ELSEVIER

Carbohydrate Research 299 (1997) 7–14

CARBOHYDRATE RESEARCH

A convenient synthesis of disaccharides containing furanoside units

Rachel Velty, Thierry Benvegnu, Muriel Gelin, Eric Privat, Daniel Plusquellec *

Laboratoire de Chimie Organique et des Substances Naturelles, associé au CNRS, Ecole Nationale Supérieure de Chimie de Rennes, Avenue du Général Leclerc, F-35700 Rennes, France

Received 26 July 1996; accepted 4 October 1996

Abstract

Pent-4-enyl 2,3,5,6-tetra-*O*-acetyl-D-glycofuranosides were synthesized in a one-pot reaction by a ferric chloride-promoted glycosylation of 4-penten-1-ol with D-glucose, D-mannose, and D-galactose, respectively, in heterogeneous media, followed by in situ acetylation. These *n*-pentenyl glycosides are efficient glycofuranosyl donors and have therefore been used for the subsequent synthesis of various furanosyl–pyranoside type or furanosyl–furanoside type disaccharides related to archaebacterial glycolipids and protozoa glycoconjugates.

Keywords: *n*-Pentenyl furanosides; Glycosidation; Glycosyl donors; Disaccharides; Furanoside units

1. Introduction

Galactofuranosyl residues have been characterized in oligosaccharides and glycoconjugates present in protozoae [1–3], fungi [4], bacteriae [5], and archaebacteriae [6] either as terminal non-reducing units [1,4], as part of the core oligosaccharides [1–3], or as repeating units in the backbone of polysaccharides [5]. Since mammalian cells do not biosynthesize glycoconjugates containing these structural units, galactofuranosyl compounds are strongly antigenic [7]. The synthesis of oligosaccharides containing glycofuranoses may therefore be useful: (i) for understanding the role of such unusual carbohydrates in microorganisms; (ii) for the study of the biosynthesis of furanosyl containing glycoconjugates; and (iii) for the design of antiparasitic drugs and the treatment of diseases caused by *trypanosoma* or *leishmania* species [1].

Some results of our research in the synthesis of simple alkyl furanosides have already been published [8] and we recently described preliminary studies concerning an improved synthetic route to *n*-pentenyl furanosides as glycosyl donors for the synthesis of analogs of archaebacterial glycolipids [9].

We now report full experimental details of the preparation of furanosyl donors and an extension of this work to the synthesis of original disaccharides containing one or two glycofuranose units.

* Corresponding author.

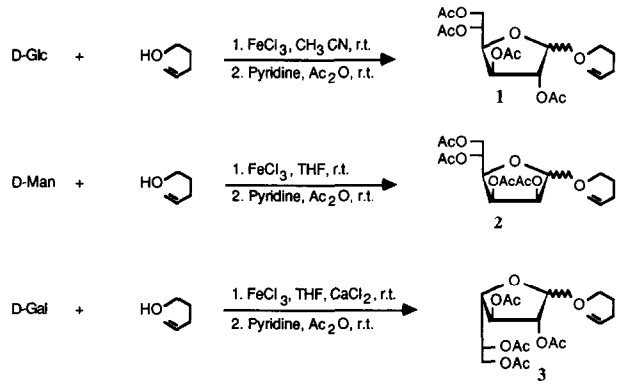
0008-6215/97/$17.00
PII S0008-6215(96)00268-6

2. Results and discussion

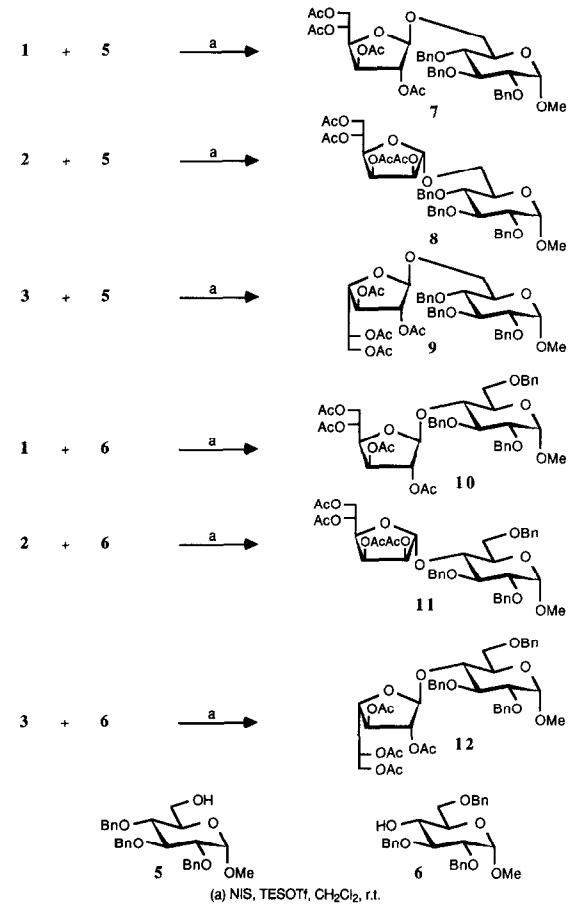
Synthesis of n-*pentenyl furanosides.*—Until now, the formation of an anomeric linkage between a furanose and an aglycone has been difficult to achieve, mainly due to: (i) the lack of an efficient method for obtaining donors in the furanosidic form; and (ii) the instability of furanosyl halides [10]. The recent application of *n*-pentenyl glycoside (NPG) chemistry [11] to galactofuranosides has revealed new perspectives on this synthetic problem [12]. Nevertheless, the Fischer conditions used by Fraser-Reid et al. to prepare *n*-pentenyl galactofuranosides proved some limitation since they led to mixtures of furanosidic and pyranosidic donors which were difficult to purify [12]. Herein, we report the mild coupling of various aldohexoses with 4-penten-1-ol in order to produce *n*-pentenyl glycosides exclusively in the furanoside cyclic form.

