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Synthesis of the trisaccharide portion of soyasaponin βg: evaluation of a new glucuronic acid acceptor

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Abstract

The synthesis of the trisaccharide portion of soyasaponin βg was successfully achieved using a new glucuronic acid acceptor: methyl 1-*O*-allyl-3,4-di-*O*-methoxymethyl-β-D-glucuronate (**9**). This compound and methyl 1-*O*-allyl-3,4-di-*O*-*tert*-butyldimethylsilyl-β-D-glucuronate (**8**) were both prepared from glucuronolactone via a glycal intermediate. The former compound **9** was successfully coupled to ethyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-1-thio-β-D-galactopyranoside (**13**) in excellent yield. Synthesis of the protected trisaccharide was then completed by the addition of a suitably protected rhamnose derivative to the disaccharide portion. The reactivity of the glucuronic acid derivative **9** was also explored with trichloroacetimidate and fluoride donors.

Keywords: DDMP saponins; Glucuronic acid glycosylation; Saponin synthesis

1. Introduction

Soyasaponin βg (**1**), a triterpenoid saponin, was first isolated and identified by our laboratory[1] as well as others[2] in 1992. Also known as Soysaponin VI[1] and Chromosaponin I,[2b] it is one of the major soybean saponins, and is found in a variety of other leguminous plants. In general, saponins are composed of oligosaccharides of various lengths which are attached to a triterpene or steroid aglycone. Soyasaponin βg (Fig. 1) is unique in that it possesses a 2,3-dihydro-2,5-dihydroxy-6-methyl-4*H*-pyran-4-one or 'DDMP' fragment attached through a glycoside bond to the C-22 hydroxyl group of the sapogenin Soyasapogenol B.

Numerous biological activities have been attributed to group B soybean saponins,[3] in particular to soyasaponin I, the non-DDMP counterpart of soyasaponin βg. Some of these activities include antiviral activity against HIV in vitro,[4] hepatoprotective effects,[5] and sialyltransferase inhibition.[6] In comparison, the biological activity of soyasaponin βg has been less studied, most likely due to the instability of this compound and the tedious extraction process required to obtain even a small quantity from natural sources. Oxygen and radical scavenging activity have been reported,[7] as well as the antimutagenic activity of saponin extracts containing a mixture of DDMP and non-DDMP saponins.[8]

Chemical synthesis offers an alternative to the extraction of low abundance saponins in natural products. The trisaccharide moiety of soyasaponin βg is composed of a β-D-glucuronic acid residue coupled in position 2 to a β-D-galactose residue, which in turn is coupled in position 2 to an α-L-rhamnose. This trisaccharide unit, also called 'fabatriose' has been shown to be essential to the hepatoprotective activity of certain β-fabatriosyl oleanene glycosides from Fabaceae plants.[5a]

The presence of a β-D-glucuronic acid residue coupled in position 2 to another sugar is common in a large variety of natural products, especially saponins. Unfortunately, the use of glucuronic acid derivatives as acceptors in glycosylation reactions remains problematic because the synthesis of the desired derivatives is not always straightforward, and the reactivity of the resulting hydroxy compound is often low. In many cases, glucose is used as a glucuronic acid equivalent,[9] and oxidation is performed at a later stage in the

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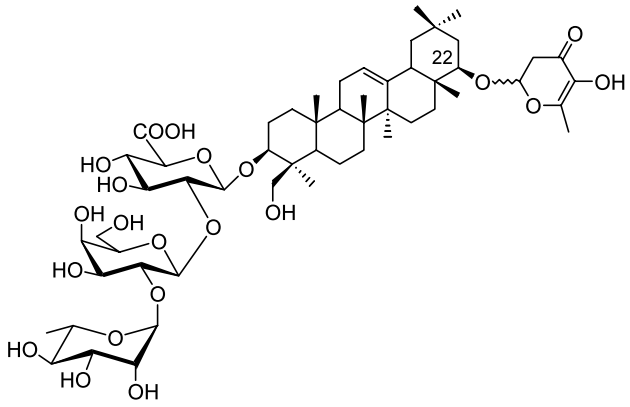


Fig. 1. Soyasaponin βg.

synthesis. This, however, involves additional protection and deprotection steps for the hydroxyl group in position 6 as well as final oxidation to the acid. To avoid these extra steps, we opted for the use of a glucuronic acid derivative in spite of the potential drawbacks.

The preparation and use of synthetic protected glucuronic acid derivatives having a free hydroxyl group in position 2 has been limited. Saito and co-workers reported the use of a 2-*O*-trichloroacetyl glucuronic acid chloride obtained by treatment of methyl 2,3,4-tri-*O*-acetyl-β-D-glucuronate with PCl_5 in toluene.[10] In the preparation of glycyrrhetinic acid α and β glycosides[11] and sarsasapogenin glycosides,[10] the glucuronic acid derivatives were first coupled to the genine, followed by selective deprotection of the trichloroacetyl group. The poor yields obtained for the synthesis of the glucuronic acid portion as well as for the glycosylation steps discouraged the use of this method.

More recently, glucuronic acid glycals were reported as being a possible source of 2-hydroxy glucuronic acid derivatives through oxidation of the glycal followed by ring opening. 2-Hydroxythioglycosides of methyl glucuronate have been described using dimethoxydioxirane as the oxidizing agent.[12] Gin and Kim reported the sulfonium mediated oxidation of glucuronic acid glycals followed by nucleophilic epoxide opening, and the use of this sugar in their synthesis of the immunologic adjuvant QS-21A.[13] We wish to report the preparation of a new glucuronic acid derivative and its use in the synthesis of the trisaccharide portion of Soyasapogenin βg. The reactivity of this compound as an acceptor in glycosylation reactions with various donors was also studied.

2. Results and discussion

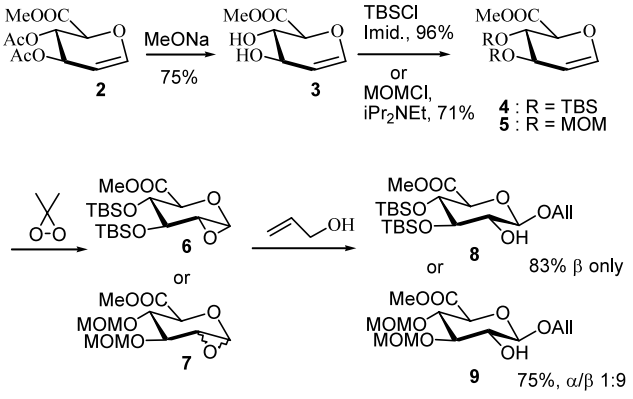
The starting point of the synthesis was methyl 3,4-di-*O*-acetyl-D-glucuronate glycal (**2**), readily available from commercially available glucuronolactone.[14] Deacetylation with sodium methoxide followed by protection with *tert*-butyldimethylsilyl (TBS) or methoxymethyl (MOM) groups led to compounds **4** and **5**. Treatment of the glycals with dimethoxydioxirane[15] led to the formation of only one epoxide in the case of the TBS derivative **6**, and a mixture of epoxides when starting from the MOM compound **5** (Scheme 1).

The orientation of the epoxide (α or β) could not be determined in an absolute manner based solely on ^1H NMR coupling constants, but ring opening of the TBS derivative by allyl alcohol gave the β anomer exclusively (**8**), indicating that the precursor was the α epoxide. Similar treatment of the MOM epoxide mixture resulted in the formation of the two easily separated anomers in an α/β ratio of 1:9, again showing that the major epoxide was α.

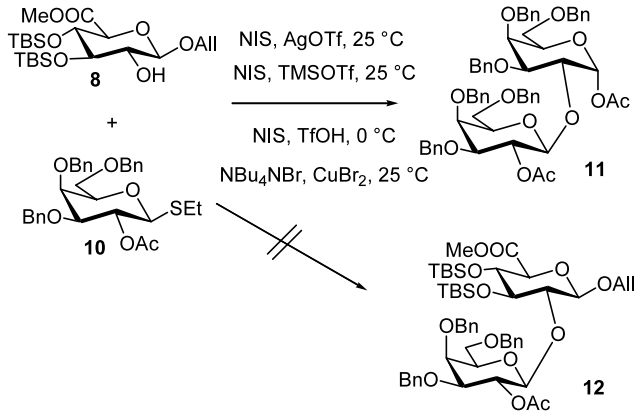
The thioglycoside ethyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-1-thio-β-D-galactopyranoside[16] **10** (Scheme 2) was chosen as a suitable galactose donor. The acetate group in position 2 could be selectively deprotected after disaccharide formation, and would also serve to promote β-glycosyeudation. Unfortunately, coupling of the TBS acceptor **8** and the thioglycoside donor **10** proved unsuccessful despite the different reaction conditions exemplified in Scheme 2.

One of the only identifiable products obtained in trace amounts was the coupling product between two galactose residues **11** as a result of acetate migration. The limited reactivity of the acceptor seemed to be the origin of the failed glycosylations for steric and/or electronic reasons. The first positive results were obtained by using the MOM glucuronic acceptor **9** with the thioglycoside **10** in the presence of trifluoromethanesulfonic acid (TfOH) and *N*-iodosuccinimide (NIS) (Scheme 3). The disaccharide **14** was synthesized in 50% yield, which tended to confirm the hypothesis of steric hindrance influencing the reactivity of the acceptor.

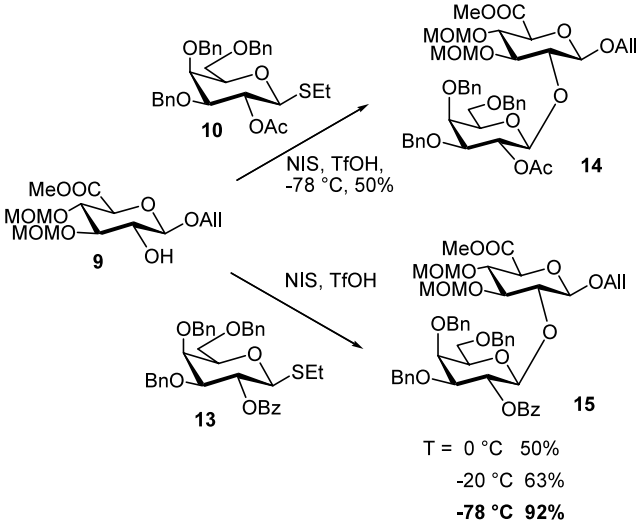
A series of reactions were then carried out to optimize disaccharide formation. Although no orthoacetate formation had been detected in the glycosylation reaction, the acetate group in position 2 was replaced with a



Scheme 1.

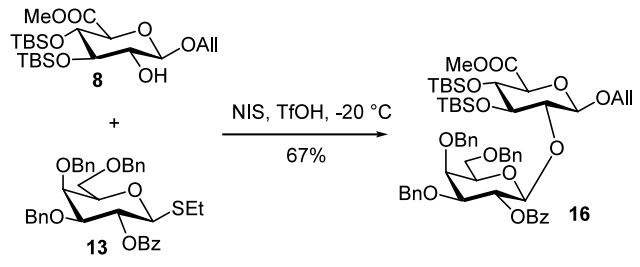


Scheme 2.



Scheme 3.

benzoate ester in an attempt to increase the yield of the reaction. Glycosylation with the galactose derivative **13** at 0 °C gave a 50% yield of disaccharide **15** and lowering the temperature to −78 °C gave 92% of the disaccharide. When these optimized conditions were applied to the coupling reaction between the thioglycoside **13** and the TBS acceptor **8**, disaccharide formation was observed for the first time (Scheme 4), but the yields were lower compared to glycosylation with **9**. The MOM



Scheme 4.

derivative was therefore used for the rest of the synthesis.

