Facile synthesis of α-D-Ara*f*-(1→5)-D-Gal*f*, the linker unit of the arabinan to the galactan in *Mycobacterium tuberculosis*[1]

Lucía Gandolfi-Donadío, Carola Gallo-Rodriguez, and Rosa M. de Lederkremer

Abstract: The arabinogalactan is a crucial constituent of the cell wall of mycobacteria. Both monosaccharides (arabinose and galactose) are found in the furanose configuration, absent in mammals. An efficient synthesis of α-D-Ara*f*-(1→5)-D-Gal*f*, the linker unit of the arabinan to the galactan, is described. The strategy relies on the use of a conveniently substituted D-galactono-1,4-lactone as a precursor of the reducing furanose ring. The glycosylation step was performed by the tin(IV) chloride promoted method using 1,2,3,5-tetra-*O*-benzoyl-α,β-D-arabinofuranose. The arabinose donor was obtained in a crystalline state in one step by benzoylation of arabinose in hot pyridine. Selective glycosylation of the exocyclic OH-5 was obtained in 75% yield to give 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-2,6-di-*O*-pivaloyl-D-galactono-1,4-lactone. Reduction with disiamylborane gave the disaccharide synthon, useful for further glycosylations. Dec-9-enyl α-D-Ara*f*-(1→5)-β-D-Gal*f*, a convenient substrate for arabinofuranosyl transferases studies, was obtained by the trichloroacetimidate method of glycosylation.

Key words: arabinofuranose, galactofuranose, *Mycobacterium* arabinogalactan, trichloroacetimidate, tin(IV) chloride.

Résumé : L'arabinogalactane est un constituant crucial de la paroi de la cellule des mycobactéries. Les deux monosaccharides, arabinose et galactose, se retrouvent dans la configuration furanose qu'on ne retrouve pas chez les mammifères. On décrit une synthèse efficace du α-D-Ara*f*-(1→5)-D-Gal*f*, l'unité de liaison de l'arabinane au galactane. La stratégie repose sur l'utilisation d'une D-galactono-1,4-lactone substituée d'une façon appropriée comme précurseur du cycle réducteur du furanose. L'étape de glycosylation a été réalisée par la méthode de catalyse à l'aide de chlorure d'étain(IV) en utilisant le 1,2,3,5-tétra-*O*-benzoyl-α,β-D-arabinofuranose. Le donneur arabinose a été obtenu à l'état cristallin en une étape benzoylation de l'arabinose dans de la pyridine à chaud. La glycosylation sélective de OH-5 exocyclique a été réalisée avec un rendement de 75 % pour conduire à la formation de la 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-2,6-di-*O*-pivaloyl-D-galactono-1,4-lactone. Sa réduction par du disiamylborane fournit le synthon disaccharide utile dans des glycosylations subséquentes. Par ailleurs, le dec-9-enyl α-D-Ara*f*-(1→5)-β-D-Gal*f*, un substrat approprié pour les études de transférases d'arabinofuranosyle a été préparé par la méthode de glycosylation au trichloroacétimidate.

Mots clés : arabinofuranose, galactofuranose, arabinogalactane *Mycobacterium*, trichloroacétimidate, chlorure d'étain(IV).

[Traduit par la Rédaction]

Introduction

Mycobacterial diseases have reemerged in the last years because of the appearance of multidrug-resistant strains of *Mycobacterium* and the relation of tuberculosis with AIDS (1). The integrity of the mycobacterial cell wall is essential for the viability of mycobacteria (2).

One of the components of this unique cell wall is arabinogalactan (AG) (3) in which both arabinose and galactose are found in the furanose form, which is absent in mammals. The galactan region consists of alternating β(1→5)- and β(1→6)-linked D-Gal*f* residues. This linear galactofuranose chain has branch points at OH-5 at which the arabinan chains are α-attached. Thus, an α-D-Ara*f*-(1→5)-D-Gal*f* linkage anchors the arabinan component to the galactan structure. The disaccharide has been previously synthesized as the *n*-octyl (4) and the ethyl glycosides (5*a*, 5*b*). These derivatives are not precursors for further elongation of the chain. In both procedures, the trichloroacetimidate method (6) was employed for the glycosylation step. The 2,3,5-tri-

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Dedicated to Professor Walter Szarek on the occasion of his 65th birthday.

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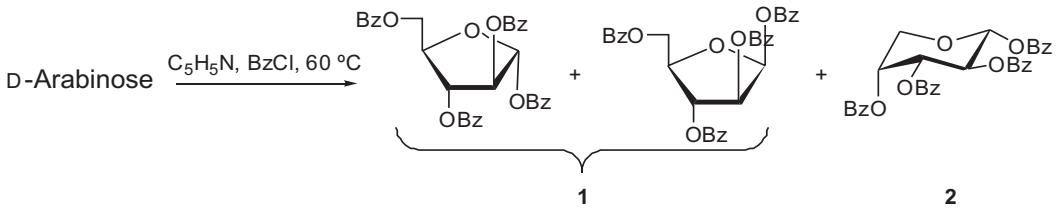
Scheme 1.



O-acyl-α-D-arabinofuranosyl trichloroacetimidate donors were prepared from D-arabinose via the methyl arabinofuranoside in five steps.

