Synthesis of 2,3,5,6-tetra-*O*-benzyl-D-galactofuranose for α-glycosidation

Gabriel Gola, Paula Libenson, Lucía Gandolfi-Donadío, and Carola Gallo-Rodriguez*

CIHIDECAR. Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Ciudad Universitaria, Pabellón II, 1428 Buenos Aires, Argentina
E-mail: cgallo@qo.fcen.uba.ar

Dedicated to Prof. Rosa M. de Lederkremer on her 70th anniversary

Absract
The synthesis of 2,3,5,6-tetra-*O*-benzyl-D-galactofuranose, a useful compound for α-glycosylation studies, is described. Direct anomeric *O*-alkylation of galactose was employed for alpha-allylation to yield pure allyl α-D-galactofuranoside, which is a versatile precursor for the synthesis of galactofuranose-containing oligosaccharides. Allyl removal of the benzylated galactofuranosyl derivative was performed using palladium (II) chloride as catalyst.

Keywords: α-Galactofuranosyl, 1,2-*cis*-glycosylation, galactofuranose, allyl galactofuranoside

Introduction

Galactose is widespread distributed in nature.[1] However, the occurrence of the furanose form, absent in mammals, is restricted to bacteria,[2] protozoa[3] and fungi.[4] For that reason, galactofuranose metabolism arises as an interesting target for chemotherapy.[5] At the present time, Gal*f* biosynthetic studies are currently being performed. Two enzymes are required for Gal*f* incorporation to glycoconjugates, a low efficiency mutase that transform UDP-Gal*p* to UDP-Gal*f*,[6] and a recently described, UDP-Gal*f* transferase,[7] which transfers the Gal*f* unit to the sugar chain.

β-Galactofuranosyl units are commonly found in *Mycobacterium tuberculosis*,[8] *Leishmania*,[9] and *Trypanosoma cruzi*[10] as examples. However, there are only few reported examples in which galactofuranose occurs in the alpha configuration. Cellulolytic bacteria like *Clostridium thermocellum* and *Bacteroides cellulosolvens* express cellulosomes, which possess O-linked oligosaccharides present galactofuranose in α configuration.[11,12] This unit is also found in the capsular polysaccharide of *Streptococcus pneumoniae* 22F[13] and in the *O*-antigenic polysaccharide from *Escherichia coli* O167.[14] α-D-Galf was found also in varianose, a complex

extracellular polysaccharide produced by the fungus *Penicillium varians*[15] and in other fungi.[16,17] More recently, α-Gal*f* unit was found in the cell wall of the fungus *Paracoccidioides brasiliensis*,[18] the ethiological agent of paracoccidioidomycosis, the most common systemic mycosis in Latin America. The existence of this unusual unit is associated to a biosynthetic pathway that would have a particular galactofuranosyltransferase in one of their steps. As this new biosynthesis has not been studied, the synthesis of specific α-galactofuranosyl linkages is necessary in order to confirm these very unusual units, and as new tools for biosynthetic studies. Moreover, the determination of α-Gal*f* units in natural components have been sometimes difficult to accomplish because the resonance of the anomeric center in ^{13}C NMR is around 100 ppm as found in α-Gal*p*. Thus, accurate confirmation by ^{1}H NMR should be required, on occasion hard to achieve because of superposition of the signals.

The preparation of 1,2-*trans* β-galactofuranosides can be accomplished through the use of several galactofuranosyl donors containing acyl protecting groups at O-2 due to neighboring group participation.[19] However, no successful general method for 1,2-*cis* glycosylation have emerged. The advances in 1,2-*cis*-*O*-glycosylation has been reviewed.[20] The construction of a 1,2-*cis* α-galactofuranosic linkage requires a galactofuranosyl derivative with a non-participant group at the C-2 position, that is the case of 2,3,5,6-tetra-*O*-benzyl-α,β-galactofuranose (**1**) and derivatives. On activation by n-pentenyl glycoside of this derivative, β-galactofuranosyl linkages were mainly obtained in spite of the benzyl group at O-2.[21] Studies on the α-glycosylation by the trichloroacetimidate method have been previously performed with several low steric demanding acceptors giving moderate diastereoselectivities.[22] Also, encourages results have been described from 1,2-*trans*-thiogalactofuranosides.[23]

The glycosidic linkage construction strongly depends on the nature of the donor and the acceptor, that is, donor and acceptor must be "matched" for best results. The Reciprocal Donor Acceptor Selectivity (RDAS) definition has been recently introduced.[24]

In our laboratory, we have extensively employed the trichloroacetimidate method[25] for β-galactofuranosyl linkages construction[26,27] allowing the synthesis of internal D-Gal*f*-containing oligosaccharides.[28,29] In order to study this methodology in the α-galactofuranosyl linkage construction, a straightfoward synthesis of **1** is needed, that after imidate activation, would allow further glycosylation studies with different acceptors.

