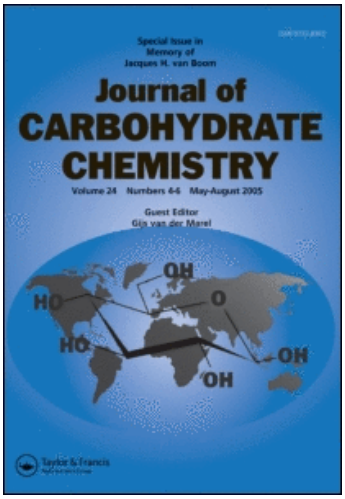

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BLOCK SYNTHESIS WITH GALACTURONATE TRICHLOROACETIMIDATES[1]

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BLOCK SYNTHESIS WITH GALACTURONATE TRICHLOROACETIMIDATES[1]

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Dedicated with great appreciation to Professor Joachim Thiem on the occasion of his 60th birthday.

ABSTRACT

The disaccharide methyl (4-*O*-benzoyl-3-*O*-benzyl-2-*O*-acetyl-α-L-rhamno pyranosyl)-(1→4)-(allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate **(13)** was obtained in an excellent yield of 88% using methyl (allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate (**12)** as the glycosyl acceptor and a slight excess of the 1,2-di-*O*-acetyl-rhamnoglycosyl donor **5a**. Disaccharide **13** is a key intermediate that can be used either as a glycosyl acceptor or glycosyl donor for the preparation of rhamnogalacturonan fragments. Here, introduction of the trichloroacetimidate function at the anomeric center gave the disaccharide glycosyl donor **28**, which could be applied in a blockwise glycosylation reaction to form the L-Rha-α(1→4)-D-GalA-α(1→4)-D-GalA trisaccharide **29**. Generally, on condition that no neighboring group effect influenced the reaction at the anomeric center of the α-trichloroacetimidate galacturonate glycosyl donors (**20**–**22**,**28**), α-glycosidic linkages were nearly exclusively formed, except in the case of the 4-*O*-methylgalactopyranosyluronate **22**.

INTRODUCTION

Pursuing our program directed at the synthesis of pectin fragments, which have a very complex structure and several biological functions and activities,[2] we looked for an option to use oligomeric galacturonates in glycosidic reactions to form higher oligomers of defined structure. The repeating units in pectin fragments are

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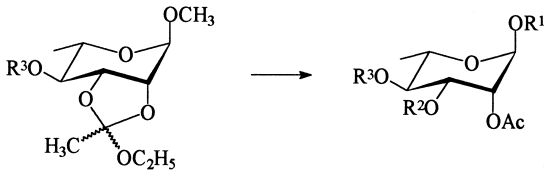
often α(1→2) or α(1→4) linked between D-galacturonic acid itself and L-rhamnose residues. Until now, the best synthetic method to prepare a D-GalA-α(1→4)-D-GalA disaccharide or a D-GalA-α(1→2)-L-Rha-α(1→4)-D-GalA trisaccharide is application of D-galactopyranosyluronic thioglycosides, in which the neighboring group in the O-2-position does not exercise an influence on the anomeric center of the glycosyl donor.[3–6] Unfortunately, there is no suitable preparative procedure to synthesize a thioglycoside starting from a D-galacturonate precursor.[7] Up to this day, the synthetic pathway to galactopyranosyluronic thioglycosides starts from selective protected thiogalactosides including the crucial oxidation step of the primary hydroxyl group.[5] Furthermore, our attempts to prepare β-D-galacturonate trichloroacetimidates for an S_N2-like α-glycosylation were unsuccessful.[7] Fortunately, the α-D-galacturonate trichloroimidates obtained provided predominantly α-glycosidic linkages and this result creates the basis both for galacturonate glycosyl donors in α-glycosylation reactions prepared directly from D-galacturonic acid and for the block synthesis with oligomeric galacturonate trichloroacetimidates.

RESULTS AND DISCUSSION

Recently, we have described the stepwise synthesis of a trisaccharide [D-GalA-α(1→2)-L-Rha-α(1→4)-D-GalA], as an analogue for the repeating unit of the backbone of rhamnogalacturonan I. The α(1→4) coupling between L-rhamnose and D-galacturonic acid derivatives was realized using the trityl-cyanoethylidene condensation.[6] Herein, we report a more efficient glycosylation procedure for this coupling as well as an option for a block synthesis with rhamnogalacturonan fragments.

In order to improve the formation of a L-Rha-α(1→4)-D-GalA disaccharide, the glycosylation step was systematically examined with several suitable rhamnopyranosyl donors (**5a**,**7**–**10**, Scheme 2), synthesis of which started from the orthoester derivative **1** (Scheme 1). The O-4 position of **1** was protected with different substituted benzoyl groups (**2a**–**2c**) to serve both as a marker in subsequent biological investigations and, after reduction of the nitro group to an amino group, as a tether for stains or dyes.

Regioselective opening[8] of the orthoester structure in **2a**–**2c** led to the O-2 acetyl protecting group of compounds **3a**–**3c** which were involved in neighboring participation in the later glycosylation, and favored formation of the desired 1,2-*trans* linked products.[10] As expected, conversion of the orthoester **1** into the diacyl derivatives **3a**–**3c** caused a considerable downfield shift of the H-2 and H-4 signals (H-2, δ 4.82 to 5.09 ± 0.02 and H-4, δ 3.49 to 5.10 ± 0.02) in the ^{1}H NMR spectra. Benzylation of **3a**–**3c** with benzyl trichloroacetimidate and a catalytic amount of trifluoromethanesulfonic acid[11] provided **4a–4c** in 63% yield. The introduction of a benzyl ether at the O-3 position functions both as a permanent protecting group and for activation of the later glycosyl donors.[10] Acetolysis[12] of **4a**–**4c** gave nearly exclusively the α-acetates **5a**–**5c** in excellent yields. Only in the case of **5a** could a small amount (7%) of the β-acetate (**5a**β) be isolated. The α stereochemistry at the anomeric center was evident only from the geminal ^{13}C—^{1}H coupling constants

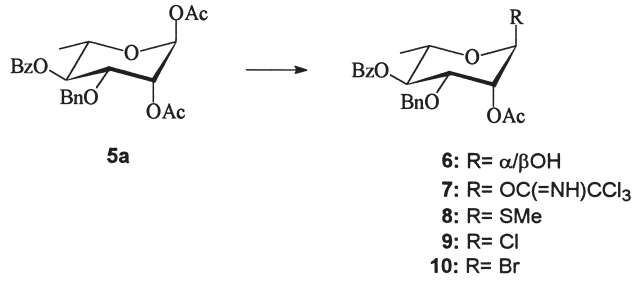


1, 2a,b,c **3a,b,c - 5a,b,c**

1: R^3= H
2a: R^3= Bz
2b: R^3= *p*MeC_6H_5CO
2c: R^3= *p*$NO_2C_6H_5CO$

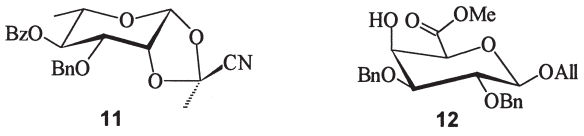
3a: R^1= CH_3 R^2= H R^3= Bz
3b: R^1= CH_3 R^2= H R^3= *p*MeC_6H_5CO
3c: R^1= CH_3 R^2= H R^3= *p*$NO_2C_6H_5CO$
4a: R^1= CH_3 R^2= Bn R^3= Bz
4b: R^1= CH_3 R^2= Bn R^3= *p*MeC_6H_5CO
4c: R^1= CH_3 R^2= Bn R^3= *p*$NO_2C_6H_5CO$
5a: R^1= Ac R^2= Bn R^3= Bz
5b: R^1= Ac R^2= Bn R^3= *p*MeC_6H_5CO
5c: R^1= Ac R^2= Bn R^3= *p*$NO_2C_6H_5CO$

Scheme 1.

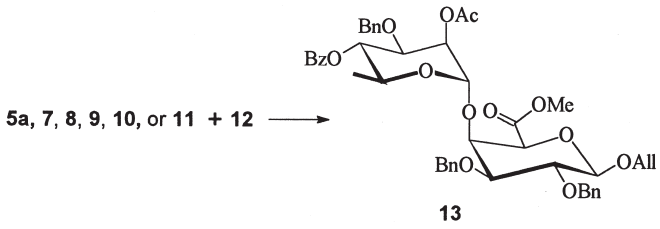


5a

6: R= α/βOH
7: R= $OC(=NH)CCl_3$
8: R= SMe
9: R= Cl
10: R= Br



11 **12**



13

Scheme 2.

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($J_{C\text{-}1,H\text{-}1}$).[6,13] Since the observed values for **5a** and **5b**,**c** are 172.6 Hz and 171.1 Hz, respectively, a comparison with $J_{C\text{-}1,H\text{-}1}$ = 161.6 Hz of **5a**β verified the expected structures.

For the preparation of the trichloroacetimidate **7,** the acetyl group at the anomeric center was removed with hydrazine acetate[14] and the resulting compound **6** treated with trichloroacetonitrile and DBU[15] to provide the compound **7** in 92% yield. Again, the value of $^{13}C—^{1}H$ coupling constant $J_{C\text{-}1,H\text{-}1}$ = 178.8 Hz established the α configuration of the trichloroacetimidate group at the anomeric center.

The reaction of **5a** with methylthiomethylsilane[15] provided the corresponding thioglycoside **8** in nearly quantitative yield. Finally, the rhamnosyl chloride **9** and the bromide **10** could be obtained in comparably good yields by treatment of **5a** with dichloromethyl methyl ether and oxalyl bromide, respectively.[16] In all cases, $^{13}C—^{1}H$ coupling constant $J_{C\text{-}1,H\text{-}1}$ with values higher than 169 Hz indicated the 1,2-*trans* configuration of the substituents at the rhamnose derivatives **8**–**10**.

For the comparative study, the rhamnoglycosyl donors **5a**,**7**–**10** were coupled with the galacturonate glycosyl acceptor **12** in a ratio of 1:1. For every glycosyl donor several promoters were tested, and the best result of each reaction type is described in the Experimental. Thus, the highest yields of the α(1→4)-coupled disaccharide **13** were achieved with the glycosyl chloride **9** (73%) and the glycosyl bromide **10** (76%) in the presence of silver trifluoromethanesulfonate.[17] Comparable results afforded the coupling of the 1-acetate **5a** with the aid of trimethylsilyl trifluoromethanesulfonate[17] (66%), in the course of which the utilization of a 1.3:1 molar ratio of donor **5a** and acceptor **12** increased effectively the yield of disaccharide **13** to 88%. Unfortunately, the glycosylation with the rhamnosyl trichloroacetimidate **7** in the presence of boron trifluoride diethyl etherate[16] gave only comparable results (50% yield) due to the trityl-cyanoethylidene condensation of the 4-*O*-tritylated acceptor **12** with the donor **11**.[6] Suprisingly low was the yield of disaccharide **13** when the thioglycoside **8** was used as glycosyl donor. Promotion with *N*-iodosuccinimide/trifluoromethanesulfonic acid[18] as well as with dimethyl(methyl-thio)sulfonium triflate[19] gave approximately 30% yields only, whereas iodonium di-*sym*-collidine perchlorate[18,20] and iodonium di-*sym*-collidine triflate[21] were completely inactive. The analytical data for compound **13** was reported in an earlier paper[6] by us and is in full agreement with the structure obtained here. Noteworthy, the value of the $^{13}C—^{1}H$ coupling constant $J_{C\text{-}1',H\text{-}1'}$ is 172.5 Hz and indicates clearly the α-linkage between L-rhamnose and D-galacturonic acid.

Before the disaccharide **13** was used as a glycosyl donor in a block synthesis, we investigated both the introduction of the trichloroacetimidate function at the anomeric center and the influence on stereoselectivity during glycosylation of several substituents in the O-3 and O-4 position of galacturonates **20**–**22** (Scheme 3), which served here as model compounds. Thus, acetylation of galacturonate **12**[5] with acetic anhydride in pyridine provided the 4-*O*-acetyl derivative **14**, whereas methylation of **12** was achieved with ethereal diazomethane under acid catalysis[22] to afford the 4-*O*-methyl derivative **16**. In the ^{1}H NMR spectra the acetylation of **12** caused the expected downfield shift of the H-4 ring proton signal from δ 4.31

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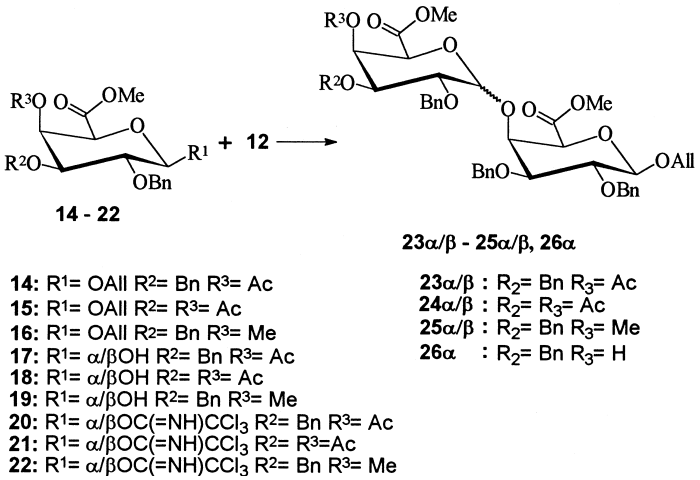


Scheme 3.