The synthesis of a closely related trisaccharide fragment of the arabinogalactan was described by two groups (5). The procedures also employed the trichloroacetimidate method for the introduction of the Ara*f* unit.

The synthesis and conformation of D-arabinofuranosides from mycobacteria have been reviewed (7).

In the present work, we optimized the conditions for the one-step preparation of crystalline tetra-*O*-benzoyl-α,β-D-arabinofuranose (**1**) from D-arabinose. The D-arabinofuranose derivative **1** was used for tin(IV) chloride promoted glycosylation.

Results and discussion

The synthetic strategy relied on the use of a conveniently substituted D-galactono-1,4-lactone as the precursor of the reducing furanose ring (8, 9). Thus, after glycosylation, the disaccharide–lactone is reduced, acting as a virtually protected anomeric center. Activation of the anomeric center would allow further construction of different oligosaccharides.

We have extensively used the tin(IV) chloride promoted glycosylation method (10–12) for the activation of a peracylated galactofuranose. We employed α,β-perbenzoylgalactofuranose, which is obtained in the crystalline state in a one step-reaction from galactose (13). This is a very simple, direct, and convenient method for the construction of the β-D-galactofuranosyl linkage. Taking into account the stereochemical relationship between arabinose and galactose, we applied this glycosylation method to perbenzoyl arabinofuranose derivatives.

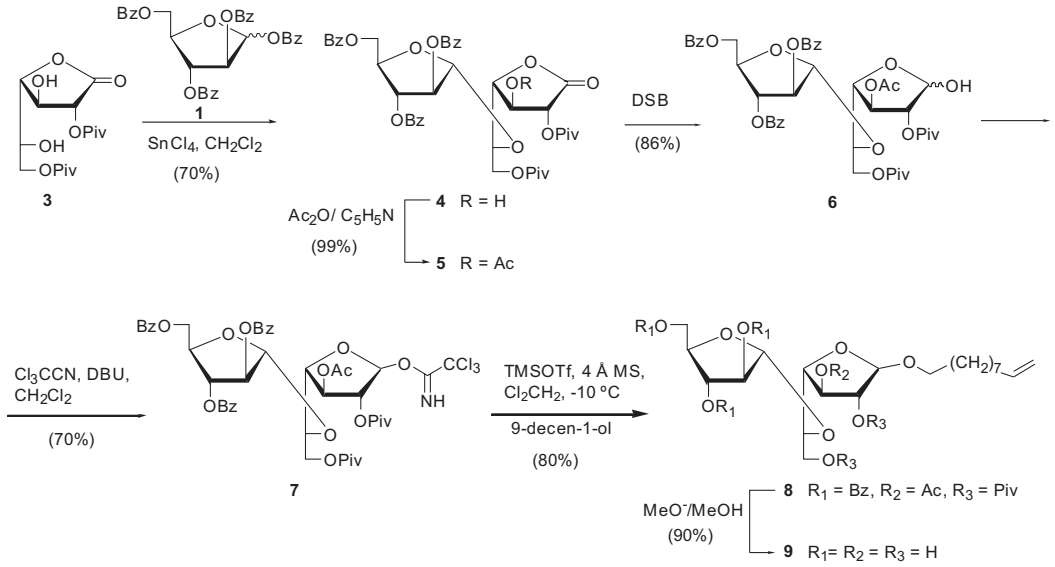
Tin(IV) chloride has been previously employed to achieve 1,2-*trans* α-arabinofuranosidic linkages. Tetra-*O*-acetyl-α-D-arabinofuranose, which was obtained in four steps as a syrup from arabinose, was used to give the expected 1,2-*trans* α-glycosidic linkage provided by the acetyl assistance in O-2 (14). On the other hand, it was described (15) that tetra-*O*-acetyl-α,β-D-arabinofuranose, obtained by ozonolysis of tri-*O*-acetyl-D-glucal, was employed as a glycosyl donor. However, the reaction gave low diastereoselectivity leading to a 2:1α:β ratio in the glycosylation of methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (15). Similar results were obtained using the L-enantiomer (16).

In the galactofuranose series, we have also noticed that glycosylation yields diminished when employing the peracetylated analog, which could be attributed to the lability of the acetyl compared with the benzoyl group in the presence of the strong Lewis acid tin(IV) chloride. Excellent yields were obtained when the benzoylated analog was employed (10–12). For that reason, we thought that 1,2,3,5-tetra-*O*-benzoyl-arabinofuranose (**1**) could be a good precursor for the tin(IV) chloride promoted glycosylation reaction. Compound **1** was synthesized, in one step, by the benzoylation of arabinose in hot pyridine (Scheme 1). The crude product was a mixture of β-furanose, α-furanose, and α-pyranose perbenzoates in a 30:27:43 ratio, respectively, as shown by the integration of the anomeric protons in the ^{1}H NMR spectrum: 6.88 (d, 0.30H, J = 4.4 Hz, H-1β furanose), 6.76 (s, 0.27H, H-1α furanose), 6.26 (d, 0.43H, J = 5.6 Hz, H-1α pyranose). No tetra-*O*-benzoyl-β-D-arabinopyranose was detected in the perbenzoylation reaction mixture. Crystallization of the crude product from ethanol gave a first crop of pure crystalline 1,2,3,4-tetra-*O*-benzoyl-α-D-arabinopyranose (**2**, 26%). Perbenzoyl arabinofuranose (**1**, 29%) crystallized from the mother liquors. On purification of a sample of the anomeric mixture by column chromatography, pure 1,2,3,5-tetra-*O*-benzoyl-α-D-arabinofuranose (**1α**) was obtained and fully characterized. Compound **1α** was previously obtained on reaction of 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl bromide with silver benzoate (17). The anomeric mixture was used for glycosylation. Although the furanose perbenzoate was isolated in a modest yield, its use as a donor in the route described in this paper has the advantage that it was obtained in a crystalline state in one step from D-arabinose.