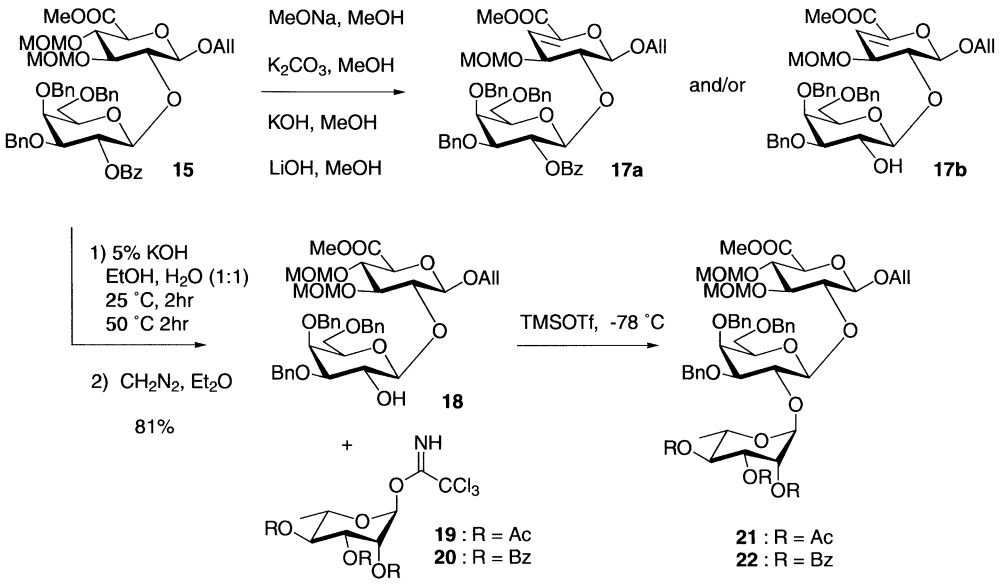
The next step was the deprotection of the benzoate ester in position 2 of the galactose residue (Scheme 5). Deprotection under strongly basic conditions resulted in total elimination of the protected hydroxyl group in position 4 of the glucuronic acid portion to give **17a** which went on to lose the benzoate ester giving **17b**. Use of milder aqueous conditions resulted in the initial saponification of the glucuronic ester, thus effectively avoiding the elimination reaction, followed by removal of the benzoate ester. Treatment of the crude reaction mixture with diazomethane gave the hydroxy disaccharide **18** in good yield.

Finally, coupling of the disaccharide **18** with 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl trichloroacetimidate[17] (**19**) in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) gave the desired trisaccharide in 44% yield. A further improvement was made by using 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl trichloroacetimidate[18] (**20**) under the same reaction conditions which gave 80% of the trisaccharide **22** (Scheme 5). This rhamnose derivative also proved to be more stable and give a cleaner reaction than the acetylated one.

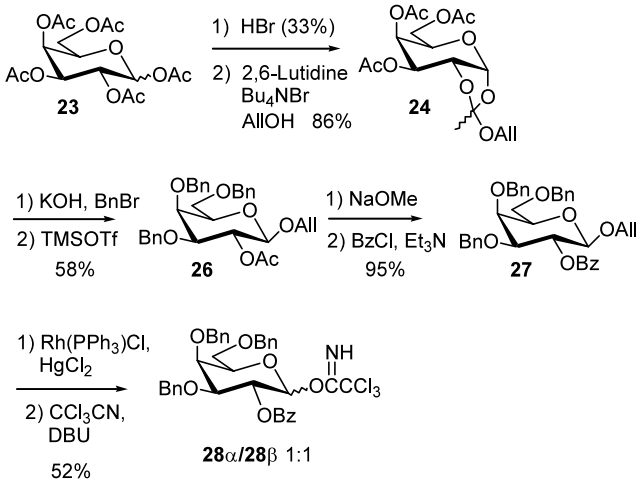
Having the glucuronic acceptor **9** in hand, it became very interesting to investigate its reactivity in the presence of different donors. Three types of glycosyl donors are routinely used in carbohydrate synthesis: thioglycosides,[19] trichloroacetimidates,[20] and glycosyl fluorides.[21,22] Having successfully used thioglycoside donors, trichloroacetimidates were then studied. 2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-α-D-galactopyranosyl trichloroacetimidate (**28α**) was synthesized from 1,2,3,4,6-penta-*O*-acetyl-D-galactose via the allyl orthoester **24** (Scheme 6). One pot deacetylation/benzylation of **24** followed by orthoester opening with TMSOTf gave **26** in good overall yield. The acetate at position 2 was then replaced with a benzoate ester **27**, and the allyl anomeric protecting group was removed with rhodium catalysis. DBU catalysis of trichloroacetimidate formation gave a 1:1 mixture of anomers **28α/28β** which were easily separated by column chromatography.

Limited disaccharide formation was observed with the trichloroacetimidate **28α** and the glucuronic derivative **9** in the presence of TMSOTf at −20 or −78 °C. The major product of the reaction was identified as being the amide **29**, resulting from acid catalyzed rearrangement.[23] (Scheme 7). To our surprise, reaction of the β anomer under identical conditions gave different results as the disaccharide became the major product.

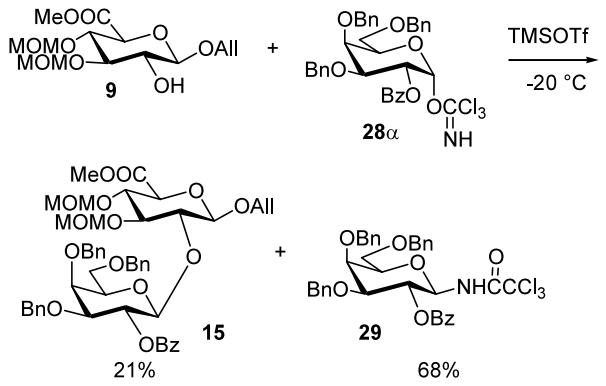
In an attempt to understand these results, two other galactose donors were prepared in order to compare the reactivity of the two anomers and to see if the ester at position 2 could influence the reaction mechanism in favor of increased disaccharide formation. The benzoate



Scheme 5.



Scheme 6.



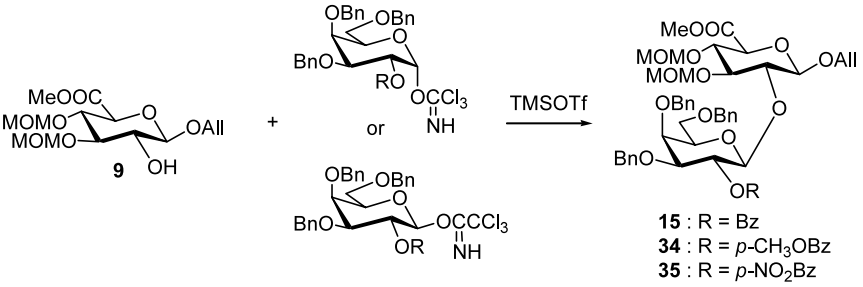
Scheme 7.

ester was replaced by a *p*-methoxybenzoate, and a *p*-nitrobenzoate. Four new trichloroacetimidates were thus synthesized from allyl 2-*O*-*p*-methoxybenzoyl-3,4,6-tri-*O*-benzyl-D-galactopyranoside (**30**) and allyl 2-*O*-*p*-nitrobenzoyl-3,4,6-tri-*O*-benzyl-D-galactopyranoside (**31**) (see Section 3). The results of the glycosylation reaction with all of the trichloroacetimidate derivatives and the MOM glucuronic acid acceptor **9** are summarized in Scheme 8.

The presence of a *p*-methoxybenzoyl in position 2 of the galactose residue had no influence on the reaction, but use of the β anomer gave more disaccharide at both temperatures. Using the *p*-nitrobenzoate trichloroacetimidates changed little in the case of the α anomer, but using the β anomer at −78 °C afforded 80% of the disaccharide.

When considering the reaction mechanism, the difference in behavior of the α and β anomers might be explained by rapid formation of the oxonium intermediate **36** (Scheme 9) in the case of the α anomer, followed by extremely fast trichloroacetamide 'capture' of the oxonium ion as well as formation of the orthoester **37** and reaction with either the acceptor hydroxyl or the trichloroacetamide. In the case of the β anomer, activation of the donor most likely results in the simultaneous formation of the orthoester intermediate and trichloroacetamide departure without passing through the oxonium intermediate, thus resulting in a smaller amount of rearrangement product.

The net increase in yield with a *p*-nitrobenzoyl protecting group in position 2 could result from an increase in the reactivity of the intermediate orthoester caused by the destabilizing effect of the electronegative *p*-nitro group. We observed that the glycosylation reaction at −78 °C was over within minutes using the



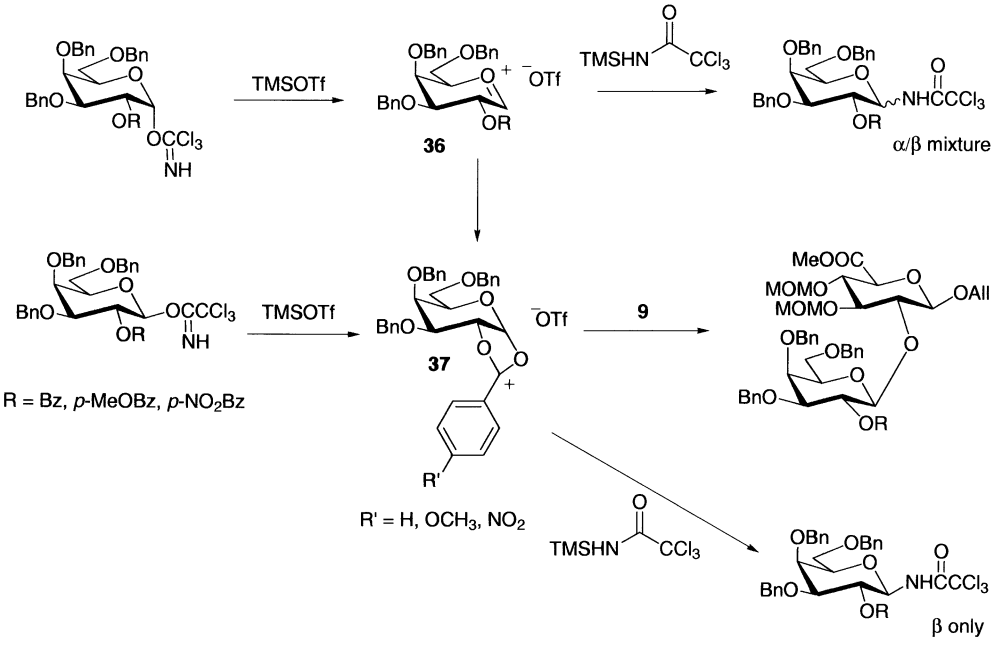
R	Disaccharide -20 °C	-78 °C
Bz (**28**α)	21%	27%
p-MeOBz (**32**α)	24%	21%
p-NO_2Bz (**33**α)	22%	24%
Bz (**28**β)	66%	65%
p-MeOBz (**32**β)	47%	62%
p-NO_2Bz (**33**β)	51%	80%

Scheme 8.

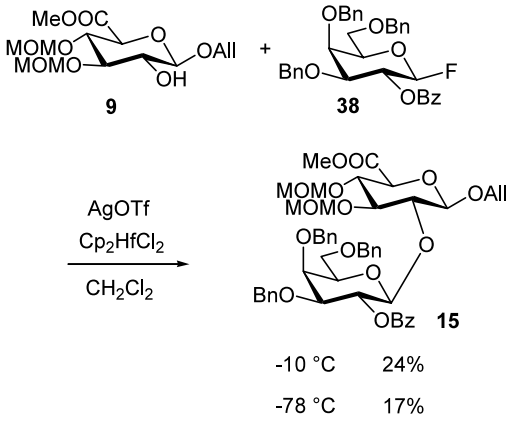
p-nitrobenzoate derivative as opposed to several hours for the benzoate and *p*-methoxybenzoate ester derivatives.

The use of the glycosyl fluoride donor, 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl fluoride[22] (**38**) failed under trifluromethanesulfonic acid catalysis.[22] Catalysis with silver trifluoromethanesulfonate and hafnocene dichloride at −10 and −78 °C gave the desired disaccharide **15** in only 24 and 17% yield, respectively (Scheme 10).