The coupling of 4-penten-1-ol with D-glucose, D-galactose, and D-mannose was investigated by using ferric chloride as promoter under heterogeneous conditions in order to avoid self-condensation of the unprotected carbohydrate (Scheme 1).

Glycosylation of 4-penten-1-ol by D-glucose (0.5 equiv) was carried out in acetonitrile at room temperature for 3 h in the presence of ferric chloride (1.5 equiv). The 4-pentenyl glucosides are water-soluble compounds, and work-up of the unprotected glycosides appeared to be difficult. Acetylation was therefore performed in situ. For this purpose, the reaction mixture was quenched with an excess of pyridine (20 equiv); acetic anhydride (6 equiv) was then added and the mixture was stirred for an additional 12 h at room temperature (Scheme 1). After work-up, the peracetylated glucofuranoside **1** was isolated by column chromatography as an inseparable mixture of



Scheme 1. Preparation of the glycofuranosyl donors **1**–**3**.



Scheme 2. Synthesis of furanosyl–pyranoside type disaccharides.

anomers (75% overall yield; $\alpha:\beta = 35/65$ from ^{1}H NMR spectra).

The next step was to ascertain whether this strategy was of general application, particularly in the D-mannose and D-galactose series. The ferric chloride promoted glycosidation of D-mannose in acetonitrile was unsuccessful, as several products were detected. After experimentation, we found that the reaction could be at best performed in tetrahydrofuran at room temperature for 40 h followed by in situ acetylation (vide supra) (Scheme 1). The *n*-pentenyl mannofuranoside **2** was isolated in 56% overall yield ($\alpha:\beta = 90/10$). The major anomer **2**α was obtained by column chromatography.

When an analogous procedure was applied to D-galactose, the reaction afforded, after 54 h at room temperature and in situ acetylation, a mixture of furanosides **3** (53%) and of the corresponding pyranosides **4** (8%) with, however, a net preference for the β-furanoside and the α-pyranoside derivatives, **3**β and **4**α, respectively. We, and others, have pre-

Table 1
^{13}C NMR (100 MHz) chemical shifts for the glycosyl moieties of **7–12** and **15**

Compound	δ (ppm) [a]											
	C-1	C-2	C-3	C-4	C-5	C-6	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′
7 [b]	97.8	80.0	81.8	77.4	69.8	66.2	105.4	80.4	73.4	77.8	68.8	63.1
8 [b]	97.8	79.7	81.4	76.1	69.5	69.0	105.8	75.7	70.5	76.0	68.1	62.7
9 [b]	97.9	79.8	82.0	77.7	69.9	66.4	105.7	81.1	76.3	79.6	69.1	62.7
10 [b]	98.0	79.7	80.7	76.2	69.5	68.3	107.7	80.4	73.1	77.9	68.1	62.8
11 [b]	98.0	79.8	81.9	77.4	69.8	67.1	105.2	75.9	70.6	76.0	68.2	62.8
12 [b]	98.1	80.0	79.9 *	73.5 *	69.9	68.3	105.0	81.6	76.6	80.5	69.4	63.1
15 [c]	106.0	88.3	82.6	80.4	76.2	65.8	105.8	81.1	76.5	80.2	69.4	62.7

[a] Recorded in $CDCl_3$; Signals marked with * may be interchanged.
[b] δ CO 170.7–169.2 ppm, δ Ar 139.0–127.0, δ CH_2Ph 75.1–71.4 ppm, δ CH_3CO 20.9–20.3 ppm, δ OCH_3 55.1 ppm.
[c] See [b] except for δ OCH_3 which is replaced by δ OCH_2 68.2 ppm, δ CH_2 31.8–22.6 ppm, δ CH_3 14.1 ppm.

viously shown that ring expansion from the kinetically favored furanosidic products to the thermodynamically more stable pyranosides could be prevented by complexation of cations from the second row of the periodical classification [8,13]. Accordingly, glycosylation of 4-penten-1-ol with D-galactose (0.5 equiv) was performed in tetrahydrofuran by using ferric chloride (1.5 equiv) as promoter and calcium chloride (0.5 equiv) as additive (Scheme 1). After acetylation, the *n*-pentenyl D-galactofuranoside **3** was isolated in 54% yield as a mixture of anomers ($\alpha:\beta = 40/60$). It is noteworthy that no pyranosides could be evidenced in the reaction mixture. On the basis of NMR studies, we assume that complexing of calcium ions with 5-OH, 6-OH, and the endocyclic oxygen atom of *n*-pentenyl galactofuranoside in an ^2E conformation may prevent any ring expansion to the corresponding pyranoside [14].