With the arabinofuranosyl donor **1**, a tin(IV) chloride promoted glycosylation reaction could be performed with a Gal*f* template acceptor. Crystalline 2,6-di-*O*-pivaloyl-D-galactone-1,4-lactone (**3**) (9), obtained in one step from D-galactone-1,4-lactone, was employed as a precursor of the galactofuranose reducing end (Scheme 2). Compound **3** was previously used in our laboratory for the construction of β-D-Gal*f*-(1→5)-β-D-Gal*f*-(1→6)-D-Gal*f* (9). Thus, on treatment of 1.3 equiv. of acceptor **3** with 1 equiv. of arabinose donor **1**, and tin(IV) chloride as the promoter in CH_2Cl_2, selective glycosylation of the exocyclic OH-5 of **3** gave 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-2,6-di-*O*-pivaloyl-D-galactono-1,4-lactone (**4**) in 70% yield. No product of condensation at the OH-3 of **3** was detected. The same regioselectivity was found when perbenzoyl galactofuranose or other galactofuranosyl derivatives were glycosylated with 2,6-di-*O*-substituted D-galactono-1,4-lactones (9, 11).

The diastereoselectivity of the glycosylation was determined from the coupling constants. In fact, the ^{1}H NMR spectrum of **4** showed a singlet at 5.44 ppm for the H-1′ and a doublet at 5.43 ppm (J = 1.7 Hz) for the H-2′, in agreement with an α-D-Ara*f* linkage. The ^{13}C NMR spectrum showed the resonance of the anomeric carbon at 107.6 ppm confirming the α-D-arabinofuranosyl linkage. The β linkage was not observed.

Scheme 2.



Previous to reducing the lactone function, acetylation of **4** was performed carefully to avoid β-elimination by-products. In this case, the ^{1}H NMR signal of H-3 in **5** was shifted 0.97 ppm downfield compared with H-3 in **4**, confirming that glycosylation had taken place regioselectively at OH-5. Further reduction of the lactone derivative **5** with disiamylborane gave 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-3-*O*-acetyl-2,6-di-*O*-pivaloyl-D-galactofuranose (**6**); the target disaccharide showed both anomers in a 1:1 α:β ratio as indicated by the integration of the anomeric protons in the ^{1}H NMR spectrum at 5.53 ppm (d, J = 4.8 Hz, H-1α) and 5.33 (s, H-1β).

To synthesize the decenyl glycoside, the trichloroacetimidate method was chosen. This method has been successfully used for β-D-galactofuranosyl glycosylation (8, 9, 18–20). Thus, activation of the anomeric center of **6** with Cl_3CCN and DBU gave a mixture of β- and α-trichloroacetimidates (**7**) in 88% yield. Disaccharide imidate **7** was stable for 1 day at –20 °C. On reaction of **7** with 1.3 equiv. of 9-decen-1-ol in CH_2Cl_2 with TMSOTf as the catalyst, decenyl β-glycoside (**8**) was obtained diastereoselectively (80%). In the ^{1}H NMR spectrum, the galactofuranosyl anomeric proton of **8** gave a signal at 4.94 (s, H-1) indicating the β-configuration. This assignment was confirmed by the ^{13}C NMR spectrum, which showed the signal of C-1 at 106.5 ppm. Full assignments for compound **8** were supported by COSY and HETCOR experiments. Sodium methoxide deprotection of **8** afforded 1-decenyl α-D-Ara*f*-(1→5)-β-D-Gal*f* (**9**) in 90% yield. The ^{1}H NMR spectrum of **9** is shown in Fig. 1.

Conclusion

A facile synthesis of a synthon for the α-D-Ara*f*-(1→5)-D-Gal*f* (**4**) unit of *M. tuberculosis* arabinogalactan was achieved in 70% yield from **1** and **3**. The aldonolactone approach followed by DSB reduction produced the disaccharide **6**, conveniently protected for further coupling in the synthesis of oligosaccharide units, useful for studies on its biosynthesis. The decenyl glycoside was also synthesized allowing further functionalization of the double bond.

Experimental section

General

TLC was performed on 0.2 mm silica gel 60 F254 aluminium-supported plates. Detection was effected by exposure to UV light or by spraying with 5% (*v*/*v*) sulfuric acid in EtOH and charring. Column chromatography was performed on silica gel 60 (230–400 mesh). Melting points are uncorrected. Optical rotations were measured at 25 °C. 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 at 500 MHz (^{1}H) and 125.8 MHz (^{13}C), or as indicated. Homo- and hetero-nuclear correlation spectroscopy experiments were performed when indicated.