In summary, the synthesis of the protected trisaccharide **22** was completed with an overall yield of 59% from the protected monosaccharides, giving a versatile carbohydrate intermediate for the synthesis of soyasaponin βg as well as other glycoconjugates. A novel glucuronic acid derivative **9** was synthesized and tested in several types of glycosylation reactions giving disaccharides in good to excellent yields. For this type of acceptor having a limited reactivity, thioglycosides were shown to be the best donors followed by trichloroacetimidates, then



Scheme 9.



Scheme 10.

glycosyl fluorides. In the case of trichloroacetimidates, the anomeric configuration of the reacting donor as well as the ester protecting group at position 2 can have an important influence on the outcome of the reaction. Work is being continued toward completion of the synthesis of soyasaponin βg.

3. Experimental

3.1. General methods

All chemicals were reagent grade and used as supplied unless otherwise noted. Dichloromethane (CH_2Cl_2) and triethylamine were refluxed over calcium hydride and distilled prior to use. Analytical thin-layer chromatography (TLC) was performed on E. Merck Silica Gel 60 F_{254} plates. Compounds were visualized by dipping in an anisaldehyde solution in ethanol and heating. Column chromatography was performed using E. Merck Geduran Silica Gel Si 60 (40–60 μM). Optical rotations were recorded on a Perkin–Elmer 241 polarimeter. ESIMS were recorded with a Thermofinnigan quadripolar mass spectrometer with positive ion data collected automatically. NMR spectra were obtained using a Bruker Avance DRX 500 spectrometer (500 MHz for ^1H and 125 MHz for ^{13}C). Elemental analyses were performed on a Perkin–Elmer CHN 2400.

3.2. Methyl 1,5-anhydro-2-deoxy-3,4-di-*O*-methoxymethyl-D-*arabino*-hex-1-enuronate (5)

Methoxymethyl chloride (1.57 g, 19.5 mmol) was added at 0 °C to a solution of glycal **3**[12] (0.566 g, 3.25 mmol) and iPr$_2$EtN (3.36 g, 26 mmol) in anhyd CH_2Cl_2 (25 mL). The mixture was then stirred for 48 h at room temperature (r.t.). The reaction mixture was evaporated to dryness and taken up in EtOAc (50 mL) which was washed with satd aq $NaHCO_3$. The aq layer was further extracted with EtOAc, and the combined extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed (1:1 cyclohexane–EtOAc) to give **5** as a colorless syrup (0.555 g, 69%), as well as 0.044 g of the mono 3-OH protected derivative which was recycled; $[\alpha]_D$ +7.6° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.65 (d, 1 H, $J_{1,2}$ 6.5 Hz, H-1), 5.01 (ddd, 1 H, $J_{2,3}$ 5.5, $J_{2,4}$ 1.7 Hz, H-2), 4.83 (dd, 1 H, $J_{4,5}$ 2.6, $J_{3,5}$ 1.8 Hz, H-5), 4.8 (s, 2 H, –OCH_2O–), 4.65 (d, 1 H, –OCH_2O–), 4.59 (d, 1 H, –OCH_2O–), 4.31 (dd, 1 H, $J_{3,4}$ 4.2 Hz, H-4), 3.8 (ddd, 1 H, H-3), 3.73 (s, 3 H, OCH_3), 3.42 (s, 3 H, OCH_3), 3.36 (s, 3 H, OCH_3). ^{13}C NMR ($CDCl_3$): δ 168.4 (*C*OOCH$_3$), 145.1 (C-1), 98.3 (C-2), 96 (–OCH_2O–), 93.9 (–OCH_2O–), 73.3 (C-5), 72, (C-4), 65.2 (C-3), 55.8 (OCH_3), 55.6 (OCH_3), 52.1 (OCH_3). Anal. Calcd for $C_{11}H_{18}O_7$: C, 50.38; H, 6.92. Found: C, 50.41; H, 6.74.

3.3. Methyl 1-*O*-allyl-3,4-di-*O*-*tert*-butyldimethylsilyl-β-D-glucuronate (8)

A solution of glycal **4**[12] (1.2 g, 3.0 mmol) in CH_2Cl_2 (10 mL) was added dropwise to an acetone solution of dimethoxydioxirane ($\sim$ 0.095 M, 54 mL, 5.1 mmol) at 0 °C, and the mixture was stirred for 2 h until an NMR sample showed the reaction to be complete. After most of the acetone was evaporated, the residue was dissolved in CH_2Cl_2, dried (Na_2SO_4), and filtered. The filtrate was then evaporated to give the crude epoxide **6**. Allyl alcohol (25 mL) was added and the reaction was stirred for 5 days at r.t. and stopped when an NMR sample of the reaction mixture showed no more starting material. The solvent was evaporated, and the residue chromatographed on silica gel (19:1 cyclohexane–EtOAc) to give **8** as a colorless syrup (1.2 g, 83%); $[\alpha]_D$ −36.5° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.92 (m, 1 H, C*H*=CH$_2$), 5.3 (dd, 1 H, *J* 17.3, *J* 1.6 Hz, CH=C*H*$_2$), 5.19 (dd, 1 H, *J* 10.4, *J* 1.3 Hz, CH=C*H*$_2$), 4.74 (d, 1 H, $J_{1,2}$ 4.5 Hz, H-1), 4.5 (ddt, 1 H, *J* 12.7, *J* 5, *J* 1.4 Hz, C*H*$_2$–CH=CH$_2$), 4.25 (dd, 1 H, $J_{3,4} = J_{4,5}$ 4.5 Hz, H-4), 4.19 (d, 1 H, H-5), 4.08 (dd, 1 H, *J* 12.7, *J* 6.4 Hz, C*H*$_2$–CH=CH$_2$), 3.81 (dd, 1 H, $J_{2,3} = J_{3,4}$ 4.5 Hz, H-3), 3.75 (s, 3 H, $COOCH_3$), 3.55 (ddd, 1 H, $J_{2,\ OH}$ 7.8, H-2), 3.08 (d, 1 H, OH), 0.92 (s, 9 H, *tert*-butyl), 0.89 (s, 9 H, *tert*-butyl), 0.19 (s, 3 H, CH_3Si), 0.12 (s, 6 H, 2 × CH_3Si), 0.1 (s, 3 H, CH_3Si); ^{13}C NMR ($CDCl_3$): δ 169.7 (*C*OOCH$_3$), 134.3 (*C*H=CH$_2$), 117.1 (CH=*C*H$_2$), 100.8 (C-1), 75.9 (C-5), 72.5 (C-3), 72.2 (C-2), 72.1 (C-4), 70.1 (*C*H$_2$–CH=CH$_2$), 52.1 (OCH_3), 25.9, 25.7 (*tert*-butyl), −4.2, −4.3, −4.4 (CH_3Si); ESIMS: *m*/*z* 499 $(M+Na)^+$; Anal. Calcd for $C_{22}H_{44}O_7Si_2$: C, 55.42; H, 9.3. Found: C, 55.19; H, 9.61.

3.4. Methyl 1-*O*-allyl-3,4-di-*O*-methoxymethyl-β-D-glucuronate (9)

A solution of glycal **5** (2.43 g, 9.3 mmol) in CH_2Cl_2 (20 mL) was added dropwise to an acetone solution of dimethoxydioxirane ($\sim$ 0.084 M, 133 mL, 11.2 mmol) at 0 °C, and the mixture was stirred for 2 h until an NMR sample showed the reaction to be complete. After most of the acetone was evaporated, the residue was dissolved in CH_2Cl_2, dried (Na_2SO_4), and filtered. The filtrate was then evaporated to give the crude epoxide **7**. Allyl alcohol (30 mL) was added and the reaction was stirred for 5 days at r.t. and stopped when an NMR sample of the reaction mixture showed no more starting material. The solvent was evaporated, and the residue chromatographed on silica gel (1:1 cyclohexane–EtOAc) to give **9** as a colorless syrup (2.12 g, 68%), as well as 0.210 g of the more polar α isomer (6.8%); $[\alpha]_D$ +34.2° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 5.95 (m, 1 H, C*H*=CH_2), 5.35 (dd, 1 H, *J* 17.2, *J* 1.4 Hz, CH=C*H*$_2$), 5.19 (dd, 1 H, *J* 10.4, *J* 1.1 Hz, CH=C*H*$_2$), 4.84 (d, 1 H, –OCH_2O–), 4.79 (d, 1 H, –OCH_2O–), 4.78 (d, 1 H, –OCH_2O–), 4.65 (d, 1 H, –OCH_2O–), 4.41 (d, 1 H, $J_{1,2}$ 7.2 Hz, H-1), 4.40 (ddt, 1 H, *J* 12.8, *J* 5.2, *J* 1.5 Hz, C*H*$_2$–CH=CH_2), 4.15 (ddt, 1 H, *J* 12.8, *J* 6.5, *J* 1.0 Hz, C*H*$_2$–CH=CH_2), 3.89 (m, 2 H, H-4, H-5), 3.82 (s, 3 H, $COOCH_3$), 3.5 (m, 5 H, H-2, H-3, OCH_3), 3.33 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$): δ 168.5 (*C*$OOCH_3$), 133.4 (*C*H=CH_2), 118.2 (CH=*C*H$_2$), 101.7 (C-1), 98.3, 98 (2 × –OCH_2O–), 86.2 (C-3), 76.5 (C-4), 75 (C-5), 72.6 (C-2), 70.3 (*C*H$_2$–CH=CH_2), 56.2, 56.1 (2 × OCH_3), 52.5 (COO*C*H$_3$); Anal. Calcd for $C_{14}H_{24}O_9$: C, 50.00; H, 7.19. Found: C, 49.79; H, 7.37.

3.5. Ethyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-1-thio-β-D-galactopyranoside (13)

Benzoyl chloride (0.453 mL, 3.9 mmol) was added to a mixture of ethyl 3,4,6-tri-*O*-benzyl-1-thio-β-D-galactopyranoside[16] (1.29 g, 2.6 mmol), triethylamine (1.09 mL, 7.8 mmol), and dimethylaminopyridine (DMAP) (0.064 g, 0.52 mmol) in CH_2Cl_2 (40 mL). The reaction was refluxed overnight, cooled, and quenched by the addition of MeOH (3 mL). The solvent was evaporated, the crude residue taken up in EtOAc, and the organic layer washed with HCl (2 N), $NaHCO_3$, and brine. After drying, (Na_2SO_4), the solvent was evaporated and the crude residue purified by column chromatography (19:1 cyclohexane–EtOAc) to give **13** (1.37 g, 88%) as a white solid; mp 80 °C; $[\alpha]_D$ +23.4° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.1 (d, 2 H, Bz–H), 7.65 (t, 1 H, Bz–H), 7.52 (t, 2 H, Bz–H), 7.45–7.2 (m, 15 H), 5.78 (t, 1 H, $J_{1,2}$ = $J_{2,3}$ 9.7 Hz, H-2), 5.09 (d, 1 H, C*H*$_2$Ph), 4.71 (m, 2 H, C*H*$_2$Ph), 4.55 (m, 4 H, H-1, C*H*$_2$Ph), 4.12 (d, 1 H, $J_{3,4}$ 2.6 Hz, H-4), 3.73 (m, 4 H, H-3, H-5, H-6a/b), 2.69 (m, 2 H, CH_3CH_2S), 1.8 (t, 3 H, CH_3CH_2S); ^{13}C NMR ($CDCl_3$): δ 165.4, 138.6, 137.8, 137.7, 133, 130.1, 129.9, 128.5, 128.3, 128.2, 128.1, 128, 127.9, 127.7, 127.5, 83.7 (C-1), 81.1 (C-3), 77.5 (C-5), 74.4, 73.6, 72.8 (C-4), 71.7, 70.2 (C-2), 68.5 (C-6), 23.7, 14.8; ESIMS: *m*/*z* 621 $(M+Na)^+$; Anal. Calcd for $C_{36}H_{38}O_6S$: C, 72.22; H, 6.40. Found: C, 72.27; H, 6.55.

