and D-GalNAc (Scheme 2).

Starting from D-GalA, the target furanose **19** was obtained in 36% yield. Conversion into the corresponding per-*O*-acyl furanose was, however, unsuccessful, probably due to the formation of highly reactive anhydride at C-6. We then decided to start with methyl galacturonate **20**.[28] Its silylation afforded **21**, which was then easily converted into **22** in 83% yield. In a similar way, starting from D-GalNAc, the corresponding per-*O*-TBS galactofuranosamine **23** was obtained in 31% yield. Subsequent acetylation quantitatively led to the oxazoline **24**. The nucleophilic attack of the *N*-acetamido group on the activated anomeric position is a common feature observed in pyranoses.[29−31] Under certain conditions, an oxazoline can also be a suitable glycosyl donor, as confirmed by the glycosylation of methanol which afforded furanoside **25** in excellent 94% yield.

CONCLUSION

In conclusion, a simple method has been developed to access peracetylated furanoses. It relies first on specific formation of

Scheme 2[a]



[a]Conditions: (a) TBSCl, imidazole, DMF, 50 °C, 2 h, 36%; (b) *p*TSA, Ac_2O, CH_2Cl_2, rt, 24 h; (c) TBSCl, imidazole, DMF, 50 °C, 5 h, 29%; (d) *p*TSA, Ac_2O, CH_2Cl_2, rt, 24 h, 83%; (e) TBSCl, imidazole, DMF, 70 °C, 2 h, 31%; (f) *p*TSA, Ac_2O, CH_2Cl_2, rt; 48 h, 99%; (g) *p*TSA, MeOH, rt, 3 h, 94%.

per-*O*-TBS intermediates directly from aldoses that present all substituent with vicinal *trans* orientation. Subsequent conversion of the TBS groups into acetyl ones was efficiently performed using acetic anhydride as an electrophile and *p*-toluenesulfonic acid as a catalyst, while keeping the integrity of the furanosidic ring. Thus, key furanose building blocks in D-Gal*f*, D/L- Ara*f*, D/L-Fuc*f*, D-Gal*f*A, and D-Gal*f*NAc series are now easily available. It is noteworthy that this two-step strategy complements well the one already proposed for peracetylated Fuc*f*[32] and allowed us both to save eight chemical steps and to significantly increase the yields. It paves the way to easy access to new potential sugar-based bioactive molecules.

EXPERIMENTAL SECTION

General Experimental Details. All reactions were carried out in oven-dried glassware. All reagents were purchased from commercial sources and were used without further purification unless noted. Dichloromethane used was stabilized on amylene and was further distilled on calcium hydride. Unless otherwise stated, all reactions were carried out at room temperature under a positive pressure of nitrogen and were monitored by TLC on silica gel 60 F_{254}. TLC spots were detected under 254 nm light or by staining with cerium ammonium molybdate solution. Column chromatography was performed on silica gel (40−63 μm). Optical rotations were measured at 20 °C. NMR spectra were recorded at 400 MHz for ^1H and 100 MHz for ^{13}C. Chemical shifts are given in δ units (ppm) and referenced to $CDCl_3$ (7.26 ppm). Coupling constants *J* are reported in hertz (Hz). Proton and carbon NMR peaks were unambiguously assigned by COSY (double quantum filtered with gradient pulse for selection), HSQC (gradient echo-anti echo selection and shape pulse) and HMBC (echo-anti echo gradient selection, magnitude mode) correlation experiments. High-resolution mass were measured by electrospray with a MS/MS ZabSpec TOF micromass used *m*-nitrobenzylic alcohol as a matrix and accelerated cesium ions for ionization (Centre Regional des Mesures Physiques de l'Ouest, Université de Rennes 1).

General Procedure A for the Formation of Per-O-TBS-glycofuranoses. To a 0.1 M solution of aldose (1 equiv) in dry DMF was added an appropriate amount of imidazole and *tert*-butyldimethylsilyl chloride. The reaction mixture was stirred at room temperature for 10 min and then heated to the appropriate temperature for 2 h before

dx.doi.org/10.1021/jo201913f | J. Org. Chem. 2012, 77, 1301−1307

placing the mixture at 4 °C overnight. The resulting precipitate was filtered off and then dried under high vacuum to yield the desired per-*O*-TBS-glycofuranose in a 1,2-*trans* configuration.

General Procedure B for the Formation of Per-O-acetylglycofuranoses. Tosic acid was previously recrystallized with neat EtOAc. To a solution of per-*O*-TBS-glycofuranose (1 equiv) and *p*-TsOH (20 equiv) in dry CH_2Cl_2 (5 mL) was added dropwise an appropriate amount of acetic anhydride. The mixture was stirred for an appropriate period at room temperature. The mixture was diluted with CH_2Cl_2 (50 mL), quenched with Et_3N, and then washed with saturated aq $NaHCO_3$ solution (3 × 50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the residue by flash chromatography (cyclohexane/EtOAc 3:2) afforded the described products.