1,2,3,5-Tetra-*O*-benzoyl-α,β-D-arabinofuranose (1αβ), 1,2,3,5-tetra-*O*-benzoyl-α-D-arabinofuranose (1α), and 1,2,3,4-tetra-*O*-benzoyl-α-D-arabinopyranose (2)

Arabinose (3.05 g, 20.3 mmol) in dry pyridine (63.9 mL) was heated in a boiling water bath for 45 min with the exclusion of moisture. The water bath was rapidly cooled to 60–65 °C and freshly distilled benzoyl chloride (11.3 mL, 97.4 mmol) was slowly added to the reaction mixture. After stirring at 60 °C for 1.3 h, water (6 mL) was added, and the stirring was continued for 30 min at room temperature. The solution was slowly poured into ice water (400 g) with vigorous stirring, affording an amorphous solid. After decantation, the remaining solid was washed five times with water. The ^{1}H NMR spectrum ($CDCl_3$) of the solid showed the anomeric signals with the following integrations: δ 6.88 (d, 0.30H, J = 4.4 Hz, H-1β furanosic), 6.76 (s, 0.27H, H-1α furanosic), 6.26 (d, 0.43H, J = 5.6 Hz, H-1α pyranosic). The

solid was dissolved in boiling EtOH (400 mL) and slow crystallization took place. After 1 day, crystals of 1,2,3,4-tetra-*O*-benzoyl-α-D-arabinopyranose (**2**, 3.02 g, 26%, R_f 0.46, hexane–EtOAc (3:1), twice developed) were obtained; mp 161 to 162 °C. $[\alpha]_D$ –113.8° (*c* 1, $CHCl_3$) (lit. value (21) mp 164 to 165 °C, MeOH–AcOH, 80:5.7; $[\alpha]_D$ –114.4° (*c* 0.848, $CHCl_3$)). ^{1}H NMR ($CDCl_3$) δ: 8.08–7.33 (m, 20H), 6.26 (d, 1H, *J* = 5.6 Hz, H-1), 5.95 (dd, 1H, *J* = 5.6, 7.3 Hz, H-2), 5.80 (ddd, 1H, *J* = 2.9, 3.6, 5.2 Hz, H-4), 5.78 (dd, 1H, *J* = 3.6, 7.3 Hz, H-3), 4.43 (dd, 1H, *J* = 5.2, 12.6 Hz, H-5a), 4.14 (dd, 1H, *J* = 2.9, 12.6 Hz, H-5b) (lit. value (22) ^{1}H NMR (acetone-d_6, 100 MHz)). ^{13}C NMR ($CDCl_3$) δ: 164.5–164.7 (*C*OPh), 133.7–128.5 (aromatic), 92.4 (C-1), 69.9 (C-3), 68.9 (C-2), 67.5 (C-4), 62.7 (C-5).

The mother liquors were kept at room temperature (20–23 °C) for 2 days and the second crop of crystals was filtered and characterized as 1,2,3,5-tetra-*O*-benzoyl-α,β-D-arabinofuranose (**1αβ**, 3.34 g, 29%, R_f 0.53 and 0.49, hexane–EtOAc (3:1), twice developed) in a 7:3 α:β ratio. ^{1}H NMR ($CDCl_3$) δ: 8.13–7.24 (m, 20H), 6.87 (d, 0.3H, *J* = 4.7 Hz, H-1 β anomer), 6.76 (s, 0.7H, H-1 α anomer), 6.11 (dd, 0.3H, *J* = 5.2, 7.0 Hz, H-3), 5.94 (dd, 0.3H, *J* = 4.7, 7.0 Hz, H-2), 5.82 (d, 0.7H, *J* = 0.8 Hz, H-2), 5.68 (dd, 0.7H, *J* = 3.7, 0.8 Hz, H-3), 4.83 (dd, 0.7H, *J* = 3.9, 12.7 Hz, H-5a), 4.82 (m, 0.7H, H-4), 4.81 (dd, 0.3H, *J* = 6.7, 14.1 Hz, H-5a), 4.73 (dd, 0.7H, *J* = 6.4, 12.7 Hz, H-5b), 4.67 (m, 0.3H, H-4), 4.66 (dd, 0.3H, *J* = 6.1, 14.1 Hz, H-5b). ^{13}C NMR ($CDCl_3$) δ: 166.2–164.6 (*C*OPh), 133.7–128.2 (aromatic), 99.8 (C-1 α anomer), 94.5 (C-1 β anomer), 83.9 (C-4 α anomer), 80.9 (C-2 α anomer), 79.8, 77.5, 76.2, 75.5, 64.7, 63.7.