(**12**)[5] to 5.78 (**14**). Otherwise, the methylation leads to an upfield shift of H-4 to δ 3.97 (**16**). The synthesis of the 3,4-di-*O*-acetyl derivative **15** has been described in an earlier paper.[5] After deallylation of compounds **14**–**16** with the aid of palladium(II) chloride,[23] the introduction of the trichloroacetimidate group at the anomeric center of resulting **17**–**19** in the presence of DBU furnished the α-D-galactopyranosyl trichloroacetimidates **20**α-**22**α after chromatographic purification in good yields (ca. 73%). Furthermore, the β-trichloroacetimidates **20**β-**22**β could be characterized by ^{1}H NMR spectroscopy obtained from enriched HPLC fractions which still contained mostly the corresponding α-anomers. Typically, the small coupling constants $J_{1,2}$ of 3.2 ± 0.2 Hz for compounds **20**α-**22**α and the considerable bigger ones of 7.8 ± 0.5 Hz for **20**β-**22**β illustrated the situation at the anomeric center.

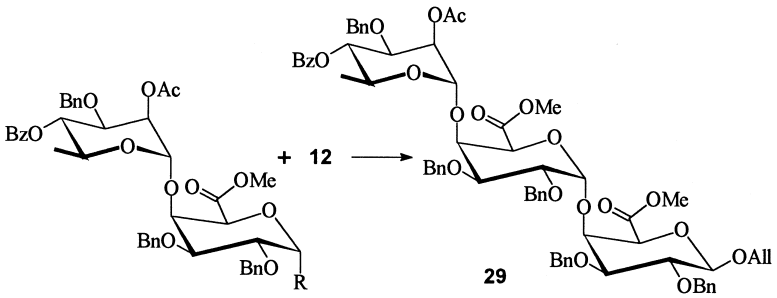
The glycosylation of the galacturonate acceptor **12** with donors **20**α-**22**α in a ratio of 1:1 promoted by trimethylsilyl trifluoromethanesulfonate revealed a peculiar effect of the chosen substitution pattern (Scheme 3). Thus, the 3,4-di-*O*-acetyl-α-D-galacturonate trichloroacetimidate **21** provided 67% yield of the α(1→4)-coupled disaccharide **24**α but only 5% of the β-coupled disaccharide **24**β was detected. By way of contrast, the more active 2,3-di-*O*-benzyl glycosyl donor **20** coupled with **12** furnished the corresponding disaccharides **23**α in a yield of 59% but no β-coupled disaccharide **23**β was observed. In earlier experiments the coupling of **12** with **20** in the presence of boron trifluoride diethyl etherate furnished the corresponding disaccharides **23**α and **23**β in a total yield of 53% and a disappointingα/β ratio of 1.6:1. The analytical data of the isolated **23**β are described in the Experimental. Finally, the methyl group in the O-4 position of the glycosyl donor **22** gave rise to the lowest stereoselectivity (nearly 1:1 disaccharide **25**α/**25**β) with a total yield of 52%. Subsequent experiments have shown that the α- or β-configuration of the trichloroacetimidate group at the anomeric center of

the donors **20**–**22** exerted no influence on the outcome of stereoselectivity of the glycosylations here investigated. Therefore, in the following experiments we used theα/β mixtures of **20**–**22**. The ^{1}H NMR spectra showed vicinal coupling constants $J_{1',2'}$ of 3.4 ± 0.3 Hz for the α-coupled disaccarides **23**α, **24**α and **25**α, whereas the β-coupled ones had a value of 7.6 Hz. Furthermore, the ^{13}C NMR signals for C-1′ of **23**α-**25**α were found to fall within the expected range of δ 99.7 ± 0.3. In the case of **23**β-**25**β values for C-1′ signals were determined at δ 102.4 ± 0.1. The other ^{1}H and ^{13}C NMR data were also fully consistent with the assigned structures.

Now, the preparation of galacturonates suitable as donors in α-glycosylation reactions can be carried out directly from commercially available D-galacturonic acid (D-GalA → **14**,**15** → **20**,**21**) avoiding the crucial oxidation step in comparison to an approach involving D-galactose-derived intermediates.

In a side-experiment, we made sure that disaccharide **23**α could serve as a precursor of a glycosyl acceptor. Thus, the deacetylation of **23**α with 0.28 M methanolic hydrochloric acid[6] provided the deprotected O-4′ position of the disaccharide **26**α in a quantitative yield. This successful cleavage of an acetyl group in **23**α was documented in its ^{1}H NMR spectrum by a significant upfield shift for the H-4′ ring proton signal from δ 5.78 (**23**α) to 4.28 (**26**α).

Encouraged by the good results of the model glycosylations, the disaccharide **13** was transformed *via* deallylation (**27**) into the α-trichloroacetimidate **28** (Scheme 4) and coupled with the glycosyl acceptor **12** under exactly the same conditions described above. Fortunately, the trisaccharide **29** was obtained after chromatographic purification in 70% isolated yield. Only traces of a trisaccharide formed as a result of a β-glycosylation were noticed in the NMR spectra of the reaction mixture. The ^{1}H and ^{13}C NMR spectra of **29** confirm the assigned structure. Thus, the stereochemistry of the glycosidic linkage between the galacturonic acid residues was established in the ^{1}H NMR spectra by the signal for H-1′ at δ 5.26 with a small coupling constant $J_{1',2'}$ of 3.1 Hz, whereas β-linked trisaccharide shows a typically larger coupling constant $J_{1',2'}$ of 7.6 Hz at δ 4.39. Additionally, the value of the C-1′ signal at δ 99.59 for **29** is shifted to δ 102.22 in the case of the β-linked derivative.



27: R= OH
28: R= OC(=NH)CCl$_3$

Scheme 4.

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In conclusion, the key intermediate **13** could be obtained in excellent 88% yield using a slight excess of the 1,2-di-*O*-acetylrhamnosyl glycosyl donor **5a**. The disaccharide **13** can be used either as a glycosyl acceptor or glycosyl donor for the preparation of rhamnogalacturonan fragments. Selective deacetylation of the O-2′-position and coupling with a suitable galacturonate glycosyl donor led to the D-GalA-α(1→2)-L-Rha-α(1→4)-D-GalA trisaccharide as described in a previous paper.[6] On the other hand, introduction of the trichloroacetimidate function at the anomeric center gave the disaccharide glycosyl donor **28**, which could be applied in a glycosylation reaction to form the L-Rha-α(1→4)-D-GalA-α(1→4)-D-GalA trisaccharide **29** in excellent yield. On condition that no neighboring group effect controlled the reaction at the anomeric center of the α-trichloroacetimidate glycosyl donors **20**–**22** and **28**, α-glycosidic linkages were nearly exclusively formed, except in the case of the 4-*O*-methyl-galactopyranosyluronate **22**. Thus, the trichloroacetimidate glycosylation procedure offers for the first time the possibility to use D-galacturonate oligomers in a block synthesis in the course of which α-glycosidic linkages were realized.

EXPERIMENTAL

General methods. Melting points were determined with a Boetius micro apparatus BHMK 05 (Rapido, Dresden) and are uncorrected. Optical rotations were measured for solutions in a 2-cm cell with an automatic polarimeter "GYROMAT" (Dr. Kernchen Co.). NMR spectra were recorded with Bruker AC-250 or ARX-300 spectrometers, at 250 MHz or 300 MHz for ^{1}H, and 62.9 MHz or 75.5 MHz for ^{13}C, respectively. Chemical shifts are given relative to the signal of internal tetramethylsilane ($\delta = 0$). First order chemical shifts and coupling constants were obtained from one-dimensional spectra, and assignment of proton resonances was based on COSY experiments. Thin-layer chromatography (TLC) on precoated plates of silica gel (Merck, Silica Gel 60, F_{254}, 0.25 mm) was performed with the following solvent systems (v/v): (A) 1:1, (B) 1.5:1, (C) 2:1, (D) 2.5:1, (E) 1:1.5, and (F) 1:2 heptane-ethyl acetate. The spots were made visible by spraying with methanolic 10% H_2SO_4 solution and charring them for 3–5 min with a heat gun. Detection of benzyl derivatives was effected by UV fluorescence. Preparative flash chromatography, MPLC and HPLC were performed by elution from columns of slurry-packed Silica Gel 60 (Merck, 40–63 μm) and Nucleosil 100–7 (Knauer, 7.0 μm), respectively, with the above mentioned solvent systems. All solvents and reagents were purified and dried according to standard procedures.[24] After classical work-up of the reaction mixtures, the organic layers as a rule, were dried over $MgSO_4$, and then concentrated under reduced pressure (rotary evaporator).

Methyl 2,3-*O*-methylorthoacetyl-α-L-rhamnopyranoside (1). To a solution of methyl α-L-rhamnopyranoside[25] (1.265 g, 7.1 mmol) in dry DMF (40 mL) was successively added camphorsulfonic acid (165 mg, 0.71 mmol) and triethyl orthoacetate (3.3 mL, 17.2 mmol). The solution was stirred for 40 min at ambient

temperature under argon (TLC, R_f 0.40, solvent A). The reaction was terminated by addition of triethylamine (1.8 mL, 12.8 mmol), and the mixture was concentrated. The residue was dissolved in chloroform (40 mL), and the organic solution was extracted with ice-water (2 × 15 mL), cold aq sat $NaHCO_3$ solution (2 × 15 mL), dried, and concentrated. The crude material was purified by MPLC (ethyl acetate gradient 0%→40% in heptane) to yield **1** (1.15 g, 65%) as a colorless syrup: ^{1}H NMR ($CDCl_3$) δ 1.16, 1.19 (2t, 6H, J = 8.2 Hz, OCH_2CH_3 *endo/exo*), 1.29 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6), 1.52, 1.62 (2s, 6H, CH_3 *endo/exo*), 2.96 (d, 1H, $J_{4,OH}$ = 15.3 Hz, OH-4), 3.36 (s, 3H, OCH_3), 3.45, 3.48 (2m, 4H, OCH_2CH_3 *endo/exo*), 3.49 (t, 1H, $J_{4,5}$ = 7.0 Hz, H-4), 3.52 (m, 1H, H-5), 4.11 (d, 1 H, $J_{1,2}$ = 1.8 Hz, H-1), 4.34 (dd, 1 H, $J_{3,4}$ = 7.0 Hz, H-3), 4.82 (dd, 1H, $J_{2,3}$ = 3.1 Hz, H-2).

Anal. Calcd for $C_{11}H_{20}O_6$ (248.28): C, 53.22; H, 8.12. Found: C, 53.16; H, 8.03.

Acylation and opening of the orthoester ring of compound 1. To a solution of **1** (546 mg, 2.2 mmol) in dry pyridine (15 mL) was added the acylation agent (2.5 mmol of benzoyl chloride, *p*-methylbenzoyl chloride or *p*-nitrobenzoyl chloride) at −20 °C under an inert atmosphere. The reaction mixture was stirred at that temperature for one hour and then kept for an additional 8 h at ambient temperature (TLC, R_f ~0.6, solvent A). Next, the slight excess of acyl chloride was destroyed by addition of methanol (1 mL), and after stirring for a further 20 min, the reaction mixture was concentrated and repeatedly co-concentrated with toluene-ethyl acetate-ethanol (5:3:1, v/v/v). In the course of this work-up the orthoester was already completely opened (TLC, R_f ~0.4, solvent A). The residue was dissolved in toluene, and the formed carbohydrate-free precipitate filtered off and washed with toluene. The filtrate and washings were combined, dried and concentrated.

The crude products were purified by HPLC (eluent solvent B).

Methyl 2-*O*-acetyl-4-*O*-benzoyl-α-L-rhamnopyranoside (3a). (642 mg, 90%; TLC, R_f 0.43, solvent A), colorless crystals: mp 152°C (ethyl acetate-heptane); $[\alpha]_D^{25}$ −31.6° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.25 (d, 3H, $J_{5,6}$ = 6.4 Hz, H-6), 2.15 (s, 3H, $OCOCH_3$), 3.38 (s, 3H, OCH_3), 3.90 (m, 1H, H-5), 4.16 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.70 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1), 5.11 (dd, 1H, $J_{2,3}$ = 3.7 Hz, H-2), 5.12 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 7.41, 7.55, 8.05 (3m, 5H, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 17.40 (C-6), 20.91 ($OCOCH_3$), 55.08 (OCH_3), 65.88 (C-5), 68.38 (C-3), 72.13 (C-2), 75.13 (C-4), 98.26 ($J_{C\text{-}1,H\text{-}1}$ = 170.9 Hz, C-1), 128.31, 128.36 129.41, 129.74, 130.01, 133.31 ($OCOC_6H_5$), 166.82 ($OCOC_6H_5$), 170.68 ($OCOCH_3$).

Anal. Calcd for $C_{16}H_{20}O_7$ (324.33): C, 59.25; H, 6.22. Found: C, 59.18; H, 6.19.

Methyl 2-*O*-acetyl-4-*O*-*p*-methylbenzoyl-α-L-rhamnopyranoside (3b). (633 mg, 85%; TLC, R_f 0.38, solvent A), colorless crystals: mp 126°C (ethyl acetate-heptane); $[\alpha]_D^{25}$ −50.7° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.23 (d, 3H,

$J_{5,6}$ = 6.4 Hz, H-6), 2.12 (s, 3H, $OCOCH_3$), 2.36 (s, 3H, $pCH_3C_6H_4OCO$), 2.76 (bs, 1H, OH-3), 3.36 (s, 3H, OCH_3), 3.90 (m, 1H, H-5), 4.12 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.67 (d, 1H, $J_{1,2}$ = 1.6 Hz, H-1), 5.08 (dd, 1H, $J_{2,3}$ = 3.7 Hz, H-2), 5.08 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 7.18, 7.88 (2m, 4H, $pCH_3C_6H_4OCO$); ^{13}C NMR ($CDCl_3$) δ 17.32 (C-6), 20.82 ($OCOCH_3$), 21.49 ($pCH_3C_6H_4OCO$), 54.97 (OCH_3), 65.84 (C-5), 68.24 (C-3), 72.47 (C-2), 74.85 (C-4), 98.20 ($J_{C\text{-}1,H\text{-}1}$ = 171.1 Hz, C-1), 126.58, 128.96, 129.69, 143.97 ($pCH_3C_6H_4OCO$), 166.78 ($pCH_3C_6H_4OCO$), 170.58 ($OCOCH_3$).