Compound **1** was previously obtained by direct benzylation of galactose to yield an inseparable mixture of benzyl 2,3,5,6-tetra-*O*-benzyl-α-D-galactofuranoside and benzyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranoside in 17:83 ratio in moderate yield.[30] Further hydrolysis of the mixture afforded the corresponding anomeric free derivatives isolated by chromatography although no yields are reported in this procedure. Compound **1** was also described in four reaction steps from penta-*O*-benzoyl-α,β-galactofuranose, *via* benzylation of methyl β-D-galactofuranoside followed by acid hydrolysis of the glycoside.[31] Another procedure was stated from the octyl glycoside,[22] obtained by glycosidation of galactose with $FeCl_3$ as a Lewis acid promoter in heterogeneous media as 1:4.9 α/β separable mixture by column chromatography.

Benzylation and further acetolysis to avoid debenzylation or ring expansion to pyranoid compound afforded 1-*O*-acyl-2,4,5,6-tetra-*O*-benzyl-α,β-D-galactofuranose.[23].

In this paper we describe a straightforward synthesis of known 2,3,5,6-tetra-*O*-benzyl-galactofuranose (**1**) *via* the alpha-allyl glycoside in three steps from galactose in high yield, useful for studies on the synthesis of α-D-galactofuranosyl linkages.