*1,2,3,5,6-Penta-O-tert-butyldimethylsilyl-β-D-galactofuranose (**1c**).* To a 0.1 M solution of D-galactose (1.25 g, 6.94 mmol) in dry DMF were added imidazole (6.8 g, 45.1 mmol) and TBSCl (7.5 g, 50.2 mmol). The reaction mixture was stirred at room temperature for 72 h. The mixture was then placed at 4 °C overnight. The resulting precipitate was filtered off and then dried under high vacuum to yield **1c** (3.82 g, 73%). Physico-chemical properties and spectroscopic data are consistent with the described compound.[15]

*1,2,3,5-Tetra-O-tert-butyldimethylsilyl-α-L-arabinofuranose (**5**).* Compound **5** was prepared from L-arabinose (0.5 g, 3.33 mmol) according to the general procedure A using imidazole (1.13 g, 16.6 mmol) and TBSCl (2.5 g, 16.6 mmol). The reaction was performed at 70 °C. A white solid was obtained (1.60 g, 79%): R_f = 0.6 (cyclohexane/EtOAc, 35:1); mp 86−90 °C; $[\alpha]_D$ −32 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.12 (1H, s, H-1), 4.00 (1H, dt, $J_{4,5a}$ = $J_{4,5b}$ = 5.6 Hz, $J_{3,4}$ = 4.4 Hz, H-4), 3.94−3.91 (2H, m, H-2, H-3), 3.67 (1H, d, H-5a), 3.66 (1H, d, H-5b), 0.89−0.88 [36H, 4s, $C(CH_3)_3$], 0.10−0.07 [24H, 5s, $Si(CH_3)_2$]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 103.9 (C-1), 85.7 (C-4), 85.5 (C-3), 79.3 (C-2), 63.6 (C-5), 63.1 (C-6), 26.1, 25.9, 25.8, 25.7 [$C(CH_3)_3$], 18.4, 18.2, 17.9 [$C(CH_3)_3$], −4.2, −4.5, −4.7, −4.8, −5.2, −5.3 [$Si(CH_3)_2$]; HRMS (ESI$^+$) calcd. for $C_{29}H_{66}O_5Si_4$ [M + Na]$^+$ 629.3880, found 629.3881.

*1,2,3,5-Tetra-O-tert-butyldimethylsilyl-β-D-arabinofuranose (**6**).* Compound **6** was prepared from D-arabinose (0.1 g, 0.67 mmol) according to the general procedure A, using imidazole (0.23 g, 3.35 mmol) and TBSCl (0.6 g, 4.02 mmol). The reaction was performed at 70 °C. A white solid was obtained (0.27 g, 66%). Physico-chemical properties and spectroscopic data are consistent with the described compound.[14]

*1,2,3,5-Tetra-O-tert-butyldimethylsilyl-β-D-fucofuranose (**7**).* Compound **7** was prepared from D-fucose (0.5 g, 3.0 mmol) according to the general procedure A, using imidazole (1.02 g, 15.0 mmol) and TBSCl (2.26 g, 15.0 mmol). The reaction was performed at 50 °C. A white solid was obtained (1.12 g, 60%): R_f = 0.65 (cyclohexane/EtOAc, 35:1); mp 55−58 °C; $[\alpha]_D$ −18 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.13 (1H, s, H-1), 3.89−3.88 (2H, m, H-2, H-3), 3.88−3.81 (2H, m, H-4, H-5), 1.16 (3H, d, *J* = 6.4 Hz, CH_3), 0.89, 0.88, 0.87 [36H, 4s, $C(CH_3)_3$], 0.09, 0.08, 0.07, 0.06, 0.05 [24H, 7s, $Si(CH_3)_2$]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 103.3 (C-1), 90.3 (C-4), 85.2 (C-3), 79.8 (C-2), 69.1 (C-5), 26.0, 25.8, 25.7 [$C(CH_3)_3$], 20.2 (CH_3), 17.9, 17.8 [$C(CH_3)_3$], −4.2, −4.4, −4.5, −4.6, −5.2 [$Si(CH_3)_2$]; HRMS (ESI$^+$) calcd for $C_{30}H_{68}O_5Si_4$ [M + Na]$^+$ 643.4036, found 643.4035.

*1,2,3,5-Tetra-O-tert-butyldimethylsilyl-β-L-fucofuranose (**8**).* Compound **8** was prepared from L-fucose (0.5 g, 3.0 mmol) according to the general procedure A, using imidazole (1.02 g, 15.0 mmol) and TBSCl (2.26 g, 15.0 mmol). The reaction was performed at 50 °C. A white solid was obtained (0.94 g, 50%): R_f = 0.65 (cyclohexane/EtOAc, 35:1); mp 55−58 °C; $[\alpha]_D$ +18 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.13 (1H, s, H-1), 3.89−3.88 (2H, m, H-2, H-3), 3.88−3.81 (2H, m, H-4, H-5), 1.16 (3H, d, ^3J = 6.4 Hz, CH_3), 0.89, 0.88, 0.87 [36H, 4s, $C(CH_3)_3$], 0.09, 0.08, 0.07, 0.06, 0.05 [24H, 7s, $Si(CH_3)_2$]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 103.3 (C-1), 90.3 (C-4), 85.2 (C-3), 79.8 (C-2), 69.1 (C-5), 26.0, 25.8, 25.7 [$C(CH_3)_3$], 20.2 (CH_3), 17.9, 17.8 [$C(CH_3)_3$], −4.2, −4.4, −4.5, −4.6, −5.2 [$Si(CH_3)_2$]; HRMS (ESI$^+$) calcd for $C_{30}H_{68}O_5Si_4$ [M + Na]$^+$ 643.4036, found 643.4036.