Anal. Calcd for $C_{17}H_{22}O_7$ (338.36): C, 60.35; H, 6.55. Found: C, 60.31, H, 6.59.

Methyl 2-*O*-acetyl-4-*O*-*p*-nitrobenzoyl-α-L-rhamnopyranoside (3c). (674 mg, 83%; TLC, R_f 0.39, solvent A), pale yellow crystals: mp 143 °C (ethyl acetate-heptane); $[\alpha]_D^{19}$ −15.6° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.26 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6), 2.17 (s, 3H, $OCOCH_3$), 2.34 (d, 1H, $J_{3,OH}$ = 8.2 Hz, OH-3), 3.39 (s, 3H, OCH_3), 3.95 (m, 1H, H-5), 4.16 (ddd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.71 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1), 5.09 (dd, 1H, $J_{2,3}$ = 3.7 Hz, H-2), 5.12 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 8.20, 8.28 (2m, 4H, $pNO_2C_6H_4OCO$); ^{13}C NMR ($CDCl_3$) δ 17.44 (C-6), 20.92 ($OCOCH_3$), 55.22 (OCH_3), 65.70 (C-5), 68.42 (C-3), 72.70 (C-2), 76.14 (C-4), 98.30 ($J_{C\text{-}1,H\text{-}1}$ = 171.2 Hz, C-1), 123.56, 130.78, 130.88, 134.96, 150.78 ($pNO_2C_6H_4OCO$), 164.78 ($pNO_2C_6H_4OCO$), 170.60 ($OCOCH_3$).

Anal. Calcd for $C_{16}H_{19}O_9N$ (369.32): C, 52.03; H, 5.19; N, 3.79. Found: C, 51.99; H, 5.25; N, 3.81.

Benzylation of 3a–3c. A solution of **3a, 3b,** or **3c** (5.7 mmol) and benzyl 2,2,2-trichloroacetimidate (1.6 mL, 8.5 mmol) in dry dichloromethane (20 mL) and dry heptane (30 mL) was treated with a catalytic amount of trifluoromethanesulfonic acid [55 μL, 0.6 mmol, dissolved in dry dichloromethane (2 mL)] under an inert atmosphere at −10°C. The reaction mixture was stirred at that temperature for 3.5 h, and then for a further 18 h at ambient temperature (TLC solvent A). The solution was passed through a layer of alkaline alumina and concentrated. After suspending the residue in heptane-diethyl ether (6:1, v/v, 70 mL) the carbohydrate-free precipitates were filtered off and washed with heptane-diethyl ether (6:1, v/v, 30 mL). The filtrate and washings were combined, concentrated, and the raw product was purified by MPLC (ethyl acetate gradient 0%→45% in heptane).

Methyl 2-*O*-acetyl-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranoside (4a). (1.51 g, 64%; TLC, R_f 0.49, solvent A), colorless foam: $[\alpha]_D^{25}$ +39.7° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.39 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6), 2.30 (s, 3H, $OCOCH_3$), 3.49 (s, 3H, OCH_3), 4.00 (m, 1H, H-5), 4.06 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.53, 4.73 (2d, 2H, J = 12.5 Hz, $CH_2C_6H_5$), 4.82 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 5.44 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 5.55 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2), 7.17–8.13 (4m, 10H, $CH_2C_6H_5$, $OCOC_6H_5$); ^{13}C NMR ($CDCl_3$) δ 17.45 (C-6), 20.88 ($OCOCH_3$), 54.93 (OCH_3), 66.41 (C-5), 68.34 (C-2), 70.96 ($CH_2C_6H_5$), 72.91 (C-4), 74.21

(C-3), 98.81 (C-1), 127.40, 127.66, 128.06, 128.25, 129.68, 129.86, 132.97, 137.58 ($CH_2C_6H_5$, $OCOC_6H_5$), 165.53 ($OCOC_6H_5$), 170.22 ($OCOCH_3$).

Anal. Calcd for $C_{23}H_{26}O_7$ (414.45): C, 66.66; H, 6.32. Found: C, 66.67; H, 6.28.

Methyl 2-*O*-acetyl-3-*O*-benzyl-4-*O*-*p*-methylbenzoyl-α-L-rhamnopyranoside (4b). (1.54 g, 63%; TLC, R_f 0.54, solvent A), colorless foam: $[\alpha]_D^{23}$ +23.2° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.24 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6), 2.17 (s, 3H, $OCOCH_3$), 2.44 (s, 3H, $pCH_3C_6H_4OCO$), 3.37 (s, 3H, OCH_3), 3.90 (m, 1H, H-5), 3.91 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.41, 4.60 (2d, 2H, J = 12.5 Hz, $CH_2C_6H_5$), 4.68 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 5.29 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 5.40 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2), 7.11–7.89 (3m, 9H, $CH_2C_6H_5$, $pCH_3C_6H_4OCO$); ^{13}C NMR ($CDCl_3$) δ 17.50 (C-6), 21.08 ($OCOCH_3$), 21.67 ($pCH_3C_6H_5OCO$), 55.04 (OCH_3), 66.50 (C-5), 68.33 (C-2), 70.92 ($CH_2C_6H_5$), 72.65 (C-4), 74.07 (C-3), 98.85 (C-1), 127.08, 127.48, 127.75, 128.17, 129.04, 129.86, 137.65, 143.82 ($CH_2C_6H_5$, $pCH_3C_6H_4OCO$), 165.72 ($pCH_3C_6H_4OCO$), 170.46 ($OCOCH_3$).

Anal. Calcd for $C_{24}H_{28}O_7$ (428.48): C, 67.28; H, 6.59. Found: C, 67.24; H, 6.65.

Methyl 2-*O*-acetyl-3-*O*-benzyl-4-*O*-*p*-nitrobenzoyl-α-L-rhamnopyranoside (4c). (1.65 g, 63%; TLC, R_f 0.50, solvent A), pale yellow foam: $[\alpha]_D^{24}$ +31.7° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.23 (d, 3H, $J_{5,6}$ = 6.4 Hz, H-6), 2.18 (s, 3H, $OCOCH_3$), 3.39 (s, 3H, OCH_3), 3.89 (m, 1H, H-5), 3.92 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.34, 4.59 (2d, 2H, J = 12.5 Hz, $CH_2C_6H_5$), 4.70 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 5.26 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 5.42 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2), 7.07–8.15 (3m, 9H, $CH_2C_6H_5$, $pNO_2C_6H_4OCO$); ^{13}C NMR ($CDCl_3$) δ 17.55 (C-6), 21.06 ($OCOCH_3$), 55.20 (OCH_3), 66.13 (C-5), 68.05 (C-2), 70.87 ($CH_2C_6H_5$), 73.89 (C-4), 73.91 (C-3), 98.83 (C-1), 123.47, 127.73, 127.93, 128.23, 130.86, 135.13, 137.44, 150.59 ($CH_2C_6H_5$, $pNO_2C_6H_4OCO$), 163.79 ($pNO_2C_6H_4OCO$), 170.37 ($OCOCH_3$).

Anal. Calcd for $C_{23}H_{25}O_9N$ (459.45): C, 60.13; H, 5.48; N, 3.05. Found: C, 60.04; H, 5.55; N, 3.12.

Acetolysis of 4a–4c. A solution of **4a, 4b,** or **4c** (3.5 mmol) in acetic anhydride-acetic acid-sulfuric acid (100:40:1, v/v/v, 15 mL) was stirred for 30 min at ambient temperature (TLC solvent A). After addition of cold aq 10% K_2SO_4 (200 mL), the solution was stirred for a further 30 min. Subsequently, the reaction mixture was extracted with chloroform (3 × 50 mL), and the combined organic phases were washed successively with cold sat aq $NaHCO_3$ (2 × 50 mL), water (2 × 50 mL), dried, and concentrated. The residue was co-concentrated with toluene (3 ×) to remove remaining traces of acetic acid. Finally, the residue was purified by MPLC (ethyl acetate gradient 0%→50% in heptane) providing nearly exclusively the α-anomers of **5a**–**5c**.

1,2-Di-*O*-acetyl-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranose (5a). (1.30 g, 84%; TLC, R_f 0.55, solvent A), colorless foam: $[\alpha]_D^{25}$ +22.7° (*c* 1.0, chlo-

roform); ^{1}H NMR ($CDCl_3$) δ 1.26 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6), 2.12, 2.18 (2s, 6H, 2 × $OCOCH_3$), 3.93 (dd, 1H, $J_{3,4}$ = 9.9 Hz, H-3), 3.96 (m, 1H, H-5), 4.43, 4.63 (2 d, 2H, J = 12.4 Hz, $CH_2C_6H_5$), 5.34 (t, 1H, $J_{4,5}$ = 9.9 Hz, H-4), 5.40 (dd, 1H, $J_{2,3}$ = 3.3 Hz, H-2), 6.08 (d, 1H, $J_{1,2}$ = 1.9 Hz, H-1), 7.10–8.01 (4m, 10H, $CH_2C_6H_5$, $OCOC_6H_5$); ^{13}C NMR ($CDCl_3$) δ 17.52 (C-6), 20.90 (2 × $OCOCH_3$), 67.26 (C-2), 68.99 (C-5), 71.11 ($CH_2C_6H_5$), 72.24 (C-4), 73.77 (C-3), 91.13 ($J_{C\text{-}1,H\text{-}1}$ = 172.6 Hz, C-1), 127.67, 127.81, 128.22, 128.37, 129.80, 129.25, 133.25, 137.29 ($CH_2C_6H_5$, $OCOC_6H_5$), 165.51 ($OCOC_6H_5$), 168.37, 170.07 (2 × $OCOCH_3$).

Anal. Calcd for $C_{24}H_{26}O_8$ (442.46): C, 65.15; H, 5.92. Found: C, 65.16; H, 5.87.

1,2-Di-*O*-acetyl-3-*O*-benzyl-4-*O*-benzoyl-β-L-rhamnopyranose (5aβ). (108 mg, 7%; TLC, R_f 0.47, solvent A), colorless foam: $[\alpha]_D^{24}$ +73.3° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.46 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6), 2.26, 2.39 (2s, 6H, 2 × $OCOCH_3$), 3.84 (m, 1H, H-5), 3.87 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.55, 4.79 (2d, 2H, J = 12.5 Hz, $CH_2C_6H_5$), 5.46 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 5.80 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2), 5.95 (d, 1H, $J_{1,2}$ = 1.2 Hz, H-1), 7.26–8.13 (4m, 10H, $CH_2C_6H_5$, $OCOC_6H_5$); ^{13}C NMR ($CDCl_3$) δ 17.41 (C-6), 20.72, 20.90 (2 × $OCOCH_3$), 66.91 (C-2), 70.66 ($CH_2C_6H_5$), 71.58 (C-5), 72.06 (C-4), 75.49 (C-3), 90.92 ($J_{C\text{-}1,H\text{-}1}$ = 161.6 Hz C-1), 127.77, 127.83, 128.25, 128.35, 128.81, 129.46, 129.77, 133.26, 136.86 ($CH_2C_6H_5$, $OCOC_6H_5$), 165.46 ($OCOC_6H_5$), 168.70, 170.52 (2 × $OCOCH_3$).

Anal. Calcd for $C_{24}H_{26}O_8$ (442.46): C, 65.15; H, 5.92. Found: C, 65.11; H, 5.86.

1,2-Di-*O*-acetyl-3-*O*-benzyl-4-*O*-*p*-methylbenzoyl-α-L-rhamnopyranose (5b). (1.49 g, 93%; TLC, R_f 0.53, solvent A), colorless syrup: $[\alpha]_D^{24}$ +15.7° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.23 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6), 2.12, 2.18 (2s, 6H, 2 × $COCH_3$), 2.43 (s, 3H, $pCH_3C_6H_4OCO$), 3.91 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 3.93 (m, 1H, H-5), 4.41, 4.61 (2d, 2H, J = 12.5 Hz, $CH_2C_6H_5$), 5.33 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 5.39 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2), 6.07 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 7.12–7.91 (3m, 9H, $CH_2C_6H_5$, $pCH_3C_6H_4OCO$); ^{13}C NMR ($CDCl_3$) δ 17.53 (C-6), 20.94, 21.72 (2 × $OCOCH_3$), 22.67 ($pCH_3C_6H_4OCO$), 67.31 (C-2), 69.09 (C-5), 71.10 ($CH_2C_6H_5$), 72.05 (C-4), 73.74 (C-3), 91.16 ($J_{C\text{-}1,H\text{-}1}$ = 171.7 Hz, C-1), 127.67, 127.83, 128.02, 128.27, 129.11, 129.90, 137.36, 144.05 ($CH_2C_6H_5$, $pCH_3C_6H_4OCO$), 165.60 ($pCH_3C_6H_4OCO$), 168.43, 170.13 (2 × $OCOCH_3$).

Anal. Calcd for $C_{25}H_{28}O_8$ (456.49): C, 65.78; H, 6.18. Found: C, 6.84; H, 6.14 %.