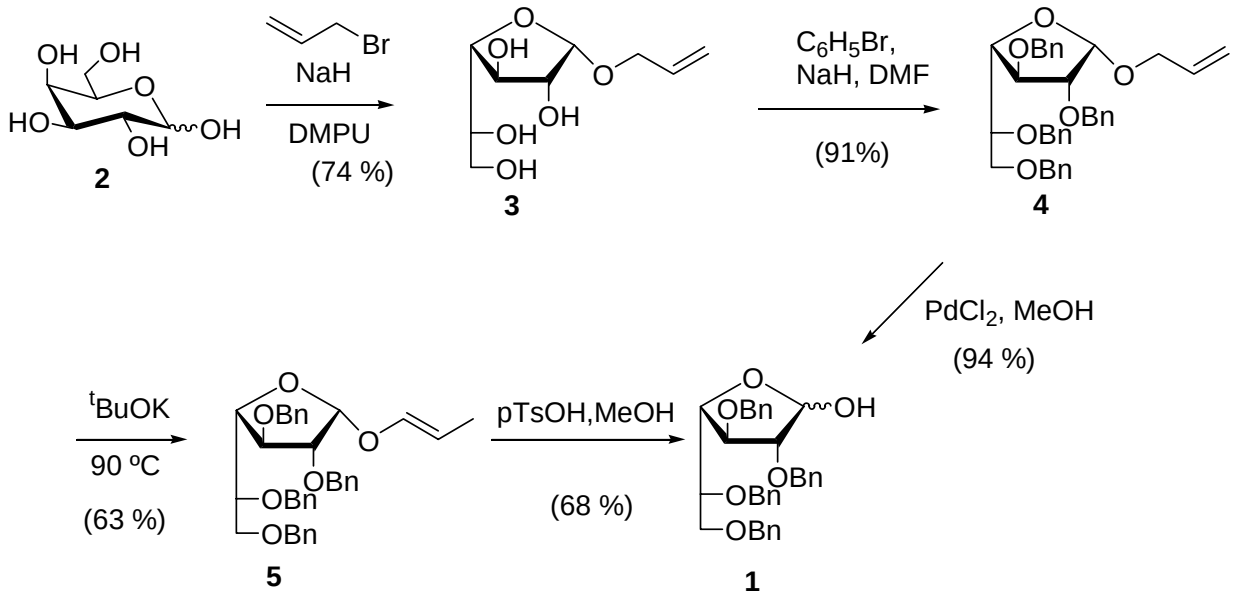
Results and Discussion

The synthesis of the target furanose derivative **1**, was successfully carried out taking advantage of the anomeric *O*-alkylation procedure of unprotected hexoses described by Klotz and Schmidt.[32] Access to pure anomeric glycosides as starting material is an important task in the oligosaccharide synthesis. Upon several hexoses and pentoses, galactose treated in the presence of sodium hydride as a base in *N*,*N*'-dimethyl-hexahydropirimidine-2-one (DMPU) as an aprotic polar solvent, didecyl sulfate as alkylating agent, gave exclusively decenyl α-galactofuranoside. This alkylation procedure was also employed to afford the corresponding benzyl and allyl α-galactofuranosides that were purified after acetylation and characterized as acetates. More recently, this reaction was also used for the synthesis of pentenyl α-D-galactofuranoside, isolated after an acetylation-deacetylation sequence.[33]

In our case, treatment of galactose (**2**) with 1.5 equivalents of allyl bromide and sodium hydride in DMPU, in a slightly modified procedure, gave allyl α-D-galactofuranoside (**3**). With the aim to avoid the acetylation-deacetylation sequence in the purification of **3**, previous removal of DMPU solvent by succesive extraction of the crude reaction mixture with hexane was performed. Thus, the viscous syrup obtained was easily purified by chromatography giving rise to crystalline allyl glycoside **3** in 74 % yield (Scheme 1) that was fully characterized. The anomeric configuration was confirmed by NMR spectroscopy. In the ^{1}H NMR spectrum, H-1 appeared at 5.08 ppm with a $J_{1,2}$ = 4.2 Hz, characteristic of α-Gal*f* configuration, also H-2 appeared as a doublet of doublets with J = 8.2 and 4.2 Hz. The ^{13}C NMR spectrum showed the resonance of the anomeric carbon at 100.9 ppm and the C-4 at 82.0 ppm, unambiguosly establishing the α-furanosic configuration. An inseparable mixture of presumably diallylated by-products was also obtained.

With the furanosic template on hand, standard benzylation of compound **3** yielded syrupy allyl 2,3,5,6-tetra-*O*-benzyl-α-D-galactofuranoside (**4**) in 91 % yield. In this case, the ^{13}C NMR spectrum showed the C-1 shielded at 98.8 ppm and C-2 deshielded at 84.2 compared to C-4 at 80.5 ppm. The inversion of these diagnostic signals has to be taking into account in benzylated α-galactofuranosyl series. In order to remove the anomeric allyl group of **4**, isomerization of the double bond,[34] followed by hydrolysis of the enol ether was performed as first attempt. Therefore, treatment of **4** with one equivalent of potassium *tert*-butoxide in anh. dimethylsulfoxide at 90 ºC afforded the isomerized vinyl 2,3,5,6-tetra-*O*-benzyl-α-D-galactofuranoside (**5**) in 63 % yield. Further hydrolysis of the resulting enol ether of **5** by

catalytic amounts of *p*-toluensulphonic acid in methanol at room temperature gave desired 2,3,5,6-tetra-O-benzyl-α-D-galactofuranose (**1**) in 68 % yield. After purification by column chromatography, **1** was obtained as mixture of α/β anomers in 56:44 ratio as shown by integration of the anomeric protons in the ^{1}H NMR spectrum: δ 5.41 (bs, H-1β), 5.27 (d, J = 4.4 Hz, H-1α). The anomeric equilibrium in a chloroformic solution was reached in 5 days giving an α/β anomeric 2:1 ratio as indicated in the ^{1}H NMR spectrum. The ^{13}C NMR spectrum of **1** showed the resonances of the anomeric carbons at 101.0 (C-1β), 96.2 (C-1α) in agreement with those reported signals previously described.[30] No methyl glycoside by-product was observed.



Scheme 1

The moderate yield obtained in the isomerization-hydrolysis deprotection sequence prompt us to follow the procedure in one step. Thus, treatment of allyl glycoside **4** with $PdCl_2$[35] in methanol-dichloromethane solution smoothly afforded **1** in 94 % yield. After purification by column chromatography, **4** crystallized on standing and, in this case, as an anomeric α/β mixture of 82:18 ratio as shown by integration of anomeric signals in the ^{1}H NMR spectrum. Recrystallization of this anomeric mixture from EtOH gave the pure α-anomer. After anomeric equilibration, compound **1** had the same physical and spectroscopic properties described.