In conclusion, the aforementioned results describe a general entry into glycofuranoside donors for glycosidic synthesis. This methodology compares favorably with the recently reported method of Fraser-Reid [12] since: (i) it gives exclusively peracetylated *n*-pentenyl furanosides in a one-pot synthesis from various aldohexoses; (ii) it avoids the use of a large excess of the expensive 4-penten-1-ol; and (iii) it represents, to our knowledge, the first synthesis of the *gluco* and the *manno* derivatives **1**, **2**.

Synthesis of disaccharides bearing furanose units. —In order to extend the scope of our methodology, we next explored the synthesis of disaccharides containing furanosyl units. Glycosidation reactions with monosaccharide acceptors were carried out by use of standard NPG coupling conditions (NIS, 1.3 equiv; TESOTf, 0.3 equiv) [11]. Glycosylation of the 6-OH free acceptor **5** [15] with *n*-pentenyl furanoside donors **1**, **2**, and **3** (Scheme 2) was first checked. The reactions proceeded smoothly and quickly (10–15 min) at room temperature in dichloromethane to provide exclusively β-linked disaccharides **7** (60%) and

Table 2
^1H NMR (400 MHz) chemical shifts for the glycosyl units of **7–12** and **15**

Compound	δ (ppm) [a]											
	H-1	H-2	H-3	H-4	H-5	H-6	H-1′	H-2′	H-3′	H-4′	H-5′	H-6′
7 [b]	4.72	3.54	3.99	3.54	3.71	3.83, 3.72	5.00	4.98	5.38	4.54	5.39	4.57, 4.20
8 [b]	4.58	3.50	4.00	3.50	3.73	3.92, 3.67	5.19	5.19	5.57	4.34	5.25	4.55, 4.00
9 [b]	4.60	3.49	4.00	3.49	3.76	3.87, 3.62	5.03	5.08	4.99	4.27	5.37	4.31, 4.19
10 [b]	4.58	3.53	3.93	3.84	3.75	3.75, 3.64	5.33	4.95	5.28	4.33	5.20	4.35, 3.97
11 [b]	4.60	3.50	3.85–3.98	3.54–3.68	3.68–3.81	3.68–3.81, 3.54–3.68	5.61	5.16	5.49	4.19	5.20	4.50, 3.85–3.98
12 [b]	4.59	3.58	3.79–3.93	3.79–3.93	3.75	3.75, 3.66	5.17	4.90	4.95	4.27	5.14	4.03, 3.79–3.93
15 [c]	5.05	3.98	4.00	4.08	3.76	3.66, 3.38	5.06	5.08	4.99	4.24	5.37	4.31, 4.19

[a] Recorded in $CDCl_3$.
[b] δ Ar 7.40–7.25 ppm, δ CH_2Ph 5.00–4.50 ppm, δ CH_3CO 2.02–1.92 ppm, δ OCH_3 3.36 ppm.
[c] See [b] except for δ OCH_3 which is replaced by δ OCH_2 3.74–3.60 ppm, δ CH_2 1.60–1.19 ppm, δ CH_3 0.87 ppm.

Table 3
^{1}H NMR (400 MHz) ^{1}H–^{1}H coupling constants for the furanosyl moiety of disaccharides **7–12** and **15**

Compound	J (Hz)						
	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'a}$	$J_{5',6'b}$	$J_{6'a,6'b}$
7	< 1 [a]	< 1 [a]	5.3	9.8	1.9	3.8	12.4
8	3.8	nd [b]	4.6	8.6	2.0	6.1	12.2
9	< 1 [a]	2.3	6.1	3.6	4.2	7.4	11.9
10	< 1 [a]	< 1 [a]	4.2	9.6	2.3	4.3	12.5
11	3.6	5.1	4.1	8.6	2.5	6.1	12.2
12	< 1 [a]	1.0	5.1	4.1	5.6	8.1	12.2
15	0.6 (1.6) [c]	1.9 (3.5) [c]	5.6 (3.0) [c]	3.9 (7.0) [c]	nd [b] (nd) [b]	7.3 (nd) [b]	11.9 (nd) [b]

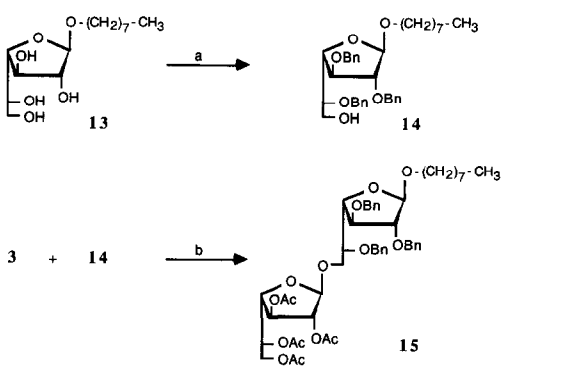
[a] Broad signals.
[b] Not determined.
[c] Coupling constants in brackets of the furanosyl reducing unit of **15**.

9 (58%), respectively, in the *gluco* and the *galacto* series whereas an α-linked disaccharide **8** was obtained from the mannosyl donor **2** (63%). All reactions resulted therefore in the specific formation of 1,2-*trans* glycosides, probably due to the C-2 ester neighboring group participation and independently of the anomeric configuration of the donor.

The glycosylation of the more sterically hindered C-4 hydroxyl group of the acceptor **6** [16] was next investigated (Scheme 2). In the same conditions as previously described, disaccharides **10**, **11**, and **12** were produced with exclusive 1,2-*trans* anomeric configuration and in yields (70–80%) slightly higher than obtained from the primary alcohol **5**. The successful preparation of disaccharide **12** will permit investigation into the synthesis of lecythophorin and chaetiacandin [4].