3.6. Methyl (2-*O*-acetyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→2)-(allyl 3,4-di-*O*-methoxymethyl-β-D-glucopyranosid)uronate (14)

A mixture of alcohol **9** (0.082 g, 0.24 mmol), donor **10** (0.196 g, 0.37 mmol), and 4 Å powdered molecular sieves (1 g) was stirred for 2 h at r.t. in CH_2Cl_2 (7 mL). The mixture was cooled to −78 °C and *N*-iodosuccinimide (0.082 g, 0.37 mmol) was added followed by the dropwise addition of a triflic acid solution (0.162 mL, 0.02 mmol, $\sim$0.15 M solution). The reaction was slowly allowed to warm, and was complete within 30 min. The reaction was quenched with triethylamine and filtered through Celite. The filtrate was washed with $NaHCO_3$, 10% $Na_2S_2O_3$, and water. The organic layer was dried (Na_2SO_4), filtered and evaporated. The crude residue was purified by column chromatography (1.5:1 cyclohexane–EtOAc) to give **14** (0.099 g, 50%) as a colorless syrup; $[\alpha]_D$ +31.9° (*c* 0.96, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.31 (m, 15 H), 5.82 (m, 1 H, C*H*=CH_2), 5.35 (dd, 1 H, $J_{2',3'}$ 10, $J_{1',2'}$ 8.2 Hz, H-2′), 5.22 (dd, 1 H, *J* 17.2, *J* 1.5 Hz, CH=C*H*$_2$), 5.09 (dd, 1 H, *J* 10.5, *J* 1.3 Hz, CH=C*H*$_2$), 4.97 (d, 1 H, C*H*$_2$Ph), 4.83 (d, 1 H, –OCH_2O–), 4.77 (m, 2 H, H-1′, C*H*$_2$Ph), 4.67 (m, 3 H, C*H*$_2$Ph, –OCH_2O–), 4.6 (d, 1 H, C*H*$_2$Ph), 4.52 (m, 2 H, H-1, –OCH_2O–), 4.41 (t, 2 H, C*H*$_2$Ph), 4.32 (m, 1 H, C*H*$_2$–CH=CH_2), 4.02 (m, 1 H, C*H*$_2$–CH=CH_2), 3.98 (d, 1 H, $J_{3',4'}$ 2.4 Hz, H-4′), 3.91 (d, 1 H, $J_{4,5}$ 9.2 Hz, H-5), 3.85 (t, 1 H, *J* 9 Hz, H-4), 3.8 (s, 3 H, OCH_3), 3.68 (t, 1 H, H-3), 3.65–3.44 (m, 4 H, H-2, H-5′, H-6a′/6b′), 3.5 (dd, 1 H, H-3′), 3.38 (s, 3 H, OCH_3), 3.31 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$): δ 169.5, 168.9, 138.4, 137.8, 137.6, 133.7, 128.4, 128.2, 128.1, 128, 127.8, 127.7, 127.5, 127.4, 117, 101.8 (C-1), 101.1 (C-1′), 98.6, 98.3, 81.4 (C-2), 80.4 (C-3′), 79.3 (C-3), 77.3 (C-4), 75 (C-5), 74.4, 73.5 (C-5′), 73.5, 72.2 (C-2′), 72.1 (C-4′), 71.7, 70.5, 68.2 (C-6′), 56.2, 52.4, 21; ESIMS: *m*/*z* 833 $(M+Na)^+$.

3.7. Methyl (2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→2)-(allyl 3,4-di-*O*-methoxymethyl-β-D-glucopyranosid)uronate (15)

A mixture of alcohol **9** (0.150 g, 0.45 mmol), donor **13** (0.4 g, 0.67 mmol), and 4 Å powdered molecular sieves (2 g) was stirred for 2 h at r.t. in CH_2Cl_2 (15 mL). The mixture was cooled to −78 °C and *N*-iodosuccinimide (0.150 g, 0.67 mmol) was added followed by the

dropwise addition of a triflic acid solution (0.297 mL, 0.04 mmol, ~0.15 M solution). The reaction was slowly allowed to warm, and was complete within 30 min. The reaction was quenched with triethylamine and filtered through Celite. The filtrate was washed with $NaHCO_3$, 10% $Na_2S_2O_3$, and water. The organic layer was dried (Na_2SO_4), filtered and evaporated. The crude residue was purified by column chromatography (1.5:1 cyclohexane–EtOAc) to give **15** (0.357 g, 92%) as a colorless syrup; $[\alpha]_D$ +19.3° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.03 (d, 2 H, Bz–H), 7.6 (t, 1 H, Bz–H), 7.47 (t, 2 H, Bz–H), 7.4–7.1 (m, 15 H), 5.84 (m, 1 H, C*H*=CH_2), 5.64 (dd, 1 H, $J_{2',3'}$ 9.9, $J_{1',2'}$ 8.2 Hz, H-2′), 5.23 (dd, 1 H, *J* 17.3, *J* 1.5 Hz, CH=CH_2), 5.1 (dd, 1 H, *J* 10.5, *J* 1.1 Hz, CH=CH_2), 5.02 (d, 1 H, CH_2Ph), 4.89 (d, 1 H, H-1′), 4.64 (m, 4 H, CH_2Ph, –OCH_2O–), 4.54 (m, 2 H, H-1, CH_2Ph), 4.5–4.4 (m, 4 H, CH_2Ph, –OCH_2O–), 4.32 (dd, 1 H, *J* 12.4, *J* 5.1 Hz, CH_2–CH=CH_2), 4.03 (m, 2 H, H-4′, CH_2–CH=CH_2), 3.85 (d, 1 H, $J_{4,5}$ 9.1 Hz, H-5), 3.77 (s, 3 H, OCH_3), 3.69 (m, 2 H, H-4, H-6a′), 3.6 (m, 5 H, H-2, H-3, H-3′, H-5′, H-6b′), 3.25 (s, 3 H, OCH_3), 3.19 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$): δ 168.9, 165.3, 138.4, 137.6, 137.5, 133.7, 132.9, 130.2, 129.7, 128.4, 128.3, 128.2, 128.1, 128, 127.9, 127.6, 127.5, 117, 101.8 (C-1), 101.2 (C-1′), 98.5, 98.2, 81.8 (C-2), 80 (C-3′), 79.7 (C-3), 77.2 (C-4), 74.9 (C-5), 74.4, 73.5 (C-5′), 73.5, 72.6 (C-2′), 72 (C-4′), 71.4, 70.6, 68.2 (C-6′), 56.1, 56, 52.4; ESIMS: *m*/*z* 895 $(M+Na)^+$; Anal. Calcd for $C_{48}H_{56}O_{15}$: C, 66.04; H, 6.47. Found: C, 66.35; H, 6.54.

3.8. Methyl (2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→2)-(allyl 3,4-di-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosid)uronate (16)

A mixture of alcohol **8** (0.030 g, 0.06 mmol), donor **13** (0.056 g, 0.09 mmol), and 4 Å powdered molecular sieves (400 mg) was stirred for 2 h at r.t. in CH_2Cl_2 (5 mL). The mixture was cooled to −78 °C and *N*-iodosuccinimide (0.021 g, 0.09 mmol) was added followed by the dropwise addition of a triflic acid solution (0.041 mL, 0.006 mmol, ~0.15 M solution). The reaction was slowly allowed to warm, and was complete within 30 min. The reaction was quenched with triethylamine and filtered through Celite. The filtrate was washed with $NaHCO_3$, 10% $Na_2S_2O_3$, and water. The organic layer was dried (Na_2SO_4), filtered and evaporated. The crude residue was purified by column chromatography (9:1 cyclohexane–EtOAc) to give **16** (0.043 g, 67%) as a colorless syrup; $[\alpha]_D$ +17.0° (*c* 0.94, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.05 (d, 2 H, Bz–H), 7.59 (t, 1 H, Bz–H), 7.45 (t, 2 H, Bz–H), 7.4–7.1 (m, 15 H), 5.91 (m, 1 H, C*H*=CH_2), 5.6 (dd, 1 H, $J_{2',3'}$ 10, $J_{1',2'}$ 8.1 Hz, H-2′), 5.28 (dl, 1 H, *J* 17.3 Hz, CH=CH_2), 5.13 (m, 2 H, H-1, CH=CH_2), 5.08 (d, 1 H, CH_2Ph), 4.75 (d, 1 H, H-1′), 4.69 (d, 1 H, CH_2Ph), 4.6 (d, 1 H, CH_2Ph), 4.51 (d, 1 H, CH_2Ph), 4.45 (m, 3 H, CH_2–CH=CH_2, CH_2Ph), 4.32 (sl, 1 H, H-5), 4.21 (dl, 1 H, $J_{3,4}$ 2.9 Hz, H-4), 4.04 (sl, 1 H, H-4′), 3.95 (dd, 1 H, *J* 12.3, *J* 5.7 Hz, CH_2–CH=CH_2), 3.71 (m, 5 H, H-3, H-6a′, OCH_3), 3.6 (m, 4 H, H-2′, H-3′, H-5′, H-6b′), 0.9 (s, 9 H, *tert*-butyl), 0.69 (s, 9 H, *tert*-butyl), 0.1 (s, 6 H, 2 × CH_3Si), −0.22 (s, 3 H, CH_3Si), −0.25 (s, 3 H, CH_3Si); ^{13}C NMR ($CDCl_3$): δ 170.2, 164.9, 138.9, 137.8, 137.7, 134.5, 132.8, 130.3, 129.9, 128.4, 128.2, 128.1, 128, 127.9, 127.8, 127.6, 127.1, 116.5, 100.5 (C-1′), 100 (C-1), 83 (C-2), 79.8 (C-3′), 79 (C-5), 74.3, 74.2 (C-3), 73.5, 72.7 (C-5′), 72.6 (C-4′), 72.1 (C-2′), 72 (C-4), 71.3, 70.4, 68.4 (C-6′), 52.1, 25.6, 25.5, −5, −5.4, −5.2; ESIMS: *m*/*z* 1036 $(M+Na)^+$; Anal. Calcd for $C_{56}H_{76}O_{13}Si_2$: C, 66.37; H, 7.56. Found: C, 66.03; H, 7.38.

3.9. Methyl (3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→2)-(allyl 3,4-di-*O*-methoxymethyl-β-D-glucopyranosid)uronate (18)

A solution of KOH (5% in 1:1 EtOH–water, 30 mL) was added to the disaccharide **15** (0.158 g, 0.018 mmol). The reaction was stirred for 2 h at r.t., and then heated to 50 °C for another 2 h. The reaction was carefully acidified with HCl (2 N), extracted with EtOAc, dried (Na_2SO_4), and concentrated. The crude residue was taken up in Et_2O (5 mL), and treated with diazomethane at 0 °C. Stirring was continued for 30 min at r.t. Evaporation of the solvent followed by column chromatography (1.5:1 cyclohexane–EtOAc) of the crude product gave **18** (0.127 g, 91%) as a colorless syrup; $[\alpha]_D$ +7.9° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.45–7.2 (m, 15 H), 5.8 (m, 1 H, C*H*=CH_2), 5.22 (dd, 1 H, *J* 17.3, *J* 1.7 Hz, CH=CH_2), 5.09 (dd, 1 H, *J* 10.5, *J* 1.5 Hz, CH=CH_2), 4.94 (d, 1 H, CH_2Ph), 4.88 (m, 2 H, –OCH_2O–), 4.82 (d, 1 H, CH_2Ph), 4.8 (d, 1 H, –OCH_2O–), 4.75 (d, 1 H, CH_2Ph), 4.68 (d, 1 H, –OCH_2O–), 4.62 (d, 1 H, CH_2Ph), 4.58 (d, 1 H, $J_{1,2}$ 6.6 Hz, H-1), 4.48 (d, 1 H, $J_{1',2'}$ 7.7 Hz, H-1′), 4.42 (d, 1 H, CH_2Ph), 4.39 (d, 1 H, CH_2Ph), 4.31 (m, 1 H, CH_2–CH=CH_2), 4.03 (m, 1 H, CH_2–CH=CH_2), 3.99 (dd, 1 H, $J_{2',3'}$ 9.8, Hz, H-2′), 3.92 (d, 1 H, $J_{3',4'}$ 2.5 Hz, H-4′), 3.88 (m, 2 H, H-4, H-5), 3.8 (s, 3 H, OCH_3), 3.7 (m, 2 H, H-2, H-3), 3.65–3.5 (m, 3 H, H-5′, H-6a′/6b′), 3.49 (d, 1 H, H-3′), 3.47 (s, 3 H, OCH_3), 3.33 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$): δ 168.7, 138.6, 138.5, 137.7, 133.7, 128.4, 128.2, 128.1, 127.9, 127.8, 127.5, 127.4, 116.7, 104.7 (C-1′), 101.9 (C-1), 98.7, 98.1, 82.4 (C-2), 82.1 (C-3), 81.5 (C-3′), 77.1 (C-4), 74.7, 74.3 (C-5), 73.5 (C-5′), 73.4, 73.3 (C-4′), 72.7, 72.3 (C-2′), 70.5, 68.3 (C-6′), 56.4, 56.3, 52.5; Anal. Calcd for $C_{41}H_{52}O_{14}\cdot 0.3\,H_2O$: C, 63.60; H, 6.85. Found: C, 63.40; H, 6.59.

