Tetrahedron 69 (2013) 10337–10350

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Concise synthesis of di- and trisaccharides related to the O-antigens from *Shigella flexneri* serotypes 6 and 6a, based on late stage mono-*O*-acetylation and/or site-selective oxidation

Pierre Chassagne [a,b,c,†], Laurent Raibaut [a,b,‡], Catherine Guerreiro [a,b], Laurence A. Mulard [a,b,*]

[a] *Institut Pasteur, Unité de Chimie des Biomolécules, 28 rue du Dr Roux, 75015 Paris, France*
[b] *CNRS UMR3523 Institut Pasteur, 28 rue du Dr Roux, 75015 Paris, France*
[c] *Université Paris Descartes Sorbonne Paris Cité, Institut Pasteur, 28 rue du Dr Roux, 75015 Paris, France*

ARTICLE INFO

Article history:
Received 10 June 2013
Received in revised form 1 October 2013
Accepted 4 October 2013
Available online 11 October 2013

Keywords:
Carbohydrates
Glycosylation
Gram negative bacteria
Lipopolysaccharide
TEMPO

ABSTRACT

Shigella flexneri serotypes 6 and 6a are closely related bacteria causing shigellosis in humans. Their O-antigens are {→4)-β-D-Gal*p*A-(1→3)-β-D-Gal*p*NAc-(1→2)-[3Ac/4Ac]-α-L-Rha*p*-(1→2)-α-L-Rha*p*-(1→}$_n$ acidic polysaccharides ({**AB$_{Ac}$CD**}$_n$), which only differ in the degree of *O*-acetylation. A concise synthesis of two disaccharides (**BC**, **B$_{Ac}$C**) and four trisaccharides, representing portions and/or analogs of the O-antigens, is described. A protected intermediate compatible with late stage 3$_C$-*O*-acetylation, and/or galactosyl (**A°**) to galacturonic acid (**A**) conversion, was designed and assembled from trichloroacetimidate and thioglycoside donors tuned for high yielding glycosylation and excellent stereocontrol. The galacturonic moiety was efficiently introduced from galactose using a TEMPO/NaOCl/$NaClO_2$-based oxidation protocol optimized for full compatibility with sensitive moieties, such as allyl ethers and acetates. Final Pd/C-mediated deprotection provided the targets, including the propyl glycoside **AB$_{Ac}$C**, its non *O*-acetylated counterpart **ABC**, and the non acidic analogs **A°B$_{Ac}$C** and **A°BC**. The **BC** and **ABC** oligosaccharides are also portions of the O-antigen from *Escherichia coli* O147, which causes diarrhea in pigs.

1. Introduction

Shigella flexneri is a human Gram negative entero-invasive bacterium that is a common cause of diarrhea worldwide.[1–3] It remains a major burden in developing countries, especially in the pediatric population.[2,4,5] All known serotypes—varying in geographic and temporal distributions—can be isolated from patients,[4] and epidemiological surveys indicate an increasing occurrence of *S. flexneri* serotype 6 (SF6) in several settings.[2,6] This serotype was identified as one to include in a multivalent *Shigella* vaccine.[4,7]

As for other *Shigellae*, the polysaccharide part—or O-antigen (O-Ag)—of the SF6 lipopolysaccharide (LPS) is thought to be a primary target of the host's humoral immune response generated following natural infection. Hence, SF6 detoxified LPS-conjugate vaccine prototypes were recently documented.[8] As part of our current effort toward a potent *Shigella* glycovaccine, we pursue a strategy that avoids the handling of LPS. Our approach is based on the molecular design of synthetic oligosaccharide haptens to serve as functional mimics of the natural O-Ag of interest.[9] Access to well-defined synthetic frame-shifted fragments of the O-Ag is a pre-required step to warrant a successful development.[10,11]

Recently, we have confirmed the molecular composition of the SF6 O-Ag (Fig. 1),[14] the basic RU of which is a linear acidic tetrasaccharide made of one D-galacturonic acid (**A**), one *N*-acetyl-D-galactosamine (**B**) and two L-rhamnose residues (**C**, **D**), with rhamnose **C** being unevenly monoacetylated at its 3- or 4-OH. Moreover, in a recent survey of *S. flexneri* O-Ag structures, Perepelov et al. distinguish between type SF6 (minor) and type SF6a (major), which differ only in their degree of 3$_C$/4$_C$-*O*-acetylation.[12] As part of our general concern for *S. flexneri* O-Ags, we initiated a careful investigation of the role of the 3$_C$/4$_C$-*O*-acetylation pattern on O-Ag properties in the case of SF6 and SF6a. Toward this aim, we first reported the synthesis of a set of SF6-specific di- to tetrasaccharides having a D-galacturonic acid (**A**) at the reducing end.[14] Herein, we describe the linear synthesis of 6 frame-shifted di- to trisaccharides having rhamnose **$_{3Ac}$C** at their reducing end. The non *O*-acetylated analogs encompassing rhamnose **C** were isolated as well, together with—whenever possible—those having rhamnose

* Corresponding author. Tel.: +33 140613820; fax: +33 145688404; e-mail address: laurence.mulard@pasteur.fr (L.A. Mulard).
† Present address: Glycom A/S, DTU, Bld 201, 2800 Kgs Lyngby, Denmark.
‡ Present address: UMR CNRS 8161, Université Lille Nord de France, Institut Pasteur de Lille, 59021 Lille, France.

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.10.011

$_{4Ac}$C. Note that the 4$_C$-*O*-acetylated regioisomers impersonate the minor *O*-acetylation pattern of the SF6 and SF6a O-Ags.[12,14] Moreover, the non *O*-acetylated oligosaccharides are representative of portions of the natural SF6 and SF6a O-Ags on the one hand[12,14] and of fragments of the closely related O-Ag from *Escherichia coli* O147 on the other hand.[13] In view of appreciating the influence of the uronate function on the O-Ag antigenic and/or immunogenic properties, analogs comprising a galactose residue (**A**°) instead of the natural galacturonic acid (**A**) were also prepared by advantageously exploiting selected intermediates.

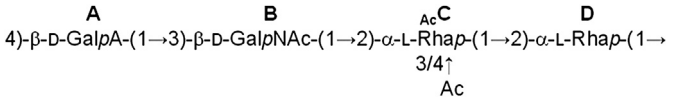


Fig. 1. Repeating unit (RU, **AB$_{Ac}$CD**) of the O-Ags from SF6 and SF6a showing the non stoichiometric acetylation at O-3$_C$/O-4$_C$.[12] The corresponding non *O*-acetylated **ABCD** tetrasaccharide defines the O-Ag from *Escherichia coli* O147.[13]

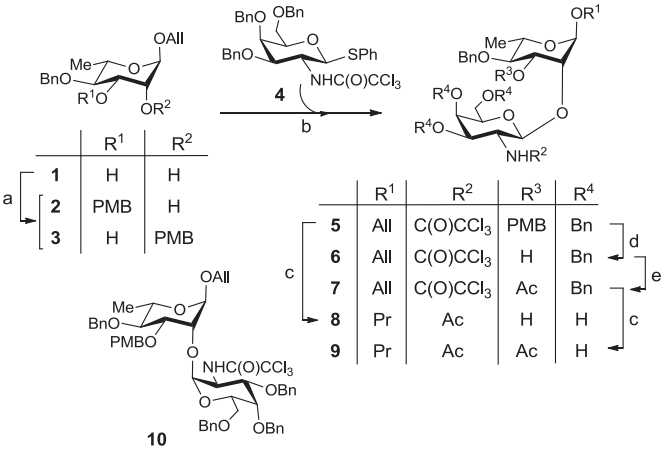
2. Results and discussion

All target oligosaccharides were prepared as α-propyl glycosides in order to block their reducing end in a form mimicking the natural linkages found in the O-Ag. The choice of propyl glycosides is in line with our previous work on this series,[14] as well as on other *S. flexneri* serotypes.[15] It is meant at facilitating the synthesis, owing to the easy access to allyl glycoside building blocks, in the absence of any anticipated major influence on antigenicity.

The strategy was designed in order to warrant the isolation of six oligosaccharides, namely the non *O*-acetylated targets **BC**-Pr (**8**), **A**°**BC**-Pr (**29**), and **ABC**-Pr (**32**) as well as their *O*-acetylated counterparts **B$_{3Ac}$C**-Pr (**9**), **A**°**B$_{3Ac}$C**-Pr (**27**), and **AB$_{3Ac}$C**-Pr (**30**). The 3$_C$-*O*-acetyl moiety (Ac) was introduced at an intermediate stage of the synthesis, to serve either as a required substituent or as a protecting group. The corresponding hydroxyl group was initially masked by use of a *para*-methoxybenzyl (PMB) ether. Thus, stepwise chain extension starting from a 3-*O*-PMB-rhamnoside acceptor serving as a common precursor to residue **C** or **$_{3Ac}$C**, enabled a careful investigation and optimization of each glycosylation step. Among the numerous *N*-protecting groups ensuring anchimeric assistance in the formation of 1,2-*trans* glycosidic linkages involving 2-acetamido-glycosyl donors,[16] such as that required in the [**B**+**C**] glycosylation, we favored the trichloroacetamide moiety owing to its powerful β-directing effect and possible conversion to an acetamide in the presence of an acetate.[17]

2.1. Synthesis of disaccharides BC-Pr (8) and B$_{3Ac}$C-Pr (9)

Tin-mediated introduction of a PMB moiety at O-3 of diol **1**[18] was achieved in a high 81% yield on a multigram scale providing the known rhamnoside acceptor **2**[19] together with the yet unreported regioisomer **3** (8%). Several 2-deoxy-2-*N*-trichloroacetyl D-galactosyl donors acting as chain terminators could be envisioned as precursors to residue **B**. We reasoned that, to prevent extensive side reactions at the 3$_C$-acetate site, the trichloroacetamide to acetamide conversion would be best performed under Pd/C hydrogen-mediated hydrodechlorination.[17] Therefore, a 3,4,6-tri-*O*-benzyl donor was selected as precursor to residue **B**. When a DCM solution of the known thiophenyl β-D-glycoside[14] **4** and rhamnoside **2** was treated with the NIS/TMSOTf activator system at 0 °C, the β-condensation product **5** (NMR data for C-1$_B$: $^1J_{CH}$ 163.5 Hz, and H-1$_B$: $^1J_{1,2}$ 8.4 Hz) was isolated as the major product (69%). However, the product of α-glycosylation **10**, identified by mass spectrometry and NMR analysis (NMR data for C-1$_B$: $^1J_{CH}$ 174.5 Hz, and H-1$_B$: $^1J_{1,2}$ 3.5 Hz), was isolated in a significant 13% yield. To our satisfaction, lowering the reaction temperature improved the α/β selectivity. Under the best conditions (−65 to −40 °C, 1.2 equiv of donor in DCM), only traces of the unwanted α-linked condensation product were formed. The isolated yield of the required β-(1→2)-linked disaccharide reached 78%. Treatment of the fully protected disaccharide **5** with Pd/C under a hydrogen atmosphere enabled the concomitant benzyl protecting group removal, allyl reduction, and hydrodechlorination of the 2$_B$-trichloroacetamide. The target **BC** propyl glycoside **8** was obtained in 77% yield following RP-HPLC purification (Scheme 1). Besides, CAN-mediated oxidative cleavage of the PMB ether in disaccharide **5** (64%) and subsequent acetylation of the unmasked hydroxyl group in alcohol **6** furnished the 3$_C$-*O*-acetyl analog **7** (97%). Likewise, an ethanolic solution of the latter was treated with Pd/C under a hydrogen atmosphere to give the **B$_{3Ac}$C**-Pr disaccharide **9** in 67% following RP-HPLC purification. The regioisomer resulting from the possible acetyl migration onto the vicinal hydroxyl group was not identified.