A sample of **1αβ** was purified by column chromatography (toluene) to yield pure 1,2,3,5-tetra-*O*-benzoyl-α-D-arabinofuranose (**1α**). Crystallization from EtOH gave: mp 100 to 101 °C (EtOH). $[\alpha]_D$ +26.7° (*c* 1, $CHCl_3$) (lit. value (17) mp 117–121 °C (EtOH). $[\alpha]_D$ +27.9° (*c* 2.13, $CHCl_3$)). ^{1}H NMR ($CDCl_3$) δ: 8.14–7.26 (m, 20H), 6.76 (s, 1H, H-1), 5.82 (d, 1H, *J* = 0.8 Hz, H-2), 5.68 (dd, 1H, *J* = 3.7, 0.8 Hz, H-3), 4.83 (dd, 1H, *J* = 3.9, 12.7 Hz, H-5a), 4.82 (m, 1H, H-4), 4.73 (dd, 1H, *J* = 6.4, 12.7 Hz, H-5b). ^{13}C NMR ($CDCl_3$) δ: 166.2–164.6 (*C*OPh), 133.8–128.3 (aromatic), 99.8 (C-1), 83.9 (C-4), 80.9 (C-2), 77.5 (C-3), 63.7 (C-5). These assignments were supported by HETCOR experiments.

2,3,5-Tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-2,6-di-*O*-pivaloyl-D-galactono-1,4-lactone (4)

To an externally cooled (0 °C) solution of tetra-*O*-benzoyl-α,β-D-arabinofuranose (**1αβ**, 1.07 g, 1.9 mmol) in dry CH_2Cl_2 (50 mL) was added $SnCl_4$ (0.22 mL, 1.9 mmol) with stirring in an argon atmosphere. After 10 min, this solution was added to a solution of compound **3** (9) (0.86 g, 2.5 mmol) in CH_2Cl_2 (50 mL) over a 25 min period and then the mixture was stirred for 3 h at 0 °C. The solution was poured into aq. $NaHCO_3$ and extracted with CH_2Cl_2 (2 × 200 mL). The organic extract was washed with water (3 × 100 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Purification of the residue by column chromatography (toluene–EtOAc, 20:1) gave 1.05 g of **4** (70% yield) as a foamy solid. R_f 0.45 (toluene–EtOAc, 3:1). $[\alpha]_D$ –28.1° (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 8.07–7.14 (m, 15H), 5.68 (dd, 1H, *J* = 1.7, 4.8 Hz, H-3′), 5.44 (bs, 1H, H-1′), 5.43 (d, 1H, *J* = 1.7 Hz, H-2′), 5.37 (d, 1H, *J* = 8.0 Hz, H-2), 4.80 (dd, 1H, *J* = 2.6, 11.2 Hz, H5a′), 4.79 (dt, 1H, *J* = 3.0, 8.0 Hz, H-3), 4.70 (m, 1H, H-4′), 4.67 (dd, 1H, *J* = 5.0, 11.2 Hz, H-5b′), 4.46 (dd, 1H, *J* = 5.5, 11.5 Hz, H-6a), 4.44 (dd, 1H, *J* = 3.5, 8.0 Hz, H-4), 4.34 (dd, 1H, *J* = 6.7, 11.5 Hz, H-6b), 4.20 (ddd, 1H, *J* = 3.5, 5.5, 6.7 Hz, H-5), 3.87 (d, 1H, *J* = 3.0, OH), 1.26, 1.19 (2s, 18H, $(CH_3)_3CCO$). ^{13}C NMR ($CDCl_3$) δ: 179.1, 177.0 ($(CH_3)_3C\mathit{C}O$), 168.7 (C-1), 166.1–165.8 (*C*OPh), 137.8–128.2 (aromatic), 107.6 (C-1′), 83.0 (C-2′), 81.2 (C-4′), 79.8 (C-4), 77.0 (C-3′), 76.4 (C-2), 74.8 (C-5), 72.4 (C-3), 63.4 (C-5′), 62.6 (C-6), 38.9, 38.7 ($(CH_3)_3\mathit{C}CO$), 27.1, 26.9 ($(\mathit{C}H_3)_3CCO$). These assignments were supported by COSY and HETCOR experiments. Anal. calcd. for $C_{42}H_{46}O_{15}$: C 63.79, H 5.86; found: C 63.72, H 6.13.