3.10. Methyl (2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→2)-(allyl 3,4-di-*O*-methoxymethyl-β-D-glucopyranosid)uronate (21)

A mixture of alcohol **18** (0.087 g, 0.11 mmol), donor **19**[17] (0.074 g, 0.17 mmol), and 4 Å powdered molecular sieves (350 mg) was stirred for 1 h at r.t. in CH_2Cl_2 (5 mL). The mixture was cooled to −78 °C followed by the dropwise addition of a 0.1 M solution of TMSOTf in CH_2Cl_2 (0.056 mL, 0.006 mmol, 0.05 equiv). The reaction was slowly allowed to warm until TLC indicated that no more rhamnose imidate was present. The reaction was quenched with triethylamine, filtered through Celite, and evaporated. The crude residue was purified by column chromatography (1:1.5 cyclohexane–Et_2O) to give the trisaccharide **21** (0.052 g, 44%) as a colorless oil; ^{1}H NMR ($CDCl_3$): δ 7.3 (m, 15 H), 5.86 (m, 1 H, C*H*=CH_2), 5.38 (dd, 1 H, $J_{2'',3''}$ 3.4, $J_{1'',2''}$ 1.6 Hz, H-2″), 5.29 (m, 3 H, H-1″, H-3″, CH=CH_2), 5.11 (dd, 1 H, J 10.5, J 1.3 Hz, CH=CH_2), 5.07 (t, 1 H, $J_{3'',4''} = J_{4'',5''}$ 13.5 Hz, H-4″), 4.88 (m, 2 H, –OCH_2O–, CH_2Ph), 4.82 (m, 2 H, –OCH_2O–), 4.7 (m, 4 H, H-1, H-1′, –OCH_2O–, CH_2Ph), 4.55 (d, 2 H, CH_2Ph), 4.45 (d, 2 H, CH_2Ph), 4.34 (m, 2 H, H-5″, CH_2–CH=CH_2), 4.21 (t, 1 H, $J_{3,4} = J_{4,5}$ 9.1 Hz, H-4), 4.02 (m, 4 H, H-2, H-2′, H-5′, CH_2–CH=CH_2), 3.95 (s, 1 H, H-4′), 3.79 (s, 3 H, OCH_3), 3.75 (dd, 1 H, $J_{2,3}$ 5.1 Hz, H-3), 3.59 (m, 4 H, H-3′, H-5′, H-6a′/6b′), 3.42 (s, 3 H, OCH_3), 3.32 (s, 3 H, OCH_3), 2.09, (s, 3 H, CO*C*H_3), 2.06 (s, 3 H, CO*C*H_3), 1.98 (s, 3 H, CO*C*H_3), 1.2 (d, 3 H, $J_{5'',6''}$ 6.2 Hz, H-6″); ^{13}C NMR ($CDCl_3$): δ 170.4, 170.2, 169.9, 169.8, 138.3, 137.6, 137.3, 133.7, 128.4, 128.2, 128, 127.9, 127.8, 127.6, 117.3, 99.9 (C-1), 99.5 (C-1′), 98.1 (C-1″), 98, 97.4, 83.3 (C-3′), 80.4 (C-3), 77.6 (C-2), 76.1 (C-4), 74.7 (C-2′), 74.5 (C-5), 74.5, 73.5, 73.3 (C-5′), 72.5 (C-4′), 72.3, 71 (C-4″), 69.2 (C-2″, C-3″), 68.4, 67.5 (C-6′), 66.3 (C-5″), 56.2, 56.1, 52.3, 20.8, 20.7, 17 (C-6″); ESIMS: m/z 1064 $(M+Na)^+$.

3.11. Methyl (2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→2)-(allyl 3,4-di-*O*-methoxymethyl-β-D-glucopyranosid)uronate (22)

A mixture of alcohol **18** (0.160 g, 0.21 mmol), donor **20**[18] (0.223 g, 0.37 mmol), and 4 Å powdered molecular sieves (800 mg) was stirred for 1 h at r.t. in CH_2Cl_2 (20 mL). The mixture was cooled to −78 °C followed by the dropwise addition of a 0.1 M solution of TMSOTf in CH_2Cl_2 (0.104 mL, 0.01 mmol, 0.05 equiv). The reaction was slowly allowed to warm, and was complete within 1 h. The reaction was quenched with triethylamine, filtered through Celite, and evaporated. The crude residue was purified by column chromatography (3:1 cyclohexane–EtOAc) to give the trisaccharide **22** (0.206 g, 80%) as a colorless oil; $[\alpha]_D$ +49.6° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.05 (t, 4 H, Bz–H), 7.84 (d, 2 H, Bz–H), 7.62 (t, 1 H, Bz–H), 7.58–7.1 (m, 23 H), 5.86 (m, 3 H, H-2″, H-3″, C*H*=CH_2), 5.67 (t, 1 H, $J_{3'',4''} = J_{4'',5''}$ 10 Hz, H-4″), 5.57 (bs, 1 H, H-1″), 5.31 (dd, 1 H, J 17.2, J 1.5 Hz, CH=CH_2), 5.11 (dd, 1 H, J 10.5, J 1.2 Hz, CH=CH_2), 5.02 (d, 1 H, –OCH_2O–), 4.96 (d, 1 H, –OCH_2O–), 4.91 (d, 1 H, CH_2Ph), 4.84 (m, 2 H, H-1′, –OCH_2O–), 4.72 (m, 5 H, H-1, H-5″, CH_2Ph, –OCH_2O–), 4.58 (d, 1 H, CH_2Ph), 4.5 (d, 1 H, CH_2Ph), 4.48 (d, 1 H, CH_2Ph), 4.34 (m, 1 H, CH_2–CH=CH_2), 4.2 (t, 1 H, $J_{3,4} = J_{4,5}$ 9.0 Hz, H-4), 4.15 (dd, 1 H, $J_{1',2'} = J_{2',3'}$ 8.0 Hz, H-2′), 4.05 (m, 3 H, H-2, H-5, CH_2–CH=CH_2), 3.98 (d, 1 H, $J_{3',4'}$ 2.5 Hz, H-4′), 3.9 (dd, 1 H, $J_{2,3}$ 5.7 Hz, H-3), 3.7 (dd, 1 H, $J_{3',4'}$ 2.7 Hz, H-3′), 3.62 (m, 6 H, H-5′, H-6a′/6b′, OCH_3), 3.49 (s, 3 H, OCH_3), 3.33 (s, 3 H, OCH_3), 1.38 (d, 3 H, $J_{5'',6''}$ 6.2 Hz, H-6″); ^{13}C NMR ($CDCl_3$): δ 169.7, 165.8, 165.4, 165.2, 138.4, 137.8, 137.3, 133.7, 133.2, 133.1, 132.9, 129.9, 129.8, 129.6, 129.5, 129.4, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.5, 117.2, 100.2 (C-1), 99.7 (C-1′), 98.3 (C-1″), 98.1, 97.6, 83.4 (C-3′), 80.4 (C-3), 77.5 (C-2), 76.3 (C-4), 74.7 (C-2′), 74.5, 74.3 (C-5), 73.5, 73.4 (C-5′), 72.7 (C-4′), 72.5, 71.8 (C-4″), 70.4 (C-2″), 70.3 (C-3″), 69.3, 68.4 (C-6′), 66.7 (C-5″), 56.4, 56.2, 52.1, 17.3 (C-6″); ESIMS: m/z 1250 $(M+Na)^+$; Anal. Calcd for $C_{68}H_{74}O_{21}$: C, 66.55; H, 6.08. Found: C, 66.32; H, 6.09.

3.12. 3,4,6-Tri-*O*-acetyl-1,2-*O*-(allyloxyethylidene)-α-D-galactopyranose (24)

A solution of HBr in AcOH (33%, 3.7 mL) was slowly added to a stirred solution of 1,2,3,4,6-penta-*O*-acetyl-D-galactopyranose (1 g, 2.6 mmol) in CH_2Cl_2 (7 mL) at 0 °C. After 90 min at r.t., the solvent was evaporated and toluene (20 mL) was distilled off three times from the residue. This was taken up in nitromethane (6.5 mL) and, after addition of 2,6-lutidine (0.45 mL, 3.84 mmol), allyl alcohol (0.70 mL, 10.2 mmol) and tetrabutylammonium bromide (0.082 g, 0.26 mmol), heated to 40 °C for 20 h. The solution was then partitioned between EtOAc and aq $NaHCO_3$. The aq layer was extracted with EtOAc (3 ×), dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (4:1 to 3:1 cyclohexane–EtOAc, 1% Et_3N) to give **24** as a colorless oil composed of an unequal mixture of endo/exo isomers (0.86 g, 86%); ^{1}H NMR ($CDCl_3$): [major isomer (a), minor isomer (b)] δ 5.9 (m, 2 H, C*H*=CH_2(a,b)), 5.82 (d, 1 H, $J_{1,2}$ 4.8 Hz, H-1a), 5.7 (d, 1 H, $J_{1,2}$ 5.2 Hz, H-1b), 5.44 (m, 3 H, H-3b, H-4b, H-4a), 5.32 (dd, 1 H, J 16.2, J 1.5 Hz, CH=CH_2(b)), 5.29 (dd, 1 H, J 17.2, J 1.6 Hz, CH=CH_2(a)), 5.2 (dd, 1 H, J 10.5, J 1.4 Hz, CH=CH_2(b)), 5.17 (dd, 1 H, J 10.5, J 1.4 Hz, CH=CH_2(a)), 5.07 (dd, 1 H, $J_{3,4}$ 6.8, $J_{2,3}$ 3.4 Hz, H-3a), 4.37 (ddd, 1 H, $J_{5,6a} = J_{5,6b}$ 6.6, $J_{4,5}$ 1.4 Hz, H-5b), 4.33 (m, 2 H, H-2a, H-5a), 4.23 (dd, 1 H, H-2b), 4.2–4.1 (m,

6 H, H-6a/b (a), H-6a/b (b),), CH_2–CH=CH_2 (a,b)), 4.06 (m, 2 H, CH_2–CH=CH_2 (a,b)), 2.15–2.05 (m, 18 H, CH_3 (a, b)), 1.72 (s, 3 H, orthoester-CH_3(a)), 1.62 (s, 3 H, orthoester-CH_3(b)); ^{13}C NMR ($CDCl_3$): δ 170.5, 170, 169.9, 169.8, 134, 133.7, 117, 116.7, 97.9, 97.4 (C-1), 73.8, 73.6 (C-2), 71.6, 71.3 (C-3), 69.1 (C-5), 66.2, 65.9 (C-4), 64.7, 64, 61.5, 61.3 (C-6), 23.8, 23.1, 20.7, 20.5; ESIMS: *m/z* 411 $(M+Na)^+$; Anal. Calcd for $C_{17}H_{24}O_{10}$: C, 52.58; H, 6.23. Found: C, 52.81; H, 6.53.