*1,2,3,5,6-Penta-O-tert-butyldimethylsilyl-α-L-altrofuranose (**9**).* Compound **9** was prepared from L-altrose (125 mg, 0.69 mmol) according to general procedure A, using imidazole (0.28 g, 4.16 mmol) and TBSCl (0.63 g, 4.16 mmol). The reaction was performed at 70 °C. Purification of the residue by flash chromatography on silica gel (cyclohexane/EtOAc 98:2) afforded the desired product **9** (91 mg, 17%) and a byproduct the **1,2,4,6-tetra-*O*-*tert*-butyldimethylsilyl-β-L-altropyranose** (70 mg, 16%) as amorphous solids.

9: R_f = 0.2 (cyclohexane); $[\alpha]_D$ −21.3 (*c* 1.0 $CHCl_3$); mp 91−94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.09 (1H, s, H-1), 4.12 (1H, dd, $J_{3,4}$ = 4.8 Hz, $J_{2,3}$ = 2.0 Hz, H-3), 4.03 (1H, dd, $J_{4,5}$ = 4.4 Hz, H-4), 3.93 (1H, d, H-2), 3.77 (1H, ddd, $J_{5,6b}$ = 5.6 Hz, $J_{5,6a}$ = 4.4 Hz, H-5), 3.71 (1H, dd, $J_{6a,6b}$ = 10.4 Hz, H-6a), 3.56 (1H, dd, H-6b), 0.89, 0.88 [45H, 4s, $C(CH_3)_3$], 0.09, 0.08, 0.07, 0.04 [30H, 9s, $Si(CH_3)_2$]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 104.0 (C-1), 86.3 (C-2), 85.7 (C-4), 79.2 (C-3), 73.8 (C-5), 64.6 (C-6), 26.1, 26.0, 25.9, 25.8, 25.7 [$C(CH_3)_3$], 18.3, 18.2, 18.0, 17.9, 17.8 [$C(CH_3)_3$], −4.1, −4.5, −4.6, −4.7, −5.2, −5.3 [$Si(CH_3)_2$]; HRMS (ESI$^+$) calcd for $C_{36}H_{82}O_6Si_5$ [M + Na]$^+$ 773.4855, found 773.4853.

1,2,4,6-Tetra-O-tert-butyldimethylsilyl-β-L-altropyranose: R_f = 0.2 (cyclohexane/EtOAc, 98:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.98 (1H, d, $J_{1,2}$ = 1.2 Hz, H-1), 4.07 (1H, dd, $J_{4,5}$ = 9.2 Hz, $J_{3,4}$ = 3.6 Hz, H-4), 3.82 (1H, dd, $J_{2,3}$ = 3.6 Hz, H-3), 3.77 (1H, dd, H-2), 3.76 (1H, dd, $J_{6a,6b}$ = 11.2 Hz, $J_{5,6a}$ = 2.8 Hz, H-6a), 3.72 (1H, dd, $J_{5,6b}$ = 4.0 Hz, H-6b), 3.51 (1H, ddd, H-5), 0.90, 0.89, 0.88 [36H, 4s, $C(CH_3)_3$], 0.11, 0.10, 0.09, 0.08, 0.07, 0.04 [24H, 8s, $Si(CH_3)_2$]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 93.8 (C-1), 74.8 (C-5), 73.0 (C-3), 71.9 (C-2), 65.8 (C-4), 62.8 (C-6), 25.9, 25.8, 25.7 [$C(CH_3)_3$], 18.3, 18.2, 17.9 [$C(CH_3)_3$], −4.1, −4.3, −4.6, −4.7, −4.9, −5.3, −5.5 [$Si(CH_3)_2$]; HRMS (ESI$^+$) calcd. for $C_{30}H_{68}O_6Si_4$ [M + Na]$^+$ 659.3991, found 659.3990.