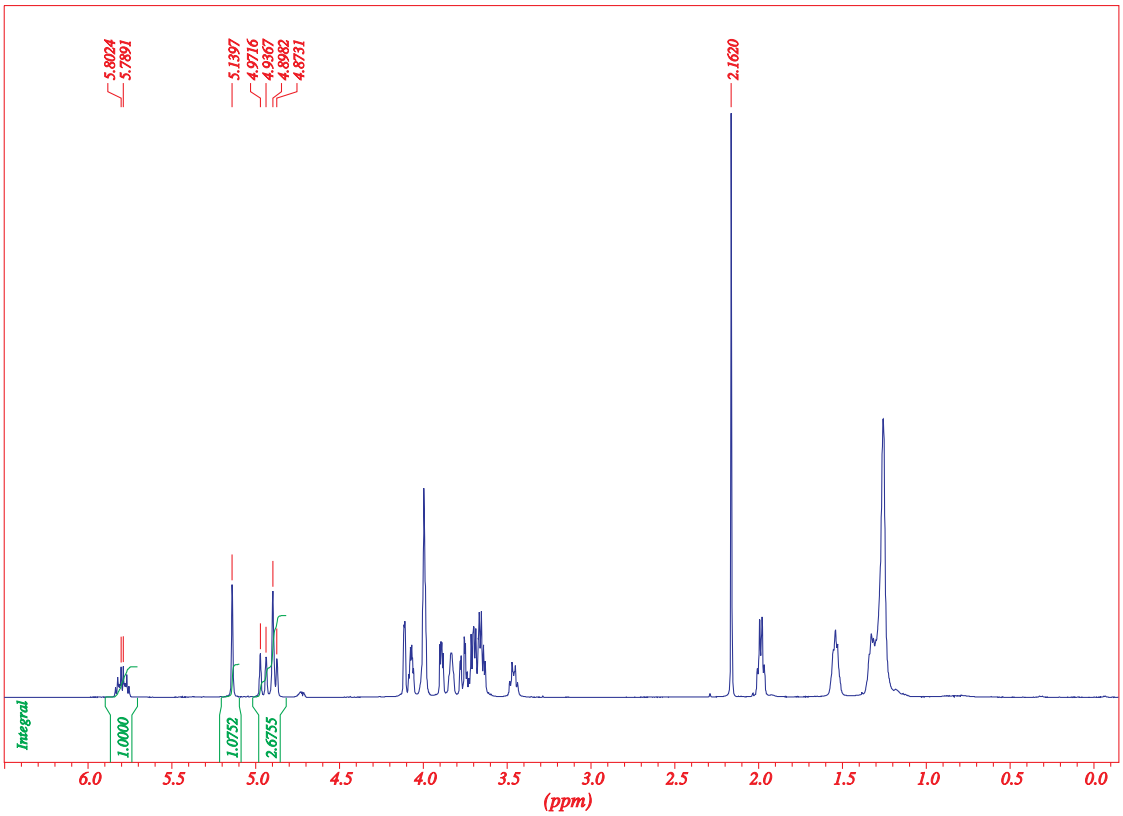
2,3,5-Tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-3-*O*-acetyl-2,6-di-*O*-pivaloyl-D-galactono-1,4-lactone (5)

To a solution of **4** (1.29 g, 1.63 mmol) in dry pyridine (13 mL), cooled at 0 °C, was added acetic anhydride (13 mL, dropwise) and the mixture was stirred at room temperature for 30 min. After cooling to 0 °C, the reaction was quenched by a slow addition of MeOH (20 mL) and the stirring continued for 30 min at room temperature. The solution was diluted with CH_2Cl_2 (200 mL) and then sequentially washed with 10% HCl (2 × 200 mL), water (200 mL), satd. aq. $NaHCO_3$ (200 mL), water, dried (Na_2SO_4), and then concentrated to give **5** (1.34 g, 99%) as a chromatographically pure syrup. R_f 0.66 (toluene–EtOAc, 3:1). $[\alpha]_D$ –21.3° (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 8.04–7.16 (m, 15H, aromatic), 5.76 (t, 1H, *J* = 6.6 Hz, H-3), 5.66 (d, 1H, *J* = 6.9 Hz, H-2), 5.63 (dd, 1H, *J* = 1.4, 4.6 Hz, H-3′), 5.59 (bs, 1H, H-1′), 5.56 (d, 1H, *J* = 1.4 Hz, H-2′), 4.80 (dd, 1H, *J* = 5.3, 13.5 Hz, H-5a′), 4.67 (m, 2H, H-4′, H-5b′), 4.55 (dd, 1H, *J* = 3.0, 6.4 Hz, H-4), 4.48 (dd, 1H, *J* = 4.4, 11.0 Hz, H-6a), 4.29 (dd, 1H, *J* = 7.1, 11.0 Hz, H-6b), 4.25 (ddd, 1H, *J* = 3.0, 4.4, 7.1 Hz, H-5), 2.11 (s, 3H, CH_3), 1.20, 1.18 (2s, 18H, $(CH_3)_3CCO$)). ^{13}C NMR ($CDCl_3$) δ: 177.6, 177.1 ($(CH_3)_3C\mathit{C}O$), 169.9 (C-1), 168.4 ($\mathit{C}OCH_3$), 166.1–165.4 (*C*OPh), 133.5–128.3 (aromatic), 107.6 (C-1′), 82.4 (C-2′), 81.7 (C-4′), 79.1 (C-4), 77.2 (C-3′), 75.4 (C-5); 72.9, 72.0 (C-2, C-3), 63.6 (C-5′), 62.4 (C-6), 38.7, 38.6 ($(CH_3)_3\mathit{C}CO$), 27.1, 26.8 ($(\mathit{C}H_3)_3CCO$), 20.5 ($CO\mathit{C}H_3$). These assignments were supported by COSY and HETCOR experiments. Anal. calcd. for $C_{44}H_{48}O_{16}$: C 63.45, H 5.81; found: C 63.48, H 5.83.