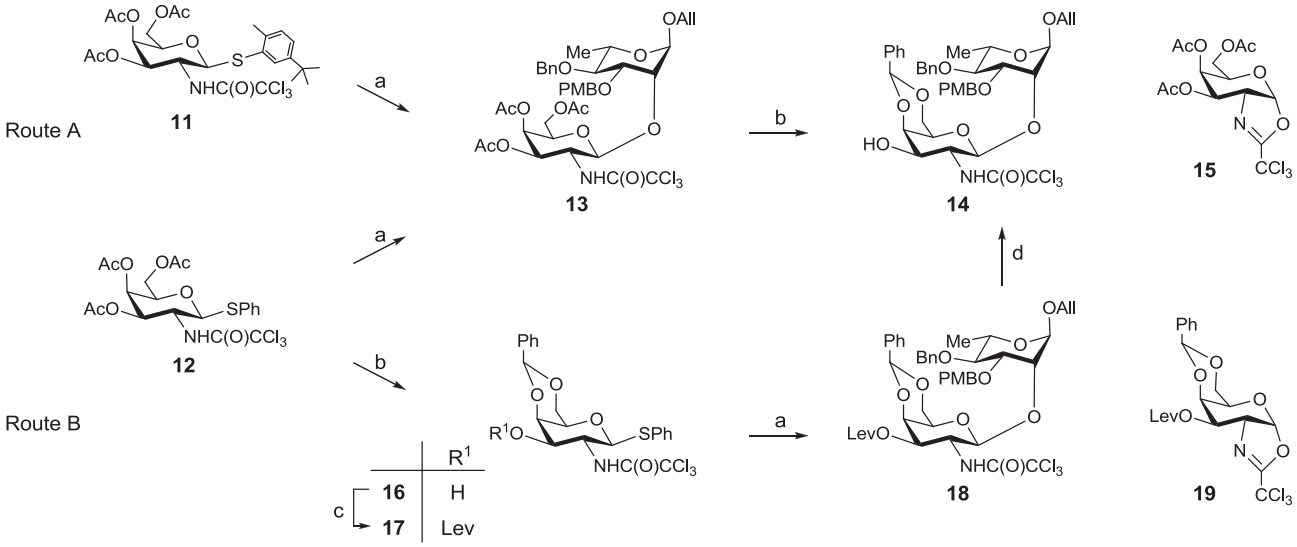


Scheme 1. Synthesis of the **BC**-Pr (**8**) and **B$_{3Ac}$C**-Pr (**9**) disaccharides. Reagents and conditions: (a) (i) Bu_2SnO, toluene, reflux, 5 h; (ii) PMBCl, TBAI, CsF, reflux, 5 h (81% for **2**, 8% for **3**); (b) NIS/TMSOTf, DCM, −65 to −40 °C, 1 h (78%); (c) H_2, Pd/C 10%, EtOH, rt, 48 h (77% for **8**, 67% for **9**); (d) CAN, MeCN/H_2O, rt, 1 h (64%); (e) Ac_2O, pyridine, rt, 24 h (97%).

2.2. Synthesis of trisaccharides A°B$_{3Ac}$C-Pr (27), A°BC-Pr (29), AB$_{3Ac}$C-Pr (30), and ABC-Pr (32)

In contrast to the above synthesis, chain elongation at the 3$_B$-OH is required to reach any of the trisaccharide targets. Thus, starting from the same rhamnoside acceptor **2**, two routes to the disaccharide acceptor **14** were investigated (Scheme 2). The simplest one (Route A) involved the readily accessible peracetylated thioglycoside **12**,[14] and functionalization post glycosylation. Several attractive odorless thioglycoside donors have been proposed in oligosaccharide synthesis.[20–22] Along this line, route A was also investigated using thioglycoside **11**, a closely related analog of donor **12**, which was easily obtained from commercially available 2-methyl-5-*tert*-butylthiophenol.[22] In the second route (Route B), the galactosamine residue was introduced using a novel orthogonally protected donor **17**.

Donors **12** and **11** were obtained in three steps from D-galactosamine hydrochloride in 64% and 56% yield, respectively. The NIS/TMSOTf-promoted condensation of allyl glycoside **2** and thioglycoside **12** or **11**, run in DCM at 0 °C, provided the desired β-(1→2)-linked disaccharide **13** (NMR data for C-1$_B$: $^1J_{CH}$ 161.5 Hz, and H-1$_B$: $^1J_{1,2}$ 8.5 Hz) in a disappointing yield (Table 1, entries 1 & 2). Identification of the known oxazoline[23] **15** (NMR data for H-1: δ 6.24 ppm, $^1J_{1,2}$ 7.0 Hz) in admixture with unreacted **2** encouraged additional investigation toward improved reaction conditions. Changing the promoter system from NIS/TMSOTf to NIS/TfOH had no influence (Table 1, entries 1 & 3). In contrast, increasing the



Scheme 2. Synthesis of disaccharides **14** and **17** from rhamnoside **2**. Reagents and conditions: (a) **2**, DCM, see Table 1; (b) (i) NaOMe, MeOH, rt; (ii) $PhCH(OMe)_2$, CSA, MeCN, rt (84% for **14**, 93% for **16**); (c) LevOH, DCC, DMAP, DCM, rt, 1 h (90%); (d) $H_2NNH_2 \cdot H_2O$, AcOH/pyridine, 0 °C to rt, 1 h (86%).

Table 1
Conditions for the synthesis of disaccharides **13** and **18** from acceptor **2**

Entry	Donor (equiv)	Promoter	Temperature	Time	Product/ Yield %
1	**12** (1.2)	NIS (1.5)/TMSOTf (0.1)	0 °C to rt	1 h	**13**/56
2	**11** (1.2)	NIS (1.5)/TMSOTf (0.1)	0 °C to rt	1 h	**13**/54
3	**12** (1.2)	NIS (1.5)/TfOH (0.1)	0 °C to rt	1 h	**13**/54
4	**12** (1.2)	NIS (1.5)/TfOH (0.1)	0 °C to rt	2 h	**13**/63
5	**11** (1.2)	NIS (1.5)/TfOH (0.1)	0 °C to rt	1.5 h	**13**/62
6	**12** (1.5)	NIS (1.5)/TfOH (0.1)	−60 °C to rt	3 h	**13**/73
7	**17** (1.1)	NIS (1.5)/TMSOTf (0.1)	0 °C to rt	45 min	**18**/64
8	**17** (1.2)	NIS (1.5)/TfOH (0.1)	0 °C to rt	1.5 h	**18**/62
9	**17** (1.2)	NIS (1.5)/TMSOTf (0.1)	−65 °C to −40 °C	20 min	**18**/69
10	**17** (1.5)	NIS (1.5)/TfOH (0.1)	−65 °C to −40 °C	1.5 h	**18**/82
11[a]	**17** (1.2)	BSP (1.3)/TTBP (2.0)/ Tf_2O (1.2)	−65 °C to −40 °C	50 min	**18**/47
12[a]	**17** (1.2)	BSP (1.5)/TTBP (1.8)/ Tf_2O (1.5)	−60 °C to rt	2 h	**18**/38

[a] Pre-activation system, inverse procedure.

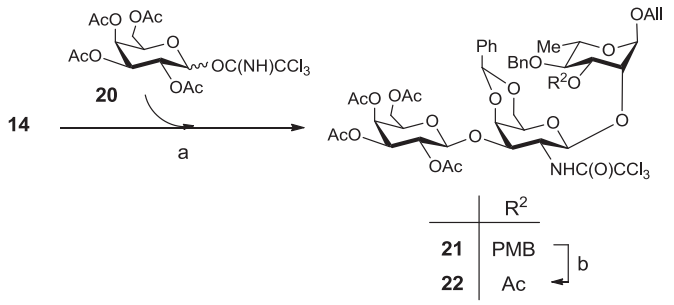
reaction time resulted in a slightly higher yield (Table 1, entries 1 & 4, 2 & 5). Under the conditions used, the choice of thioglycoside donor **11** versus **12** had no noticeable impact on the outcome of the glycosylation reaction. Finally, lowering the temperature at which the promoter was added favored glycosylation over oxazoline formation. Under the best identified conditions (Table 1, entry 6), disaccharide **13** was isolated in an acceptable 73% yield (Scheme 2). To our satisfaction, the corresponding α-(1→2)-linked condensation product was not detected. Zemplén deacetylation of intermediate **13** gave the corresponding triol, which was readily converted into acceptor **14** by regioselective 4,6-*O*-benzylidenation (84% over two steps). Following this route, compound **14** was prepared in 61% yield over three steps starting from rhamnoside **2**.

In route B, phenyl thioglycoside **17** served as a pre-functionalized galactosaminyl donor, which is easily accessible from triacetate **12**. Zemplén deacetylation of the latter followed by acetylation gave benzylidene acetal[24] **16** (93% over two steps). Next, reaction of the latter with levulinic acid and DCC in the presence of DMAP gave the fully protected **17** (90%). Condensation of donor **17** and acceptor **2** under conditions applied to donors **11** or **12** led to similar observations (Table 1). The glycosylation product had the desired 1,2-trans stereochemistry (NMR data for C-1_B: $^1J_{CH}$ 162.4 Hz, and H-1_B: $^1J_{1,2}$ 8.4 Hz). Despite being present in diminished amounts owing to extended reaction time, oxazoline **19** was identified repeatedly as a side-product during protocol optimization. Alike in the synthesis of disaccharide **13**, the 1,2-*cis* linked isomer was not observed. This outcome diverges from previous reports involving donors closely related to thioglycoside **17**.[24] It substantiates the powerful β-directing effect of the trichloroacetamido moiety in 4,6-*O*-benzylidene protected galactosamine donors, and confirms the hypothesis that despite its rigidity, the 1,3-dioxane ring in *galacto*-derivatives does not interfere with a β-coupling transition state in the absence of any donor/acceptor mismatched pairing.[24] Furthermore, excess of donor **17**, longer reaction time, and lower reaction temperature resulted in a higher yield of disaccharide **18** (Table 1, entries 7–10), whereas changing the promoter system from NIS/TfOH to BSP/TTBP/Tf_2O[25] impaired the glycosylation outcome (Table 1, entries 11 & 12). Under the best identified conditions (−65 to 40 °C, 1.5 equiv of donor **17** in DCM), the fully protected **BC** disaccharide **18** was isolated in 82% yield (Scheme 2 and Table 1, entry 10). Conventional hydrazinolysis of the 3_B-levulinoyl ester gave alcohol **14** (86% from **18**). This second route provided acceptor **14**, serving as precursor to trisaccharides **27**, **29**, **30**, and **32**, in two steps and 71% yield from allyl rhamnoside **2**. When referring to acceptor consumption, comparison of the two routes to the **BC** intermediate **14** supports our preference for the pre-functionalized donor **17**. However, since route B involves two extra functionalization steps, it may not necessarily be favored when engaging easily accessible acceptors, such as rhamnoside **2**. Interestingly, the conditions and outcome of the [**17**+**2**] condensation resemble that of the [**12**+**2**] coupling, which suggests that the protecting pattern of donor **B** does not interfere.