In conclusion, in this work we synthesized 2,3,5,6-tetra-*O*-benzyl-galactofuranose (**5**) *via* the alpha-allyl glycoside in three steps from galactose (63% overall) useful for α-glycosylation studies. Allyl α-D-galactofuranoside was easily obtained crystalline in one step from galactose by direct O-anomeric alkylation. Compound **3** could be useful as starting material in Gal*f*-containing oligosaccharide synthesis being a good precursor of galactofuranosic units.

Experimental Section

General Procedures. TLC was performed on 0.2 mm silica gel 60 F254 (Merck) aluminum supported plates. Detection was effected by exposure to UV light or by spraying with 10 % (v/v) sulfuric acid in EtOH and charring. Column chromatography was performed on silica gel 60 (230-400 mesh, Merck). Melting points were determined with a Thomas-Hoover apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 343 polarimeter. High resolution mass spectra (HRMS) were recorded on a VG ZAB2SE (1996) high resolution mass spectrometer, with Opus V3.1 and DEC 3000 Alpha Station. NMR spectra were recorded with a Bruker AC 200 spectrometer at 200 MHz (^{1}H) and 50.3 MHz (^{13}C) or with a Bruker AM 500 spectrometer at 500 MHz (^{1}H) and 125 MHz (^{13}C). Homo and heteronuclear correlation spectroscopy experiments were performed when indicated.

Allyl α-D-galactofuranoside (3). Dried finelly ground galactose (3.30 gr, 18.3 mmol) was partially dissolved in DMPU (46 ml) in an argon atmosphere. This mixture was cannula-added to a flask containing 60 % suspension oil sodium hydride (1.05 g, 27.5 mmol) previously washed twice with hexane and dried. After cooling to 0º C, allyl bromide (6.4 ml, 73.9 mmol) was added and the suspension was stirred at 25 ºC for 36 h until TLC examination showed consumption of galactose. The resulting solution was cooled to 0º C and the sodium hydride excess was destroyed by addition of MeOH (1.8 ml). The solution was extracted 12 times with hexane (100 ml) to give a viscous syrup that was dissolved in methanol and evaporated. NaBr was precipitated by addition of 9:1 Cl_2CH_2: MeOH (50 ml) and the supernatant decanted. Purification of the supernatant by column chromatography (9:1 Cl_2CH_2-MeOH) afforded 2.98 gr of pure crystalline **3** (74 %) that after recrystallization from MeOH gave: R_f 0.38 (8:2 Cl_2CH_2-MeOH), $[\alpha]_D$ +95.6 º (*c* 1, H_2O); mp 157-158 ºC; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.00 (dddd, 1 H, *J* = 5.5, 6.0, 10.4, 17.2 Hz, C*H*=CH_2), 5.39 (ddt, 1 H, *J* = 17.4, 1.7, 1.6 Hz, HC=C*H*$_a$H), 5.30 (ddt, 1 H, *J* = 10.4, 1.2, 1.7 Hz, HC=C*H*$_b$H), 5.08 (d, 1 H, *J* = 4.2 Hz, H-1), 4.32 (ddt, 1 H, *J* = 12.9, 5.5, 1.4 Hz, OC*H*$_a$H-CH=), 4.20 (dd, 1 H, *J* = 8.2, 6.5 Hz, H-3), 4.17 (dd, 1 H, *J* = 8.2, 4.2 Hz, H-2), 4.14 (ddt, 1 H, *J* = 12.9, 6.2, 1.3 Hz, OC*H*$_b$H-CH=), 3.82 (t, 1 H, *J* = 6.6 Hz, H-4), 3.79-3.75 (m, 1 H, H-5), 3.75 (dd, 1 H, *J* = 3.9, 13.1 Hz, H-6a), 3.63 (dd, 1 H, *J* = 8.1, 13.1 Hz, H-6b); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 134.4 (*C*H=CH_2), 118.9 (CH=*C*H_2), 100.9 (C-1), 82.0 (C-4), 77.1 (C-2), 75.2 (C-3), 73.6 (C-5), 69.6 (O*C*H_2-CH=), 63.0 (C-6). The assignments were supported by homo and heteronuclear correlation spectroscopy experiments. Anal. Calcd for $C_9H_{16}O_9$: C, 49.09; H, 7.32. Found: C, 48.90; H, 7.41.