1,2-Di-*O*-acetyl-3-*O*-benzyl-4-*O*-(*p*-nitrobenzoyl)-α -L-rhamnopyranose (5c). (1.60 g, 94%; TLC, R_f 0.53, solvent A), colorless foam: $[\alpha]_D^{23}$ +18.4° (*c* 0.5, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.24 (d, 3H, $J_{5,6}$ = 6.4 Hz, H-6), 2.15, 2.20 (2s, 6H, $OCOCH_3$), 3.93 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 3.96 (m, 1H, H-5), 4.38, 4.63 (2d, 2H, J = 12.5 Hz, $CH_2C_6H_5$), 5.33 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 5.43 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2), 6.08 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 7.09–8.28 (3m, 9H, $CH_2C_6H_5$,

p$NO_2C_6H_4OCO$); ^{13}C NMR ($CDCl_3$) δ 17.56 (C-6), 20.79, 21.93 (2 × OCO*C*H_3), 67.05 (C-2), 68.69 (C-5), 71.07 (*C*$H_2C_6H_5$), 73.25 (C-4), 73.63 (C-3), 91.06 ($J_{C\text{-}1,H\text{-}1}$ = 171.7 Hz, C-1), 123.53, 127.92, 128.05, 128.31, 130.89, 134.92, 137.14, 150.84 ($CH_2C_6H_5$, *p*$NO_2C_6H_4OCO$), 163.69 (*p*$NO_2C_6H_4OCO$), 168.31, 170.02 (2 × O*C*OCH_3).

Anal. Calcd for $C_{24}H_{25}O_{10}N$ (487.46): C, 59.14; H, 5.17; N, 2.87. Found: C, 59.06; H, 5.26; N, 2.95.

2-*O*-Acetyl-4-*O*-benzoyl-3-*O*-benzyl-α,β-L-rhamnopyranose (6). A solution of 5a (1.18 g, 2.7 mmol) and hydrazine acetate (247 mg, 2.7 mmol) in dry acetonitrile (10 mL) was stirred for 4 h at 40°C (TLC, R_f 0.35, solvent A). Subsequently, the reaction mixture was concentrated, the residue dissolved in chloroform (30 mL), and the organic layer extracted with brine (2 × 15 mL), water (2 × 15 mL), dried, and concentrated. The crude product was purified by HPLC (eluent solvent A) to yield **6** (961 mg, 90%, 10:1 ratio of the α,β -anomers) as a colorless foam: ^1H NMR ($CDCl_3$) δ 1.23 (d, $J_{5,6}$ = 6.1 Hz, H-6α), 1.29 (d, $J_{5,6}$ = 6.1 Hz, H-6β), 2.18 (s, $OCOCH_3$α), 2.24 (s, $OCOCH_3$β), 3.22 (bs, 1-OHα/β), 3.64 (m, H-5β), 4.01 (dd, $J_{3,4}$ = 9.8 Hz, H-3α), 4.10 (dd, $J_{3,4}$ = 9.8 Hz H-3β), 4.14 (m, H-5α), 4.39, 4.63 (2d, J = 12.5 Hz, C*H*$_2C_6H_5$β), 4.42, 4.61 (2d, J = 12.5 Hz, C*H*$_2C_6H_5$α), 5.22 (d, $J_{1,2}$ = 0.9 Hz, H-1β), 5.22 (d, $J_{1,2}$ = 2.1 Hz, H-1α), 5.24 (t, $J_{3,4}$ = 9.8 Hz, H-4β), 5.30 (t, $J_{3,4}$ = 9.8 Hz, H-4α), 5.43 (dd, $J_{2,3}$ = 3.4 Hz, H-2α), 5.56 (dd, $J_{2,3}$ = 3.4 Hz, H-2β), 7.05–8.00 (4m, $CH_2C_6H_5$α/β, $OCOC_6H_5$α/β); ^{13}C NMR ($CDCl_3$) δ 17.55 (C-6β), 17.58 (C-6α), 21.00 (OCO*C*H_3β), 21.08 (OCO*C*H_3α), 66.66 (C-5α/β), 68.75 (C-2α), 69.09 (C-2β), 70.74 (*C*$H_2C_6H_5$β), 70.77 (*C*$H_2C_6H_5$α), 72.27 (C-4β), 72.89 (C-4α), 73.62 (C-3α), 75.97 (C-3β), 92.48 ($J_{C\text{-}1,H\text{-}1}$ = 173.2 Hz, C-1α), 93.03 ($J_{C\text{-}1,H\text{-}1}$ = 161.6 Hz, C-1β), 127.57, 127.76, 127.84, 127.96, 128.19, 128.28, 128.34, 128.40, 128.67, 128.75, 128.87, 129.49, 129.77, 129.81, 133.15, 133.30, 137.09, 137.50 ($CH_2C_6H_5$α/β, $OCOC_6H_5$α/β), 165.72 (O*C*OC_6H_5α/β), 170.61 (O*C*OCH_3α), 170.62 (O*C*OCH_3β).

Anal. Calcd for $C_{22}H_{24}O_7$ (400.43): C, 65.99; H, 27.97. Found: C, 66.05; H, 28.01.

2-*O*-Acetyl-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl trichloroacetimidate (7). To a solution of **6** (100 mg, 0.25 mmol) in dry dichloromethane (4 mL) were added trichloroacetonitrile (760 μL, 7.6 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 21 μL, 0.15 mmol) under argon at −20 °C. The reaction mixture was stirred at that temperature for one hour, and then, for an additional 30 min at room temperature (TLC, R_f 0.59, solvent A). Finally, the mixture was concentrated, the residue suspended in chloroform (20 mL) and filtered over Celite. The remaining solids were washed with chloroform (3 × 10 mL), the combined filtrate and washings were dried, and concentrated. The residue was purified by HPLC (eluent solvent D) to provide **7** (125 mg, 92%) as a colorless foam: $[\alpha]_D^{24}$ +7.3° (*c* 1.0, chloroform); ^1H NMR ($CDCl_3$) δ 1.28 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6), 2.21 (s, 3H, $OCOCH_3$), 4.00 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.07 (m, 1H, H-5), 4.44, 4.62 (2d, 2H, J = 12.5 Hz, C*H*$_2C_6H_5$), 5.39 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 5.54 (dd,

1H, $J_{2,3}$ = 3.4 Hz, H-2), 6.25 (d, 1H, $J_{1,2}$ = 2.1 Hz, H-1), 7.09–7.99 (4m, 10H, $CH_2C_6H_5$, $OCOC_6H_5$), 8.71 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 17.53 (C-6), 20.93 ($OCOCH_3$), 66.84 (C-2), 69.65 (C-5), 71.22 ($CH_2C_6H_5$), 72.01 (C-4), 73.22 (C-3), 90.72 [C(═NH)CCl_3], 95.09 ($J_{C\text{-}1,H\text{-}1}$ = 178.8 Hz, C-1), 127.81, 127.89, 127.96, 128.23, 128.37, 128.60, 128.83, 129.51, 129.83, 133.28, 136.94 ($CH_2C_6H_5$, $OCOC_6H_5$), 159.82 [C(═NH)CCl_3], 165.58 ($OCOC_6H_5$), 170.07 ($OCOCH_3$).

Anal. Calcd for $C_{24}H_{24}O_7NCl_3$ (544.82): C, 52.91; H, 20.56; N, 2.57; Cl, 19.52. Found: C, 52.96; H, 20.59; N, 2.62; Cl, 19.40.

Methyl 2-*O*-acetyl-4-*O*-benzoyl-3-*O*-benzyl-1-thio-α-L-rhamnopyranoside (8). To a solution of **5a** (664 mg, 1.5 mmol) in dry dichloromethane (10 mL) were added methylthiotrimethylsilane (2.1 mL, 14.7 mmol) and boron trifluoride diethyl etherate (1.0 mL, 7.3 mmol) under argon at 0 °C. After one hour at that temperature, the reaction mixture was stirred at room temperature for 8 h (TLC, R_f 0.61, solvent A). Then, the reaction was terminated by addition of *N*-ethyldiisopropylamine (3 mL). Finally, the mixture was diluted with chloroform (30 mL), extracted with water (2 × 15 mL), dried, and concentrated. The residue was purified by HPLC (eluent solvent D) to give **8** (633 mg, 98%) as a colorless foam: $[\alpha]_D^{24}$ −49.3° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.25 (d, 3H, $J_{5,6}$ = 6.4 Hz, H-6), 1.84 (s, 3H, $OCOCH_3$), 2.17 (s, 3H, SCH_3), 3.87 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.20 (m, 1H, H-5), 4.38, 4.58 (2d, 2H, J = 12.5 Hz, $CH_2C_6H_5$), 5.14 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1), 5.32 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 5.49 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2), 7.09–7.97 (4m, 10H, $CH_2C_6H_5$, $OCOC_6H_5$); ^{13}C NMR ($CDCl_3$) δ 13.74 (SCH_3), 17.49 (C-6), 21.05 ($OCOCH_3$), 67.14 (C-5), 69.78 (C-2), 71.07 ($CH_2C_6H_5$), 72.97 (C-4), 74.44 (C-3), 83.73 ($J_{C\text{-}1,H\text{-}1}$ = 169.3 Hz, C-1), 127.66, 127.95, 128.22, 128.33, 128.63, 128.80, 129.72, 129.79, 133.13, 137.21 ($CH_2C_6H_5$, $OCOC_6H_5$), 165.59 ($OCOC_6H_5$), 170.28 ($OCOCH_3$).

Anal. Calcd $C_{23}H_{26}O_6S$ (430.52): C, 64.17; H, 6.09; S, 7.45. Found: C, 64.19; H, 6.05; S, 7.58.

2-*O*-Acetyl-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl chloride (9). To a stirred solution of **5a** (266 mg, 0.6 mmol) in dry dichloromethane (6 mL) were added dichloromethyl methyl ether (58 μL, 0.7 mmol) and a catalytic amount of anhydrous $ZnBr_2$ (2.3 mg, 0.001 mmol) under argon at room temperature. After stirring for 15 min (TLC, R_f 0.57, solvent A), the mixture was filtered through cotton wool, and concentrated. After drying under high vacuum, the chromatographically pure syrup **9** (246 mg, 98%) was used without further purification: $[\alpha]_D^{25}$ −8.7° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.29 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6), 2.19 (s, 3H, $OCOCH_3$), 4.18 (m, 1H, H-5), 4.22 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.42, 4.61 (2d, 2H, J = 12.5 Hz, $CH_2C_6H_5$), 5.36 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 5.52 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2), 6.03 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 7.11–7.61 (4m, 10H, $CH_2C_6H_5$, $OCOC_6H_5$); ^{13}C NMR ($CDCl_3$) δ 17.17 (C-6), 20.91 ($OCOCH_3$), 69.77 (C-5), 70.62 (C-2), 71.33 ($CH_2C_6H_5$), 72.01 (C-4), 72.59 (C-3), 90.05 ($J_{C\text{-}1,H\text{-}1}$ = 183.9 Hz, C-1), 127.80, 127.98, 128.28, 128.39, 128.69, 129.22, 129.40, 129.45, 129.80, 129.84, 133.31, 137.04 ($CH_2C_6H_5$, $OCOC_6H_5$), 165.51 ($OCOC_6H_5$), 169.99 ($OCOCH_3$).

Anal. Calcd for $C_{22}H_{23}O_6Cl$ (418.87): C, 63.08; H, 5.53; Cl, 8.46. Found: C, 63.11; H, 5.49; Cl, 8.41.

2-*O*-Acetyl-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl bromide (10). To a solution of **5a** (443 mg, 1.0 mmol) in dry dichloromethane (6 mL) was added oxalyl bromide (139 μL) under argon at −40 °C. After an additional hour at that temperature, the reaction mixture was kept for 4 h at ambient temperature (TLC, R_f 0.60, solvent A). Next, the mixture was concentrated and repeatedly co-concentrated with toluene. Finally, the residue was rapidly processed by HPLC (eluent solvent D) to provide **10** (454 mg, 98%) as a colorless syrup: $[\alpha]_D^{23}$ −63.6° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.28 (d, 3H, $J_{5,6}$ = 6.10 Hz, H-6), 2.18 (s, 3H, $OCOCH_3$), 4.12 (m, 1H, H-5), 4.34 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.41, 4.60 (2d, 2H, J = 12.2 Hz, $CH_2C_6H_5$), 5.37 (t, 1H, $J_{4,5}$ = 9.8 Hz, H-4), 5.57 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2), 6.36 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1), 7.11–8.01 (4m, 10H, $CH_2C_6H_5$, $OCOC_6H_5$); ^{13}C NMR ($CDCl_3$) δ 17.05 (C-6), 20.93 ($OCOCH_3$), 69.65 (C-5), 71.12 (C-2), 71.97 ($CH_2C_6H_5$), 72.74 (C-4), 73.38 (C-3), 85.39 ($J_{C\text{-}1,H\text{-}1}$ = 184.6 Hz, C-1), 127.84, 127.98, 128.08, 128.31, 128.42, 129.45, 129.80, 129.89, 133.34, 137.01 ($CH_2C_6H_5$, $OCOC_6H_5$) 165.50 ($OCOC_6H_5$), 169.92 ($OCOCH_3$).

Anal. Calcd for $C_{22}H_{23}O_6Br$ (463.87): C, 57.03; H, 5.00; Br, 17.23. Found: C, 57.00; H, 4.96; Br, 17.15.

Methyl (4-*O*-benzoyl-3-*O*-benzyl-2-*O*-acetyl-α-L-rhamnopyranosyl)-(1→4)-(allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate (13). A. *via* donor 5a. Compound **5a** (221 mg, 0.5 mmol), methyl (allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid) uronate[5] (**12**, 214 mg, 0.5 mmol), and molecular sieves (4 Å, 4.0 g) were dried under high vacuum at ambient temperature for one hour. Then, the solids were suspended in dry dichloromethane (8 mL), and the reaction mixture was stirred for two hours, under argon, at room temperature in the dark. Subsequently, trimethylsilyl trifluoromethanesulfonate (150 μL, 0.9 mmol) was added, and stirring was continued for a further 18 h (TLC, R_f 0.53, solvent A). The reaction mixture was then passed through a layer of alkaline alumina by elution with chloroform. The eluate was washed with water (2 × 10 mL), dried, and concentrated. Finally, the residue was purified by HPLC (eluent solvent B) to yield starting materials **5a** (15 mg, 7%) and **12** (21 mg, 10%), and desired **13** (268 mg, 66%) as a colorless foam. The analytical data of **13** is in full agreement with the data from the literature.[6] The utilization of a 1.3:1 molar ratio of glycosyl donor **5a** and acceptor **12** increased effectively the yield of **13** (357 mg, 88%).