3.13. 3,4,6-Tri-*O*-benzyl-1,2-*O*-(allyloxyethylidene)-α-D-galactopyranose (25)

To a solution of orthoester **24** (1.03 g, 2.8 mmol) and benzyl bromide (1.5 g, 8.9 mmol) in dry THF (7 mL) was added powdered KOH (1.75 g, 31.2 mmol) and the mixture was refluxed for 3 h with stirring. After the mixture was cooled, EtOAc was added, and the solution was successively washed with water (3 × 20 mL), a satd $NaHCO_3$ soln (2 × 20 mL), and water (2 × 20 mL). The organic layer was dried (Na_2SO_4), evaporated, and the crude residue was purified by column chromatography (19:1 to 9:1 cyclohexane–EtOAc, 1% Et_3N) to give **25** as a colorless oil composed of an unequal mixture of isomers (endo/exo) (1.2 g, 81%); ^{1}H NMR ($CDCl_3$): [major isomer (a), minor isomer (b)] δ 7.4 (m, 30 H), 5.96 (m, 2 H, CH=CH_2(a,b)), 5.81 (d, 1 H, $J_{1,2}$ 4.4 Hz, H-1a), 5.65 (d, 1 H, $J_{1,2}$ 4.5 Hz, H-1b), 5.34 (m, 2 H, CH=CH_2(a,b)), 5.2 (m, 2 H, CH=CH_2(a,b)), 5.0 (d, 2 H, CH_2Ph), 4.88 (d, 2 H, CH_2Ph), 4.74 (m, 2 H, CH_2Ph), 4.68 (d, 2 H, CH_2Ph), 4.54 (m, 5 H, CH_2Ph, H-2a), 4.42 (dd, 1 H, $J_{2,3}$ 5.7 Hz, H-2b), 4.2–4.05 (m, 8 H, H-4(a,b), H-5(a,b), CH_2–CH=CH_2 (a,b)), 4.0 (dd, 1 H, $J_{2,3}$ 6.0, $J_{3,4}$ 2.1 Hz, H-3b), 3.69 (m, 5 H, H-3a, H-6a/b (a), H-6a/b (b)), 1.68 (s, 3 H, orthoester-CH_3(a)), 1.65 (s, 3 H, orthoester-CH_3(b)); ^{13}C NMR ($CDCl_3$): δ 138.4, 138.3, 138.1, 138, 137.9, 137.8, 134.6, 134.4, 128.1, 127.9, 127.8, 127.7, 127.5, 122.3, 121.8, 116.6, 116.3, 97.7, 96.9 (C-1), 80.3, 80.2 (C-3), 79.7, 79.2 (C-2), 74.5, 73.5, 73.4, 73.2 (C-4), 73.1, 73 (C-5), 71.5, 71.4, 68 (C-6), 63.7, 63.5, 24.9, 24; ESIMS: *m/z* 555 $(M+Na)^+$; Anal. Calcd for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81. Found: C, 72.47; H, 7.13.

3.14. Allyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranose (26)

To a solution of orthoester **25** (6.7 g, 12.6 mmol) in CH_2Cl_2 (40 mL) was added 4 Å molecular sieves (2 g), and the mixture was stirred for 30 min. The solution was cooled to 0 °C, and TMSOTf (0.251 mL, 1.38 mmol) was added. After stirring for 2 h, the reaction was quenched by the addition of Et_3N, diluted with CH_2Cl_2, washed with water (2 ×), dried (Na_2SO_4), and concentrated. Column chromatography (6:1 cyclohexane–EtOAc) of the residue gave **26** (5.33 g, 77%) as a white solid; mp 64 °C; $[\alpha]_D$ −5.3° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.35 (m, 15 H), 5.89 (m, 1 H, CH=CH_2), 5.47 (dd, 1 H, $J_{2,3}$ 10.0, $J_{1,2}$ 8.0 Hz, H-2), 5.3 (dd, 1 H, *J* 17.2, *J* 1.5 Hz, CH=CH_2), 5.19 (dd, 1 H, *J* 10.5, *J* 1.4 Hz, CH=CH_2), 5.0 (d, 1 H, CH_2Ph), 4.73 (d, 1 H, CH_2Ph), 4.65 (d, 1 H, CH_2Ph), 4.58 (d, 1 H, CH_2Ph), 4.52 (d, 1 H, CH_2Ph), 4.48 (d, 1 H, CH_2Ph), 4.45 (d, 1 H, H-1), 4.38 (dd, 1 H, *J* 13.4, *J* 4.7 Hz, CH_2–CH=CH_2), 4.1 (dd, 1 H, *J* 13.4, *J* 6 Hz, CH_2–CH=CH_2), 4.02 (d, 1 H, $J_{3,4}$ 2.5 Hz, H-4), 3.69 (m, 2 H, H-6), 3.62 (t, 1 H, $J_{5,6}$ 5.9 Hz, H-5), 3.58 (dd, 1 H, H-3); ^{13}C NMR ($CDCl_3$): δ 169.5, 138.4, 138, 137.8, 133.9, 128.4, 128.2, 128.1, 128, 127.8, 127.7, 127.5, 127.4, 116.9, 100.2 (C-1), 80.3 (C-3), 74.4, 73.6 (C-5), 73.55, 72.5 (C-4), 71.9, 71.3 (C-2), 69.2, 68.6 (C-6), 21; ESIMS: *m/z* 555 $(M+Na)^+$; Anal. Calcd for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81. Found: C, 72.03; H, 6.54.

3.15. Allyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranose (27)

To a freshly prepared solution of NaOMe (0.1 M, 200 mL) was added the acetate **26** (5.97 g, 11.2 mmol), and the reaction was stirred for 2 h at r.t., and then heated to 50 °C overnight. The mixture was neutralized with Amberlite IR 120 (H^+ form), and concentrated to give the deacetylated product (5.4 g, 98%), as a white solid, pure enough for use in the next step.

Benzoyl chloride (1.35 mL, 11.7 mmol) was added to a mixture of the above alcohol (2.86 g, 5.8 mmol), triethylamine (3.25 mL, 23.3 mmol), and DMAP (0.142 g, 1.2 mmol) in CH_2Cl_2 (50 mL). The reaction was refluxed overnight, cooled, and quenched by the addition of MeOH (3 mL). The solvent was evaporated, the crude residue taken up in EtOAc, and the organic layer washed with HCl (2 N), $NaHCO_3$, and brine. After drying, (Na_2SO_4), the solvent was evaporated and the crude residue purified by column chromatography (19:1 to 4:1 cyclohexane–EtOAc) to give **27** (2.95 g, 85%) as a white solid; mp 101 °C; $[\alpha]_D$ +20.7° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.05 (d, 2 H, Bz–H), 7.6 (t, 1 H, Bz–H), 7.49 7.6 (t, 2 H, Bz–H), 7.42–7.1 (m, 15 H), 5.78 (m, 1 H, CH=CH_2), 5.7 (dd, 1 H, $J_{2,3}$ 10, $J_{1,2}$ 8 Hz, H-2), 5.21 (dd, 1 H, *J* 17.3, *J* 1.6 Hz, CH=CH_2), 5.09 (dd, 1 H, *J* 10.5, *J* 1.3 Hz, CH=CH_2), 5.02 (d, 1 H, CH_2Ph), 4.68 (d, 2 H, CH_2Ph), 4.58 (d, 1 H, H-1), 4.51 (m, 3 H, CH_2Ph), 4.33 (ddt, 1 H, *J* 13.4, *J* 4.7, *J* 1.6 Hz, CH_2–CH=CH_2), 4.09 (ddt, 1 H, *J* 13.4, *J* 6.2 *J* 1.4 Hz, CH_2–CH=CH_2), 4.04 (d, 1 H, $J_{3,4}$ 2.7 Hz, H-4), 3.7 (m, 4 H, H-3, H-5, H-6a/b); ^{13}C NMR ($CDCl_3$): δ 165.3, 138.4, 137.8, 137.6, 133.8, 132.8, 130.2, 129.8, 128.4, 128.3, 128.2, 127.9, 127.8, 127.6, 127.5, 117, 100.1 (C-1), 79.9 (C-3), 74.4, 73.7 (C-5), 73.6, 72.3 (C-4), 71.8 (C-2), 71.1, 69.3, 68.6 (C-6); ESIMS: *m/z* 617 $(M+Na)^+$; Anal. Calcd for $C_{37}H_{38}O_7$: C, 74.73; H, 6.44. Found: C, 74.88; H, 6.36.

3.16. 2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-α/β-D-galactopyranosyl trichloroacetimidate (28)

To a stirring solution of **27** (2.58 g, 4.33 mmol) in a mixture of toluene (41 mL), EtOH (95%, 105 mL), and water (14 mL) was added tris(triphenylphosphine)rhodium(I) chloride (0.681 g, 0.74 mmol) followed by 1,4-diazabicyclo[2.2.2]octane (DABCO) (0.365 g, 3.2 mmol). The mixture was stirred at r.t. for 1 h, and then refluxed for 17 h. The resulting brown solution was evaporated, and the residue dissolved in 9:1 acetone–water (150 mL). To this solution was added mercury(II) chloride (11 g, 43.3 mmol) followed by yellow mercury(II) oxide (0.047 g, 0.21 mmol), and the reaction was stirred at r.t. for 6 h. The solvent was then evaporated, the residue diluted with CH_2Cl_2, and filtered through a pad of Celite. The pad was rinced with CH_2Cl_2, and the combined filtrates were washed with 20% aq NaI and water. The organic layer was dried (Na_2SO_4), evaporated, and the crude residue purified by column chromatography (4:1 cyclohexane–EtOAc) to give the deprotected 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α/β-D-galactopyranoside as an oily mixture of epimers (1.98 g, 83%).

To a solution of the above compound (1 g, 1.8 mmol) in CH_2Cl_2 (25 mL) was added trichloroacetonitrile (1.8 mL) followed by a catalytic amount of DBU (several drops). The reaction was stirred at r.t. for 4 h. The solvent was then evaporated and the crude residue purified by column chromatography (19:1 to 9:1 cyclohexane–EtOAc, 1% Et_3N) to give the α trichloroacetimidate **28**α as an oil (0.400 g, 32%) and the β trichloroacetimidate **28**β as a white solid (0.390 g, 31%).

α Anomer: $[\alpha]_D$ +89.5° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.45 (s, 1 H, NH), 8.0 (d, 2 H, Bz–H), 7.6 (t, 1 H, Bz–H), 7.5–7.25 (m, 17 H), 6.69 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 5.85 (dd, 1 H, $J_{2,3}$ 9.9 Hz, H-2), 5.05 (d, 1 H, CH_2Ph), 4.77 (d, 1 H, CH_2Ph), 4.69 (d, 1 H, CH_2Ph), 4.68 (d, 1 H, CH_2Ph), 4.54 (d, 1 H, CH_2Ph), 4.49 (d, 1 H, CH_2Ph), 4.28 (m, 2 H, H-4, H-5), 4.22 (bs, 1 H, H-3), 3.75 (dd, 1 H, $J_{6a,6b}$ 9.2, $J_{6a,5}$ 9.0 Hz, H-6a), 3.66 (dd, 1 H, $J_{6b,5}$ 5.5 Hz, H-6b); ^{13}C NMR ($CDCl_3$): δ 165.6, 160.5 (C=NH), 138.2, 137.7, 137.6, 133.1, 129.8, 129.6, 128.4, 128.3, 128.2, 128.1, 128, 127.9, 127.8, 127.7, 94.6 (C-1), 75.5 (C-3), 74.9, 73.6 (C-4), 73.5, 72.3 (C-5), 72.1, 70.1 (C-2), 68.1 (C-6).