2,3,5-Tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-3-*O*-acetyl-2,6-di-*O*-pivaloyl-D-galactofuranose (6)

A solution of bis(2-butyl-3methyl)borane (9.24 mmol) in anhydr. THF (2.6 mL), cooled to 0 °C and under an argon atmosphere, was added to a flask containing previously dried compound **5** (1.28 g, 1.54 mmol). The resulting solution was stirred for 22 h at room temperature and then processed as previously described (23). The organic layer was washed with water, dried (Na_2SO_4), and concentrated. Boric acid was eliminated by coevaporation with MeOH (5 × 20 mL) at room temperature. The residue was purified by column chromatography (toluene–EtOAc, 15:1) to give

Fig. 1. ^{1}H NMR spectrum of compound **9** (D_2O, 500 MHz, acetone was used as internal reference).



1.05 g (86%) of **6** (syrup) as a 2:3 α:β anomeric mixture. R_f 0.43 (toluene–EtOAc, 3:1). $[\alpha]_D$ –2.4° (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) anomeric protons δ: 5.67 (bs, 0.5H, H-1′ for β anomer), 5.63 (bs, 0.5H, H-1′ for α anomer), 5.53 (d, 0.5H, J = 4.7 Hz, H-1 α anomer), 5.33 (bs, 0.5H, H-1 β anomer). ^{13}C NMR ($CDCl_3$) δ: 178.0–177.4 (($CH_3)_3CCO$)), 170.6, 170.1 ($COCH_3$), 166.1–165.3 ($COPh$), 133.7–125.3 (aromatic), 107.6 (C-1′β anomer), 106.5 (C-1′α anomer), 100.6 (C-1 β anomer), 95.0 (C-1 α anomer), 82.8, 82.1, 82.0, 81.7, 81.2, 80.9, 80.3, 77.7, 77.2, 77.1, 76.9, 76.7, 75.5, 75.2, 63.7, 63.6, 63.5, 63.0, 38.7 (($CH_3)_3CCO$)), 27.1, 27.0, 26.9 (($CH_3)_3CCO$), 20.7, 20.6 (CH_3). These assignments were supported by COSY and HETCOR experiments. Anal. calcd. for $C_{44}H_{50}O_{16}$: C 63.30, H 6.04; found: C 63.65, H 6.44.

9-Decenyl 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-3-*O*-acetyl-2,6-di-*O*-pivaloyl-D-galactofuranoside (8)

To a stirred solution of **6** (314 mg, 0.40 mmol) and trichloroacetonitrile (0.20 mL, 2.0 mmol) in dry CH_2Cl_2 (10 mL), cooled to 0 °C, DBU (28.4 µL, 0.18 mmol) was slowly added. After 1 h, the solution was concentrated under reduced pressure, and the residue was purified by column chromatography (toluene–EtOAc–TEA, 40:1:0.4) to give 342 mg (88%) of *O*-(2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-3-*O*-acetyl-2,6-di-*O*-pivaloyl-α,β-D-galactofuranosyl) trichloroacetimidate (**7**) as an amorphous solid (R_f 0.33 and 0.47 in toluene–EtOAc–TEA (9:1:0.09) for the α and β anomers, respectively). Compound **7** was stable for 1 day at –20 °C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 8.61 (s, 0.8H, N*H*), 8.44 (s, 0.2H, N*H*), 6.55 (d, 0.2H, J = 4.6 Hz, H-1 α anomer), 6.30 (s, 0.8H, H-1 β anomer). ^{13} C NMR ($CDCl_3$, 25 MHz) for the β anomer δ: 177.8, 177.0 (($CH_3)_3CCO$), 170.0 (CH_3CO), 166.2–165.2 ($COPh$), 160.2 ($NHCOCl_3$), 133.5–125.3 (aromatic), 106.5 (C-1′), 102.8 (C-1), 97.9 (C-1 α anomer), 84.0, 82.1, 81.3, 80.4, 77.6, 75.8, 74.3, 63.6, 63.4, 38.6 (($CH_3)_3CCO$ × 2), 27.1, 26.9 (($CH_3)_3CCO$), 20.6 (CH_3CO).

A vigorously stirred suspension of the trichloroacetimidate **7** (241 mg, 0.25 mmol), 9-decen-1-ol (60.4 µL, 0.33 mmol), and powdered activated 4 Å molecular sieves (0.5 g) in anhydr. CH_2Cl_2 (9 mL) was cooled to –20 °C, and TMSOTf (13.3 µL, 0.073 mmol) was slowly added. After 30 min of stirring, the mixture was filtered into aq. $NaHCO_3$ (15 mL) and then extracted with CH_2Cl_2 (2 × 25 mL). The organic layer was washed with water (3 × 40 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (toluene–EtOAc, 45:1) affording **8** (243 mg, 80%) as a syrup. R_f 0.60 (toluene–EtOAc, 9:1). $[\alpha]_D$ –23.9° (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 8.07–7.26 (m, 15H, aromatic), 5.80 (ddt, 1H, J = 6.7, 10.2, 17.2 Hz, C*H*=CH_2), 5.65 (s, 1H, H-1′), 5.61 (dd, 1H, J = 1.5, 5.0 Hz, H-3′), 5.57 (d, 1H, J = 1.5 Hz, H-2′), 5.23 (dd, 1H, J = 1.7, 5.5 Hz, H-3), 5.07 (d, 1H, J = 1.7 Hz, H-2), 4.98 (ddt, 1H, J = 1.2, 1.7, 17.2 Hz, HC=CH_aH), 4.94 (bs, 1H, H-1), 4.92 (ddt, 1H, J = 1.3, 2.5, 10.2 Hz, HC=CH_bH), 4.80 (dd, 1H, J = 3.2, 11.4 Hz, H-5a′), 4.71 (m, 1H, H-4′), 4.67 (dd, 1H, J = 4.8, 11.4 Hz, H-5b′), 4.36 (m, 1H, H-5), 4.24–4.30 (m, 3H, H-6a, H-6b, H-4), 3.67 (dt, 1H, J = 6.7, 9.7 Hz, CH_aHO), 3.40 (dt, 1H, J = 6.5, 9.7 Hz, CH_bHO), 2.07 (s, 3H, CH_3), 2.04 (m, 2H, CH_2), 1.58 (m, 2H, CH_2), 1.27 (m, 12H, CH_2), 1.17, 1.16 (2s, 18H,