2D-COSY ^{1}H NMR and ^{1}H–^{13}C correlation spectra allowed the assignment of most of ^{1}H and ^{13}C signals, allowing to ascertain the anomeric configuration of the furanoid rings (Tables 1–3). The low field resonances (δ 105.0–107.7 ppm) observed for the anomeric carbon C-1′ of **7–12** were similar to previously published data [8,17,18]. Moreover, the values obtained for $J_{1',2'}$ < 1 Hz for **7**, **9**, **10**, **12** and $J_{1',2'}$ 3–4 Hz for mannofuranosides **8** and **11** are indicative of a *trans* relationship between H-1′ and H-2′. To our knowledge, compounds **7**, **8**, **10**, and **11** are the first examples of synthetic disaccharides possessing a gluco- or manno-furanose moiety as non-reducing unit.

In order to extend the scope of this methodology, disaccharides composed of two galactofuranose units were then prepared. A (1 → 6) β-D-galactofuranoside dimer was found in natural products, notably as a constituent of archaebacterial lipid membranes [6] or as the terminal unit in the highly immunogenic arabinogalactans [19]. Octyl β-D-galactofuranoside **13** [8] was selected as an appropriate precursor for **15** (Scheme 3). Thus, **13** was converted into octyl 2,3,5-tri-*O*-benzyl-β-D-galactofuranoside **14** via the known tritylation–benzylation–detritylation sequence [20]. Coupling of **3** and **14** in the presence of NIS (1.3 equiv) and TESOTf (0.3 equiv) at room temperature for 15 min afforded, after purification by column chromatography, the disaccharide **15** in 55% yield. No trace of the α-isomer could be observed. The ^{13}C NMR spectrum of **15** showed (Table 1), in the low field region, two close signals (δ 105.8 and 106.0 ppm). In the ^{1}H NMR spectra (Tables 2 and 3), the anomeric protons H-1 and H-1′ appeared, respectively, at δ 5.05 ($J_{1,2}$ 1.6 Hz) and 5.06 ppm ($J_{1',2'}$ 0.6 Hz). These results confirmed the presence of two furanose rings having the β-anomeric configuration [20].



(a) i) 4-Anisylchlorodiphenylmethane, pyridine, DMAP, 50°C; ii) BnBr, NaH, DMF, r.t.; iii) HOAc, H_2O, 70°C; (b) NIS, TESOTf, CH_2Cl_2, r.t.

Scheme 3. Synthesis of a furanosyl–furanoside type disaccharide.

3. Experimental

General methods.—All reactions were performed under nitrogen in an oven-dried glassware. For the coupling reactions, the carbohydrate derivatives were dissolved in a small quantity of toluene and placed under vacuum for 2 h prior to use. All melting points were determined using a Kofler apparatus and are uncorrected. Elemental analyses were made by the Service de Microanalyse de l'ENSCR, Rennes (France). Thin layer chromatography (TLC) was performed on Silica Gel 60 F_{254} non-activated plates (E. Merck). UV light and a soln of 5% H_2SO_4 in EtOH were used to develop the plates. For column chromatography, 60H (5–40 μm) Silica Gel (E. Merck) was used. Optical rotations were measured using a Perkin–Elmer 341 polarimeter. ^1H and ^{13}C NMR spectra were recorded, respectively, at 400 and 100 MHz using a Bruker ARX 400 spectrometer. All reagents were purchased from Acros or Fluka Chemika Co. Acceptors **5**, **6**, and compound **13** were prepared as described previously [8,15,16].

*Pent-4-enyl 2,3,5,6-tetra-*O*-acetyl-α,β-*D*-gluco-furanoside* (**1**).—To a suspension of D-glucose (0.45 g, 2.5 mmol) in dry MeCN (7.5 mL) was added 4-penten-1-ol (0.5 mL, 5 mmol). The soln was cooled to 0 °C before $FeCl_3$ (1.22 g, 7.5 mmol) was added in small portions. The mixture was stirred for 3 h at room temperature under nitrogen followed by the addition of dry pyridine (8 mL, 97.5 mmol) at 0 °C. After stirring for 15 min at room temperature, acetic anhydride (2.8 mL, 30 mmol) was introduced into the reaction mixture at 0 °C. The resulting soln was maintained at room temperature under vigorous stirring overnight before being diluted with CH_2Cl_2 (30 mL), washed with water (20 mL), 5% aq HCl (until discoloration), and satd aq NaCl (20 mL), successively. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by column chromatography (7:3 petroleum ether–EtOAc) afforded **1** (0.78 g, 75%) as a colorless oil containing an inseparable mixture of anomers ($\alpha:\beta = 35/65$ determined from H-3 signal integration), R_f 0.56 (3:2 petroleum ether–EtOAc).