β Anomer: mp 142 °C; $[\alpha]_D$ +45° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.57 (s, 1 H, NH), 8.0 (d, 2 H, Bz–H), 7.59 (t, 1 H, Bz–H), 7.5–7.15 (m, 17 H), 5.94 (dd, 1 H, $J_{2,3}$ 9.8, $J_{1,2}$ 8.2 Hz, H-2), 5.86 (d, 1 H, H-1), 5.05 (d, 1 H, CH_2Ph), 4.7 (m, 2 H, CH_2Ph), 4.5 (m, 3 H, CH_2Ph), 4.11 (d, 1 H, $J_{3,4}$ 1.8 Hz, H-4), 3.89 (t, 1 H, *J* 6.1 Hz, H-5), 3.75 (m, 3 H, H-3, H-6a/b); ^{13}C NMR ($CDCl_3$): δ 165, 161.7 (C=NH), 138.1, 137.6, 137.3, 133, 129.8, 129.7, 128.4, 128.3, 128.2, 128, 127.9, 127.8, 127.7, 96.8 (C-1), 79.3 (C-3), 74.8 (C-5), 74.7, 73.5, 72.2 (C-4), 71.7, 70.6 (C-2), 68 (C-6); Anal. Calcd for $C_{36}H_{34}Cl_3NO_7$: C, 61.86; H, 4.9; N, 2.0. Found: C, 61.90; H, 4.92; N, 1.96.

3.17. Preparation of disaccharides using glycosyl trichloroacetimidates

Two reactions were carried out with each glycosyl trichloroacetimidate (α or β): coupling at −20 or −78 °C. General procedure: a mixture of methyl 1-*O*-allyl-3,4-di-*O*-methoxymethyl-β-D-glucuronate (**9**) (1.0 equiv), α or β glycosyl trichloroacetimidate (1.5 equiv), and 4 Å powdered molecular sieves was stirred for 1 h at r.t. in CH_2Cl_2. The mixture was cooled and TMSOTf (0.05 equiv, 0.1 M in CH_2Cl_2) was added. The reaction was quenched with triethylamine, filtered through Celite, and evaporated. The crude residue was purified by column chromatography to give the disaccharide.

3.18. Methyl (2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→2)-(allyl 3,4-di-*O*-methoxymethyl-β-D-glucopyranosid)uronate (15)

3.18.1. Using the α glycosyl trichloroacetimidate. Coupling of the acceptor **9** (30 mg, 89 μmol) and donor **28**α (93 mg, 130 μmol) using TMSOTf (44 μL, 4 μmol) according to the general procedure at −20 °C for 20 min gave, after purification (1.5:1 cyclohexane–EtOAc), the disaccharide **15** (0.016 g, 21%) as well as the rearrangement product **29** (0.054 g, 68%). Reaction at −78 °C (2 h) gave 27% of the disaccharide and 69% of the rearrangement product.

3.18.2. Using the β glycosyl trichloroacetimidate. Coupling of the acceptor **9** (25 mg, 74 μmol) and donor **28**β (78 mg, 111 μmol) using TMSOTf (37 μL, 3.7 μmol) according to the general procedure at −20 °C for 20 min gave, after purification (1.5:1 cyclohexane–EtOAc), the disaccharide **15** (0.043 g, 66%) identical to the above described product as well as the rearrangement product **29** (0.033 g, 42%). Reaction at −78 °C (2 h) gave 65% of the disaccharide and 15% of the rearrangement product.

For the rearrangement product 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-*N*-trichloroacetyl-β-D-galactopyranosylamine **29**: ^1H NMR ($CDCl_3$): δ 7.99 (m, 2 H, Bz–H), 7.65 (m, 2 H, NH, Bz–H), 7.5–7.2 (m, 17 H), 5.68 (t, 1 H, *J* 9.6 Hz, H-2), 5.16 (t, 1 H, *J* 9.0 Hz, H-1), 5.0 (d, 1 H, CH_2Ph), 4.68 (m, 3 H, CH_2Ph), 4.5 (d, 2 H, CH_2Ph), 4.15 (d, 1 H, $J_{3,4}$ 2.3 Hz, H-4), 3.85 (m, 2 H, H-3, H-5), 3.7 (m, 2 H, H-6a/6b); ^{13}C NMR ($CDCl_3$): δ 166.9, 162.1, 138, 137.6, 137.3, 133.6, 129.9, 129.1, 128.6, 128.5, 128.4, 128.3, 128, 127.9, 127.8, 80.7 (C-1), 79.6 (C-3), 75.6 (C-5), 75.1, 73.6, 72.9 (C-4), 72.3, 71.2 (C-2), 67.7 (C-6); ESIMS: *m*/*z* 722 $(M+Na)^+$.

3.19. Allyl 2-*O*-*p*-methoxybenzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside (30)

Allyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranose (**26**) was treated with NaOMe as indicated for compound **27**. The resulting deacetylated product (0.536 g, 1.1 mmol) in THF (15 mL) was treated with 1,3-dicyclohexylcarbodiimide (DCC) (0.811 g, 3.9 mmol), and the reaction was stirred for 30 min at r.t. *p*-Methoxybenzoic acid (0.831 g, 5.5 mmol) was then added followed by DMAP (38 mg, 0.3 mmol). The reaction was refluxed for 16 h. After cooling, the solvent was evaporated, the residue taken up in EtOAc and filtered over Celite. The pad was rinced with EtOAc, and the combined filtrates washed with HCl (2 N), $NaHCO_3$ (satd), and brine. The solution was dried (Na_2SO_4), and the solvent evaporated. The crude product was purified by column chromatography (4:1 cyclohexane–EtOAc) to give **30** (0.386 g, 57%) as a white solid; mp 67 °C; $[\alpha]_D$ +18.1° (*c* 0.78, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.07 (d, 2 H, Bz–H), 7.45–7.2 (m, 15 H), 7.0 (d, 2 H, Bz–H), 5.81 (m, 1 H, C*H*=CH_2), 5.73 (dd, 1 H, $J_{2,3}$ 9.5, $J_{1,2}$ 8.4 Hz, H-2), 5.25 (d, 1 H, *J* 17.3 Hz, CH=CH_2), 5.12 (d, 1 H, *J* 10.5 Hz, CH=CH_2), 5.07 (d, 1 H, CH_2Ph), 4.71 (d, 2 H, CH_2Ph), 4.6 (d, 1 H, H-1), 4.53 (m, 3 H, CH_2Ph), 4.37 (dd, 1 H, *J* 13.5, *J* 3.5 Hz, CH_2–CH=CH_2), 4.14 (ddd, 1 H, *J* 13.5, *J* 6.2, *J* 0.9 Hz, CH_2–CH=CH_2), 4.08 (d, 1 H, $J_{3,4}$ 2.2 Hz, H-4), 3.95 (s, 3 H, OCH_3), 3.72 (m, 4 H, H-3, H-5, H-6a/b); ^{13}C NMR ($CDCl_3$): δ 165, 163.3, 138.5, 137.9, 137.8, 133.9, 131.9, 128.5, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 122.7, 117, 113.5, 100.2 (C-1), 79.9 (C-3), 74.4, 73.7 (C-5), 73.6, 72.4 (C-4), 71.7, 71.6 (C-2), 69.3, 68.7 (C-6), 55.5; ESIMS: *m*/*z* 647 $(M+Na)^+$; Anal. Calcd for $C_{38}H_{40}O_8 \cdot 0.2$ cyclohexane: C, 73.39; H, 6.66. Found: C, 73.09; H, 6.95.

3.20. Allyl 2-*O*-*p*-nitrobenzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside (31)

Allyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranose (**26**) was treated with NaOMe as indicated for compound **27**. The resulting de-acetylated product (0.498 g, 1.0 mmol) in THF (13 mL) was treated with DCC (0.754 g, 3.7 mmol), and the reaction was stirred for 30 min at r.t. *p*-Nitrobenzoic acid (0.848 g, 5.1 mmol) was then added followed by DMAP (34 mg, 0.3 mmol). Stirring was continued for 30 min when TLC indicated complete conversion of the starting material. The solvent was evaporated, the residue taken up in EtOAc and filtered over Celite. The pad was washed with EtOAc, and the combined filtrates washed with HCl (2 N), $NaHCO_3$ (satd), and brine. The solution was dried (Na_2SO_4), and the solvent evaporated. The crude product was purified by column chromatography (4:1 cyclohexane–EtOAc) to give **31** (0.587 g, 90%) as a pale yellow solid; mp 88 °C; $[\alpha]_D$ +7.7° (*c* 0.68, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.33 (d, 2 H, Bz–H), 8.18 (d, 2 H, Bz–H), 7.45–7.15 (m, 15 H), 5.78 (m, 1 H, C*H*=CH_2), 5.7 (dd, 1 H, $J_{2,3}$ 10, $J_{1,2}$ 8.0 Hz, H-2), 5.21 (dd, 1 H, *J* 17.3, *J* 1.3 Hz, CH=CH_2), 5.1 (dd, 1 H, *J* 10.4, *J* 0.9 Hz, CH=CH_2), 5.04 (d, 1 H, CH_2Ph), 4.71 (m, 2 H, CH_2Ph), 4.59 (d, 1 H, H-1), 4.5 (m, 3 H, CH_2Ph), 4.35 (dd, 1 H, *J* 13.4, *J* 4.6 Hz, CH_2–CH=CH_2), 4.09 (m, 2 H, H-4, CH_2–CH=CH_2), 3.7 (m, 4 H, H-3, H-5, H-6a/b); ^{13}C NMR ($CDCl_3$): δ 163.4, 150.5, 138.2, 137.7, 137.5, 135.6, 133.7, 130.8, 128.5, 128.3, 128.2, 128, 127.9, 127.8, 127.7, 127.6, 123.4, 117.2, 99.8 (C-1), 79.7, (C-3), 74.6, 73.7 (C-5), 73.6, 72.7 (C-2), 72.1 (C-4), 71.5, 69.3, 68.5 (C-6); ESIMS: *m*/*z* 662 $(M+Na)^+$; Anal. Calcd for $C_{37}H_{37}NO_9$: C, 69.47; H, 5.83; N, 2.19. Found: C, 69.07; H, 5.86; N, 2.18.

3.21. 2-*O*-*p*-Methoxybenzoyl-3,4,6-tri-*O*-benzyl-α/β-D-galactopyranosyl trichloroacetimidate (32)

The anomeric allyl group was first removed in the same manner as for compound **28**. To a solution of the crude alcohol (0.339 g, 0.46 mmol) and trichloroacetonitrile (2 mL) in anhyd CH_2Cl_2 (15 mL) was added anhyd K_2CO_3 (0.500 g). The mixture was stirred overnight, the solid material was filtered off and the solvent evaporated. The oily residue was purified by column chromatography (9:1 cyclohexane–EtOAc, 1% Et_3N) to give the α trichloroacetimidate **32**α as an oil (0.082 g, 19%) and the β trichloroacetimidate **32**β as an amorphous white solid (0.265 g, 63%).

α Anomer: $[\alpha]_D$ +77.4° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.47 (s, 1 H, NH), 7.9 (d, 2 H, Bz–H), 7.45–7.2 (m, 15 H), 6.95 (d, 2 H, Bz–H), 6.69 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.85 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2), 5.09 (d, 1 H, CH_2Ph), 4.79 (d, 1 H, CH_2Ph), 4.71 (d, 2 H, CH_2Ph), 4.56 (d, 1 H, CH_2Ph), 4.51 (d, 1 H, CH_2Ph), 4.27 (m, 3 H, H-3, H-4, H-5), 3.92 (s, 3 H, OCH_3), 3.78 (dd, 1 H, $J_{6a,6b}$ 9.1, $J_{5,6a}$ 8.0 Hz, H-6a), 3.69 (dd, 1 H, $J_{5,6b}$ 5.4 Hz, H-6b); ^{13}C NMR ($CDCl_3$): δ 165.3, 163.5, 160.5 (C=NH), 138.3, 137.7, 131.9, 128.5, 128.4, 128.3, 128.2, 128, 127.9, 127.8, 127.7, 122, 113.5, 94.7 (C-1), 75.6 (C-3), 74.9, 73.6 (C-4), 73.5, 72.3 (C-5), 72.2, 69.8 (C-2), 68.1 (C-6), 55.4.