((CH_3)$_3$CCO). ^{13}C NMR ($CDCl_3$) δ: 177.9, 177.4 ((CH_3)$_3$*C*CO), 170.2 (CH_3*C*O), 166.1–165.2 (*C*OPh), 139.1 (*C*H=CH_2), 133.5–128.3 (aromatic), 114.1 (CH=*C*H$_2$), 106.5 (C-1′), 105.3 (C-1), 82.2 (C-2′), 81.9 (C-2), 81.0 (C-4′), 80.9 (C-4), 77.7 (C-3′), 76.9 (C-3), 74.6 (C-5), 67.6 (CH_2O), 63.7 (C-5′), 63.6 (C-6), 38.7, 38.6, ((CH_3)$_3$*C*CO), 33.8, 29.4, 29.3, 29.0, 28.9, 27.1, 26.9, 26.0 (*C*H$_3$)$_3$CCO), 20.7 (CH_3). These assignments were supported by COSY and HETCOR experiments. Anal. calcd. for $C_{54}H_{68}O_{16}$: C 66.65, H 7.04; found: C 66.48, H 7.09.

9-Decenyl α-D-arabinofuranosyl-(1→5)-β-D-galactofuranoside (9)

Compound **8** (112 mg, 0.12 mmol) was suspended in 0.48 mol/L sodium methoxide in a methanol solution (1.7 mL) and cooled at 0 °C. After stirring for 1 h at 0 °C, the resulting solution was warmed to room temperature, stirred for 2 h, and water (0.5 mL) was added. The solution was passed through a column containing Amberlite IR-120 plus (H^+) resin (3 mL) and the column washed with MeOH–H_2O (9:1). The combined eluates were evaporated and the remaining methyl benzoate was eliminated by five successive coevaporations with water. The residue was dissolved in water, further purified through a C8-Maxi-Clean cartridge, and the solution lyophilized. Glycoside **9** (49 mg, 90%) was obtained as a hygroscopic syrup. R_f 0.86 (*n*-propanol–EtOH–H_2O, 7:1:1). $[\alpha]_D$ –4.4° (*c* 0.6, H_2O). ^{1}H NMR (D_2O) δ: 5.79 (ddt, 1H, *J* = 6.7, 10.4, 17.0 Hz, C*H*=CH$_2$), 5.14 (d, 1H, *J* = 1.9 Hz, H-1′), 4.95 (ddt, 1H, *J* = 1.5, 3.7, 17.0 Hz, HC=C*H*$_a$H), 4.90 (bs, 1H, H-1), 4.88 (ddt, 1H, *J* = 1.1, 2.2, 10.4 Hz, HC=C*H*$_b$H), 4.11 (dd, 1H, *J* = 1.9, 3.7 Hz, H-2′), 4.07 (ddd, 1H, *J* = 3.3, 5.9, 6.1 Hz, H-4′), 4.01–3.98 (m, 3H, H-2, H-3, H-4), 3.89 (dd, 1H, *J* = 3.7, 6.1 Hz, H-3′), 3.83 (m, 1H, H-5), 3.76 (dd, 1H, *J* = 3.3, 12.6 Hz, H-5a′), 3.74–3.63 (m, 3H, H-6a, H-6b, C*H*$_a$HO), 3.65 (dd, 1H, *J* = 5.9, 12.6 Hz, H-5b′), 3.46 (dt, 1H, *J* = 6.7, 10.0 Hz, C*H*$_b$HO), 1.98 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 1.36–1.22 (m, 10H, CH_2). ^{13}C NMR (D_2O) δ: 140.3 (*C*H=CH$_2$), 114.6 (CH=*C*H$_2$), 109.1 (C-1′), 107.6 (C-1), 84.4 (C-4′), 82.4 (C-2′), 81.9, 81.7 (C-4, C-2), 78.4 (C-5), 77.0, 76.9 (C-3′, C-3), 69.6 (CH_2O), 62.1 (C-6), 61.8 (C-5′), 34.0, 29.6, 29.5, 29.4, 29.2, 29.1, 26.1. HRMS (FAB+) *m*/*z* calcd. for $C_{21}H_{38}O_{10}Na$: 473.2363 (M + Na^+); found: 473.2356. Anal. calcd. for $C_{21}H_{38}O_{10}\cdot 0.5H_2O$: C 54.89, H 8.55; found: C 54.86, H 8.68.

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