*1,2,3,5,6-Penta-O-acetyl-D-galactofuranose (**10**).* Compound **10** was prepared from **3** (0.1 g, 0.13 mmol) according to the general procedure B, using acetic anhydride (0.63 mL, 6.65 mmol) and *p*-TsOH (0.49 g, 2.6 mmol). The reaction was stirred for 48 h. An anomeric mixture (α/β 1:5) was obtained as a colorless oil (43 mg, 83%). Physico-chemical properties and spectroscopic data are consistent with the described compound.[33]

*1,2,3,5-Tetra-O-acetyl-L-arabinofuranose (**14**).* Compound **14** was prepared from **5** (0.1 g, 0.16 mmol) according to the general procedure B, using acetic anhydride (0.62 mL, 6.40 mmol) and *p*-TsOH (3.2 g, 0.61 mmol). The reaction was stirred for 48 h. An anomeric mixture (α/β 1:5) was obtained as a colorless oil (31.2 mg, 61%): R_f = 0.43 (cyclohexane/EtOAc, 1:1). **14*α***: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.37 (1H, d, $J_{1,2}$ = 4.0 Hz, H-1), 5.35−5.34 (2H, m, H-2, H-3), 4.41−4.33 (1H, m, H-5a), 4.28−4.18 (2H, m, H-4, H-5b), 2.10, 2.08 (12H, 4s, CH_3CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 170.2, 169.2 (CO), 93.7 (C-1), 79.6 (C-4), 75.2 (C-2), 74.6 (C-3), 64.5 (C-5), 21.0, 20.7 ($COCH_3$). **14*β***: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (1H, s, H-1), 5.21 (1H, dd, $J_{2,3}$ = 1.6 Hz, $J_{1,2}$ = 0.4 Hz, H-2), 5.04 (1H, ddd, $J_{3,4}$ = 4.8 Hz, ^4J = 0.8 Hz, H-3), 4.41−4.33 (2H, m, H-4, H-5a), 4.28−4.18 (1H, m, H-5b), 2.12, 2.11, 2.09 (12H, 3s, CH_3CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 169.9, 169.4, 169.2 (CO), 99.3 (C-1), 82.3 (C-4), 80.5 (C-2), 76.8 (C-3), 63.0 (C-5), 21.0, 20.6, 20.4 ($COCH_3$); HRMS (ESI$^+$) calcd. for $C_{13}H_{18}O_9$ [M + Na]$^+$ 341.0848, found 341.0847. Anal. Calcd for $C_{13}H_{18}O_9$: C, 49.06; H, 5.70. Found: C, 48.85; H, 5.77.

*1,2,3,5-Tetra-O-acetyl-D-fucofuranose (**15**).* Compound **15** was prepared from **7** (0.1 g, 0.16 mmol) according to the general procedure B, using acetic anhydride (0.61 mL, 6.40 mmol) and *p*-TsOH (3.2 g, 0.61 mmol). The reaction was stirred for 24 h. An anomeric mixture (α/β 1:5) was obtained as a colorless oil (42.7 mg, 80%). Physico-chemical properties and spectroscopic data are consistent with the described compound.[32]

*1,2,3,5-Tetra-O-acetyl-D-arabinofuranose (**16**).* Compound **16** was prepared from **6** (0.1 g, 0.16 mmol) according to the general procedure B, using acetic anhydride (0.62 mL, 6.40 mmol) and *p*-TsOH (3.2 g, 0.61 mmol). The reaction was stirred for 48 h. An anomeric mixture (α/β 1:5) was obtained as a colorless oil (28.9 mg,

dx.doi.org/10.1021/jo201913f | J. Org. Chem. 2012, 77, 1301−1307

57%): R_f = 0.43 (cyclohexane/EtOAc, 1:1). **15*α***: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.37 (1H, d, $J_{1,2}$ = 4.0 Hz, H-1), 5.35−5.34 (2H, m, H-2, H-3), 4.41−4.33 (1H, m, H-5a), 4.28−4.18 (2H, m, H-4, H-5b), 2.10, 2.08 (12H, 4s, CH_3CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 170.2, 169.2 (CO), 93.7 (C-1), 79.6 (C-4), 75.2 (C-2), 74.6 (C-3), 64.5 (C-5), 21.0, 20.7 ($COCH_3$). **15*β***: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (1H, s, H-1), 5.21 (1H, dd, $J_{2,3}$ = 1.6 Hz, $J_{1,2}$ = 0.4 Hz, H-2), 5.04 (1H, ddd, $J_{3,4}$ = 4.8 Hz, ^4J = 0.8 Hz, H-3), 4.41−4.33 (2H, m, H-4, H-5a), 4.28−4.18 (1H, m, H-5b), 2.12, 2.11, 2.09 (12H, 3s, CH_3CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 169.9, 169.4, 169.2 (CO), 99.3 (C-1), 82.3 (C-4), 80.5 (C-2), 76.8 (C-3), 63.0 (C-5), 21.0, 20.6, 20.4 ($COCH_3$); HRMS (ESI$^+$) calcd for $C_{13}H_{18}O_9$ [M + Na]$^+$ 341.0848, found 341.0845. Anal. Calcd for $C_{13}H_{18}O_9$: C, 49.06; H, 5.70. Found: C, 49.09; H, 5.67.