The introduction of the galacturonic acid residue could be envisioned according to either the 'post glycosylation oxidation' or the 'pre glycosylation oxidation' strategies.[26] The latter route remains poorly exemplified for the formation of β-D-galacturonate linkages.[27] In contrast, several reports attest of the efficiency of the former, which advantageously allows the synthesis of both the uronic targets and their non oxidized analogs. Interest in this strategy has increased following the introduction of the 2,2,6,6-tetramethyl-1-piperidinyloxy reagent (TEMPO). In combination with an appropriate co-oxydant, TEMPO was successfully used for the careful oxidation of either rather heavily protected oligosaccharides[28] or lightly protected ones.[29] In view of its selectivity for primary hydroxyl groups, TEMPO was herein selected as an attractive agent to oxidize the 6-OH of a β-linked terminal D-galactopyranosyl residue within a partially protected **A**◦**BC** trisaccharide. Accordingly, the known

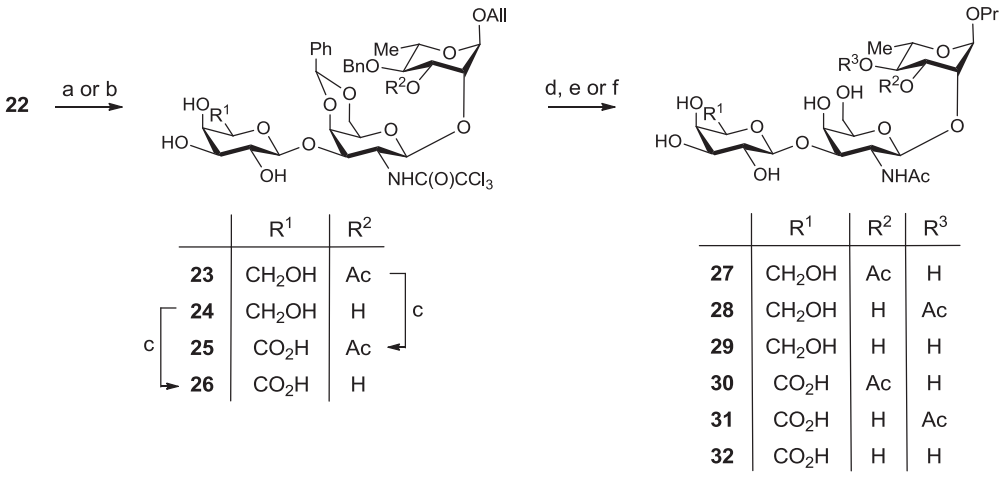
peracetylated trichloroacetimidate donor[30] **20**, was thought to suit the requirements for both protecting group orthogonality and synthetic efficacy. Indeed, the 'anomalous' difference in stability of vicinal versus isolated *O*-acetyl protecting groups under Zemplén conditions[31,32] was occasionally found attractive,[33,34] and even valuable for the preparation of site-specifically *O*-acetylated oligosaccharides.[17,35] In designing a precursor to residue **A**, we rationalized that the strategy primarily developed for the synthesis of *S. flexneri* 3a oligosaccharides[17,35] could be adapted to a suitable **A**°**BC** intermediate without affecting a 3_C-acetate.

Conventional reaction of trichloroacetimidate **20** and acceptor **14** in the presence of catalytic TMSOTf gave the fully protected **A**°**BC** (**21**, 72%). CAN-mediated oxidative cleavage of the PMB ether and consecutive *O*-acetylation readily furnished pentaacetate **22** (82% over two steps). Upon scale-up, the [**20**+**14**] glycosylation, PMB removal, and *O*-acetylation steps provided pentaacetate **22** in a good 74% overall yield (Scheme 3). Chemoselective deacetylation of trisaccharide **22** was attempted using either potassium carbonate or methanolic sodium methoxide. The latter was the most selective. Performing the transesterification at 0 °C in the presence of 0.15 equiv of NaOMe gave the key tetraol **23** in a satisfactory 70% yield together with pentaol **24** (14%). Otherwise, treatment of the fully protected **22** under harsher conditions (0.5 equiv NaOMe, rt) enabled its efficient conversion into the same **24** (92%), which is the key intermediate to trisaccharides **A**°**BC**-Pr and **ABC**-Pr (Scheme 4). ^{1}H NMR analysis, especially of the chemical shift of H-3_C in the two products of transesterification—δ_H at 5.05 and 3.93 for **23** and **24**, respectively—ascertained the site of *O*-acetylation in tetraol **23**.



Scheme 3. Synthesis of trisaccharide **22** from disaccharide **14**. Reagents and conditions: (a) TMSOTf, toluene, −10 °C, 20 min (72%); (b) (i) CAN, MeCN/H_2O, rt, 30 min; (ii) Ac_2O, pyridine, DMAP, rt, 2 h (82% from **21** over two steps, 74% from **14** over three steps).

In view of the possible sensitivity of allyl ether and/or acetates to oxidative conditions,[36,37] such as in the 'Anelli's method',[38,39] and of the propensity of β-galactopyranosides to form 3,6-lactones upon TEMPO-mediated oxidation,[40] the conversion of monoacetate **23** to the corresponding uronic acid **25** was investigated under various conditions (Table 2). The poor solubility of intermediate **23** both in DCM and in water was incompatible with the biphasic system recommended as being critical for a high yielding oxidation step. Hence, all reactions were run in a homogenous MeCN/water (or MeCN/aqueous buffer) system. The use of TEMPO in combination with 1,3-dibromo-5,5-dimethylhydantoin was favored owing to its compatibility with *O*-acetyl groups.[41] Yet, this reagent system was rapidly abandoned since in our hands the desired oxidation product **25** was formed within complex mixtures (not shown). Under Anelli's conditions, modified according to J. Xie[42] for compatibility with an allyl aglycone, the reaction was slow, while degradation gradually increased. Nevertheless, repeated addition of TEMPO improved the conversion and the target trisaccharide **25** was isolated in an acceptable 49% yield (Table 2, entry 1). In an attempt to increase the conversion, trisaccharide **23** was engaged in a two-step oxidation process according to Huang and collaborators.[43] However, the remaining unreacted alcohol **23** suggested lack of completion, possibly due to solvent limitation, and the procedure was not investigated further (Table 2, entry 2). The orthogonality of TEMPO/BAIB ([bis(acetoxy)iodo]benzene)[44] to alkenes was exemplified previously.[14,45,46] Herein, tetraol **23** was reacted with excess TEMPO and BAIB providing oxidation product **25**, albeit in a rather low and poorly reproducible 39% yield (not shown). Therefore, inspired by the work of Zhao and collaborators[36] and of Kovensky's team,[47] a combination of TEMPO, NaOCl, and $NaOCl_2$ in buffer was investigated. However, in view of the substantial timelength of the reported oxidation procedure (4–14 days),[47] the amount of TEMPO was increased—0.3 versus 0.05 equiv—to speed up the transformation and prevent acetate cleavage. The initial transformation was clean though far from completion, reaching a moderate 35% yield of trisaccharide **25** (Table 2, entry 3). The presence of unreacted tetraol **23** suggested a rupture in the catalytic cycle. In the absence of any isolated chlorinated side-product, the amount of TEMPO was thought to interfere. This assumption along with the possible visual follow-up of the reaction progress[36] encouraged the implementation of a sequential procedure. The new proposed protocol involved the repeated addition of small portions of NaOCl and a slightly increased reaction temperature. The slow **23**→**25** conversion was kept under control, and under optimized conditions (Table 2, entry 4), isolation



	R^1	R^2
23	CH_2OH	Ac
24	CH_2OH	H
25	CO_2H	Ac
26	CO_2H	H

	R^1	R^2	R^3
27	CH_2OH	Ac	H
28	CH_2OH	H	Ac
29	CH_2OH	H	H
30	CO_2H	Ac	H
31	CO_2H	H	Ac
32	CO_2H	H	H

Scheme 4. Synthesis of the propyl glycosides **27**, **29**, **30**, and **32** from a common trisaccharide precursor **22**. Reagents and conditions: (a) NaOMe, MeOH, 0 °C, 2.5 h (70% for **23**); (b) NaOMe, MeOH, rt, 2 h (92% for **24**); (c) TEMPO, NaOCl, $NaClO_2$, MeCN/phosphate buffer, 45 °C, 24 h (90% for **25**, 86% for **26**); (d) Pd/C, MeOH, 30 °C, H-Cube™ 'full H_2' mode, 73% for **27**/**28** (5:1); (e) (i) Pd/C, H_2, MeOH, rt, 1 day, (ii) Pd/C, H_2, Et_3N, MeOH/H_2O, rt, 2 days (51% for **29**, 70% for **32**); (f) (i) Pd/C, H_2, THF/H_2O, rt, 1 day, (ii) Pd/C, H_2, Et_3N, THF/H_2O, rt, 2 days (47%/16% for **30**/**31**).

Table 2
Oxidation of tetraol **23** into uronic acid **25**

Entry	Oxidation system: reagent (equiv)	Medium	Duration	Temperature	Yield %
1	TEMPO (1.1), NaOCl, NaBr, $NaHCO_3$ then TEMPO (0.5) twice	MeCN/H_2O (2:1)	6 h	rt	49
2	TEMPO (0.3), NaBr, nBu_4NBr, NaOCl, $NaHCO_3$ then $NaClO_2$, 2-methyl-2-butene	MeCN/H_2O (1:1)	1 h	rt	n.d.
3	TEMPO (1.1), NaOCl, NaBr, $NaHCO_3$ then TEMPO (0.5) twice	MeCN/Phosphate buffer pH 6.7 (1:1)	4 days	35 °C	37
4	TEMPO (0.3), NaOCl, $NaClO_2$	MeCN/Phosphate buffer pH 6.7 (1:1)	24 h	45 °C	90

n.d. not determined.

of the oxidized **25** reached an excellent reproducible 90% yield. When pentaol **24** was reacted with TEMPO/NaOCl/$NaOCl_2$ under the same conditions, the corresponding uronic acid derivative **26** was isolated in a similar yield (86%), which validated the process in our hands (Scheme 4).