1α: ^1H NMR ($CDCl_3$): δ 5.87–5.74 (m, 1 H, =CH), 5.54 (dd, 1 H, $J_{3,4}$ 5.1, $J_{3,2}$ 2.8 Hz, H-3), 5.27 (d, 1 H, $J_{1,2}$ 4.6 Hz, H-1), 5.28–5.24 (m, 1 H, H-5), 5.07–4.95 (m, 2 H, $=CH_2$), 4.92 (dd, 1 H, H-2), 4.54 (dd, 1 H, $J_{6a,6b}$ 12.2, $J_{6a,5}$ 2.4 Hz, H-6a), 4.38 (dd, 1 H, $J_{4,5}$ 8.9 Hz, H-4), 4.17–4.10 (m, 1 H, H-6b), 3.75–3.44 (m, 2 H, OCH_2), 2.13 (m, 2 H, CH_2), 2.11–2.00 (4 s, 12 H, CH_3CO), 1.71–1.63 (m, 2 H, CH_2); ^{13}C NMR ($CDCl_3$): δ 170.4–169.1 (CO), 137.7 (=CH), 114.9 ($=CH_2$) 100.1 (C-1), 78.2 (C-2), 74.4 (C-3), 73.9 (C-4), 68.0 (C-5), 67.9 (OCH_2), 62.8 (C-6), 29.9 and 28.5 (CH_2), 20.6–20.3 (CH_3CO).

1β: ^1H NMR ($CDCl_3$): δ 5.87–5.74 (m, 1 H, =CH), 5.36 (d, 1 H, $J_{3,4}$ 5.1 Hz, H-3), 5.23–5.21 (m, 1 H, H-5), 5.07–4.95 (m, 2 H, $=CH_2$), 5.00 and 4.98 (2 s, 2 H, H-1, H-2), 4.62 (dd, 1 H, $J_{6a,6b}$ 12.3, $J_{6a,5}$ 2.3 Hz, H-6a), 4.49 (dd, 1 H, $J_{4,5}$ 9.4 Hz, H-4), 4.14 (dd, 1 H, $J_{6b,5}$ 4.9 Hz, H-6b), 3.75–3.44 (m, 2 H, OCH_2), 2.13 (m, 2 H, CH_2), 2.11–2.00 (4 s, 12 H, CH_3CO), 1.71–1.63 (m, 2 H, CH_2); ^{13}C NMR ($CDCl_3$): δ 170.4–169.1 (CO), 137.8 (=CH), 114.9 ($=CH_2$), 106.2 (C-1), 80.1 (C-2), 77.9 (C-4), 73.2 (C-3), 68.6 (C-5), 67.5 (OCH_2), 63.1 (C-6), 29.9 (CH_2), 28.4 (CH_2), 20.6–20.3 (CH_3CO). Anal. Calcd for $C_{19}H_{28}O_{10}$ (mixture of anomers): C, 54.80; H, 6.78. Found: C, 54.40; H, 6.77.

*Pent-4-enyl 2,3,5,6-tetra-*O*-acetyl-α-*D*-manno-furanoside* (**2**).—To a suspension of D-mannose (0.45 g, 2.5 mmol) in dry THF (9 mL) was added 4-penten-1-ol (0.5 mL, 5 mmol) and $FeCl_3$ (1.22 g, 7.5 mmol) at 0 °C. The mixture was stirred for 40 h at room temperature under nitrogen followed, as for **1**, by the addition of dry pyridine (8 mL, 97.5 mmol) and Ac_2O (2.8 mL, 30 mmol) at 0 °C. The same procedure (stirring overnight, work-up, and column chromatography) was then applied to give anomer **2α** (0.52 g, 50%) as a colorless oil; $[\alpha]_D^{20}$ +102° (*c* 1, CH_2Cl_2); R_f 0.4 (3:2 petroleum ether–EtOAc); ^1H NMR ($CDCl_3$): δ 5.80 (m, 1 H, =CH), 5.57 (t, 1 H, H-3), 5.27 (ddd, 1 H, H-5), 5.18 (dd, 1 H, $J_{2,3}$ 5.1 Hz, H-2), 5.10 (d, 1 H, $J_{1,2}$ 2.9 Hz, H-1), 5.02–4.97 (m, 2 H, $=CH_2$), 4.56 (dd, 1 H, $J_{6a,6b}$ 12.2, $J_{6a,5}$ 2.3 Hz, H-6a), 4.38 (dd, 1 H, $J_{4,5}$ 8.8 Hz, H-4), 4.14 (dd, 1 H, $J_{6b,5}$ 5.6 Hz, H-6b), 3.69–3.47 (2 dt, 2 H, OCH_2), 2.11 (m, 2 H, CH_2), 2.07–2.01 (4 s, 12 H, CH_3CO), 1.71–1.64 (m, 2 H, CH_2); ^{13}C NMR ($CDCl_3$): δ 170.2–169.0 (CO), 137.6 (=CH), 114.7 ($=CH_2$), 104.7 (C-1), 76.0 (C-2), 75.3 (C-4), 70.3 (C-3), 67.9 (C-5), 67.7 (OCH_2), 62.6 (C-6), 29.8 (CH_2), 28.3 (CH_2), 20.4–20.0 (CH_3CO). Anal. Calcd for $C_{19}H_{28}O_{10}$: C, 54.80; H, 6.78. Found: C, 55.01; H, 6.96.