Allyl 2,3,5,6-tetra-*O*-benzyl-α-D-galactofuranoside (4). A 60 % suspension of sodium hydride in oil (2.86 g, 71.5 mmol) was washed twice with hexane under an argon atmosphere and DMF (10 mL) was added. The suspension was cooled to 0 ºC with stirring and a solution of allyl α-D-galactofuranoside (**3**, 1.75 g, 7.94 mmol) in DMF (15 ml) and then benzyl bromide (8.5 ml, 71.5 mmol) were slowly added. The mixture was stirred at room temperature for 3 h. After cooling to 0 ºC, the reaction was quenched by slowly addition of MeOH (18 ml) and stirred for

20 min. The reaction mixture was diluted with Cl_2CH_2 (200 ml), and washed with water (4 x 200 ml), dried ($NaSO_4$) and concentrated. The residue was purified by column chromatography (toluene) to give compound **4** (4.21 g, 91 %) as a colorless syrup (R_f 0.35, 20:1 toluene-EtOAc), $[\alpha]_D$ +34.1º (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.36-7.23 (m, 20 H, aromatic), 5.86 (dddd, 1 H, *J* = 17.3, 10.5, 6.5, 5.2 Hz, C*H*=CH$_2$), 5.24 (dc, 1 H, *J* = 17.3, 1.5 Hz, HC=C*H*$_a$H), 5.15 (dc, 1 H, *J* = 10.5, 1.5 Hz, HC=C*H*$_b$H), 4.91 (d, 1 H, *J* = 4.4 Hz, H-1), 3.73-3.71 (m, 2 H, C*H*$_2$Ph), 4.64, 4.60 (2 d, 2 H, *J* = 11.8 Hz, C*H*$_2$Ph), 4.55, 4.50 (2 d, 2 H, *J* = 11.8 Hz, C*H*$_2$Ph), 4.48, 4.44 (2 d, 2 H, *J* = 12.1 Hz, C*H*$_2$Ph), 4.32 (t, 1 H, *J* = 7.3 Hz, H-3), 4.16 (ddt, 1 H, *J* = 12.9, 5.2, 1.5 Hz, OC*H*$_a$H-CH=), 4.05 (dd, 1 H, *J* = 7.5, 4.4 Hz, H-2), 3.97 (dd, 1 H, *J* = 6.9, 6.2 Hz, H-4), 3.91 (ddt, 1 H, *J* = 12.9, 6.5, 1.5 Hz, OC*H*$_b$H-CH=), 3.69 (dt, 1 H, *J* = 6.2, 4.0 Hz, H-5), 3.63 (dd, 1 H, *J* = 10.4, 4.0 Hz, H-6a), 3.57 (dd, 1 H, *J* = 10.4, 6.3 Hz, H-6b); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 138.9-137.7 (aromatic), 134.2 (*C*H=CH$_2$), 127.5-126.2 (aromatic), 117.4 (CH=*C*H$_2$), 98.8 (C-1), 84.2 (C-2), 81.0 (C-3), 80.5 (C-4), 79.6 (C-5), 73.3, 73.0, 72.4, 72.3 (*C*H$_2$Ph), 70.4 (C-6), 68.1 (O*C*H$_2$-CH=). The assignments were supported by homo and heteronuclear correlation spectroscopy experiments. HRMS (FAB+) *m/z* calculated for $C_{37}H_{40}O_6Na$ (M + Na^+) requires 603.2723; found: 603.2718. Anal. Calcd for $C_{37}H_{40}O_6.0.75H_2O$: C, 74.98; H, 7.03. Found: C, 74.81; H, 6.94.