B. *via* donor 7. Compound **7** (272 mg, 0.5 mmol), glycosyl acceptor **12** (214 mg, 0.5 mmol), and molecular sieves (4 Å, 4.0 g) were dried under high vacuum at ambient temperature for 30 min. The solids were then suspended in dry dichloromethane (12 mL), and the reaction mixture was stirred for one hour, under argon, at room temperature in the dark. After cooling to −30°C, boron trifluoride diethyl etherate (123 μL, 1.0 mmol) was added, and stirring was continued for two hours at that temperature. Next, the reaction mixture was allowed to warm-up to

room temperature and stirring was continued for a further 18 h (TLC solvent A). Subsequently, the reaction mixture was passed through a layer of alkaline alumina by elution with chloroform. The eluate (ca. 40 mL) was extracted with cold aq sat $NaHCO_3$ (2 × 20 mL), water (2 × 20 mL), dried and concentrated. Finally, the residue was purified by HPLC (eluent solvent C) to provide starting material **12** (45 mg, 21%), syrupy **6** (26 mg, 13%) as a by-product, and desired **13** (207 mg, 51%).

C. *via* donor 8. Glycosyl donor **8** (215 mg, 0.5 mmol), acceptor **12** (214 mg, 0.5 mmol), and molecular sieves (4 Å, 4.0 g) were dried under high vacuum at ambient temperature for one hour. The solids were then suspended in dry dichloromethane (7 mL), and the suspension was stirred for two hours, under argon, at room temperature in the dark. Subsequently, to the reaction mixtue were added *N*-iodosuccinimide (158 mg, 0.7 mmol), and after chilling to −40°C, a solution of trifluoromethanesulfonic acid (6 μL) in dry diethyl ether (4 mL). After stirring for two hours at that temperature, the equal amount of *N*-iodosuccinimide and trifluoromethanesulfonic acid was again added. After an additional two hours, the chilling was terminated, and the mixture was stirred for 18 h at ambient temperature (TLC solvent A). A solution of *N*-ethyldiisopropylamine (3 mL) in methanol (4 mL) was then added, the reaction mixture was passed through a layer of alkaline alumina by elution with chloroform. The eluate (ca. 40 mL) was extracted with cold aq 10% sodium thiosulfate (2 × 20 mL), ice-water (20 mL), cold aq 3% hydrochloric acid (2 × 20 mL), ice-water (20 mL), cold sat aq $NaHCO_3$ (2 × 20 mL), ice-water (2 × 20 mL), dried, and concentrated. Finally, the residue was purified by HPLC (eluent solvent solvent B) to afford starting material **12** (114 mg, 53%), syrupy **6** (10 mg, 5%) as a by-product, and desired **13** (122 mg, 30%).

D. *via* donor 9. Glycosyl donor **9** (209 mg, 0.5 mmol), acceptor **12** (214 mg, 0.5 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (123 mg, 0.6 mmol), and molecular sieves (4 Å, 4.0 g) were dried under high vacuum at ambient temperature for one hour. The solids were then suspended in dry dichloromethane (10 mL), and the suspension was stirred for one hour, under argon, at room temperature in the dark. Subsequently, after chilling to −65°C, silver trifluoromethanesulfonate (141 mg, 0.55 mmol) was added. After stirring for two hours at that temperature, the chilling was terminated and the mixture was stirred for 18 h at ambient temperature (TLC solvent A). The reaction mixture was then passed through a layer of alkaline alumina by elution with chloroform. The eluate (ca. 40 mL) was extracted with cold aq 3% hydrochloric acid (2 × 20 mL), ice-water (20 mL), cold sat aq $NaHCO_3$ (2 × 20 mL), ice-water (2 × 20 mL), dried, and concentrated. Finally, the residue was purified by HPLC (eluent solvent B) to yield starting material **12** (13 mg, 6%), syrupy **6** (10 mg, 5%) as a by-product, and desired **13** (296 mg, 73%).

E. *via* donor 10. Exactly the same procedure as above (pathway D) was used for the glycosylation with **10** (232 mg, 0.5 mmol) to give starting material **12** (17 mg, 8%), syrupy **6** (8 mg, 4%) as a by-product, and desired **13** (308 mg, 76%).Methyl (allyl 4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate

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(**14**). To a stirred solution of methyl (allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate (**12**, 429 mg, 1.0 mmol) in dry pyridine (10 mL) was added acetic anhydride (5 mL) at 0°C. After 5 h at ambient temperature (TLC, R_f 0.45, solvent A), the mixture was poured into ice-water (60 mL), and the aqueous layer was extracted with chloroform (2 × 25 mL). The combined organic extracts were diluted with heptane (100 mL), washed with cold aq 1% hydrochloric acid (2 × 20 mL), ice-water (1 × 20 mL), cold aq sat $NaHCO_3$ (1 × 20 mL), ice-water (1 × 20 mL), dried, and concentrated. The residue was purified by HPLC (eluent solvent C) to provide **14** (461 mg, 98 %) as a colorless foam: $[\alpha]_D^{23}$ +35.8° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 2.12 (s, 3H, $OCOCH_3$), 3.61 (d, 1H, $J_{3,4}$ = 3.4 Hz, H-3), 3.69 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 3.77 (s, 3H, OCH_3), 4.15 (d, 1H, H-5), 4.15 (m, 1H, $CH_2CH{=}CH_2$), 4.45 (d, 1H, $J_{1,2}$ = 7.3 Hz, H-1), 4.50 (m, 1H, $CH_2CH{=}CH_2$), 4.54, 4.72, 4.76, 4.90 (4d, 4H, J = 10.7 Hz, J = 11.3 Hz, 2 × $CH_2C_6H_5$), 5.20, 5.34 (2m, 2H, $CH_2CH{=}CH_2$), 5.78 (dd, 1H, $J_{4,5}$ = 0.9 Hz, H-4), 5.95 (m, 1H, CH_2-$CH{=}CH_2$), 7.26–7.33 (m, 10H, $CH_2C_6H_5$); ^{13}C NMR ($CDCl_3$) δ 20.81 ($OCOCH_3$), 52.63 (OCH_3), 67.72 (C-4), 70.53, 72.22 (2 × $CH_2C_6H_5$), 72.48 (C-5), 75.42 ($CH_2CH{=}CH_2$), 78.23 (C-2), 78.58 (C-3), 102.35 (C-1), 117.64 ($CH_2CH{=}CH_2$), 127.64, 127.80, 127.95, 128.04, 128.10, 128.25, 128.36, 128.40, 128.86, 129.83, 137.51, 138.36 (2 × $CH_2C_6H_5$), 133.66 ($CH_2CH{=}CH_2$), 167.36 (C-6), 170.04 ($OCOCH_3$).

Anal. Calcd for $C_{26}H_{30}O_8$ (470.52): C, 66.37; H, 6.43. Found: C, 66.34; H, 6.40.

Methyl (allyl 2,3-di-*O*-benzyl-4-*O*-methyl-β-D-galactopyranosid)uronate (16). To a solution of **12** (429 mg, 0.1 mmol) in dry dichloromethane (10 mL) were successively added boron trifluoride diethyl etherate (20 μL, 0.15 mmol) and, dropwise, an ethereal diazomethane solution (until the yellow color of the reaction mixture persisted) under argon at 0 °C. When the reaction was complete (TLC, R_f 0.32, solvent A), the excess of diazomethane was destroyed with boron trifluoride diethyl etherate. The solution was then passed through a layer of alkaline alumina, and concentrated. The residue was applied to a HPLC (eluent solvent A) to provide **16** (367 mg, 83%) as a colorless foam: $[\alpha]_D^{26}$ −9.7° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 3.52 (dd, 1H, $J_{3,4}$ = 3.1 Hz, H-3), 3.54 (s, 3H, H_3CO-4) 3.80 (dd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 3.81 (s, 3H, OCH_3), 3.97 (dd, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 3.99 (d, 1H, H-5), 4.13, 4.48 (2m, 2H, $CH_2CH{=}CH_2$), 4.38 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1), 4.73, 4.92 (2d, 2H, J = 10.7 Hz, $CH_2C_6H_5$), 4.76 (s, 2H, $CH_2C_6H_5$), 5.18, 5.32 (2m, 2H, $CH_2CH{=}CH_2$), 5.94 (m, 1H, $CH_2CH{=}CH_2$), 7.23–7.39 (m, 10H, 2 × $CH_2C_6H_5$); ^{13}C NMR ($CDCl_3$) δ 52.53 (OCH_3), 61.19 (H_3CO-4), 70.13, 72.98 (2 × $CH_2C_6H_5$), 73.60 (C-5), 75.33 ($CH_2CH{=}CH_2$), 77.61 (C-2), 78.87 (C-3), 80.85 (C-4), 102.29 (C-1), 117.23 ($CH_2CH{=}CH_2$), 127.60, 127.66, 127.75, 127.86, 127.98, 128.16, 128.27, 128.40, 128.48, 128.89, 138.05, 138.51 (2 × $CH_2C_6H_5$), 133.92 ($CH_2CH{=}CH_2$), 168.87 (C-6).

Anal. Calcd for $C_{25}H_{30}O_7$ (442.51): C, 67.86; H, 6.83. Found: C, 67.90; H, 6.81.

Deallylation of 14–16. To a stirred solution of **14**, **15** or **16** (0.5 mmol) in a mixture of acetic acid and water (20:1, 15 ml) were added sodium acetate trihydrate (681 mg, 5 mmol) and palladium(II)chloride (355 mg, 2.0 mmol). After stirring for 4–6 h at 40–45°C (TLC solvent A), the reaction mixture was filtered, and the solids were washed with chloroform. The combined filtrate and washings (~30 mL) were extracted with sat aq $NaHCO_3$ (3 × 15 mL), water (2 × 15 mL), dried, and concentrated. The residue was purified by HPLC (eluent solvent E).

Methyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α/β-D-galactopyranuronate (17). (164 mg, 79%; TLC, R_f 0.20, solvent A, R_f 0.41, solvent F, 4:1 ratio of the α,β-anomers), colorless syrup: ^{1}H NMR ($CDCl_3$) δ 2.10, 2.11 ($OCOCH_3$), 3.51 (d, $J_{1,OH}$ = 2.5 Hz, HO-1), 3.60 (dd, $J_{3,4}$ = 3.1 Hz, H-3β), 3.67 (dd, $J_{2,3}$ = 10.1 Hz, H-2β), 3.73, 3.76 (2s, OCH_3α/β), 3.82 (dd, $J_{3,4}$ = 3.7 Hz, H-3α), 4.02 (dd, $J_{2,3}$ = 9.8 Hz, H-2α), 4.16 (d, H-5β), 4.52–4.84 (d,s, 2 × CH_2C$_6$H$_5$α/β), 4.76 (d, $J_{1,2}$ = 7.6 Hz, H-1β), 4.80 (d, H-5α), 5.37 (d, $J_{1,2}$ = 3.4 Hz, H-1α), 5.78 (dd, $J_{4,5}$ = 0.91 Hz, H-4β), 5.85 (dd, $J_{4,5}$ = 1.5 Hz, H-4α), 7.27–7.36 (m, 2 × $CH_2C_6H_5$α/β); ^{13}C NMR ($CDCl_3$) δ 20.72, 20.80 ($OCOCH_3$), 52.54, 52.70 (OCH_3α/β), 67.51 (C-4β), 68.48 (C-4α), 72.03, 73.77 (2 × $CH_2C_6H_5$), 72.22 (C-5β), 72.48 (C-5α), 77.93 (C-2β), 78.43 (C-3β), 78.56 (C-2α), 79.14 (C-3α), 92.07 (C-1α), 97.33 (C-1β), 127.67, 127.73, 127.80, 127.83, 127.88, 127.95, 127.98, 128.02, 128.11, 128.19, 128.27, 128.34, 128.37, 128.93, 129.52, 137.39, 137.62, 137.85, 138.23 (2 × $CH_2C_6H_5$α/β), 167.04, 168.31 (C-6α/β), 169.89, 169.93 ($OCOCH_3$α/β).

Anal. Calcd $C_{23}H_{26}O_8$ (430.45): C, 64.18; H, 6.08. Found: C, 64.20; H, 6.09.

Methyl 2,3-di-*O*-acetyl-4-*O*-benzyl-α/β-D-galactopyranuronate (18). (153 mg, 80%; TLC, R_f 0.22, solvent A, R_f 0.46, solvent F): colorless foam. For further analytical data see Ref. 5.