*1,2,3,5-Tetra-O-acetyl-L-fucofuranose (**17**).* Compound **17** was prepared from **8** (0.1 g, 0.16 mmol) according to the general procedure B, using acetic anhydride (0.61 mL, 6.44 mmol) and *p*-TsOH (3.2 g, 0.61 mmol). The reaction was stirred for 24 h. An anomeric mixture (α/β 1:4) was obtained as a colorless oil (44.5 mg, 84%): R_f = 0.42 (cyclohexane/EtOAc, 1:1). **18*α***: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30 (1H, d, $J_{1,2}$ = 4.6 Hz, H-1), 5.50 (1H, t, $J_{2,3}$ = $J_{3,4}$ = 6.6 Hz, H-3), 5.30 (1H, dd, H-2), 5.07−5.12 (1H, m, H-5), 3.97 (1H, t, $J_{4,5}$ = 6.6 Hz, H-4), 2.12, 2.09, 2.08, 2.07 (12H, 4s, CH_3CO), 1.21 (3H, d, J = 6.4 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 170.0, 169.5 (C═O), 93.2 (C-1), 82.3 (C-4), 75.6 (C-2), 73.7 (C-3), 69.9 (C-5), 21.2, 20.8, 20.6 (CH_3CO), 15.8 (C-6). **18*β***: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.18 (1H, br s, H-1), 5.17 (1H, dd, $J_{1,2}$ = 1.0, $J_{2,3}$ = 1.8 Hz, H-2), 5.15 (1H, qd, $J_{4,5}$ = 4,6 Hz, $J_{5,6}$ = 6.3 Hz, H-5), 5.08 (1H, dd, $J_{3,4}$ = 5.1 Hz, H-3), 4.21 (1H, dd, H-4), 2.12, 2.11, 2.08 (12H, 4s, CH_3CO), 1.30 (3H, d, H-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 169.9, 169.5, 169.3 (CO), 99.2 (C-1), 84.9 (C-4), 81.0 (C-2), 75.6 (C-3), 68.6 (C-5), 21.2, 21.1, 20.8 (CH_3CO),16.0 (C-6); HRMS (ESI$^+$) calcd for $C_{14}H_{20}O_9$ [M + Na]$^+$ 355.1005, found 355.1005. Anal. Calcd for $C_{14}H_{20}O_9$: C, 50.60; H, 6.07. Found: C, 50.98; H, 6.22.

*tert-Butyldimethylsilyl 1,2,3,5-Tetra-O-tert-butyldimethylsilyl-β-D-galactofuranuronate (**19**).* Compound **19** was prepared from D-galacturonic acid (0.5 g, 2.5 mmol) according to general procedure A, using 1.02 g of imidazole (15.0 mmol) and 2.64 g of TBSCl (17.5 mmol). The reaction was performed at 50 °C. A white solid was obtained (0.70 g, 36%): R_f = 0.41 (cyclohexane/EtOAc, 4:1); $[\alpha]_D$ −23.3 (*c* 1.0, $CHCl_3$); mp 133−137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.22 (1H, d, $J_{1,2}$ = 3.2 Hz, H-1), 4.26 (1H, dd, $J_{3,4}$ = 4.0 Hz, $J_{4,5}$ = 3.2 Hz, H-4), 4.23 (1H, d, H-5), 4.18 (1H, dd, $J_{2,3}$ = 3.6 Hz, H-3), 3.92 (1H, dd, H-2), 0.93, 0.92, 0.88 [45H, 4s, C$(CH_3)_3$], 0.28, 0.27, 0.13, 0.08, 0.07 [30H, 7s, Si$(CH_3)_2$]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2 (CO), 103.2 (C-1), 85.9 (C-4), 85.7 (C-2), 79.4 (C-3), 74.0 (C-5), 25.9, 25.8, 25.7, 25.5 [C$(CH_3)_3$], 18.4, 17.9, 17.8, 17.6 [C$(CH_3)_3$], −4.1, −4.2, −4.3, −4.6, −4.9, −5.2 [Si$(CH_3)_2$]; HRMS (ESI$^+$) calcd for $C_{36}H_{80}O_7NaSi_5$ [M + Na]$^+$ 787.4643, found 787.4641.

*Methyl 1,2,3,5-Tetra-O-tert-butyldimethylsilyl-β-D-galactofuranuronate (**21**).* To a 0.14 M solution of methyl-D-galacturonate[28] (0.58 g, 2.8 mmol) in dry DMF were added imidazole (1.14 g, 16.7 mmol) and TBSCl (2.52 g, 16.7 mmol). The reaction was performed at 50 °C for 5 h. The mixture was then diluted with EtOAc (20 mL) and washed with water (20 mL). The resulting aqueous layer was further extracted with EtOAc (20 mL). The combined organic layers were then washed with water (3 × 20 mL) and brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/toluene 4:1) afforded **21** as a colorless oil (545 mg, 29%): R_f = 0.38 (cyclohexane/toluene, 3:2); $[\alpha]_D$ −39.3 (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (1H, d, $J_{1,2}$ = 1.5 Hz, H-1), 4.32 (1H, d, $J_{5,4}$ = 5.0 Hz, H-5), 4.22 (1H, dd, $J_{3,4}$ = 4.1 Hz, H-4), 4.12 (1H, dd, $J_{2,3}$ = 2.2 Hz, H-3), 3.93 (1H, dd, H-2), 3.72 (3H, s, CO_2CH_3), 0.92, 0.89, 0.88, 0.87 [36H, 4s, C$(CH_3)_3$], 0.11, 0.09, 0.08, 0.07, 0.06, 0.05 [24H, 8s, Si$(CH_3)_2$]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1 (CO), 103.8 (C-1), 86.9 (C-4), 85.6 (C-2), 79.2 (C-3), 73.4 (C-5), 52.0 (CO_2CH_3), 26.0, 25.9, 25.8 [C$(CH_3)_3$], 18.6, 18.1, 18.0, 17.9 [C$(CH_3)_3$], −4.2, −4.3, −4.5, −4.6, −4.8, −5.1 [Si$(CH_3)_2$]; HRMS (ESI$^+$) calcd for $C_{31}H_{68}O_7Si_4$ [M + Na]$^+$ 687.3940, found 687.3934. Anal. Calcd for $C_{31}H_{68}O_7Si_4$: C, 55.97; H, 10.30. Found: C, 56.01; H, 10.18.