β Anomer: $[\alpha]_D$ +41° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.58 (s, 1 H, NH), 7.98 (d, 2 H, Bz–H), 7.45–7.2 (m, 15 H), 6.95 (d, 2 H, Bz–H), 5.95 (t, 1 H, $J_{1,2} = J_{2,3}$ 8.2 Hz, H-2), 5.89 (d, 1 H, H-1), 5.09 (d, 1 H, CH_2Ph), 4.71 (d, 2 H, CH_2Ph), 4.6–4.5 (m, 3 H, CH_2Ph), 4.14 (d, 1 H, $J_{3,4}$ 1.8 Hz, H-4), 3.93 (s, 3 H, OCH_3), 3.9 (t, 1 H, $J_{5,6a} = J_{5,6b}$ 6.7 Hz, H-5), 3.81–3.71 (m, 3 H, H-3, H-6a/b); ^{13}C NMR ($CDCl_3$): δ 164.7, 163.4, 161.8 (C=NH), 138.2, 137.7, 137.5, 131.8, 128.5, 128.4, 128.3, 128.1, 127.9, 127.8, 122.3, 113.5, 96.9 (C-1), 79.3 (C-3), 74.8 (C-5), 74.7, 73.6, 72.3 (C-4), 71.7, 70.3 (C-2), 68 (C-6), 55.4; Anal. Calcd for $C_{37}H_{36}Cl_3N_1O_7 \cdot$

0.8 cyclohexane: C, 63.04; H, 5.77; N, 1.76. Found: C, 62.97; H, 5.72; N, 1.81.

3.22. 2-*O*-*p*-Nitrobenzoyl-3,4,6-tri-*O*-benzyl-α/β-D-galactopyranosyl trichloroacetimidate (33)

The anomeric allyl group was first removed in the same manner as for compound **28**. To a solution of the crude alcohol (0.356 g, 0.59 mmol) and trichloroacetonitrile (2 mL) in anhyd CH_2Cl_2 (15 mL) was added anhyd K_2CO_3 (0.500 g). The mixture was stirred overnight, the solid material was filtered off and the solvent evaporated. The oily residue was purified by column chromatography (6:1 cyclohexane–EtOAc, 1% Et_3N) to give the α trichloroacetimidate **33**α as an oil (0.172 g, 39%) and the β trichloroacetimidate **33**β as an amorphous white solid (0.115 g, 26%).

α Anomer: $[\alpha]_D$ +97.6° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.45 (s, 1 H, NH), 8.3 (d, 2 H, Bz–H), 8.1 (d, 2 H, Bz–H), 7.45–7.26 (m, 15 H), 6.7 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.86 (dd, 1 H, $J_{2,3}$ 10.3 Hz, H-2), 5.08 (d, 1 H, CH_2Ph), 4.79 (d, 1 H, CH_2Ph), 4.71 (d, 1 H, CH_2Ph), 4.61 (d, 1 H, CH_2Ph), 4.56 (d, 1 H, CH_2Ph), 4.51 (d, 1 H, CH_2Ph), 4.29 (m, 3 H, H-3, H-4, H-5), 3.79 (dd, 1 H, $J_{6a,6b}$ 9.0, $J_{5,6a}$ 8.0 Hz, H-6a), 3.7 (dd, 1 H, $J_{5,6b}$ 5.4 Hz, H-6b); ^{13}C NMR ($CDCl_3$): δ 163.7, 160.6 (C=NH), 150.6, 138.1, 137.6, 137.4, 134.9, 130.8, 128.5, 128.4, 128.3, 128.2, 128.1, 128, 127.9, 127.8, 123.5, 94.3 (C-1), 75.2 (C-3), 75.1, 73.6, 73.2 (C-4), 72.4 (C-5), 71.8, 70.7 (C-2), 68 (C-6).

β Anomer: $[\alpha]_D$ +48.8° (*c* 0.67, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.62 (s, 1 H, NH), 8.3 (d, 2 H, Bz–H), 8.11 (d, 2 H, Bz–H), 7.46–7.15 (m, 15 H), 5.93 (m, 2 H, H-1, H-2), 5.06 (d, 1 H, CH_2Ph), 4.73 (m, 2 H, CH_2Ph), 4.54 (m, 3 H, CH_2Ph), 4.2 (d, 1 H, $J_{3,4}$ 2.0 Hz, H-4), 3.92 (m, 1 H, H-5), 3.83–3.72 (m, 3 H, H-3, H-6a/b); ^{13}C NMR ($CDCl_3$): δ 163.2, 161.5 (C=NH), 150.5, 138, 137.6, 137.2, 135.1, 130.8, 128.5, 128.4, 128.3, 128.1, 128, 127.9, 127.8, 123.5, 96.5 (C-1), 79.1 (C-3), 74.9, 74.8 (C-5), 73.6, 72 (C-4), 71.6, 71.5 (C-2), 67.8 (C-6); Anal. Calcd for $C_{36}H_{33}Cl_3N_2O_7 \cdot 0.8$ cyclohexane: C, 60.40; H, 5.29; N, 3.45. Found: C, 60.35; H, 5.43; N, 3.47.

3.23. Methyl (2-*O*-*p*-methoxybenzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→2)-(allyl 3,4-di-*O*-methoxymethyl-β-D-glucopyranosid)uronate (34)

3.23.1. Using the α-glycosyl trichloroacetimidate. Coupling of the acceptor **9** (25 mg, 74 μmol) and donor **32**α (81 mg, 111 μmol) using TMSOTf (37 μL, 3.7 μmol) according to the general procedure at −20 °C for 30 min gave, after purification (1.5:1 cyclohexane–EtOAc), the disaccharide **34** (0.010 g, 24%) as a white powder as well as the trichloroacetamide rearrangement product (0.065 g, 80%). Reaction at −78 °C (2 h) gave 21% of the disaccharide and 70% of the rearrangement product.

3.23.2. Using the β-glycosyl trichloroacetimidate. Coupling of the acceptor **9** (25 mg, 74 μmol) and donor **32**β (81 mg, 111 μmol) using TMSOTf (37 μL, 3.7 μmol) according to the general procedure at −20 °C for 20 min gave, after purification (1.5:1 cyclohexane–EtOAc) the disaccharide **34** (0.033 g, 47%) as well as the rearrangement product (0.026 g, 32%). Reaction at −78 °C (2 h) gave 62% of the disaccharide and 30% of the rearrangement product.

Disaccharide **34**: mp 127 °C; $[\alpha]_D$ +19.2° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.02 (d, 2 H, Bz–H), 7.42–7.18 (m, 15 H), 6.98 (d, 2 H, Bz–H), 5.87 (m, 1 H, CH=CH_2), 5.65 (dd, 1 H, $J_{2',3'}$ 9.8, $J_{1',2'}$ 8.2 Hz, H-2′), 5.25 (dd, 1 H, *J* 17.2, *J* 1.3 Hz, CH=CH_2), 5.1 (d, 1 H, *J* 10.5 Hz, CH=CH_2), 5.06 (d, 1 H, CH_2Ph), 4.9 (d, 1 H, H-1′), 4.69 (m, 4 H, –OCH_2O–, CH_2Ph), 4.58 (m, 2 H, H-1, –OCH_2O–), 4.5 (d, 1 H, CH_2Ph), 4.46 (m, 3 H, –OCH_2O–, CH_2Ph), 4.35 (dd, 1 H, *J* 12.4, *J* 5.3 Hz, CH_2–CH=CH_2), 4.05 (m, 2 H, H-4′, CH_2–CH=CH_2), 3.95 (s, 3 H, OCH_3), 3.89 (d, 1 H, $J_{4,5}$ 9.2 Hz, H-5), 3.8 (s, 3 H, OCH_3), 3.71 (m, 2 H, H-4, H-6a′), 3.61 (m, 5 H, H-2, H-3, H-3′, H-5′, H-6b′), 3.27 (s, 3 H, OCH_3), 3.23 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$): δ 168.9, 165, 163.3, 138.4, 137.6, 137.5, 133.7, 131.8, 128.4, 128.3, 128.2, 128, 127.9, 127.6, 127.5, 122.7, 117.1, 113.6, 101.9 (C-1), 101.3 (C-1′), 98.6, 98.2, 81.8 (C-2), 80.1 (C-3′), 79.8 (C-3), 77.1 (C-4), 74.9 (C-5), 74.4, 73.6, 73.5 (C-5′), 72.3 (C-2′), 72.1 (C-4′), 71.5, 70.6, 68.3 (C-6′), 56.2, 56.1, 55.4, 52.4; ESIMS: *m*/*z* 925 $(M+Na)^+$; Anal. Calcd for $C_{49}H_{58}O_{16}$: C, 65.18; H, 6.47. Found: C, 64.79; H, 6.43.

3.24. Methyl (2-*O*-*p*-nitrobenzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→2)-(allyl 3,4-di-*O*-methoxymethyl-β-D-glucopyranosid)uronate (35)

3.24.1. Using the α-glycosyl trichloroacetimidate. Coupling of the acceptor **9** (27 mg, 80 μmol) and donor **33**α (90 mg, 120 μmol) using TMSOTf (40 μL, 4.0 μmol) according to the general procedure at −20 °C for 30 min gave, after purification (32:1 to 6:1 toluene–EtOAc) the disaccharide **35** (0.016 g, 22%) as well as the rearrangement product (0.059 g, 66%). Reaction at −78 °C (20 min) gave 24% of the disaccharide and 78% of the rearrangement product.

3.24.2. Using the β-glycosyl trichloroacetimidate. Coupling of the acceptor **9** (26 mg, 77 μmol) and donor **33**β (86 mg, 116 μmol) using TMSOTf (38 μL, 3.8 μmol) according to the general procedure at −20 °C for 20 min gave, after purification (32:1 to 6:1 toluene–EtOAc) the disaccharide **35** (0.037 g, 51%) as well as the rearrangement product (0.024 g, 28%). Reaction at −78 °C (20 min) gave 80% of the disaccharide and 20% of the rearrangement product.

Disaccharide **35**: mp 134 °C; $[\alpha]_D$ +27.4° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.33 (d, 2 H, Bz–H),

8.17 (d, 2 H, Bz–H), 7.45–7.15 (m, 15 H), 5.88 (m, 1 H, C*H*=CH_2), 5.65 (dd, 1 H, $J_{2',3'}$ 10, $J_{1',2'}$ 8.1 Hz, H-2′), 5.25 (dd, 1 H, *J* 17.3, *J* 1.6 Hz, CH=CH_2), 5.14 (dd, 1 H, *J* 10.5, *J* 1.4 Hz, CH=CH_2), 5.05 (d, 1 H, CH_2Ph), 4.92 (d, 1 H, H-1′), 4.71–4.62 (m, 4 H, –OCH_2O–, CH_2Ph), 4.55 (m, 2 H, H-1, –OCH_2O–), 4.5–4.4 (m, 4 H, –OCH_2O–, CH_2Ph), 4.35 (ddt, 1 H, *J* 12.4, *J* 5.1, *J* 1.5 Hz, CH_2–CH=CH_2), 4.09 (d, 1 H, $J_{3',4'}$ 2.2 Hz, H-4′), 4.05 (dd, 1 H, *J* 12.4, *J* 6.0 Hz, CH_2–CH=CH_2), 3.88 (d, 1 H, $J_{4,5}$ 9.1 Hz, H-5), 3.8 (s, 3 H, OCH_3), 3.74–3.6 (m, 6 H, H-3′, H-3, H-4, H-5′, H-6a/b′), 3.58 (dd, 1 H, *J* 7.1, *J* 6.9 Hz, H-2), 3.25 (s, 3 H, OCH_3), 3.23 (s, 3 H, OCH_3); ^{13}C NMR ($CDCl_3$): δ 168.8, 163.4, 150.5, 138.2, 137.5, 137.3, 135.6, 133.6, 130.7, 128.5, 128.3, 128.2, 128, 127.9, 127.8, 127.6, 123.5, 117.2, 101.7 (C-1), 101 (C-1′), 98.3, 98.2, 81.6 (C-2), 79.8 (C-3′), 79.3 (C-3), 77.2 (C-4), 75 (C-5), 74.6, 73.6 (C-2′, C-5′), 71.8 (C-4′), 71.3, 70.6, 68.1 (C-6′), 56.2, 56.1, 52.4; ESIMS: *m/z* 940 $(M+Na)^+$; Anal. Calcd for $C_{48}H_{55}NO_{17}$: C, 62.81; H, 6.04; N, 1.53. Found: C, 62.86; H, 6.16; N, 1.61.

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