Methyl 2,3-di-*O*-benzyl-4-*O*-methyl-α/β-D-galactopyranuronate (19). (155 mg, 77%; TLC, R_f 0.21, solvent A, R_f 0.44, solvent F; 4:1 ratio of the α,β-anomers), colorless crystals: mp 49–51 °C, ^{1}H NMR ($CDCl_3$) δ 3.29 (d, $J_{1,OH}$ = 7.3 Hz, HO-1), 3.53, 3.55 (2s, H_3CO-4α/β), 3.58 (dd, $J_{2,3}$ = 9.7 Hz, H-2β), 3.78, 3.79 (2s, OCH_3α/β), 3.88 (dd, $J_{3,4}$ = 3.1 Hz, H-3β), 3.98 (dd, $J_{2,3}$ = 8.5 Hz, H-2α), 3.99 (dd, $J_{4,5}$ = 0.91 Hz, H-4β), 4.00 (d, H-5β), 4.01 (dd, $J_{3,4}$ = 3.1 Hz, H-3α), 4.07 (dd, $J_{4,5}$ = 1.2 Hz, H-4α), 4.60 (d, H-5α), 4.60–4.84 (d,s, 2 × CH_2C$_6$H$_5$α/β), 4.77 (d, $J_{1,2}$ = 7.6 Hz, H-1β), 5.34 (d, $J_{1,2}$ = 2.7 Hz, H-1α), 7.27–7.38 (m, 2 × $CH_2C_6H_5$α/β); ^{13}C NMR ($CDCl_3$) δ 52.38 (OCH_3α) 52.51 (OCH_3β), 61.19 (H_3CO-4α), 61.25 (H_3CO-4β), 70.36, 72.88 (2 × $CH_2C_6H_5$α), 73.60, 75.74 (2 × $CH_2C_6H_5$β), 73.66 (C-5β), 73.71 (C-5α), 75.07 (C-3β), 75.74 (C-3α), 77.58 (C-2β), 78.23 (C-2α), 80.74 (C-4α), 80.87 (C-4β), 91.92 (C-1α), 97.48 (C-1β), 127.54, 127.60, 127.66, 127.76, 127.84, 127.92, 128.02, 128.07, 128.19, 128.25, 128.33, 128.37, 128.48, 128.83, 128.90, 137.83, 138.00, 138.17, 138.26 (2 × $CH_2C_6H_5$α/β), 168.74 (C-6β), 169.52 (C-6α).

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Anal. Calcd for $C_{22}H_{26}O_7$ (402.44): C, 65.66; H, 6.51. Found: C, 65.71; H, 6.47.

Introduction of the trichloracetimidate group at the anomeric center of 17–19. To a solution of **17, 18** or **19** (1.0 mmol) in dry dichloromethane (7 mL) was added trichloroacetonitrile (3.7 mL, 37 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 28 μL, 0.2 mmol) under argon at −20°C. The reaction mixture was stirred at that temperature for one hour, and then for an additional hour at room temperature (TLC, $R_f \sim 0.4$, solvent A). Finally, the mixture was concentrated, the residue suspended in ethyl acetate (40 mL) and filtered over Celite. The remaining solids were washed with ethyl acetate (3 × 10 mL), the combined filtrate and washings were dried, and concentrated. The residue was purified by HPLC (eluent solvent B).

Methyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α-D-galactopyranosyluronate trichloroacetimidate (20α). (408 mg, 71%; TLC, R_f 0.39, solvent A), colorless syrup: $[\alpha]_D^{25}$ +86.4° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 2.10 (s, 3H, $OCOCH_3$), 3.75 (s, 3H, OCH_3), 4.06 (4d, 2H, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 3.1 Hz, H-2, H-3), 4.61, 4.71, 4.76, 4.78 (4d, 4H, J = 11.3 Hz, J = 11.9 Hz, 2 × $CH_2C_6H_5$), 4.70 (d, 1H, H-5), 5.89 (dd, 1H, $J_{4,5}$ = 1.5 Hz, H-4), 6.66 (d, 1H, $J_{1,2}$ = 3.1 Hz, H-1), 7.27–7.32 (m, 10H, 2 × $CH_2C_6H_5$), 8.64 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 20.66 ($OCOCH_3$), 52.71 (OCH_3), 68.25 (C-4), 71.15 (C-5), 72.07, 73.21 (2 × $CH_2C_6H_5$), 74.16, 74.41 (C-2, C-3), 90.91 [C(═NH)CCl_3], 93.27 (C-1), 127.39, 127.60, 127.74, 128.04, 128.24, 128.30, 137.42, 137.93 (2 × $CH_2C_6H_5$, 4 signals are isochronic), 160.54 [C(═NH)CCl_3], 167.32 (C-6), 169.78 ($OCOCH_3$).

Anal. Calcd $C_{25}H_{26}O_8NCl_3$ (574.84): C, 52.24; H, 4.56; N, 2.45; Cl, 18.50. Found: C, 52.20; H, 4.52; N, 2.39; Cl, 18.46.

Methyl 4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranosyluronate trichloroacetimidate (20β). (~2%, enriched fractions still contained mostly the α-anomer; TLC, R_f 0.40, solvent A), colorless syrup: ^{1}H NMR ($CDCl_3$) δ 2.11 (s, $OCOCH_3$), 3.76 (s, OCH_3), 4.00 (dd, 1H, $J_{3,4}$ = 3.1 Hz, H-3), 4.11 (dd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 4.64–4.82 (d,s, 4H, 2 × $CH_2C_6H_5$), 4.67 (d, 1H, H-5), 5.88 (d, 1H, $J_{1,2}$ = 7.3 Hz, H-1), 5.86 (dd, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 7.27–7.34 (m, 10H, 2 × $CH_2C_6H_5$), 8.64 (s, NH); ^{13}C NMR ($CDCl_3$) δ 20.78 ($OCOCH_3$), 52.80 (OCH_3), 67.92 (C-4), 71.31, 72.50 (2 × $CH_2C_6H_5$), 71.53 (C-5), 74.74, 74.95 (C-2, C-3), 90.94 [C(═NH)CCl_3], 94.41 (C-1), 127.51, 127.86, 128.16, 128.51, 128.76, 128.93, 137.39, 137.54 (2 × $CH_2C_6H_5$, 4 signals are isochronic), 160.55 [C(═NH)CCl_3], 166.85 (C-6), 169.60 ($OCOCH_3$).

Methyl 3,4-di-*O*-acetyl-2-*O*-benzyl-α-D-galactopyranosyluronate trichloroacetimidate (21α). (395 mg, 75%; TLC, R_f 0.44, solvent A), colorless foam: $[\alpha]_D^{24}$ +58.5° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.93, 2.00 (2s, 6H, $OCOCH_3$), 3.66 (s, 3H, OCH_3), 4.01 (dd, 1H, $J_{2,3}$ = 10.7 Hz, H-2), 4.56, 4.63 (2d, 2H, J = 11.9 Hz, $CH_2C_6H_5$), 4.72 (d, 1H, H-5), 5.35 (dd, 1H, $J_{3,4}$ = 3.4 Hz, H-3), 5.75 (dd, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 6.63 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 7.22–7.28 (m, 5H, $CH_2C_6H_5$), 8.63

(s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 20.43, 20.66 (2 × OCO*C*H_3), 52.71 (OCH_3), 68.78 (C-3), 68.92 (C-4), 70.59 (C-5), 72.00 (C-2), 72.94 (*C*$H_2C_6H_5$), 90.71 [C(═NH)*C*Cl_3], 93.79 (C-1), 127.48, 127.73, 127.86, 128.25, 128.33, 137.31 (CH_2*C*$_6H_5$), 160.56 [*C*(═NH)CCl_3], 166.76 (C-6), 169.49, 169.83 (2 × O*C*OCH_3).

Anal. Calcd for $C_{20}H_{22}O_9NCl_3$ (526.75): C, 45.60; H, 4.21; N, 2.66; Cl, 20.19. Found: C, 45.49; H, 4.18; N, 2.78; Cl, 20.06.

Methyl 3,4-di-*O*-acetyl-2-*O*-benzyl-β-D-galactopyranosyluronate trichloroacetimidate (21β). (~2%, only the α-anomer was isolated pure, while the enriched fractions of the β-anomer still contained α-anomer; TLC, R_f 0.41, solvent A), colorless foam: ^{1}H NMR ($CDCl_3$) δ 1.88, 2.03 (2s, 6H, OCOCH_3), 3.66 (s, 3H, OCH_3), 3.89 (dd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 4.53, 4.83 (2d, 2H, J = 12.8 Hz, C*H*$_2C_6H_5$), 4.39 (d, 1H, H-5), 5.06 (dd, 1H, $J_{3,4}$= 3.4 Hz, H-3), 5.65 (dd, 1H, $J_{4,5}$ = 1.5 Hz, H-4), 5.78 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1), 7.24–7.28 (m, 5H, CH_2C_6*H*$_5$), 8.72 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 20.52, 20.66 (2 × OCOCH_3), 52.69 (OCH_3), 68.43 (C-3), 71.76 (C-5), 73.02 (*C*$H_2C_6H_5$), 74.77 (C-4), 74.98 (C-2), 90.83 [C(═NH)*C*Cl_3], 97.87 (C-1), 127.52, 127.77, 127.86, 127.90, 128.38, 137.45 (CH_2*C*$_6H_5$), 160.99 [*C*(═NH)CCl_3], 165.93 (C-6), 169.51, 169.68 (2 × O*C*OCH_3).

Methyl 2,3-di-*O*-benzyl-4-*O*-methyl-α-D-galactopyranosyluronate trichloroacetimidate (22α). (399 mg, 73%; TLC, R_f 0.47, solvent A), colorless syrup: $[\alpha]_D^{24}$ +28.8° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 3.55 (s, 3H, H_3CO-4), 3.80 (s, 3H, OCH_3), 4.01 (dd, 1H, $J_{3,4}$ = 3.1 Hz, H-3), 4.10 (dd, 1H, $J_{4,5}$ = 1.5 Hz, H-4), 4.20 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 4.56 (d, 1H, H-5), 4.73 (s, 2H, C*H*$_2C_6H_5$), 4.53, 4.82 (2d, 2H, J = 11.9 Hz, C*H*$_2C_6H_5$), 6.65 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 7.26–7.38 (m, 10H, 2 × CH_2C_6*H*$_5$), 8.59 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 52.65 (OCH_3), 61.52 (H_3CO-4), 72.89, 73.12 (2 × *C*$H_2C_6H_5$), 73.07 (C-5), 75.23 (C-2), 76.70 (C-3), 78.37 (C-4), 90.91 [C(═NH)*C*Cl_3], 94.56 (C-1), 127.40, 127.54, 127.73, 127.78, 128.25, 128.37, 138.00, 138.12 (2 × CH_2*C*$_6H_5$, 4 signals are isochronic), 160.62 [*C*(═NH)CCl_3], 168.61 (C-6).

Anal. Calcd $C_{24}H_{26}O_7NCl_3$ (546.83): C, 52.72; H, 4.79; N, 2.56; Cl, 19.45. Found: C, 52.65; H, 4.68; N, 2.82; Cl, 19.31.

Methyl 2,3-di-*O*-benzyl-4-*O*-methyl-β-D-galactopyranosyluronate trichloroacetimidate (22β). (~2%, enriched fractions still contained mostly the α-anomer; TLC, R_f 0.48, solvent A); ^{1}H NMR ($CDCl_3$) δ 3.27 (s, 3H, H_3CO-4), 3.81 (s, 3H, OCH_3), 4.02 (dd, 1H, H-3), 4.08 (dd, 1H, H-4), 4.12 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 4.48 (d, 1H, H-5), 4.72–4.85 (d,s, 4H, 2 × C*H*$_2C_6H_5$), 4.77 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1), 7.27–7.38 (m, 10H, 2 × CH_2C_6*H*$_5$), 8.59 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 51.16 (OCH_3), 61.47 (H_3CO-4), 69.39 (C-5), 72.54, 73.04 (2 × *C*$H_2C_6H_5$), 75.26 (C-2), 77.10 (C-3), 77.31 (C-4), 90.93 [C(═NH)*C*Cl_3], 95.21 (C-1), 127.40, 127.64, 127.72, 127.95, 128.03, 128.30, 137.95, 138.08 (2 × CH_2*C*$_6H_5$, 4 signals are isochronic), 160.98 [*C*(═NH)CCl_3], 167.81 (C-6).

Glycosylation of Acceptor 12 with the Glycosyl Donors 20, 21, or 22. The Compounds **20**αβ, **21**αβ or **22**αβ (0.5 mmol), glycosyl acceptor **12** (214 mg, 0.5

mmol), and molecular sieves (4 Å, 4.0 g) were dried under high vacuum at ambient temperature for one hour. The solids were then suspended in dry dichloromethane (8 mL), and the reaction mixture was stirred for two hours under an inert atmosphere at room temperature in the dark. After cooling to −70°C, trimethylsilyl trifluoromethanesulfonate (83 μL, 0.5 mmol) was added, and stirring was continued for 3 h at that temperature. The reaction mixture was then allowed to warm-up to room temperature and stirring was continued for an additional 18 h (TLC solvent A). Now, the reaction mixture was passed through a layer of alkaline alumina by elution with chloroform. The eluate (ca. 30 mL) was extracted with cold aq sat $NaHCO_3$ (2 × 15 mL), water (2 × 15 mL), dried, and concentrated.