*Methyl 1,2,3,5-Tetra-O-acetyl-β-D-galactofuranuronate (**22**).* To a 0.1 M solution of **21** (0.3 g, 0.45 mmol) in CH_2Cl_2 were added acetic anhydride (1.7 mL, 18.04 mmol) and *p*-TsOH (1.7 g, 9.0 mmol). The reaction was stirred at room temperature for 24 h. The mixture was diluted with CH_2Cl_2 (25 mL), quenched with Et_3N, and then washed with saturated aq $NaHCO_3$ solution (3 × 25 mL) and brine (25 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the residue by flash chromatography (cyclohexane/EtOAc 7:3) afforded **22** (141 mg, 83%) as an anomeric mixture (α/β 1:4): R_f = 0.17 (cyclohexane/EtOAc, 7:3). **22*α***: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (1H, d, $J_{1,2}$ = 4.7 Hz, H-1), 5.53 (1H, dd, $J_{3,2}$ = 7.5 Hz, $J_{3,4}$ = 6.4 Hz, H-3), 5.31 (1H, dd, H-2), 5.26 (1H, d, $J_{5,4}$ = 4.7 Hz, H-5), 4.42 (1H, dd, H-4), 3.72 (3H, s, CO_2CH_3), 2.18, 2.09, 2.06 (12H, 4s, CH_3CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 169.8, 169.2 (CO), 167.2 (CO_2CH_3), 98.8 (C-1), 79.5 (C-4), 74.9 (C-2), 73.3 (C-3), 71.6.9 (C-5), 52.8 (CO_2CH_3), 21.1, 20.6, 20.5 (CH_3CO). **22*β***: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (1H, br s, H-1), 5.34 (1H, d, $J_{5,4}$ = 3.4 Hz, H-5), 5.18 (1H, dd, $J_{2,1}$ = 0.6, $J_{2,3}$ = 1.8 Hz, H-2), 5.06 (1H, dd, $J_{3,4}$ = 5.1 Hz, H-3), 4.59 (1H, dd, H-4), 3.75 (3H, s, CO_2CH_3), 2.17, 2.10, 2.09, 2.08 (12H, 4s, CH_3CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 169.9, 169.5, 168.9 (CO), 167.3 (CO_2CH_3), 99.2 (C-1), 83.2 (C-4), 80.5 (C-2), 76.6 (C-3), 70.9 (C-5), 52.9 (CO_2CH_3), 21.0, 20.7, 20.6, 20.5 (CH_3CO); HRMS (ESI$^+$) calcd for $C_{15}H_{20}O_{11}$ [M + Na]$^+$ 399.0903, found 399.0898.

*2-Acetamido-2-deoxy-1,3,5,6-tetra-O-tert-butyldimethylsilyl-D-galactofuranose (**23**).* Compound **23** was prepared from *N*-acetylgalactosamine (1.0 g, 4.52 mmol) according to the general procedure A, using imidazole (2.46 g, 36.2 mmol) and TBSCl (5.45 g, 36.2 mmol). The reaction was performed at 70 °C. A white solid was obtained (0.95 g, 31%): R_f = 0.5 (cyclohexane/EtOAc, 9:1); mp 144−148 °C; $[\alpha]_D$ −3.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.75 (1H, d, $J_{2\text{-NH}}$ = 9.2 Hz, NH), 5.13 (1H, s, H-1), 4.23 (1H, dd, $J_{3,4}$ = 3.6 Hz, $J_{4,5}$ = 2.0 Hz, H-4), 4.21 (1H, d, H-2), 4.01 (1H, d, H-3), 3.83 (1H, ddd, $J_{5,6a}$ = 7.6 Hz, $J_{5,6b}$ = 5.6 Hz, H-5), 3.68 (1H, dd, $J_{6a,6b}$ = 9.6 Hz, H-6a), 3.62 (1H, dd, H-6b), 1.94 (3H, s, $COCH_3$), 0.93, 0.89, 0.88, 0.87 [36H, 4s, C$(CH_3)_3$], 0.16, 0.13, 0.10, 0.09, 0.07, 0.05 [24H, 7s, Si$(CH_3)_2$]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7 (CO), 102.0 (C-1), 85.8 (C-4), 77.9 (C-3), 72.9 (C-5), 63.9 (C-6), 63.4 (C-2), 26.1, 25.9, 25.6 [C$(CH_3)_3$], 23.4 ($COCH_3$), 18.4, 17.8 [C$(CH_3)_3$], −4.0, −4.4, −4.5, −4.8, −5.3, −5.4 [Si$(CH_3)_2$]; HRMS (ESI$^+$) calcd. for $C_{32}H_{71}NO_6Si_4$ [M + Na]$^+$ 700.4256, found 700.4251.