Having all four trisaccharides **23**–**26** in hands, we next focused on their final conversion into the propyl glycosides **27**, **29**, **30**, and **32**, respectively. In a first attempt, Pd/C-catalyzed hydrogenolysis of the benzyl ether and benzylidene acetal of the 3_C-*O*-acetyl intermediate **23**, along with concomitant hydrodechlorination of the 2_B-protecting group into an acetamide and allyl to propyl conversion, was performed in a microfluidic flow reactor (H-Cube™) using a diluted methanolic solution (60 mL/mmol) and a hydrogen pressure of 10 bar. Under these conditions, adding Et_3N to the reaction mixture was found to be crucial in order to avoid extensive repeated turnovers. Finally, the required trisaccharide **27** (**A**°**B$_{3Ac}$C**-Pr) was obtained in admixture with its regioisomer **28** (**A**°**B$_{4Ac}$C**-Pr) following RP column chromatography (73%, 5:1 ratio). Although an additional round of RP purification had enabled the isolation of each one of the pure monoacetates, the 4-*O*-acetylated **28** was not stable in solution. It rapidly evolved into a 2:1 mixture of trisaccharides **27** and **28**. Alternatively, the corresponding uronic acid **25** was subjected to the same transformation, albeit in THF/H_2O at ambient hydrogen pressure.[14] The 4_C-*O*-acetyl trisaccharide **AB$_{4Ac}$C**-Pr (**31**) was isolated in a meaningful 16% yield in addition to the **AB$_{3Ac}$C**-Pr (**30**) derivative (47%), following RP-HPLC purification. We have previously reported the successful obtaining of the closely related *O*-acetylated SF6 tetrasaccharide **B$_{3Ac}$CDA**-Pr following catalytic hydrogenation under neutral conditions of a precursor having the same set of protecting groups as allyl glycosides **23** and **25**.[14] In the present case, the hydrodechlorination under neutral conditions of trichloroacetamides **23** and **25** stopped at the chloroacetamide stage as indicated from LC–MS monitoring of the reaction (not shown). The acetamide targets were present as traces only and basic conditions were needed to reach completion of the 2_B-$NHCl_3Ac \rightarrow 2_B$-NHAc conversion. This different behavior may originate from a more hindered environment of the trichloroacetamide moiety within trisaccharides **23** and **25** in comparison to its location in tetrasaccharide **B$_{3Ac}$CDA**-Pr. In fact, *O*-acetyl migration at the very last step of a synthesis is not without precedent. In one exemple, although performing the hydrogenolysis of *O*-acetylated oligosaccharides protected in the form of benzylidene acetal, benzyl, and *p*-methoxybenzyl ether, under slightly acidic conditions could prevent migration, a mixture of regioisomers was still isolated following purification.[48] Herein, the basic conditions required for an efficient reduction of the trichloroacetamide in **23** and **25** favored the 3_C-*O*-acetyl migration to the vicinal 4_C-OH. Indeed, *O*-acetyl intramolecular migration was shown to already occur at pH 6.8.[49] Interestingly, we recently revealed the structure of the O-Ag from SF6 strain 2924-71, showing that acetylation—when present—occurred either at OH-4_C (minor form) or at OH-3_C (major form).[14] The 4_C-*O*-acetylated trisaccharides **28** and **31** are therefore of high interest toward the determination of the SF6 immunodominant epitopes. Toward the same goal, the non *O*-acetylated trisaccharides **24** and **26** were transformed into the corresponding propyl glycosides **A**°**BC**-Pr (**29**) and **ABC**-Pr (**32**) in 51% and 70% yield, respectively.

3. Conclusion

Seven oligosaccharides representing portions of the O-Ags of the human enteric pathogens SF6 and SF6a or of *E. coli* O147, were synthesized by appropriate combination of thioglycoside and trichloroacetimidate donors tuned for high yielding glycosylation and optimal stereocontrol of the newly installed glycosidic linkages. Fine adjustment of an oxidation protocol involving the TEMPO/NaOCl/$NaClO_2$ system, enabled the efficient chemoselective Gal*p* to Gal*p*A conversion within trisaccharide substrates comprising secondary hydroxyl groups, in addition to allyl and *O*-acetyl moieties, known for their sensitivity to standard oxidation medium. Combined with an efficient PMB→Ac replacement protocol, this newly established oxidation procedure enabled the site-directed transformation of a fully protected trisaccharide intermediate into seven functionalized targets. All RP-HPLC purified oligosaccharides will serve at investigating the molecular network of O-Ag/antibody interactions governing the serotyping for these enteric pathogens.

4. Experimental section

4.1. General

Anhydrous (anhyd) solvents—including toluene (Tol), dichloromethane (DCM), tetrahydrofuran (THF), *N*,*N*-dimethylformamide (DMF), methanol (MeOH), and pyridine—were delivered on molecular sieves and used as received. Additional solvents cited in the text are abbreviated as Chex (cyclohexane), MeCN (acetonitrile), and EtOAc (ethyl acetate), in addition to acetone. Reactions requiring anhyd conditions were run under an argon (Ar) atmosphere, using dried glassware. 4 Å Molecular sieves were activated before use by heating under high vacuum. Analytical thin-layer chromatography (TLC) was performed with silica gel $60F_{254}$, 0.25 mm pre-coated TLC aluminum foil plates. Compounds were visualized using UV_{254} and/or orcinol (1 mg mL^{-1}) in 10% aq H_2SO_4 with charring. Flash column chromatography was carried out using silica gel (particle size 40–63 μm, unless indicated otherwise). RP-HPLC purification was carried out using a Kromasil 5 μm C18 100 Å 10×250 mm semi-preparative column. Unless stated otherwise, analytical RP-HPLC of the final compounds (λ=215 nm) used a Symmetry 3.5 μm C_{18} 300 Å 2.1×100 mm analytical column eluting with a 0–35% linear gradient of MeCN in 0.01 N aq TFA over 20 min at a flow rate of 0.35 mL min^{-1}. NMR spectra were recorded at 303 K on a Bruker Avance spectrometer equipped with a BBO probe at 400 MHz (^1H) and 100 MHz (^{13}C). Spectra were recorded in deuterated chloroform ($CDCl_3$), deuterated methanol (MeOD), and deuterated water (D_2O). Chemical shifts (δ) are reported in parts per million (ppm) relative to residual solvent peak ($CHCl_3$, MeOH), and DSS (4,4-dimethyl-4-silapentane-1-sulfonic acid) in the case of D_2O at 7.28/77.0, 2.50/39.5 and 0.00/0.00 ppm for the ^1H and ^{13}C spectra, respectively. Coupling constants are reported in hertz (Hz). Elucidations of chemical structures were based on ^1H, COSY, DEPT-135, HSQC, decoupled HSQC, ^{13}C, decoupled ^{13}C, and HMBC. Signals are reported as s (singlet), d (doublet), t (triplet), dd (doublet of doublet), q (quadruplet), qt (quintuplet), dt (doublet of triplet), dq (doublet of quadruplet), ddd (doublet of doublet of doublet), m (multiplet). The signals can also be described as broad (prefix b), pseudo (prefix p),

overlapped (suffix $_o$) or partially overlapped (suffix $_{po}$). Of the two magnetically non-equivalent geminal protons at C-6, the one resonating at lower field is denoted H-6a, and the one at higher field is denoted H-6b. Interchangeable assignments are marked with an asterisk. Sugar residues are lettered according to the lettering of the RU of the SF6 O-Ag and identified by a subscript in the listing of signal assignments. LC–MS analysis was performed on a Waters Q-TOFmicro mass spectrometer equipped with an electrospray ion source (ESI) coupled to an Alliance HPLC equipped with a Waters Symmetry 3.5 μm C_{18} 100 Å 2.1×100 mm column. HRMS spectra were recorded on a WATERS QTOF Micromass instrument in the positive-ion electrospray ionization (ESI^+) mode. Solutions were prepared using 1:1 MeCN/H_2O containing 0.1% formic acid. Optical rotations were measured at 25 °C, in $CHCl_3$ solutions, except where indicated otherwise, with a BS Bellingham automatic polarimeter, Model ADP220.

4.2. Allyl 4-*O*-benzyl-3-*O*-*para*-methoxybenzyl-α-L-rhamnopyranoside (2) and allyl 4-*O*-benzyl-2-*O*-*para*-methoxybenzyl-α-L-rhamnopyranoside (3)

Bu_2SnO (37.2 g, 149.5 mmol, 1.1 equiv) was added to a solution of diol **1** (40.0 g, 135.8 mmol) in anhyd Tol (1.1 L). The mixture was stirred for 5 h at reflux using a 'Dean–Stark' apparatus and subsequently concentrated under reduced pressure to give a 0.4 M solution. After cooling to rt, dry CsF (21.05 g, 138.6 mmol, 1.0 equiv), dry TBAI (65.25 g, 175.6 mmol, 1.3 equiv), and 4-methoxybenzyl chloride (20.3 mL, 149.5 mmol, 1.1 equiv) were added. The reaction mixture was stirred for 5 h at reflux, at which time monitoring by TLC (Chex/EtOAc 6:4) showed the conversion of the starting material (R_f 0.22) into a major less polar product (R_f 0.51). The temperature was lowered to 0 °C, salts were removed by filtration (Tol wash), and volatiles were evaporated under reduced pressure. The residue was purified by flash chromatography (Chex/EtOAc 9:1 to 7:3) to give by order of elution, the yet undescribed regioisomer **3** (4.1 g, 8%) and acceptor **2** (48.1 g, 81%), both as orange-yellow oils. Alcohol **2** had $[\alpha]^{25}_D$ −41 (*c* 1.0), lit.[19] $[\alpha]^{25}_D$ −22 (*c* 1.0). ^1H NMR ($CDCl_3$), δ 7.43–7.29 (m, 7H, H_{Ar}), 6.95–6.89 (m, 2H, H_{ArPMB}), 5.96 (m, 1H, CH=$_{All}$), 5.34 (m, 1H, J_{trans}=17.2 Hz, J_{gem}=1.7 Hz, =CH_{2All}), 5.24 (m, 1H, J_{cis}=10.4 Hz, =CH_{2All}), 4.96 (d, 1H, *J*=11.1 Hz, H_{Bn}), 4.91 (d, 1H, $J_{1,2}$=1.5 Hz, H-1), 4.69 (d, 1H, H_{Bn}), 4.68 (d, 1H, *J*=11.2 Hz, H_{PMB}), 4.64 (d, 1H, H_{PMB}), 4.21 (m, 1H, H_{All}), 4.08 (br dd, 1H, H-2), 4.01 (m, 1H, H_{All}), 3.93 (dd, 1H, $J_{2,3}$=3.2 Hz, $J_{3,4}$=9.2 Hz, H-3), 3.48 (dq, 1H, $J_{4,5}$=9.4 Hz, $J_{5,6}$=6.1 Hz, H-5), 3.78 (s, 3H, CH_{3PMB}), 3.58 (pt, 1H, H-4), 2.23 (br s, 1H, OH-2), 1.41 (d, 3H, H-6). ^{13}C NMR ($CDCl_3$), δ 159.5 (C_{IVPMB}), 138.8 (C_{IVAr}), 134.1 (CH=$_{All}$), 130.6 (C_{IVAr}), 130.3–127.7 (7C, C_{Ar}), 117.2 (=CH_{2All}), 114.0 (2C, C_{ArPMB}), 98.6 (C-1), 80.1, 79.9 (2C, C-3, C-4), 75.3 (C_{Bn}), 71.7 (C_{PMB}), 68.6 (C-2), 67.8 (CH_{2All}), 67.7 (C-5), 55.2 (CH_{3PMB}), 18.0 (C-6). HRMS (ESI^+): *m*/*z* 437.1929 (calcd for $C_{24}H_{30}O_6Na$ $[M+Na]^+$: *m*/*z* 437.1940).