Methyl (methyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α-D-galactopyranosyluronate)-(1→4)-(allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate (23α). The crude disaccharide was purified by HPLC (eluent solvent B) to provide unchanged acceptor **12** (40 mg, 18%) and the disaccharides **23**α (206 mg, 59%; TLC, R_f 0.38, solvent A), colorless foam: $[\alpha]_D^{24}$ +66.5° (*c* 1.0, chloroform), ^{1}H NMR ($CDCl_3$) δ 1.99 (s, 3H, $OCOCH_3$), 3.45 (dd, 1H, $J_{3,4}$ = 2.8 Hz, H-3), 3.48, 3.53 (2s, 6H, OCH_3, OCH_3'), 3.67 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 3.79 (dd, 1H, $J_{2',3'}$ = 10.1 Hz, H-2′), 3.95 (d, 1H, H-5), 4.04 (dd, 1H, $J_{3'4'}$ = 3.1 Hz, H-3′), 4.17 (m, 1H, $OCH_2CH{=}CH_2$), 4.39 (d, 1H, $J_{1,2}$ = 7.63 Hz, H-1), 4.52 (m, 1H, $OCH_2CH{=}CH_2$), 4.46 (dd, 1H, H-4), 4.46–4.97 (d,s, 8H, 4 × $CH_2C_6H_5$), 5.03 (d, 1H, H-5′), 5.18 (d, 1H, $J_{1',2'}$ = 3.4 Hz, H-1′), 5.24, 5.36 (2m, 2H, $OCH_2CH{=}CH_2$), 5.78 (dd, 1H, $J_{4',5'}$ = 1.4 Hz, H-4′), 5.99 (m, 1H, $OCH_2CH{=}CH_2$), 7.27–7.37 (m, 20H, 4 × $CH_2C_6H_5$); ^{13}C NMR ($CDCl_3$) δ 20.67 ($OCOCH_3$), 52.12 (OCH_3), 52.29 (OCH_3'), 68.80 (C-4′), 69.65 (C-5′), 71.85, 72.45, 72.97, 70.53 (4 × $CH_2C_6H_5$), 73.44 (C-2′), 73.51 (C-5), 74.91 ($OCH_2CH{=}CH_2$), 75.74 (C-3), 76.01 (C-4), 77.21 (C-2), 79.51 (C-3′), 100.11 (C-1′), 102.79 (C-1), 117.49 ($OCH_2CH{=}CH_2$), 127.39, 127.51, 127.54, 127.67, 127.86, 127.92, 128.04, 128.11, 128.14, 128.25, 128.28, 128.37, 128.83, 128.86, 137.79, 137.91, 138.20, 138.40 (4 × $CH_2C_6H_5$, 6 signals are isochronic), 133.89 ($OCH_2CH{=}CH_2$), 168.05, 168.51 (C-6′,C-6), 169.86 ($OCOCH_3$).

Anal. Calcd for $C_{47}H_{52}O_{14}$ (840.92): C, 67.13; H,6.23. Found: C, 67.12, H, 6.24.

Here additionally, is the analytical data of disaccharide **23**β isolated in a 24% yield (α:β ratio of 1.6:1) when boron trifluoride was used as a promoter. (TLC, R_f 0.28, solvent A), colorless foam: $[\alpha]_D^{24}$ +63.7° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 2.06 (s, 3H, $OCOCH_3$), 3.50 (dd, 1H, $J_{3'4'}$ = 3.4 Hz, H-3′), 3.58 (dd, 1H, $J_{3,4}$ = 2.8 Hz, H-3), 3.63 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 3.73, 3.91 (2s, 6H, OCH_3, OCH_3'), 3.77 (dd, 1H, $J_{2',3'}$ = 9.8 Hz, H-2′), 3.90 (d, 1H, H-5′), 4.09 (d, 1H, H-5), 4.13 (m, 1H, $OCH_2CH{=}CH_2$), 4.42 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1), 4.50 (m, 1H, $OCH_2CH{=}CH_2$), 4.60 (dd, 1H, H-4), 4.14, 4.53 (2d, 2H, J = 10.7 Hz, $CH_2C_6H_5$), 4.68, 4.76 (2d, 2H, J = 12.2 Hz, $CH_2C_6H_5$), 4.74 (s, 2H, $CH_2C_6H_5$), 4.75, 5.11 (2d, 2H, J = 11.0 Hz, $CH_2C_6H_5$), 4.83 (d, 1H, $J_{1',2'}$ = 7.6 Hz, H-1′), 5.19, 5.32 (2m, 2H, $OCH_2CH{=}CH_2$), 5.65 (dd, 1H, $J_{4',5'}$ = 0.9 Hz, H-4′), 5.93 (m, 1H, $OCH_2CH{=}CH_2$), 7.19–7.46 (m, 20H, 4 × $CH_2C_6H_5$); ^{13}C NMR ($CDCl_3$) δ

20.67 ($OCOCH_3$), 52.29 (OCH_3), 52.70 (OCH_3'), 67.74 (C-4′), 70.30, 72.08, 73.04, 75.24 ($4 \times CH_2C_6H_5$), 72.09 (C-5′), 72.85 (C-4), 73.37 (C-2′), 74.01 (C-5), 75.12 ($OCH_2CH{=}CH_2$), 80.84 (C-3), 79.28 (C-2), 78.27 (C-3′), 102.37 (C-1), 102.67 (C-1′), 117.38 ($OCH_2CH{=}CH_2$), 127.23, 127.49, 127.54, 127.64, 127.81, 127.89, 127.92, 128.05, 128.19, 128.30, 137.67, 138.14, 138.50, 138.90 ($4 \times CH_2C_6H_5$, 10 signals are isochronic), 133.86 ($OCH_2CH{=}CH_2$), 166.98, 167.73 (C-6, C-6′), 169.95 ($OCOCH_3$).

Anal. Calcd for $C_{47}H_{52}O_{14}$ (840.92): C, 67.13; H, 6.23. Found: C, 67.11; H, 6.20.

Methyl (methyl 3,4-di-*O*-acetyl-2-*O*-benzyl-α/β-D-galactopyranosyluronate)-(1→4)-(allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate (24α, 24β). The crude disaccharide was purified by HPLC (eluent solvent B) to provide unchanged acceptor **12** (15 mg, 7%) and desired **24**α (266 mg, 67%; TLC, R_f 0.25, solvent A) as a colorless foam: $[\alpha]_D^{23}$ +83.7° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.93, 1.96 (2s, 6H, $OCOCH_3$), 3.409 (s, 3H, OCH_3), 3.42 (dd, 1H, $J_{3,4}$ = 3.1 Hz, H-3), 3.57 (s, 3H, OCH_3'), 3.75 (dd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 3.88 (dd, 1H, $J_{2',3'}$ = 10.7 Hz, H-2′), 3.93 (d, 1H, H-5), 4.15 (m, 1H, $CH_2CH{=}CH_2$), 4.38 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1), 4.48 (m, 1H, $CH_2CH{=}CH_2$), 4.49 (dd, 1H, $J_{4,5}$ = 0.7 Hz, H-4), 4.55, 4.74 (2d, 2H, J = 12.8 Hz, $CH_2C_6H_5$), 4.57, 4.68 (2d, 2H, J = 12.5 Hz, $CH_2C_6H_5$), 4.81, 4.97 (2d, 2H, , J = 10.7 Hz, $CH_2C_6H_5$), 5.10 (d, 1H, $J_{4',5'}$ = 1.8 Hz, H-5′), 5.20 (m, 1H, $CH_2CH{=}CH_2$), 5.29 (d, 1H, $J_{1',2'}$ = 3.7 Hz, H-1′), 5.30 (dd, 1H, $J_{3',4'}$ = 3.4 Hz, H-3′), 5.34 (m, 1H, $CH_2CH{=}CH_2$), 5.69 (dd, 1H, $J_{4',5'}$ = 1.5 Hz, H-4′), 5.96 (m, 1H, $CH_2CH{=}CH_2$), 7.21–7.41 (m, 15H, $3 \times CH_2C_6H_5$); ^{13}C NMR ($CDCl_3$) δ 20.44, 20.76 ($2 \times OCOCH_3$), 52.13 (OCH_3), 52.30 (OCH_3'), 69.13 (C-5′), 69.18 (C-3′), 69.78 (C-4′), 70.31, 72.35, 72.56 ($3 \times CH_2C_6H_5$), 71.74 (C-2′), 73.38 (C-5), 75.09 ($CH_2CH{=}CH_2$), 75.79 (C-4), 77.77 (C-2), 79.34 (C-3), 99.41 (C-1′), 102.81 (C-1), 117.35 ($CH_2CH{=}CH_2$), 127.33, 127.48, 127.64, 127.72, 127.89, 128.22, 128.28, 128.40, 128.92, 137.76, 137.97, 138.21 ($3 \times CH_2C_6H_5$), 133.91 ($CH_2CH{=}CH_2$), 168.04 (C-6′), 168.22 (C-6), 169.67, 169.7049 ($2 \times OCOCH_3$).

Anal. Calcd for $C_{42}H_{48}O_{15}$ (792.83): C, 63.63; H, 6.10. Found: C, 63.60; H, 6.11.

Disaccharide 24β. (20 mg, 5%; TLC, 0.23, solvent A), colorless foam: $[\alpha]_D^{22}$ +54.8° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 2.04, 2.11 (2s, 6H, $OCOCH_3$), 3.50 (dd, 1H, $J_{3,4}$ = 3.1 Hz, H-3), 3.70 (dd, 1H, $J_{2',3'}$ = 10.1 Hz, H-2′) 3.76 (s, 3H, OCH_3'), 3.81 (dd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 3.98 (s, 3H, OCH_3), 4.01 (d, 1H, H-5), 4.09 (d, 1H, H-5′), 4.22 (m, 1H, $CH_2CH{=}CH_2$), 4.46 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1), 4.51 (d, 1H, $J_{1',2'}$ = 7.6 Hz, H-1′), 4.56 (dd, 1H, H-4), 4.58 (m, 1H, $CH_2CH{=}CH_2$), 4.66–5.15 (6d, 6H, $3 \times CH_2C_6H_5$), 5.27, 5.40 (2m, 2H, $CH_2CH{=}CH_2$), 5.40 (dd, 1H, $J_{3',4'}$ = 3.4 Hz, H-3′), 5.63 (dd, 1H, $J_{4',5'}$ = 0.9 Hz, H-4′), 6.02 (m, 1H, $CH_2CH{=}CH_2$), 7.28–7.47 (m, 15H, $3 \times CH_2C_6H_5$); ^{13}C NMR ($CDCl_3$) δ 20.56, 20.97 ($2 \times OCOCH_3$), 52.09, 52.27 (OCH_3, OCH_3'), 67.96 (C-5′), 70.33, 72.30, 72.51 ($3 \times CH_2C_6H_5$), 71.75 (C-2′), 73.38 (C-5), 73.85 (C-3′),

74.66 (C-4′), 75.12 (CH$_2$CH═CH$_2$), 75.74 (C-4), 77.71 (C-2), 79.29 (C-3), 102.34 (C-1′), 102.76 (C-1), 117.33 (CH$_2$CH═CH$_2$), 127.33, 127.48, 127.64, 127.72, 127.89, 128.22, 128.28, 128.40, 128.92, 137.71, 137.92, 138.59 (3 × CH$_2$$C_6H_5$), 133.86 (CH$_2$$C$H═CH$_2$), 166.40 (C-6′), 167.61 (C-6), 169.64, 169.99 (2 × OCOCH$_3$).

Anal. Calcd for $C_{42}H_{48}O_{15}$ (792.83): C, 63.63; H, 6.10. Found: C, 63.75; H, 6.08.

Methyl (methyl 2,3-di-*O*-benzyl-4-*O*-methyl-α/β-D-galactopyranosyluronate)-(1→4)-(allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate (25α, 25β). The 1.3:1 α/β-mixture of **25**α,**25**β was purified by HPLC (eluent solvent B) to provide unchanged acceptor **12** (51 mg, 24%) and a not separated mixture of **25**α and **25**β (211 mg, 52%; TLC, R_f 0.26, solvent A) as a colorless syrup: ^{1}H NMR (CDCl$_3$) δ 3.45 (s, 3H, OCH$_3$), 3.53 (s, OCH$_3$′β), 3.53 (s, OCH$_3$′α), 3.55 (dd, $J_{3',4'}$ = 3.1 Hz, H-3′β), 3.58 (dd, 1H, $J_{3,4}$ = 3.4 Hz, H-3), 3.67 (dd, $J_{2',3'}$ = 9.8 Hz, H-2′β), 3.76 (dd, 1H, $J_{2,3}$ = 9.5 Hz, H-2), 3.81 (s, 3H, H$_3$CO-4), 3.81 (dd, $J_{3',4'}$ = 3.4 Hz, H-3′α), 3.93 (d, H-5′β), 3.97 (dd, H-4′β), 4.00 (dd, $J_{2',3'}$ = 9.5 Hz, H-2′α), 4.08 (dd, H-4′α), 4.09 (d, 1H, H-5), 4.17 (m, 1H, CH_2CH═CH$_2$), 4.32 (dd, 1H, H-4), 4.39 (d, $J_{1',2'}$ = 7.6 Hz, H-1′β), 4.51 (m, 1H, CH_2CH═CH$_2$), 4.54 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1), 4.54–4.95 (d, s, 4 × CH_2C$_6$H$_5$), 4.88 (d, 1H, H-5′α), 5.16 (d, $J_{1',2'}$ = 3.1 Hz, H-1′α), 5.20, 5.36 (2m, 2H, OCH$_2$CH═CH_2), 5.96 (m, 1H, CH$_2$CH═CH$_2$), 7.26–7.38 (m, 4 CH$_2$C$_6$$H_5$); ^{13}C NMR (CDCl$_3$) δ 51.95 (OCH$_3$′β), 52.22 (OCH$_3$′α), 52.71 (OCH$_3$), 61.12 (H$_3$CO-4), 67.75, 67.81, 70.57, 71.24, 72.36, 72.51, 72.57, 73.12, 73.38, 73.74, 73.85, 76.83, 77.20, 77.59, 77.83, 78.40, 79.44, 79.47, 79.74 (C-1, C-2, C-3, C-4, 2 × CH$_2$C$_6$H$_5$, CH$_2$CH═CH$_2$, C-2′α/β, C-3′α/β, C-4′α/β, C-5′α/β, 2 × CH$_2$C$_6$H$_5$′α/β), 99.46 (C-1′α), 102.40 (C-1′β), 102.79 (C-1), 117.55 (CH$_2$CH═CH$_2$), 127.28, 127.36, 127.45, 127.49, 127.60, 127.75, 127.83, 127.89, 128.08, 128.14, 128.20, 128.25, 128.31, 128.34, 128.52, 128.84 137.35, 138.03, 137.91, 138.30, 138.41, 138.53, (2 × CH$_2$$C_6H_5$, 2 × CH$_2$$C_6H_5$′α/β), 133.91 (CH$_2$$C$H═CH$_2$), 168.02 (C-6′β), 168.13 (C-6), 169.66 (C-6′α).