*Pent-4-enyl 2,3,5,6-tetra-*O*-acetyl-α,β-*D*-galacto-furanoside* (**3**).—To a suspension of D-galactose (0.9 g, 5 mmol) and $CaCl_2$ (0.56 g, 5 mmol) in dry THF (7.5 mL) was added 4-penten-1-ol (1 mL, 10 mmol). The soln was cooled to 0 °C before adding $FeCl_3$ (2.43 g, 15 mmol) by small portions. The mixture was stirred for 62 h at room temperature under

nitrogen followed by the addition of dry pyridine (16 mL, 195 mmol) at 0 °C and, after stirring for 15 min at room temperature, Ac_2O (5.7 mL, 60 mmol) was added. The resulting soln was maintained at room temperature under vigorous stirring overnight. Following the same work-up as described for **1**, compound **3** (1.12 g, 54%) was isolated after column chromatography (7:3 petroleum ether–EtOAc) as a colorless oil and as an inseparable mixture of anomers ($\alpha:\beta = 40/60$ from H-5 signal integration) [12], R_f 0.46 (3:2 petroleum ether–EtOAc).

3α: ^{1}H NMR ($CDCl_3$): δ 5.86–5.75 (m, 1 H, =CH), 5.60 (dd, 1 H, H-3), 5.21 (m, 1 H, H-5), 5.17 (d, 1 H, $J_{1,2}$ 4.6 Hz, H-1), 5.06–4.94 (m, 3 H, H-2, $=CH_2$), 4.34 (m, 1 H, H-6a), 4.15 (m, 1 H, H-6b), 3.75–3.34 (m, 2 H, OCH_2), 2.15–2.08 (m, 2 H, CH_2), 2.14–2.05 (4 s, 12 H, CH_3CO), 1.73–1.61 (m, 2 H, CH_2); ^{13}C NMR ($CDCl_3$): δ 170.2–169.4 (CO), 137.7 (=CH), 114.7 ($=CH_2$), 99.4 (C-1), 77.3 (C-4), 76.5 (C-2), 73.4 (C-3), 70.5 (C-5), 67.5 (OCH_2), 62.0 (C-6), 29.8 (CH_2), 28.3 (CH_2), 20.6–20.3 (CH_3CO).

3β: ^{1}H NMR ($CDCl_3$): δ 5.86–5.75 (m, 1 H, =CH), 5.38 (m, 1 H, H-5), 5.06–4.94 (m, 4 H, H-1, H-2, $=CH_2$), 4.36–4.32 (m, 1 H, H-6a), 4.26–4.19 (m, 2 H, H-4, H-6b), 3.75–3.34 (m, 2 H, OCH_2), 2.15–2.08 (m, 2 H, CH_2), 2.14–2.05 (m, 12 H, CH_3CO), 1.73–1.61 (m, 2 H, CH_2); ^{13}C NMR ($CDCl_3$): δ 170.2–169.4 (CO), 137.7 (=CH), 114.8 ($=CH_2$), 105.2 (C-1), 81.1 (C-2), 79.6 (C-4), 76.3 (C-3), 69.0 (C-5), 66.7 (OCH_2), 62.4 (C-6), 29.9 (CH_2), 28.3 (CH_2), 20.6–20.3 (CH_3CO). Anal. Calcd for $C_{19}H_{28}O_{10}$ (mixture of anomers): C, 54.80; H, 6.78. Found: C, 54.69; H, 6.84.

General procedure for the synthesis of disaccharides **7 – 12** and **15**.—To a soln of the glycosyl acceptor (0.1 M, 0.8 equiv) and of the pentenyl glycoside (1.0 equiv) in dry dichloromethane at room temperature was added *N*-iodosuccinimide (NIS, 1.3 equiv) followed by triethylsilyl trifluoromethanesulfonate (TESOTf, 0.3 equiv). The mixture was stirred under nitrogen until TLC analysis indicated complete disappearance of the starting acceptor (10–15 min). Several drops of Et_3N were added to the reaction mixture until it turned into a yellow soln. The resulting soln was diluted with CH_2Cl_2 and was washed successively with 10% aq $Na_2S_2O_3$, 0.5% aq HCl (until neutral pH), and satd aq NaCl. The combined organic layers were dried over $MgSO_4$ and the solvent was removed in vacuo. The crude residue was then subjected to flash column chromatography.

Methyl 6-O-(2,3,5,6-tetra-O-acetyl-β-D-glucofuranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (**7**).—From **5** (0.4 g, 0.86 mmol) and **1** (0.45 g, 1.08 mmol). The crude product was subjected to flash column chromatography using a 3:2 to 1:1 petroleum ether–Et_2O step-gradient mixture to provide disaccharide **7** (0.4 g, 60%) as a colorless oil; $[\alpha]_D^{20}$ +16° (*c* 1, CH_2Cl_2); R_f 0.3 (2:3 petroleum ether–Et_2O). Anal. Calcd for $C_{42}H_{50}O_{15}$: C, 63.47; H, 6.34. Found: C, 63.10; H, 6.44.

Methyl 6-O-(2,3,5,6-tetra-O-acetyl-α-D-mannofuranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (**8**).—From **5** (0.4 g, 0.86 mmol) and **2** (0.45 g, 1.08 mmol). The crude product obtained after work-up was subjected to flash column chromatography using 7:3 petroleum ether–Et_2O to provide disaccharide **8** (0.43 g, 63%) as a white amorphous solid; $[\alpha]_D^{20}$ +99° (*c* 1, CH_2Cl_2); R_f 0.34 (3:7 petroleum ether–Et_2O). Anal. Calcd for $C_{42}H_{50}O_{15}$: C, 63.47; H, 6.34. Found: C, 63.42; H, 6.37.