Alcohol **3** had $[\alpha]^{25}_D$ −18 (*c* 1.0). ^1H NMR ($CDCl_3$), δ 7.41–7.27 (m, 7H, H_{Ar}), 6.95–6.90 (m, 2H, H_{ArPMB}), 5.87 (m, 1H, CH=$_{All}$), 5.27 (m, 1H, J_{trans}=17.2 Hz, J_{gem}=1.7 Hz, =CH_{2All}), 5.19 (m, 1H, J_{cis}=10.4 Hz, =CH_{2All}), 4.93 (d, 1H, *J*=11.1 Hz, H_{Bn}), 486 (d, 1H, $J_{1,2}$=1.4 Hz, H-1), 4.70 (d, 1H, *J*=11.5 Hz, H_{Bn}), 4.67 (d, 1H, H_{Bn}), 4.53 (d, 1H, H_{Bn}), 4.16 (m, 1H, H_{All}), 4.01–3.92 (m, 2H, H-3, H_{All}), 3.84 (s, 3H, CH_{3PMB}), 3.75 (dd, 1H, $J_{2,3}$=3.9 Hz, H-2), 3.71 (dq, 1H, $J_{4,5}$=9.4 Hz, $J_{5,6}$=6.3 Hz, H-5), 3.32 (pt, 1H, $J_{3,4}$=9.3 Hz, H-4), 2.23 (d, 1H, $J_{OH,3}$=9.5 Hz, OH-3), 1.35 (d, 3H, H-6). ^{13}C NMR ($CDCl_3$), δ 159.5 (C_{IVPMB}), 138.6 (C_{IVAr}), 133.8 (CH=$_{All}$), 129.8 (C_{IVAr}), 129.7–127.7 (7C, C_{Ar}), 117.2 (=CH_{2All}), 114.0 (2C, C_{ArPMB}), 96.1 (C-1), 82.4 (C-4), 78.3 (C-2), 75.1, 72.7 (2C, C_{Bn}), 71.6 (C-3), 67.7 (CH_{2All}), 67.2 (C-5), 55.3 (CH_{3PMB}), 18.0 (C-6). HRMS (ESI^+): *m*/*z* 437.1835 (calcd for $C_{24}H_{30}O_6Na$ $[M+Na]^+$: *m*/*z* 437.1940).

4.3. Allyl (3,4,6-tri-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-galactopyranosyl)-(1→2)-4-*O*-benzyl-3-*O*-*para*-methoxybenzyl-α-L-rhamnopyranoside (5)

A mixture of acceptor **2** (300 mg, 0.72 mmol), donor **4** (597 mg, 0.87 mmol, 1.2 equiv), and powdered 4 Å MS (750 mg) in anhyd DCM (8.3 mL) was stirred at rt under an Ar atmosphere for 1 h. The reaction mixture was cooled to −65 °C, then NIS (244 mg, 1.09 mmol, 1.5 equiv) and TMSOTf (13 μL, 72 μmol, 0.1 equiv) were added. The reaction mixture was stirred for 1 h, while the bath temperature was allowed to reach −40 °C. Since a TLC control (Tol/EtOAc 9:1) indicated that no acceptor (R_f 0.10) nor donor (R_f 0.42) remained, and that a new product (R_f 0.22) was present, the reaction was quenched with Et_3N. Solids were filtered, and the filtrate was concentrated to dryness. The residue was purified by flash chromatography (Tol/EtOAc 95:5 to 9:1) to give disaccharide **5** (568 mg, 78%) as a light yellow solid. The β-condensation product **5** had $[\alpha]^{25}_D$ −10 (*c* 1.0). ^1H NMR ($CDCl_3$), δ 7.41–7.26 (m, 22H, H_{Ar}), 6.91 (d, 1H, $J_{NH,2}$=7.1 Hz, NH), 6.82 (m, 2H, *J*=8.8 Hz, H_{ArPMB}), 5.85 (m, 1H, CH=$_{All}$), 5.23 (m, 1H, J_{trans}=17.2 Hz, J_{gem}=1.6 Hz, =CH_{2All}), 5.14 (m, 1H, J_{cis}=10.4 Hz, =CH_{2All}), 4.96 (d_{po}, 1H, $J_{1,2}$=8.4 Hz, H-1_B), 4.93 (d_{po}, 1H, *J*=11.7 Hz, H_{Bn}), 4.92 (d, 1H, *J*=10.9 Hz, H_{Bn}), 4.82 (d, 1H, $J_{1,2}$=1.6 Hz, H-1_C), 4.68 (d, 1H, *J*=11.4 Hz, H_{Bn}), 4.63 (d, 1H, *J*=11.5 Hz, H_{Bn}), 4.60–4.55 (m, 4H, H_{Bn}), 4.50 (d, 1H, *J*=11.8 Hz, H_{Bn}), 4.46 (d, 1H, *J*=11.8 Hz, H_{Bn}), 4.13–4.02 (m, 2H, H-2_B, H_{All}), 4.00 (dd_{po}, 1H, $J_{2,3}$=10.8 Hz, $J_{3,4}$=2.4 Hz, H-3_B), 3.99–3.96 (m, 2H, H-4_B, H-2_C), 3.90 (m, 1H, H_{All}), 3.84 (dd, 1H, $J_{2,3}$=3.1 Hz, $J_{3,4}$=9.4 Hz, H-3_C), 3.78 (s, 3H, CH_{3PMB}), 3.68 (dq_{po}, 1H, $J_{4,5}$=9.4 Hz, $J_{5,6}$=6.2 Hz, H-5_C), 3.66 (dd_{po}, 1H, $J_{5,6a}$=7.0 Hz, $J_{6a,6b}$=8.8 Hz, H-$6a_B$), 3.58 (dd_{po}, 1H, $J_{5,6b}$=5.4 Hz, H-$6b_B$), 5.55 (pt_{po}, 1H, H-5_B), 3.45 (t, 1H, H-4_C), 1.31 (d, 3H, H-6_C). ^{13}C NMR ($CDCl_3$), δ 161.6 (NHCO), 159.3 (C_{IVPMB}), 138.8, 138.4, 138.0, 137.7 (4C, C_{IVAr}), 134.0 (CH=$_{All}$), 130.7 (C_{IVAr}), 129.7–127.5 (22C, C_{Ar}), 116.8 (=CH_{2All}), 113.9 (2C, C_{ArPMB}), 100.5 (C-1_B, $^1J_{CH}$=163.5 Hz), 98.6 (C-1_C, $^1J_{CH}$=175.4 Hz), 92.9 (CCl_3), 80.8 (C-4_C), 79.6 (C-3_C), 78.7 (C-3_B), 75.5 (C_{Bn}), 74.9 (C-2_C), 74.6 (C_{Bn}), 73.7 (C-5_B), 73.6 (C_{Bn}), 72.3 (3C, $2C_{Bn}$, C-4_B), 68.7 (C-6_B), 67.9 (C-5_C), 67.6 (CH_{2All}), 55.5 (C-2_B), 55.2 (CH_{3PMB}), 17.9 (C-6_C). HRMS (ESI^+): *m*/*z* 1012.2973 (calcd for $C_{53}H_{58}Cl_3NO_{11}Na$ $[M+Na]^+$: *m*/*z* 1012.2949).

4.4. Allyl (3,4,6-tri-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-galactopyranosyl)-(1→2)-4-*O*-benzyl-α-L-rhamnopyranoside (6)

Water (3.7 mL) and CAN (1.61 g, 2.94 mmol, 4.0 equiv) were added to a solution of disaccharide **5** (727 mg, 0.74 mmol) in MeCN (37 mL). After stirring for 1 h at rt, a TLC follow up (Chex/EtOAc 8:2) indicated the complete conversion of the *p*-methoxybenzyl derivative **5** (R_f 0.44) into a more polar product (R_f 0.25). The reaction was quenched by adding satd aq $NaHCO_3$. The reaction mixture was diluted with water and the aq phase was extracted three times with DCM. The combined extracts were washed with brine, dried by passing through a phase separator filter, and evaporated. The residue was purified by flash chromatography (Chex/EtOAc 8:2 to 7:3) to give alcohol **6** (552 mg, 64%) as a white solid. The latter had $[\alpha]^{25}_D$ −3 (*c* 1.0). ^1H NMR ($CDCl_3$), δ 7.40–7.27 (m, 20H, H_{Ar}), 6.97 (d, 1H, $J_{NH,2}$=6.9 Hz, NH), 5.85 (m, 1H, CH=$_{All}$), 5.24 (m, 1H, J_{trans}=17.2 Hz, J_{gem}=1.6 Hz, =CH_{2All}), 5.13 (m, 1H, J_{cis}=10.4 Hz, =CH_{2All}), 5.07 (d_{po}, 1H, $J_{1,2}$=7.9 Hz, H-1_B), 4.92 (d, 1H, *J*=11.3 Hz, H_{Bn}), 4.91 (br s, 1H, H-1_C), 4.84 (d, 1H, *J*=11.1 Hz, H_{Bn}), 4.70 (d, 1H, *J*=11.4 Hz, H_{Bn}), 4.66 (d, 1H, *J*=11.0 Hz, H_{Bn}), 4.59 (d, 1H, *J*=11.7 Hz, H_{Bn}), 4.56 (d, 1H, *J*=11.7 Hz, H_{Bn}), 4.51 (d, 1H, *J*=11.8 Hz, H_{Bn}), 4.48 (d, 1H, *J*=11.8 Hz, H_{Bn}), 4.14–4.01 (m, 4H, H-2_B, H_{All}, H-3_B, H-4_B), 4.01–3.96 (m, 2H, H-2_C, H-3_C), 3.91 (m, 1H, H_{All}), 3.69 (dq_{po}, 1H, $J_{4,5}$=9.5 Hz, $J_{5,6}$=6.2 Hz, H-5_C), 3.68–3.60 (m, 3H, H-$6a_B$, H-5_B, H-$6b_B$), 3.32 (pt, 1H, $J_{3,4}$=9.2 Hz, H-4_C), 2.37 (d, 1H, $J_{OH,3}$=7.3 Hz, OH-3_C), 1.32 (d, 3H, H-6_C). ^{13}C NMR ($CDCl_3$), δ 162.0 (NHCO), 138.5,

138.3, 137.8, 137.3 (4C, C_{IVAr}), 133.9 (CH=$_{All}$), 128.6–127.7 (20C, C_{Ar}), 116.9 (=CH_{2All}), 101.4 (C-1_B, $^1J_{CH}$=164.9 Hz), 98.4 (C-1_C, $^1J_{CH}$=171.2 Hz), 92.7 (CCl_3), 82.4 (C-4_C), 79.0 (C-3_C), 78.2 (C-3_B), 75.1, 74.7 (2C, C_{Bn}), 73.8 (C-5_B), 73.6 (C_{Bn}), 72.2 (2C, C_{Bn}, C-4_B), 71.5 (C-2_C), 68.5 (C-6_B), 67.7 (CH_{2All}), 67.3 (C-5_C), 55.7 (C-2_B), 18.0 (C-6_C). HRMS (ESI$^+$): *m*/*z* 892.2393 (calcd for $C_{45}H_{50}Cl_3NO_{10}Na$ [M+Na]$^+$: *m*/*z* 892.2398).