Vinyl 2,3,5,6-tetra-*O*-benzyl-α-D-galactofuranoside (5). To a solution of allyl 2,3,5,6-tetra-*O*-benzyl-α-D-galactofuranoside (**4**, 2.94 g, 5.06 mmol) in anh. dimethysulfoxide (12 ml) was added a solution of potassium *tert*-butoxide (0.57 g, 5.08 mmol) in dimethysulfoxide (15 ml), and the mixture was stirred at 90 ºC. After 40 min., the isomerization was complete (R*f* 0.39 20:1 toluene-ethyl acetate, twice developed). The reddish mixture was cooled to room temperature and water (4 ml) was added. After addition of CH_2Cl_2 (200 ml), the mixture was washed with water (3 x 300 ml) and the organic layer was dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (toluene) to give 1.85 g of crystalline compound **5** (63 %) that was recrystallized from ethanol. R_f 0.48 (20:1 toluene-EtOAc twice developed), $[\alpha]_D$ +41.5º (*c* 1, $CHCl_3$); mp 33-34ºC (EtOH). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38-7.23 (m, 20 H, aromatic), 6.13 (dc, 1 H, *J* = 6.2, 1.7 Hz, -OC*H*=CH), 5.10 (d, 1 H, *J* = 4.3 Hz, H-1), 4.73, 4.57 (2 d, 2 H, *J* = 11.6 Hz, C*H*$_2$Ph), 4.70, 4.66 (2 d, 2 H, *J* = 11.8 Hz, C*H*$_2$Ph), 4.65, 4.50 (2 d, 2 H, *J* = 11.6 Hz, C*H*$_2$Ph), 4.56 (dc, 1 H, *J* = 6.8, 6.2 Hz, -OCH=C*H*), 4.49, 4.44 (2 d, 2 H, *J* = 12.0 Hz, C*H*$_2$Ph), 4.32 (t, 1 H, *J* = 7.2 Hz, H-3), 4.12 (dd, 1 H, *J* = 7.3, 4.3 Hz, H-2), 4.02 (t, 1 H, *J* = 6.9 Hz, H-4), 3.70 (ddd, 1 H, *J* = 6.9, 6.2, 4.1 Hz, H-5), 3.62 (dd, 1 H, *J* = 10.4, 4.1 Hz, H-6a), 3.55 (dd, 1 H, *J* = 10.4, 6.2 Hz, H-6b), 1.63 (dd, 1 H, *J* = 6.8, 1.7 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 142.1 (-O*C*H=CH), 138.9-138.1 (aromatic), 128.5-127.3 (aromatic), 103.7 (-OCH=*C*H), 100.3 (C-1), 84.2 (C-2), 81.3, 81.2 (C-3, C-4), 80.0 (C-5), 73.4, 73.3, 72.4, 72.3 (*C*H$_2$Ph), 70.2 (C-6), 9.7 (CH_3). HRMS (FAB+) *m/z* calculated for $C_{37}H_{40}O_6Na$ (M + Na^+) requires 603.2723; found: 603.2719. Anal. Calcd for $C_{37}H_{40}O_6.0.75H_2O$: C, 74.98; H, 7.03. Found: C, 74.88; H, 6.77.

2,3,5,6-Tetra-*O*-benzyl-α-D-galactofuranose (1)