*(3′,5′,6′-Tri-O-acetyl-1′,2′-dideoxy-α-D-galactofuranoso)-4,5-dihydro-2-methyl-[2,1-d]-2-oxazole (**24**).* Compound **24** was prepared from **23** (0.1 g, 0.15 mmol) according to the general procedure B, using acetic anhydride (0.56 mL, 5.98 mmol) and *p*-TsOH (3.0 g, 0.57 mmol). The reaction was stirred for 48 h. Purification of the residue by flash chromatography (CH_2Cl_2/MeOH 95:5) afforded the desired compound as a colorless oil (48 mg, 99%): R_f = 0.2 (CH_2Cl_2/MeOH 95:5); $[\alpha]_D$ −1.2 (*c* 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (1H, d, $J_{1',2'}$ = 5.2 Hz, H-1′), 5.14 (1H, d, $J_{2',3'}$ = 1.2 Hz, H-3′), 5.01 (1H, ddd, $J_{4',5'}$ = 9.2 Hz, $J_{5',6'b}$ = 6.0 Hz, $J_{5',6'a}$ = 3.6 Hz, H-5′), 4.53 (1H, dd, H-2′), 4.33 (1H, dd, $J_{6'a,6'b}$ = 12.4 Hz, H-6′a), 4.19 (1H, d, H-4′), 4.12 (1H, dd, H-6′b), 2.09 (6H, 2s, CH_3CO), 2.07 (3H, s, CH_3), 2.05 (3H, s, CH_3CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 169.8, 169.7 (CO), 167.1 (C-2), 107.3 (C-1′), 84.4 (C-4′), 77.7 (C-3′), 76.4 (C-2′), 69.6 (C-5′), 62.8 (C-6′), 20.8, 20.7 (CH_3CO), 14.3 (CH_3); HRMS (ESI$^+$) calcd. for $C_{14}H_{19}NO_8$ [M + Na]$^+$ 352.1003, found 352.1003.

*1-Methyl-2-acetamido-2-deoxy-3,5,6-tri-O-acetyl-D-galactofuranoside (**25**).* Compound **25** was prepared from **23** (0.1 g, 0.15 mmol). The general procedure B was applied, using acetic anhydride (0.55 mL, 5.90 mmol) and *p*-TsOH (3.0 g, 0.57 mmol). The reaction was stirred for 48 h. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and then washed with saturated aq $NaHCO_3$ solution (3 × 50 mL) and brine (50 mL). The combined organic layers were evaporated, and the resulting residue was dissolved with MeOH (15 mL). Tosic acid (2.8 mg, 0.02 mmol) was then added, and the mixture was stirred for 3 h at room temperature. The solvent was evaporated and the residue

dx.doi.org/10.1021/jo201913f | J. Org. Chem. 2012, 77, 1301−1307

dissolved with CH_2Cl_2 (50 mL). The mixture was washed with saturated aq $NaHCO_3$ solution (3 × 50 mL) and brine (50 mL) and then evaporated under reduced pressure. Purification by flash chromatography (CH_2Cl_2/MeOH 95:5) afforded **22** as a colorless oil (50.3 mg, 94%). Physico-chemical properties and spectroscopic data are consistent with the described compound.[27]

■ ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: laurent.legentil@ensc-rennes.fr; vincent.ferrieres@ensc-rennes.fr.

Present Address

[§]Institut de Chimie Organique et Analytique, Université d'Orléans - CNRS- UMR 6005, Rue de Chartres, 45067 Orléans Cedex 2, France.

■ ACKNOWLEDGMENTS

We are grateful to CNRS and the "Ministère de l'enseignement supérieur et de la recherche" for financial supports, and to the "Centre Regional des Mesures Physiques de l'Ouest (Université de Rennes 1)" for the registration of the mass spectra. We thank a reviewer for useful comments.