4.5. Allyl (3,4,6-tri-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-galactopyranosyl)-(1→2)-3-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranoside (7)

Alcohol **6** (410 mg, 0.47 mmol) was dissolved in dry pyridine (2.4 mL). Acetic anhydride (45 μL, 4.7 mmol, 10 equiv) was added at rt and the reaction mixture was stirred under an Ar atmosphere for 24 h. At this time, a TLC control (Tol/EtOAc 7:3) showed the total conversion of disaccharide **6** (R_f 0.27) into a less polar product (R_f 0.41). Volatiles were evaporated and co-evaporated three times with Tol. The residue was purified by flash chromatography (Chex/EtOAc 9:1 to 8:2) to give acetate **7** (416 mg, 97%) as a white foam. Disaccharide **7** $[\alpha]^{25}_D$ −8 (*c* 1.0). ^{1}H NMR ($CDCl_3$), δ 7.41–7.24 (m, 20H, H_{Ar}), 7.00 (d, 1H, $J_{NH,2}$=7.0 Hz, NH), 5.86 (m, 1H, CH=$_{All}$), 5.28 (dd$_{po}$, 1H, $J_{3,4}$=9.5 Hz, H-3_C), 5.26 (m$_{po}$, 1H, J_{trans}=17.3 Hz, J_{gem}=1.6 Hz, =CH_{2All}), 5.14 (m, 1H, J_{cis}=10.4 Hz, =CH_{2All}), 5.03 (d, 1H, $J_{1,2}$=8.2 Hz, H-1_B), 4.88 (d, 1H, *J*=11.3 Hz, H_{Bn}), 4.83 (d, 1H, $J_{1,2}$=1.7 Hz, H-1_C), 4.68 (d$_{po}$, 1H, *J*=11.2 Hz, H_{Bn}), 4.65 (d$_{po}$, 1H, *J*=11.4 Hz, H_{Bn}), 4.58 (br d, 2H, *J*=11.0 Hz, H_{Bn}), 4.56 (d, 1H, *J*=11.2 Hz, H_{Bn}), 4.51 (d, 1H, *J*=11.7 Hz, H_{Bn}), 4.46 (d, 1H, *J*=11.7 Hz, H_{Bn}), 4.36 (dd, 1H, $J_{2,3}$=11.0 Hz, $J_{3,4}$=2.8 Hz, H-3_B), 4.16 (dd$_{po}$, 1H, $J_{2,3}$=3.1 Hz, H-2_C), 4.13 (m$_{po}$, 1H, H_{All}), 4.02 (d, 1H, H-4_B), 3.95 (m, 1H, H_{All}), 3.83 (m$_{po}$, 1H, H-2_B), 3.80 (dq$_{po}$, 1H, $J_{4,5}$=9.4 Hz, $J_{5,6}$=6.2 Hz, H-5_C), 3.68–3.63 (m, 2H, H-6a$_B$, H-5_B), 3.56 (dd, 1H, $J_{5,6b}$=9.1 Hz, $J_{6a,6b}$=12.3 Hz, H-6b$_B$), 3.53 (pt, 1H, H-4_C), 2.10 (s, 3H, CH_{3Ac}), 1.33 (d, 3H, H-6_C). ^{13}C NMR ($CDCl_3$), δ 170.7 (CO_{Ac}), 161.5 (NHCO), 138.4, 138.3, 137.9, 137.6 (4C, C_{IVAr}), 133.8 (CH=$_{All}$), 128.5–127.2 (20C, C_{Ar}), 117.0 (=CH_{2All}), 99.6 (C-1_B, $^1J_{CH}$=164.3 Hz), 98.6 (C-1_C, $^1J_{CH}$=171.9 Hz), 92.9 (CCl_3), 79.5 (C-4_C), 76.7 (C-3_B), 75.3 (C-2_C), 75.1, 74.8, 73.6 (3C, C_{Bn}), 73.5 (2C, C-3_C, C-5_B), 72.8 (C-4_B), 72.5 (C_{Bn}), 68.2 (C-6_B), 67.8 (CH_{2All}), 67.7 (C-5_C), 56.3 (C-2_B), 21.2 (CH_{3Ac}), 17.9 (C-6_C). HRMS (ESI$^+$): *m*/*z* 934.2661 (calcd for $C_{47}H_{52}Cl_3NO_{11}Na$ [M+Na]$^+$: *m*/*z* 934.2504).

4.6. Propyl 2-acetamido-2-deoxy-β-D-galactopyranosyl-(1→2)-α-L-rhamnopyranoside (8)

To a stirred solution of alcohol **5** (94 mg, 94 μmol) in EtOH (4 mL), was added 10% Pd/C (100 mg). The suspension was stirred under a hydrogen atmosphere for 48 h. After this time, MS analysis of the crude reaction mixture indicated a single molecular weight corresponding to that of the target disaccharide. The reaction mixture was filtered over a pad of Celite®. Evaporation of the volatiles, freeze-drying, and purification of the crude material by preparative RP-HPLC (0–35% linear gradient of MeCN in 0.08% aq TFA over 16 min, then 35–100% linear gradient of MeCN in 0.08% aq TFA over 4 min, at a flow rate of 5.5 mL min^{-1}) gave disaccharide **8** (29.3 mg, 77%) as a white solid following freeze-drying. Compound **8** had $[\alpha]^{25}_D$ −3 (*c* 1.0, water). ^{1}H NMR (D_2O), δ 4.83 (d, 1H, $J_{1,2}$=1.5 Hz, H-1_C), 4.48 (d, 1H, $J_{1,2}$=8.4 Hz, H-1_B), 3.86 (dd, 1H, $J_{2,3}$=3.1 Hz, H-2_C), 3.78 (d$_{po}$, 1H, $J_{3,4}$=2.7 Hz, H-4_B), 3.75 (dd$_{po}$, 1H, $J_{2,3}$=10.8 Hz, H-2_B), 3.67 (dd$_{po}$, 1H, $J_{3,4}$=9.7 Hz, H-3_C), 3.66–3.56 (m, 3H, H-6a$_B$, H-6b$_B$, H-3_B), 3.56–3.46 (m, 3H, H-5_C, H-5_B, OCH_{2Pr}), 3.35 (dt, 1H, *J*=6.3 Hz, *J*=9.7 Hz, OCH_{2Pr}), 3.19 (pt, 1H, $J_{4,5}$=9.6 Hz, H-4_C), 1.91 (s, 3H, CH_{3NHAc}), 1.48 (m, 2H, CH_{2Pr}), 1.13 (d, 3H, $J_{5,6}$=6.3 Hz, H-6_C), 0.76 (t, 3H, *J*=7.4 Hz, CH_{3Pr}). ^{13}C NMR (D_2O), δ 177.6 (NHCO), 105.6 (C-1_B, $^1J_{CH}$=163.8 Hz), 101.1 (C-1_C, $^1J_{CH}$=173.6 Hz), 81.1 (C-2_C), 77.5 (C-5_B), 74.9 (C-4_C), 73.3 (C-3_B), 72.5 (C-3_C), 72.2 (OCH_{2Pr}), 71.1 (C-5_C), 70.3 (C-4_B), 63.5 (C-6_B), 55.2 (C-2_B), 24.7 (CH_{3NHAc}), 24.5 (CH_{2Pr}), 19.1 (C-6_C), 12.3 (CH_{3Pr}). HRMS (ESI$^+$): *m*/*z* 432.1834 (calcd for $C_{17}H_{31}NO_{10}Na$ [M+Na]$^+$: *m*/*z* 432.1846). RP-HPLC (215 nm): t_R=10.4 min.

4.7. Propyl 2-acetamido-2-deoxy-β-D-galactopyranosyl-(1→2)-3-*O*-acetyl-α-L-rhamnopyranoside (9)

To a stirred solution of acetate **7** (99 mg, 108 μmol) in EtOH (4.4 mL), was added 10% Pd/C (100 mg). The suspension was stirred under a hydrogen atmosphere for 48 h. After this time, MS analysis of the crude reaction mixture indicated a single molecular weight corresponding to that of the target disaccharide. The reaction mixture was filtered over a pad of Celite®. Evaporation of the volatiles, freeze-drying, and purification of the crude material by preparative RP-HPLC (0–35% linear gradient of MeCN in 0.08% aq TFA over 16 min, then 35–100% linear gradient of MeCN in 0.08% aq TFA over 4 min, at a flow rate of 5.5 mL min^{-1}) gave disaccharide **9** (32.5 mg, 67%) as a white solid following freeze-drying. Compound **9** had $[\alpha]^{25}_D$ +5 (*c* 1.0, water). ^{1}H NMR (D_2O), δ 4.91 (dd, 1H, $J_{2,3}$=3.0 Hz, $J_{3,4}$=10.0 Hz, H-3_C), 4.83 (d, 1H, $J_{1,2}$=1.5 Hz, H-1_C), 4.28 (d, 1H, $J_{1,2}$=8.3 Hz, H-1_B), 3.98 (pt, 1H, H-2_C), 3.78 (d$_{po}$, 1H, $J_{3,4}$=3.4 Hz, H-4_B), 3.74 (dd$_{po}$, 1H, $J_{2,3}$=10.8 Hz, H-2_B), 3.59–3.56 (m, 4H, H-5_C, H-6a$_B$, H-6b$_B$, H-3_B), 3.52 (dt, 1H, *J*=7.1 Hz, *J*=9.7 Hz, OCH_{2Pr}), 3.47 (dd, 1H, $J_{5,6a}$=4.7 Hz, $J_{5,6b}$=7.7 Hz, H-5_B), 3.41–3.34 (m, 2H, H-4_C, OCH_{2Pr}), 2.05 (s, 3H, CH_{3Ac}), 1.95 (s, 3H, CH_{3NHAc}), 1.47 (m, 2H, CH_{2Pr}), 1.16 (d, 3H, $J_{5,6}$=6.2 Hz, H-6_C), 0.78 (t, 3H, *J*=7.4 Hz, CH_{3Pr}). ^{13}C NMR (D_2O), δ 177.1 (NHCO), 176.0 (CO_{Ac}), 105.8 (C-1_B, $^1J_{CH}$=163.3 Hz), 101.1 (C-1_C, $^1J_{CH}$=175.7 Hz), 79.1 (C-2_C), 77.3 (C-5_B), 75.4 (C-3_C), 72.8 (C-3_B), 72.6 (C-4_C), 72.2 (OCH_{2Pr}), 71.2 (C-5_C), 70.2 (C-4_B), 63.4 (C-6_B), 55.1 (C-2_B), 24.9 (CH_{3NHAc}), 24.5 (CH_{2Pr}), 23.1 (CH_{3Ac}), 19.1 (C-6_C), 12.4 (CH_{3Pr}). HRMS (ESI$^+$): *m*/*z* 474.1945 (calcd for $C_{19}H_{33}NO_{11}Na$ [M+Na]$^+$: *m*/*z* 474.1951). RP-HPLC (215 nm, Aeris Peptide Phenomenex 3.6 μm C_{18} 100 Å 2.1×100 mm analytical column, 0–20% linear gradient of MeCN in 0.08% aq TFA over 20 min at 0.3 mL min^{-1}): t_R=15.3 min.