Anal. Calcd for $C_{46}H_{52}O_{13}$ (812.91): C, 67.97; H,6.45. Found: C, 67.90; H, 6.52.

Methyl (methyl 2,3-di-*O*-benzyl-α-D-galactopyranosyluronate)-(1→4)-(allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate (26α). A suspension of **23**α (210 mg, 0.25 mmol) in methanolic hydrochloric acid (0.28 M, 15 mL, prepared by adding 0.3 mL acetyl chloride to 15 mL dry methanol) was stirred for 72 h under an inert atmosphere at ambient temperature (TLC, solvent A). The reaction mixture was then neutralized by filtration through a layer of alkaline alumina. Evaporation of the eluate provided analytical pure **26**α (198 mg, 99%; TLC, R_f 0.18, solvent A) as a colorless foam: $[\alpha]_D^{24}$ +56.6° (*c* 1.0, chloroform); ^{1}H NMR (CDCl$_3$) δ 2.35 (bs, 1H, 4′-OH), 3.37 (dd, 1H, $J_{3,4}$ = 2.8 Hz, H-3), 3.46, 3.47 (2s, 6H, OCH$_3$, OCH$_3$′), 3.60 (dd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 3.75 (dd, 1H, $J_{3'4'}$ = 3.4

Hz, H-3′), 3.87 (d, 1H, H-5), 3.91 (dd, 1H, $J_{2',3'}$ = 10.1 Hz, H-2′), 4.09 (m, 1H, $OCH_2CH{=}CH_2$), 4.28 (dd, 1H, H-4′), 4.32 (d, 1H, $J_{1,2}$ = 7.63 Hz, H-1), 4.39 (dd, 1H, H-4), 4.45 (m, 1H, $OCH_2CH{=}CH_2$), 4.48–4.88 (d,s, 8H, 4 × $CH_2C_6H_5$), 4.88 (d, 1H, H-5′), 5.11 (d, 1H, $J_{1',2'}$ = 3.4 Hz, H-1′), 5.15, 5.29 (2m, 2H, $OCH_2CH{=}CH_2$), 5.91 (m, 1H, $OCH_2CH{=}CH_2$), 7.16–7.31 (m, 20H, 4 × $CH_2C_6H_5$); ^{13}C NMR ($CDCl_3$) δ 52.08, 52.25 (OCH_3, OCH_3′), 68.35 (C-4′), 70.47 (C-5′), 70.56, 72.32, 72.34, 72.93 (4 × $CH_2C_6H_5$), 73.50(C-5), 73.91 (C-2′), 74.95 ($OCH_2CH{=}CH_2$), 75.66 (C-3′), 76.96 (C-4), 77.64 (C-2), 79.73 (C-2), 99.60 (C-1′), 102.84 (C-1), 117.48 ($OCH_2CH{=}CH_2$), 127.35, 127.47, 127.61, 127.67, 127.83, 128.00, 128.15, 128.22, 128.28, 128.31, 128.45, 128.78, 128.87, 137.81, 137.87, 138.28, 138.35 (4 × $CH_2C_6H_5$), 133.93 ($OCH_2CH{=}CH_2$), 168.07, 169.41 (C-6′, C-6).

Anal. Calcd for $C_{45}H_{50}O_{13}$ (798.88): C, 67.66; H, 6.31. Found: C, 67.70; H, 6.29.

Methyl (4-*O*-benzoyl-3-*O*-benzyl-2-*O*-acetyl-α-L-rhamnopyranosyl)-(1→4)-2,3-di-*O*-benzyl-α-D-galactopyranuronate (27). The deallylation of **13** (406 mg, 0.5 mmol) was carried out exactly as described for the preparation of **17**–**19**. After processing (TLC, R_f 0.18, solvent A), the crude product was purified by HPLC (eluent solvent E) to yield **27** (289 mg, 75%) as a colorless foam: $[\alpha]_D^{24}$ +42.9° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 3H, $J_{5',6'}$ = 6.1 Hz, H-6′), 2.10 (s, 3H, $OCOCH_3$), 3.75 (s, 3H, OCH_3), 3.81 (m, 1H, H-5′), 3.86 (dd, 1H, $J_{3',4'}$ = 10.1 Hz, H-3′), 3.89 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 4.00 (dd, 1H, $J_{3,4}$ = 3.7 Hz, H-3), 4.28, 4.55 (2d, 2H, J = 12.2 Hz, $CH_2C_6H_5$′), 4.48 (dd, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 4.67 (d, 1H, H-5), 4.73, 4.80 (2d, 2H, J = 12.5 Hz, $CH_2C_6H_5$), 4.73 (s, 2H, $CH_2C_6H_5$), 5.16 (d, 1H, $J_{1',2'}$ = 1.8 Hz, H-1′), 5.23 (t, 1H, $J_{4',5'}$ = 10.1 Hz, H-4′), 5.36 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 5.58 (dd, 1H, $J_{2',3'}$ = 3.1 Hz, H-2′), 7.04–8.00 (5m, 20H, 3 × $CH_2C_6H_5$, $OCOC_6H_5$); ^{13}C NMR ($CDCl_3$) δ 17.56 (C-6′), 21.06 ($OCOCH_3$), 52.47 (OCH_3), 67.24 (C-5′), 68.18 (C-2′), 70.19 (C-5), 71.12 ($CH_2C_6H_5$), 72.62 (C-4′), 73.03, 73.59 (2 × $CH_2C_6H_5$), 74.27 (C-3′), 74.62 (C-2), 76.03 (C-4), 77.09 (C-3), 92.09 (C-1), 99.73 (C-1′), 127.42, 127.64, 127.69, 127.81, 128.11, 128.34, 128.48, 128.54, 128.60, 129.77, 133.10, 137.64, 137.65, 137.68 (3 × $CH_2C_6H_5$, $OCOC_6H_5$), 165.69 ($OCOC_6H_5$), 168.78 (C-6), 169.95 ($OCOCH_3$).

Anal. Calcd for $C_{43}H_{46}O_{13}$ (770.83): C, 67.70; H, 6.02. Found: C, 67.53; H, 6.13.

Methyl (4-*O*-benzoyl-3-*O*-benzyl-2-*O*-acetyl-α-L-rhamnopyranosyl)-(1→4)-2,3-di-*O*-benzyl-α-D-galactopyranosyluronate trichloroacetimidate (28). The trichloroacetimidate group was introduced in **27** (385 mg, 0.5 mmol) as described for **20**–**22** (TLC, R_f 0.51, solvent A). Finally, the raw product was purified by HPLC (eluent solvent C) to afford **28** (316 mg, 69%) as a colorless foam: $[\alpha]_D^{24}$ +51.8° (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.21 (s, 3H, $J_{5',6'}$ = 6.4 Hz, H-6′), 2.12 (s, 3H, $OCOCH_3$), 3.75 (s, 3H, OCH_3), 3.82 (m, 1H, H-5′), 3.84 (dd,

1H, $J_{3',4'}$ = 9.8 Hz, H-3′), 4.08 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 4.09 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2), 4.27, 4.55 (2d, 2H, J = 12.2 Hz, CH_2C$_6$H$_5$), 4.51 (dd, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 4.61 (d, 1H, Hz, H-5), 4.78 (s, 2H, CH_2C$_6$H$_5$), 4.80, 4.87 (2d, 2H, J = 11.6 Hz, CH_2C$_6$H$_5$), 5.20 (d, 1H, $J_{1',2'}$ = 1.8 Hz, H-1′), 5.24 (t, 1H, $J_{4',5'}$ = 9.8 Hz, H-4′), 5.60 (dd, 1H, $J_{2',3'}$ = 3.1 Hz, H-2′), 6.66 (d, 1H, $J_{1,2}$ = 2.13 Hz, H-1), 7.03–7.95 (5m, 20H, 3x CH$_2$C$_6$*H*$_5$, OCOC$_6$*H*$_5$), 8.66 (s, 1 H, NH); ^{13}C NMR (CDCl$_3$) δ 17.58 (C-6′), 21.05 (OCO*C*H$_3$), 52.54 (OCH$_3$), 67.34 (C-5′), 68.10 (C-2′), 71.01 (*C*H$_2$C$_6$H$_5$), 72.38 (C-5), 72.54 (C-4′), 72.86, 73.24 (2 × *C*H$_2$C$_6$H$_5$), 74.09 (C-2), 74.30 (C-3′), 76.12 (C-4), 77.02 (C-3), 90.98 [C(═NH)*C*Cl$_3$], 94.30 (C-1), 99.93 (C-1′), 127.48, 127.58, 127.66, 127.75, 127.81, 127.93, 127.99, 128.02, 128.11, 128.19, 128.33, 128.49, 128.66, 129.48, 129.55, 129.77, 129.89, 133.10, 137.56, 137.64, 137.77 (3 × CH$_2$*C*$_6$H$_5$, OCO*C*$_6$H$_5$), 160.56 [*C*(═NH)CCl$_3$], 165.64 (O*C*OC$_6$H$_5$), 167.89 (C-6), 169.87 (O*C*OCH$_3$).

Anal. Calcd for C$_{45}$H$_{46}$O$_{13}$NCl$_3$ (915.22): C, 59.00; H, 5.06; N, 1.53; Cl, 1.16. Found: C, 58.92; H, 5.01; N, 1.59; Cl, 1.14.

Methyl (4-*O*-benzoyl-3-*O*-benzyl-2-*O*-acetyl-α-L-rhamnopyranosyl)-(1→4)-(methyl 2,3-di-*O*-benzyl-α-D-galactopyranosyluronate)-(1→4)-(allyl 2,3-di-*O*-benzyl-β-D-galactopyranosid)uronate (29). The glycosylation of **12** (214 mg, 0.5 mmol) with the donor **28** (458 mg, 0.5 mmol) was processed as described for the synthesis of **23** with **20** (TLC, R_f 0.28, solvent A). The crude trisaccharide was purified by HPLC (eluent solvent B) to provide unchanged acceptor **12** (18 mg, 17%) and desired **29** (407 mg, 70%) as a colorless foam: $[\alpha]_D^{23}$ +29.6° (*c* 1.0, chloroform); ^{1}H NMR (CDCl$_3$) δ 1.17 (d, 3H, $J_{5'',6''}$ = 6.1 Hz, H-6″), 2.04 (s, 3H, OCOCH$_3$), 3.45 (dd, 1H, $J_{3,4}$ = 3.1 Hz, H-3), 3.47 (s, 3H, OCH$_3$), 3.67 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 3.69 (s, 3H, OCH$_3$′), 3.75 (m, 1H, H-5″), 3.79 (dd, 1H, $J_{3'',4''}$ = 10.1 Hz, H-3″), 3.91 (dd, 1H, $J_{2',3'}$ = 9.8 Hz, H-2′), 3.98 (d, 1H, H-5), 4.07 (dd, 1H, $J_{3',4'}$ = 3.4 Hz, H-3′), 4.19, 4.36 (2m, 2H, CH_2CH═CH$_2$), 4.41 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1), 4.49 (dd, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 4.56 (dd, 1H, $J_{4',5'}$ = 1.2 Hz, H-4′), 4.46–4.99 (d and s, 10H, 5 × CH_2C$_6$H$_5$), 4.84 (d, 1H, H-5′), 5.10 (d, 1H, $J_{1'',2''}$ = 1.5 Hz, H-1″), 5.16 (t, 1H, $J_{4'',5''}$ = 10.1 Hz, H-4″), 5.23 (m, 1H, CH$_2$CH═CH_2), 5.26 (d, 1H, $J_{1',2'}$ = 3.1 Hz, H-1′), 5.37 (m, 1H, OCH$_2$CH═CH_2), 5.49 (dd, 1H, $J_{2'',3''}$ = 3.4 Hz, H-2″), 6.00 (m, 1H, CH$_2$C*H*═CH$_2$), 6.99–7.95 (5m, 30H, 5 × CH$_2$C$_6$*H*$_5$, OCOC$_6$*H*$_5$); ^{13}CNMR (CDCl$_3$) δ 17.61 (C-6″), 21.02 (OCO*C*H$_3$), 52.03 (OCH$_3$), 52.41 (OCH$_3$′), 66.99 (C-5″), 67.49 (C-5), 68.10 (C-2″), 70.65 (C-5′), 70.81, 71.27, 72.21, 72.68, 73.12 (5 × *C*H$_2$C$_6$H$_5$), 72.42 (C-4″), 72.82 (C-2′), 73.53 (C-3′), 74.77 (*C*H$_2$CH═CH$_2$), 74.88 (C-3″), 75.73 (C-4), 76.11 (C-4′), 77.65 (C-2), 79.40 (C-3), 99.59 (C-1′), 100.03 (C-1″), 102.81 (C-1), 117.59 (CH$_2$CH═*C*H$_2$), 127.14, 127.26, 127.48, 127.52, 127.58, 127.64, 127.75, 127.81, 127.86, 127.92, 128.02, 128.08, 128.11, 128.17, 128.23, 128.30, 128.33, 128.42, 128.46, 128.61, 128.81, 129.69, 129.77, 130.62, 133.01, 137.45, 137.73, 137.79, 138.09, 138.20 (5 × CH$_2$*C*$_6$H$_5$, OCO*C*$_6$H$_5$), 133.83 (CH$_2$*C*H═CH$_2$), 165.64 (O*C*OC$_6$H$_5$), 168.11 (C-6), 169.07 (C-6′), 169.67 (O*C*OCH$_3$).

Anal. Calcd for C$_{67}$H$_{72}$O$_{18}$ (1165.30): C, 69.06; H, 6.24. Found: C, 68.97; H, 6.28.

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