Methyl 6-O-(2,3,5,6-tetra-O-acetyl-β-D-galactofuranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (**9**).—From **5** (0.42 g, 0.91 mmol) and **3** (0.47 g, 1.13 mmol). The crude product was subjected to flash column chromatography using a 3:2 to 1:1 petroleum ether–Et_2O step-gradient mixture to provide disaccharide **9** (0.58 g, 58%) as a colorless oil; $[\alpha]_D^{20}$ +11° (*c* 1, CH_2Cl_2); R_f 0.24 (2:3 petroleum ether–Et_2O). Anal. Calcd for $C_{42}H_{50}O_{15}$: C, 63.47; H, 6.34. Found: C, 63.69; H, 6.43.

Methyl 4-O-(2,3,5,6-tetra-O-acetyl-β-D-glucofuranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**10**).—From **6** (0.4 g, 0.86 mmol) and **1** (0.45 g, 1.08 mmol). Chromatography of the crude residue using 1:1 petroleum ether–Et_2O provided the disaccharide **10** (0.48 g, 70%) as an amorphous solid; $[\alpha]_D^{20}$ +28° (*c* 1, CH_2Cl_2); R_f 0.29 (2:3 petroleum ether–Et_2O). Anal. Calcd for $C_{42}H_{50}O_{15}$: C, 63.47; H, 6.34. Found: C, 63.27; H, 6.40.

Methyl 4-O-(2,3,5,6-tetra-O-acetyl-α-D-mannofuranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**11**).—From **6** (0.45 g, 0.96 mmol) and **2** (0.5 g, 1.20 mmol). Chromatography of the crude residue using 19:1 CH_2Cl_2–acetone provided the disaccharide **11** (0.61 g, 80%) as a white solid; mp 162–165 °C; $[\alpha]_D^{20}$ +99° (*c* 1, CH_2Cl_2); R_f 0.23 (3:7 petroleum ether–Et_2O). Anal. Calcd for $C_{42}H_{50}O_{15}$: C, 63.47; H, 6.34. Found: C, 63.20; H, 6.40.

Methyl 4-O-(2,3,5,6-tetra-O-acetyl-β-D-galactofuranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**12**).—From **6** (0.18 g, 0.38 mmol) and **3** (0.2 g, 0.48 mmol). Chromatography of the crude residue using 2:3 petroleum ether–Et_2O provided disaccha-

ride **12** (0.24 g, 80%) as a yellow oil; $[\alpha]_D^{20}$ +28° (*c* 1, CH_2Cl_2); R_f 0.28 (2:3 petroleum ether–Et_2O). Anal. Calcd for $C_{42}H_{50}O_{15}$: C, 63.47; H, 6.34. Found: C, 63.27; H, 6.33.

Octyl 2,3,5-tri-O-benzyl-β-D-galactofuranoside (**14**).—Octyl β-D-galactofuranoside (**13**) [8] (0.4 g, 1.37 mmol) and DMAP (0.02 g, 0.14 mmol) were dissolved in dry pyridine (10 mL). 4-Anisylchlorodiphenylmethane (MMTrCl) (0.46 g, 1.50 mmol) was added at 0 °C and the reaction mixture was stirred at room temperature for 64 h. The soln was coevaporated with toluene and the residue was subjected to column chromatography (4:1 CH_2Cl_2–acetone) to afford the corresponding 6-*O*-tritylated compound (0.43 g, 56%). To a soln of this compound (0.37 g, 0.66 mmol) in dry DMF (6 mL), was added sodium hydride (60% dispersion in mineral oil, 0.16 g, 3.96 mmol) at 0 °C. After stirring for 15 min, benzyl bromide (0.47 mL, 3.96 mmol) was introduced dropwise. The reaction mixture was stirred for 3 h. MeOH (2 mL) was added and the mixture was evaporated to dryness. The residue was redissolved in CH_2Cl_2 (150 mL), extracted with water (3 × 20 mL) and brine (20 mL), dried ($MgSO_4$), evaporated, and chromatographed on silica gel using a 19:1 to 85:15 petroleum ether–Et_2O step-gradient mixture to give a yellow oil (0.46 g, 84%). Part of this oil (0.20 g, 0.24 mmol) was dissolved in AcOH (2 mL) and heated to 70 °C. Water (0.5 mL) was then added dropwise. This soln was stirred at 70 °C for 5 h, coevaporated with EtOH (4 × 5 mL) and chromatographed on silica gel using CH_2Cl_2 and then a 49:1 CH_2Cl_2–acetone mixture to provide **14** (0.096 g, 71%) as a yellow oil; $[\alpha]_D^{20}$ −46° (*c* 1, CH_2Cl_2); R_f 0.21 (CH_2Cl_2); ^1H NMR (CD_3OD): δ 7.36–7.21 (m, 15 H, CH–Ar), 5.00 (s, 1 H, H-1), 4.69–4.30 (m, 6 H, CH_2Ph), 4.11 (dd, 1 H, $J_{4,5}$ 6.8, $J_{4,3}$ 3.7 Hz, H-4), 3.98–3.94 (m, 2 H, H-3, H-2), 3.74–3.64 (m, 3 H, H-5, OCH_2), 3.60 (dd, 1 H, $J_{6a,5}$ 5.8 Hz, H-6a), 3.39 (m, 1 H, $J_{6b,6a}$ 9.6, $J_{6b,5}$ 6.4 Hz, H-6b), 1.60–1.53 (m, 2 H, CH_2), 1.36–1.28 (m, 10 H, CH_2), 0.89 (t, 3 H, CH_3); ^{13}C NMR (CD_3OD): δ 139.7–128.7 (Ar), 107.3 (C-1), 89.4 (C-2), 84.2 (C-3), 82.0 (C-4), 80.1 (C-5), 74.3–72.8 (CH_2Ph), 68.5 (OCH_2), 62.8 (C-6), 33.0–23.7 (CH_2), 14.5 (CH_3). Anal. Calcd for $C_{35}H_{46}O_6$: C, 74.70; H, 8.24. Found: C, 75.04; H, 8.47.