4.8. Allyl (3,4,6-tri-*O*-benzyl-2-deoxy-2-trichloroacetamido-α-D-galactopyranosyl)-(1→2)-4-*O*-benzyl-3-*O*-*para*-methoxybenzyl-α-L-rhamnopyranoside (10)

A mixture of acceptor **2** (51 mg, 0.12 mmol), donor **4** (99 mg, 0.15 mmol, 1.2 equiv), and powdered 4 Å MS (100 mg) in anhyd DCM (1.4 mL) was stirred at rt under an Ar atmosphere for 1 h. The reaction mixture was cooled to 0 °C, then NIS (41 mg, 0.18 mmol, 1.5 equiv) and TMSOTf (2 μL, 12 μmol, 0.1 equiv) were added. The reaction mixture was stirred for 45 min, while the bath temperature reached rt. Since a TLC control (Tol/EtOAc 9:1) indicated that no acceptor (R_f 0.10) nor donor (R_f 0.42) remained, and that a new compound (R_f 0.22) was present, the reaction was quenched with Et_3N. Solids were filtered, and the filtrate was concentrated to dryness. The residue was purified by flash chromatography (Tol/EtOAc 95:5 to 9:1) to give by order of elution the product of α-D-glycosylation **10** (15 mg, 13%) and disaccharide **5** (82 mg, 69%), both as light yellow solids. The α-condensation product **10** had ^{1}H NMR ($CDCl_3$), δ 7.39–7.17 (m, 22H, H_{Ar}), 6.83 (d, 1H, $J_{NH,2}$=9.3 Hz, NH), 6.80 (m, 2H, *J*=8.7 Hz, H_{ArPMB}), 5.84 (m, 1H, CH=$_{All}$), 5.22 (m, 1H, J_{trans}=17.2 Hz, J_{gem}=1.5 Hz, =CH_{2All}), 5.17 (m, 1H, J_{cis}=10.5 Hz, =CH_{2All}), 4.99 (d$_{po}$, 1H, *J*=11.3 Hz, H_{Bn}), 4.97 (d$_{po}$, 1H, $J_{1,2}$=3.5 Hz, H-1_B), 4.87 (d, 1H, *J*=10.9 Hz, H_{Bn}), 4.76–4.68 (m, 4H, 2H_{Bn}, H-2_B, H-1_C), 4.60 (d, 1H, *J*=11.3 Hz, H_{Bn}), 4.56 (d, 1H, *J*=10.9 Hz, H_{Bn}), 4.54 (d, 1H, *J*=12.1 Hz, H_{Bn}), 4.47 (d, 1H, *J*=11.6 Hz, H_{Bn}), 4.41–4.32 (m, 3H, 2H_{Bn}, H-5_B), 4.13 (br s$_o$, 1H, H-4_B), 4.11 (m$_o$, 1H, H_{All}), 4.07 (pt, 1H, $J_{1,2}$=2.0 Hz, H-2_C), 3.90 (m$_o$, 1H, H_{All}), 3.88 (dd$_o$, 1H, $J_{2,3}$=3.2 Hz, $J_{3,4}$=9.6 Hz, H-3_C), 3.81 (dd, 1H, $J_{2,3}$=10.9 Hz, $J_{3,4}$=2.4 Hz, H-3_B), 3.76 (s, 3H, CH_{3PMB}), 3.69–3.62 (m, 2H, H-5_C, H-

6a$_B$), 3.46 (dd, 1H, $J_{5,6b}$=5.5 Hz, $J_{6a,6b}$=8.7 Hz, H-6b$_B$), 3.21 (pt, 1H, $J_{4,5}$=9.4 Hz, H-4$_C$), 1.21 (d, 3H, $J_{5,6}$=6.2 Hz, H-6$_C$). ^{13}C NMR ($CDCl_3$), δ 161.8 (NHCO), 158.8 (C$_{IVPMB}$), 138.5, 138.4, 138.0, 137.6 (4C, C$_{IVAr}$), 133.5 (CH=$_{All}$), 130.4 (C$_{IVAr}$), 129.1–127.6 (22C, C$_{Ar}$), 117.5 (=CH$_{2All}$), 113.7 (2C, C$_{ArPMB}$), 96.4 (C-1$_B$, $^1J_{CH}$=174.5 Hz), 95.7 (C-1$_C$, $^1J_{CH}$=172.6 Hz), 92.9 (CCl_3), 80.4 (C-4$_C$), 79.1 (C-3$_C$), 78.6 (C-3$_B$), 75.2, 74.6, 73.6 (3C, C$_{Bn}$), 72.9 (C-2$_C$), 72.2 (C-4$_B$), 71.2 (2C, C$_{Bn}$), 70.2 (C-5$_B$), 68.6 (C-6$_B$), 68.0 (CH$_{2All}$), 67.8 (C-5$_C$), 55.2 (CH$_{3PMB}$), 51.1 (C-2$_B$), 18.2 (C-6$_C$). HRMS (ESI$^+$): m/z 1012.2949 (calcd for $C_{53}H_{58}Cl_3NO_{11}Na$ [M+Na]$^+$: m/z 1012.2973).

4.9. 2-Methyl-5-*tert*-butylphenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-1-thio-β-D-galactopyranoside (11)

NaOMe (25% in MeOH, 15.9 mL, 69.6 mmol, 3.0 equiv) was slowly added to a solution of D-galactosamine hydrochloride (5.00 g, 23.18 mmol) in anhyd MeOH (100 mL) stirred at 0 °C under an Ar atmosphere. After 15 min, trichloroacetic anhydride (6.4 mL, 34.8 mmol, 1.5 equiv) was added dropwise, keeping the reaction temperature close to 0 °C. The mixture was stirred for 2 h, until a TLC control (iPrOH/H_2O/NH_3 4:1:0.5) showed the complete conversion of the starting material (R_f 0) to a less polar product (R_f 0.51). The reaction was quenched with Dowex-H$^+$ resin, the resin was filtered and volatiles were evaporated. The residue was dissolved in anhyd pyridine (35 mL) and acetic anhydride (35.0 mL, 247.8 mmol, 15.0 equiv) was slowly added over 30 min at 0 °C. After stirring for 16 h at rt, a TLC control (DCM/EtOAc 9:1) showed the conversion of the intermediate (R_f 0) into less polar compounds (R_f 0.68, 0.56). Solvents were evaporated and co-evaporated three times with Tol. The residue was purified by flash chromatography (DCM/EtOAc 95:5 to 6:4) to give a mixture (10.30 g, 90%) of the peracylated galactosamine. 2-Methyl-5-*tert*-butylthiophenol (2.50 mL, 22.6 mmol, 3.4 equiv) and $BF_3 \cdot OEt_2$ (2.55 mL, 20.0 mmol, 3.0 equiv) were added at rt to a solution of the latter (4.00 g, 6.66 mmol) in anhyd DCM (23 mL). After being stirred for 2.5 h under an Ar atmosphere, a TLC control (Tol/EtOAc 7:3) of the reaction mixture showed the conversion of the peracylated galactosamine isomers (R_f 0.23, 0.28) into a major more polar product (R_f 0.41). The reaction was quenched with satd aq $NaHCO_3$. DCM was added, and the layers were separated. The organic phase was washed with H_2O and brine, dried by passing through a phase separator filter, and volatiles were evaporated. The residue was purified by flash chromatography (Tol/EtOAc 95:5 to 75:15) to give thioglycoside **11** (3.11 g, 56%, three steps) as a white foam. Compound **11** had $[\alpha]^{25}_D$ +5 (c 1.0). ^{1}H NMR ($CDCl_3$), δ 7.63 (d, 1H, J=2.1 Hz, H$_{Ar}$), 7.28 (dd, 1H, J=8.0 Hz, H$_{Ar}$), 7.17 (d, 1H, H$_{Ar}$), 6.73 (d, 1H, $J_{NH,2}$=9.0 Hz, NH), 5.46 (dd, 1H, $J_{3,4}$=3.3 Hz, $J_{4,5}$=0.9 Hz, H-4), 5.31 (dd, 1H, $J_{2,3}$=10.9 Hz, H-3), 4.91 (d, 1H, $J_{1,2}$=10.4 Hz, H-1), 4.29 (m, 1H, H-2), 4.21 (dd$_{po}$, 1H, $J_{5,6a}$=6.9 Hz, $J_{6a,6b}$=11.3 Hz, H-6a), 4.18 (dd$_{po}$, 1H, $J_{5,6b}$=6.3 Hz, H-6b), 3.98 (dt, 1H, H-5), 2.40 (s, 3H, Me$_{Ar}$), 2.20, 2.05, 2.02 (3s, 9H, CH$_{3Ac}$), 1.34 (s, 9H, ^{t}Bu). ^{13}C NMR ($CDCl_3$), δ 170.4, 170.2 (3C, CO$_{Ac}$), 161.8 (NHCO), 149.8, 137.5, 131.6 (3C, C$_{IVAr}$), 130.7, 130.2, 128.4 (3C, C$_{Ar}$), 92.3 (CCl_3), 88.0 (C-1), 74.7 (C-5), 70.7 (C-3), 66.9 (C-4), 61.7 (C-6), 51.8 (C-2), 34.5 (C$_{IV^tBu}$), 31.4 (9C, CH$_{3^tBu}$), 20.8, 20.7, 20.6, 20.5 (4C, 3CH$_{3Ac}$, C$_{MeAr}$). HRMS (ESI$^+$): m/z 634.0815 (calcd for $C_{25}H_{32}Cl_3NO_8SNa$ [M+Na]$^+$: m/z 634.0812).

4.10. Allyl (3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-galactopyranosyl)-(1→2)-4-*O*-benzyl-3-*O*-*para*-methoxybenzyl-α-L-rhamnopyranoside (13)

4.10.1. Route 1. A mixture of acceptor **2** (400 mg, 0.97 mmol), donor **12** (786 mg, 1.45 mmol, 1.5 equiv), and powdered 4 Å MS (900 mg) in anhyd DCM (11 mL) was stirred at rt under an Ar atmosphere for 1 h, and then cooled to −60 °C. NIS (326 mg, 1.45 mmol, 1.5 equiv) and TfOH (10 μL, 116 μmol, 0.12 equiv) were added, and stirring went on for 3 h while the cooling bath reached rt. Since an LC–MS profile and a TLC control (DCM/EtOAc 9:1 and Chex/EtOAc 6:4) indicated that no acceptor (R_f 0.32, 0.43) nor donor (R_f 0.25, 0.33) remained, but that a major new product (R_f 0.32, 0.45) was present, the reaction was quenched by adding Et_3N. Solids were filtered, and the filtrate was concentrated to dryness. The residue was purified by flash chromatography (Tol/EtOAc 9:1 to 8:2) to give first oxazoline **15**[23] contaminated by some remaining acceptor and then disaccharide **13** (598 mg, 73%) as a yellow foam.