(a) from vinyl 2,3,5,6-tetra-O-benzyl-α-D-galactofuranoside (5). To solution of **5** (1.34 g, 2.31 mmol) in methanol (20 ml) was added *p*-toluensulphonic acid (43.4 mg, 0.23 mmol) and the reaction mixture was stirred at room temperature After 30 min of stirring, water was added (40 ml) and the resulting mixture was extracted with CH_2Cl_2, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (15:1 toluene-ethyl acetate) to give 0.85 g of syrupy compound **1** (68 %). R_f 0.22 (20:1 toluene-EtOAc). Anomeric equilibrium of **1** in a chloroformic solution for 5 days gave a 2:1 α/β anomeric mixture: $[\alpha]_D$ –22.6 (*c* 1, $CHCl_3$) [lit.[31] $[\alpha]_D$ –16.0 (*c* 1, $CHCl_3$); lit.[30] $[\alpha]_D$ -15 (*c* 1, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.35-7.20 (m, 20 H, aromatic), 5.41 (s, 0.33 H, H-1 β anomer), 5.26 (d, 0.67 H, *J* = 4.7 Hz, H-1 α anomer), 4.77 (d, 0.67 H, *J* = 11.5 Hz, C*H*$_2$Ph), 4.72 (d, 0.33 H, *J* = 11.9 Hz, C*H*$_2$Ph), 4.67 (d, 0.67 H, *J* = 11.4 Hz, C*H*$_2$Ph), 4.60 (d, 0.33 H, *J* = 11.9 Hz, C*H*$_2$Ph), 4.52-4.44 (m, C*H*$_2$Ph), 4.39-4.35 (m, 0.99 H, H-4 β anomer, C*H*$_2$Ph β anomer), 4.11 (t, 0.67 H, *J* = 4.7 Hz, H-3), 4.09 (dd, 0.67 H, *J* = 2.5, 4.7 Hz, H-4), 4.08 (d, 0.67 H, *J* = 11.9 Hz, C*H*$_2$Ph), 4.05 (dd, 0.33 H, *J* = 2.3, 4.7 Hz, H-3), 4.01 (t, 0.67 H, *J* = 4.7 Hz, H-2), 3.95 (d, 0.33 H, *J* = 2.3 Hz, H-2), 3.77 (m, 0.33 H, H-5), 3.73 (dd, 0.67 H, *J* = 6.5, 9.9 Hz, H6-a), 3.68 (dd, 0.67 H, *J* = 5.2, 9.9 Hz, H6-b), 3.65 (dd, 0.33 H, *J* = 4.5, 10.3 Hz, H-6a), 3.61 (ddd, 0.67 H, *J* = 2.5, 5.2, 6.5 Hz, H-5), 3.61 (dd, 0.33 H, *J* = 6.3, 10.3 Hz, H-6b); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 137.9-138.1 (aromatic), 128.5-126.3 (aromatic), 100.9 (C-1 β anomer), 96.2 (C-1 α anomer), 87.1 (C-2 β anomer), 84.5 (C-2 α anomer), 83.1 (C-3 β anomer), 82.0 (C-3 α anomer), 81.5 (C-4 α anomer), 77.0 (C-5 α anomer), 73.6, 73.5, 73.4, 73.3, 72.0, 71.8, 71.7, 71.6 (*C*H_2Ph), 70.8, 70.6 (C-6 α anomer). ^{13}C NMR anomeric carbon resonances of **1** are described in literature and are in accordance with the recorded values.[30]

(b) from allyl 2,3,5,6-tetra-O-benzyl-α-D-galactofuranoside (4). To a solution of **4** (2.28 g, 3.93 mmol) in 3:2 CH_2Cl_2-methanol (50 ml) was added a suspension of $PdCl_2$ (80 mg) in methanol (36 ml) and the mixture was stirred at room temperature. After 4 h of stirring, TLC examination showed the disappearance of the starting material **4** and isomerized **5**. The mixture was diluted with CH_2Cl_2 (200 ml), filtered through a Celite bed and the filtrate concentrated in vacuo. Purification of the residue by column chromatography (15:1 toluene-ethyl acetate) gave 2.0 g of pure compound **5** (94 %) that crystallized on standing. After recrystallization from EtOH have mp 78-80 ºC (α-anomer). Once reached the anomeric equilibrium, compound **1** gave the same spectroscopic and physical properties as described above.

Acknowledgments

This work was supported by grants from Agencia Nacional de Promoción Científica y Tecnológica (ANPCyT, BID 1201/OC-AR, PICT 12306), Universidad de Buenos Aires and Fundación Antorchas. C. Gallo-Rodriguez is a research member of CONICET. L. Gandolfi-Donadio is a fellow from CONICET. P. Libenson is a student fellow from UBA.