■ REFERENCES

(1) Peltier, P.; Euzen, R.; Daniellou, R.; Nugier-Chauvin, C.; Ferrières, V. *Carbohydr. Res.* **2008**, *343*, 1897−1923.
(2) Richards, M.; Lowary, T. *ChemBioChem* **2009**, *10*, 1920−1938.
(3) Rose, N.; Zheng, R.; Pearcey, J.; Zhou, R.; Completo, G.; Lowary, T. *Carbohydr. Res.* **2008**, *343*, 2130−2139.
(4) Seidel, M.; Alderwick, L.; Sahm, H.; Besra, G.; Eggeling, L. *Glycobiology* **2007**, *17*, 210−219.
(5) Kleczka, B.; Lamerz, A.-C.; van Zandbergen, G.; Wenzel, A.; Gerardy-Schahn, R.; Wiese, M.; Routier, F. *J. Biol. Chem.* **2007**, *282*, 10498−10505.
(6) Pedersen, L.; Turco, S. *Cell. Mol. Life Sci.* **2003**, *60*, 259−266.
(7) Dureau, R.; Robert-Gangneux, F.; Gangneux, J.-P.; Nugier-Chauvin, C.; Legentil, L.; Daniellou, R.; Ferrieres, V. *Carbohydr. Res.* **2010**, *345*, 1299−1305.
(8) Peltier, P.; Beláňová, M.; Dianišková, P.; Zhou, R.; Blake Zheng, R.; Pearcey, J.; Joe, M.; Brennan, P.; Nugier-Chauvin, C.; Ferrières, V.; Lowary, T.; Daniellou, R.; Mikušová, K. *Chem. Biol.* **2011**, *17*, 1356−1366.
(9) Eppe, G.; Peltier, P.; Daniellou, R.; Nugier-Chauvin, C.; Ferrières, V.; Vincent, S. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 814−816.
(10) Bordoni, A.; de Lederkremer, R.; Marino, C. *Biorg. Med. Chem.* **2010**, *18*, 5339−5345.
(11) Chlubnova, I.; Filipp, D.; Spiwok, V.; Dvorakova, H.; Daniellou, R.; Nugier-Chauvin, C.; Kralova, B.; Ferrieres, V. *Org. Biomol. Chem.* **2010**, *8*, 2092−2102.
(12) Varela, O.; Marino, C.; de Lederkremer, R. *Carbohydr. Res.* **1986**, *155*, 247−251.
(13) Ferrières, V.; Bertho, J.-N.; Plusquellec, D. *Carbohydr. Res.* **1998**, *311*, 25−35.
(14) Lee, R.; Mikusova, K.; Brennan, P.; Besra, G. *J. Am. Chem. Soc.* **1995**, *117*, 11829−11832.
(15) Baldoni, L.; Marino, C. *J. Org. Chem.* **2009**, *74*, 1994−2003.
(16) Witschi, M.; Gervay-Hague, J. *Org. Lett.* **2010**, *12*, 4312−4315.
(17) Oriyama, T.; Oda, M.; Gono, J.; Koga, G. *Tetrahedron Lett.* **1994**, *35*, 2027−2030.
(18) Ganem, B.; Small, V. *J. Org. Chem.* **1974**, *39*, 3728−3730.
(19) Chandra, K. L.; Saravanan, P.; Singh, V. K. *Tetrahedron Lett.* **2001**, *42*, 5309−5311.
(20) Du, T.-J.; Wu, Q.-P.; Liu, H.-X.; Chen, X.; Shu, Y.-N.; Xi, X.-D.; Zhang, Q.-S.; Li, Y.-Z. *Tetrahedron* **2011**, *67*, 1096−1101.
(21) Boto, A.; Hernández, D.; Hernández, R.; Suárez, E. *J. Org. Chem.* **2006**, *71*, 1938−1948.
(22) Furneaux, R.; Rendle, P.; Sims, I. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2011−2014.
(23) Chlubnova, I.; Sylla, B.; Nugier-Chauvin, C.; Daniellou, R.; Legentil, L.; Kralova, B.; Ferrieres, V. *Nat. Prod. Rep.* **2011**, *28*, 937−952.
(24) Allam, A.; Behr, J.-B.; Dupont, L.; Nardello-Rataj, V.; Plantier-Royon, R. *Carbohydr. Res.* **2010**, *345*, 731−739.
(25) Arbatsky, N.; Shashkov, A.; Mamyan, S.; Knirel, Y.; Zych, K.; Sidorczyk, Z. *Carbohydr. Res.* **1998**, *310*, 85−90.
(26) Poulin, M.; Nothaft, H.; Hug, I.; Feldman, M.; Szymanski, C.; Lowary, T. *J. Biol. Chem.* **2010**, *285*, 493−501.
(27) Rauter, A.; Almeida, T.; Xavier, N. M.; Siopa, F.; Vicente, A.; Lucas, S.; Marques, J.; Ramôa Ribeiro, F.; Guisnet, M.; Ferreira, M. *J. Mol. Catal. A: Chem.* **2007**, *275*, 206−213.
(28) Brown, J. A.; Fry, S. C. *Carbohydr. Res.* **1993**, *240*, 95−106.
(29) Wolfrom, M.; Winkley, M. *J. Org. Chem.* **1966**, *31*, 3711−3713.
(30) Cai, Y.; Ling, C.-C.; Bundle, D. *Org. Lett.* **2005**, *7*, 4021−4024.
(31) Cai, Y.; Ling, C.-C.; Bundle, D. *J. Org. Chem.* **2008**, *74*, 580−589.
(32) Euzen, R.; Ferrières, V.; Plusquellec, D. *J. Org. Chem.* **2005**, *70*, 847−855.
(33) Gelin, M.; Ferrières, V.; Plusquellec, D. *Eur. J. Org. Chem.* **2000**, 1423−1431.