Octyl 6-O-(2,3,5,6-tetra-O-acetyl-β-D-galactofuranosyl)-2,3,5-tri-O-benzyl-β-D-galactofuranoside (**15**).—From **14** (0.11 g, 0.19 mmol) and **3** (0.10 g, 0.24 mmol) as previously described. The crude product was purified by flash chromatography using a 3:2 to 2:3 petroleum ether–Et_2O step-gradient mixture to provide disaccharide **15** (0.1 g, 55%) as a pale yellow oil; $[\alpha]_D^{20}$ −50° (*c* 1, CH_2Cl_2); R_f 0.45 (2:3 petroleum ether–Et_2O). Anal. Calcd for $C_{49}H_{64}O_{15}$: C, 65.90; H, 7.22. Found: C, 66.30; H, 7.39.

Acknowledgements

We are grateful to the CNRS and the Region Bretagne for a grant to R.V.; to M. Lefeuvre and C. Penverne for assistance, respectively, in NMR experiments and microanalyses; and to N. Voisin for typing this manuscript.

References

[1] R.M. de Lederkremer and W. Colli, *Glycobiology*, 5 (1995) 547–552.
[2] S. Merello, M.T. Xavier, and A.J. Parodi, *Molec. Biochem. Parasitol.*, 69 (1995) 73–79.
[3] (a) M.J. McConville and A. Bacic, *Molec. Biochem. Parasitol.*, 38 (1990) 57–68; (b) M.J. McConville, S.W. Homans, J.E. Thomas-Oates, A. Dell, and A. Bacic, *J. Biol. Chem.*, 265 (1990) 7385–7394.
[4] W.A. Ayer and N. Kawahara, *Tetrahedron Lett.*, 36 (1995) 7953–7956.
[5] M. Nagaoka, S. Hashimoto, H. Shibata, I. Kimura, K. Kimura, H. Sawada, and T. Yokokura, *Carbohydr. Res.*, 281 (1996) 285–291.
[6] (a) G.D. Sprott, *J. Bioenerg. Biomembr.*, 24 (1992) 555–566; (b) Y. Koga, M. Nishihara, H. Morii, and M. Akagawa-Matsushita, *Microbiol. Rev.*, 57 (1993) 164–182.
[7] M. de Arruda, W. Colli, and B. Zingales, *Eur. J. Biochem.*, 182 (1989) 413–421.
[8] (a) J.N. Bertho, V. Ferrières, and D. Plusquellec, *J. Chem. Soc., Chem. Commun.*, (1995) 1391–1393; (b) V. Ferrières, J.N. Bertho, and D. Plusquellec, *Tetrahedron Lett.*, 36 (1995) 2749–2752.
[9] R. Velty, T. Benvegnu, and D. Plusquellec, *Synlett*, (1996) 817–819.
[10] (a) J.W. Green, *Adv. Carbohydr. Chem.* 21 (1966) 95–142; (b) R.M. de Lederkremer, V.B. Nahmad, and O. Varela, *J. Org. Chem.*, 59 (1994) 690–692 and refs therein.
[11] B. Fraser-Reid, U.E. Udodong, Z. Wu, H. Ottoson, J.R. Merritt, C.S. Rao, C. Roberts, and R. Madsen, *Synlett*, (1992) 927–942.
[12] A. Arasappan and B. Fraser-Reid, *Tetrahedron Lett.*, 36 (1995) 7967–7970.
[13] S.J. Angyal, *Chem. Soc. Rev.*, 9 (1980) 415–428.
[14] V. Ferrières, Thèse de Doctorat de l'Université de Rennes I, Rennes, (1994) pp 77–84.
[15] A. Liptak, I. Jodal, and P. Nanasi, *Carbohydr. Res.*, 44 (1975) 1–11.

[16] P.J. Garegg, H. Hultberg, and S. Wallin, *Carbohydr. Res.*, 108 (1982) 97–101.
[17] C. Gallo-Rodriguez, O. Varela, and R.M. de Lederkremer, *J. Org. Chem.*, 61 (1996) 1886–1889.
[18] (a) R.G.S. Ritchie, N. Cyr, B. Korsch, H.J. Koch, and A.S. Perlin, *Can.J. Chem.*, 53 (1975) 1424–1433.; (b) K. Bock and C. Pedersen, *Adv. Carbohyd. Chem. Biochem.*, 41 (1983) 27–66.; (c) N.B. D'Accorso, I.M.E. Thiel, and M. Schuller, *Carbohydr. Res.*, 124 (1983) 177–184.
[19] M. McNeill, S.J. Wallner, S.W. Hunter, and P.J. Brennan, *Carbohydr. Res.*, 166 (1987) 299–308.
[20] G.H. Veeneman, S. Notermans, P. Hoogerhout, and J.H. van Boom, *Recl. Trav. Chim. Pays-Bas.*, 108 (1989) 344–350.