References

1. Lederkremer, R. M.; Gallo-Rodriguez, C. *Adv. Carbohydr. Chem. Biochem.* **2004**, *59*, 9.
2. Lindberg, B. *Adv. Carbohydr. Chem. Biochem.* **1990**, *48*, 279.
3. Lederkremer, R. M.; Colli W. *Glycobiology* **1995**, *5*, 547.
4. Notermans, S.; Veeneman, G. H.; Van Zuylen, C. W. E. M.; Hoogerhout, P.; Van Boom, J. H. *Mol. Immunol.* **1988**, *25*, 975.
5. Pedersen, L. L.; Turco, S. J. *Cell. Mol. Life Sci* **2003**, *60*, 259.
6. Sanders, D. A. R.; Staines, A. G.; McMahon, S. A.; McNeil, M. R.; Whitfield, C.; Naismith, J. H. *Nat. Struct. Biol.* **2001**, *8*, 858.
7. Kremer, L.; Dover, L. G.; Morehouse, C.; Hitchin, P.; Everett, M.; Morris, H.R., Dell, A.; Brennan, P. J.; McNeil, M. R.; Flaherty, C.; Duncan, K.; Besra, G. S. *J. Biol. Chem*. **2001**, *276*, 26430.
8. Crick, D. C.; Mahaprata, S.; Brennan, P. J. *Glycobiology* **2001**, *11*, 107.
9. Turco, S. J.; Descoteaux, A. *Annu. Rev. Microbiol.* **1992**, *46*, 65.
10. Jones, C.; Todeschini, A. R.; Agrellos, O. A.; Previato, J. O.; Mendonca-Previato, L. *Biochemistry* **2004**, *43*, 11889.
11. Gerwig, G. J.; de Waard, P.; Kamerling, J. P.; Vliegenthart, J. F. G.; Morgenstern, E.; Lamed, R; Bayer, E. A. *J. Biol. Chem.* **1989**, *264*, 1027.
12. Gerwig, G. J.; Kamerling, J. P.; Vliegenthart, J. F. G.; Morag, E.; Lamed, R; Bayer, E. A. *J. Biol. Chem.* **1993**, *268*, 26956; *Eur. J. Biochem.* **1992**, *205*, 799.
13. Richards, J. C.; Perry, M. B.; Kniskern, P. J. *Can. J. Chem.* **1988**, *67*,1038.
14. Linnerborg, M.; Wollin, R.; Wildmalm, G. *Eur. J. Biochem.* **1997**, *246*, 565.
15. Jansson, P. E; Lindberg, B. *Carbohydr. Res*. **1980**, *82*, 97.
16. Kogan,G. ; Matulová, M.; Michalková, E. *Z. Naturfosch*. **2002**, *57c*, 452.
17. Parra, E.; Jiménez-Barbero, J.; Bernabé, M.; Leal, J. A.; Prieto, A.; Gomez-Miranda, B. *Carbohydr. Res.* **1994**, *251*, 315.
18. Ahrazem, O.; Prieto, A.; San-Blas, G.; Leal, J. A.; Jimenez-Barbero, J.; Bernabé, M. *Glycobiology* **2003**, *13*, 743.
19. Lowary, T. L. *Curr. Opinion Chem. Biol.* **2003**, *7*, 749.
20. Demchenko, A. V. *Curr. Org. Chem.* **2003**, *7*, 35.
21. Arasappan, A.; Fraser-Reid, B. *Tetrahedron Lett.* **1995**, *36*, 7967.
22. Guelin, M.; Ferrieres, V.; Plusquellec D. *Carbohydr. Lett.* **1997**, *2*, 381.
23. Guelin, M.; Ferrieres, V.; Plusquellec D. *Eur. J. Org. Chem.* **2000**, 1423.
24. Fraser-Reid, B.; López, J. C.; Gómez, A. M.; Uriel, C *Eur. J. Org. Chem.* **2004**, 1387.
25. Schmidt, R. R., Jung, K.-H. In *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Marcel Dekker, 1997; pp 283-312.
26. Gallo-Rodriguez,C.; Gandolfi, L.; Lederkremer, R. M. *Org. Lett.* **1999**, *1*, 245.
27. Gallo-Rodriguez, C.; Gil Libarona, M. A.; Mendoza, V. M.; Lederkremer, R. M. *Tetrahedron* **2002**, *58*, 9373.

28. Gandolfi-Donadio, L.; Gallo-Rodriguez, C.; Lederkremer, R. M. *J. Org. Chem.* **2002**, *67*, 4430.
29. Gandolfi-Donadio, L.; Gallo-Rodriguez, C.; Lederkremer, R. M. *J. Org. Chem.* **2003**, *68*, 6928.
30. Decoster, E.; Lacombe, J.-M.; Strebler, J.-L; Ferrari, B.; Pavia, A. A. *J. Carbohydr. Chem.* **1983**, *2*, 329.
31. Kovensky, J.; McNeil, M.; Sinay, P. *J. Org. Chem.* **1999**, *64*, 6202.
32. Klotz, W.; Schmidt, R. R. *Liebigs Ann. Chem.* **1993**, 683.
33. Guelin, M.; Ferrieres, V.; Lefeuvre, M.; Plusquellec D. *Eur. J. Org. Chem.* **2003**, 1285.