4.10.2. Route 2. A mixture of acceptor **2** (243 mg, 0.59 mmol), donor **11** (431 mg, 0.70 mmol, 1.2 equiv), and powdered 4 Å MS (500 mg) in anhyd DCM (6.7 mL) was stirred at rt under an Ar atmosphere for 1 h, and then cooled to 0 °C. NIS (198 mg, 0.88 mmol, 1.5 equiv) and TfOH (6 μL, 70 μmol, 0.12 equiv) were added, and the reaction mixture was stirred at that temperature for 3 h while the cooling bath reached rt. Since a TLC control (DCM/EtOAc 9:1 and Chex/EtOAc 6:4) indicated that no acceptor (R_f 0.32, 0.43) nor donor (R_f 0.25, 0.33) remained, but that a major new product (R_f 0.32, 0.45) was present, the reaction was quenched by adding Et_3N. Solids were filtered and the filtrate was concentrated to dryness. The residue was purified by flash chromatography (Tol/EtOAc 9:1 to 8:2) to give disaccharide **13** (308 mg, 62%) as a yellow foam. Disaccharide **13** had $[\alpha]^{25}_D$ −20 (c 1.0). ^{1}H NMR ($CDCl_3$), δ 7.35–7.14 (m, 7H, H$_{Ar}$), 6.82 (d, 2H, J=8.6 Hz, H$_{ArPMB}$), 5.60 (d, 1H, $J_{NH,2}$=8.5 Hz, NH), 5.81 (m, 1H, CH=$_{All}$), 5.25 (d, 1H, $J_{3,4}$=3.2 Hz, H-4$_B$), 5.19 (m, 1H, J_{trans}=17.2 Hz, J_{gem}=1.7 Hz, =CH$_{2All}$), 5.11 (m, 1H, J_{cis}=10.4 Hz, =CH$_{2All}$), 4.93 (dd, 1H, $J_{2,3}$=11.1 Hz, H-3$_B$), 4.79 (d, 1H, J=10.9 Hz, H$_{Bn}$), 4.75 (d, 1H, $J_{1,2}$=1.7 Hz, H-1$_C$), 4.62 (d, 1H, J=11.1 Hz, H$_{Bn}$), 4.57 (d, 1H, $J_{1,2}$=8.5 Hz, H-1$_B$), 4.51 (d, 1H, H$_{Bn}$), 4.46 (d, 1H, H$_{Bn}$), 4.15 (m, 1H, H-2$_B$), 4.12–3.97 (m, 3H, H-6a$_B$, H-6b$_B$, H$_{All}$), 3.87 (m, 1H, H$_{All}$), 3.85 (m, 1H, H-2$_C$), 3.80 (dd, 1H, $J_{2,3}$=3.1 Hz, $J_{3,4}$=9.2 Hz, H-3$_C$), 3.75 (s, 3H, CH$_{3PMB}$), 3.71 (pt, 1H, $J_{5,6a}$=6.5 Hz, $J_{5,6b}$=7.0 Hz H-5$_B$), 3.62 (dq, 1H, $J_{4,5}$=9.5 Hz, $J_{5,6}$=6.2 Hz, H-5$_C$), 3.31 (pt, 1H, H-4$_C$), 2.08, 1.99, 1.91 (3s, 9H, CH$_{3Ac}$), 1.24 (d, 3H, H-6$_C$). ^{13}C NMR ($CDCl_3$), δ 170.3, 170.2, 170.1 (3C, CO$_{Ac}$), 161.8 (NHCO), 159.6, 138.6 (2C, C$_{IVAr}$), 133.7 (CH=$_{All}$), 130.4 (C$_{IVAr}$), 129.8, 128.4, 127.7, 127.5, 126.4 (7C, C$_{Ar}$), 117.2 (=CH$_{2All}$), 114.2 (2C, C$_{Ar}$), 101.7 (C-1$_B$), 98.2 (C-1$_C$), 92.3 (CCl_3), 81.0 (C-4$_C$), 79.9 (C-3$_C$), 76.6 (C-2$_C$), 75.5 (C$_{Bn}$), 73.4 (C$_{Bn}$), 71.0 (C-5$_B$), 70.8 (C-3$_B$), 67.9 (C-5$_C$), 67.7 (CH$_{2All}$), 66.6 (C-4$_B$), 61.2 (C-6$_B$), 55.3 (CH$_{3PMB}$), 52.6 (C-2$_B$), 20.6, 20.5 (3C, CH$_{3Ac}$), 17.9 (C-6$_C$). HRMS (ESI$^+$): m/z 868.1815 (calcd for $C_{38}H_{46}Cl_3NO_{14}Na$ [M+Na]$^+$: m/z 868.1882).

4.11. Phenyl 4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-1-thio-β-D-galactopyranoside (16)

A solution of thioglycoside **12** (9.45 g, 17.41 mmol) in anhyd MeOH (131 mL) was treated with 0.5 M methanolic NaOMe (7.0 mL, 3.48 mmol, 0.2 equiv). The solution was stirred for 2 h at rt under an Ar atmosphere. A TLC control (Chex/EtOAc 6:4 and DCM/MeOH 8:2) showed the total conversion of the starting material (R_f 0.28, 1.0) into a more polar product (R_f 0, 0.61). The reaction was quenched with Dowex-H$^+$ resin, the resin was filtered and volatiles were evaporated to give the corresponding crude triol. Benzaldehyde dimethylacetal (5.2 mL, 34.8 mmol, 2.0 equiv) and CSA (404 mg, 1.74 mmol, 0.1 equiv) were successively added to a solution of the latter in anhyd MeCN (450 mL). The mixture was stirred under an Ar atmosphere for 16 h, at which time a TLC control (Chex/EtOAc 1:1) showed the conversion of the triol (R_f 0) into a less polar compound (R_f 0.32). The reaction was quenched with Et_3N, and volatiles were evaporated. The residue was purified by flash chromatography (Chex/EtOAc 6:4 to 4:6) to give acetal **16** (8.18 g, 93%) as a white solid. Thioglycoside **16** had $[\alpha]^{25}_D$ −12 (c 1.0), lit.[24] $[\alpha]^{25}_D$ −11 (c 1.0). ^{1}H NMR ($CDCl_3$), δ 7.72–7.29 (m, 10H, H$_{Ar}$), 6.79 (d, 1H, $J_{NH,2}$=7.6 Hz, NH), 5.58 (s, 1H, CHPh), 5.12 (d, 1H, $J_{1,2}$=10.2 Hz, H-1),

4.43 (dd, 1H, $J_{5,6a}$=1.6 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 4.27 (d, 1H, $J_{3,4}$=3.6 Hz, $J_{4,5}$=0.7 Hz, H-4), 4.19 (ptd, 1H, $J_{2,3}$=$J_{3,OH}$=10.3 Hz, H-3), 4.08 (dd, 1H, $J_{5,6b}$=1.7 Hz, H-6b), 3.79 (ptd, 1H, H-2), 3.63 (m, 1H, H-5), 2.61 (d, 1H, OH-3). ^{13}C NMR ($CDCl_3$), δ 162.0 (NHCO), 137.4 (C_{IVAr}), 134.0 (2C, C_{Ar}), 130.7 (C_{IVAr}), 129.4–126.5 (8C, C_{Ar}), 101.3 (CHPh), 92.4 (CCl_3), 83.8 (C-1, $^1J_{CH}$=160.6 Hz), 75.0 (C-4), 70.5 (C-3), 70.2 (C-5), 69.3 (C-6), 54.2 (C-2). HRMS (ESI$^+$): *m/z* 526.0053 (calcd for $C_{21}H_{20}Cl_3NO_5SNa$ [M+Na]$^+$: *m/z* 526.0026).

4.12. Phenyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-levulinoyl-2-trichloroacetamido-1-thio-β-D-galactopyranoside (17)

Levulinic acid (1.6 mL, 15.3 mmol, 2.0 equiv), DCC (2.83 g, 13.7 mmol, 1.8 equiv), and DMAP (186 mg, 1.52 mmol, 0.2 equiv) were added to a solution of alcohol **16** (3.85 g, 7.63 mmol) in DCM (27 mL). The mixture was stirred for 1 h at rt under an Ar atmosphere. At this time, a TLC control (Tol/EtOAc, 7:3) showed the conversion of alcohol **16** (R_f 0.17) into a less polar product (R_f 0.31). The reaction mixture was filtered over a pad of Celite®, diluted with DCM, and the organic phase was washed with 10% aq HCl, satd aq $NaHCO_3$, and brine, dried by passing through a phase separator filter, and concentrated. The residue was purified by flash chromatography (Tol/EtOAc, 8:2 to 7:3) to give the fully protected **17** (4.1 g, 90%) as a white powder. Thioglycoside **17** had $[\alpha]^{25}_D$ −3 (*c* 1.0). ^{1}H NMR ($CDCl_3$), δ 7.64–7.16 (m, 10H, H_{Ar}), 6.62 (d, 1H, $J_{NH,2}$=8.1 Hz, NH), 5.44 (s, 1H, CHPh), 5.33 (dd, 1H, $J_{2,3}$=10.9 Hz, $J_{3,4}$=3.3 Hz, H-3), 5.08 (d, 1H, $J_{1,2}$=10.1 Hz, H-1), 4.32 (dd, 1H, $J_{5,6a}$=1.4 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 4.25 (d, 1H, H-4), 4.05 (ptd, 1H, H-2), 3.97 (dd, 1H, $J_{5,6b}$=1.5 Hz, H-6b), 3.57 (m, 1H, H-5), 2.61–2.39 (m, 4H, CH_{2Lev}), 1.93 (s, 3H, CH_{3Lev}). ^{13}C NMR ($CDCl_3$), δ 206.4 (CO_{Lev}), 172.0 (CO_{2Lev}), 161.4 (NHCO), 137.6, 134.0, 130.8, 129.2, 129.0, 128.5, 128.2, 126.5 (12C, C_{Ar}), 100.9 (CHPh), 92.4 (CCl_3), 84.3 (C-1, $^1J_{CH}$=148.9 Hz), 73.2 (C-4), 71.1 (C-3), 69.9 (C-5), 69.2 (C-6), 50.8 (C-2), 37.7 (CH_{2Lev}), 29.6 (CH_{3Lev}), 28.1 (CH_{2Lev}). HRMS (ESI$^+$): *m/z* 624.0410 (calcd for $C_{26}H_{26}Cl_3NO_7SNa$ [M+Na]$^+$: *m/z* 624.0393).

4.13. Allyl (4,6-*O*-benzylidene-2-deoxy-3-*O*-levulinoyl-2-trichloroacetamido-β-D-galactopyranosyl)-(1→2)-4-*O*-benzyl-3-*O*-*para*-methoxybenzyl-α-L-rhamnopyranoside (18) and 2-trichloromethyl-4,5-dihydro-(4,6-*O*-benzylidene-1,2-dideoxy-3-*O*-levulinoyl-α-D-galactopyranoso)[2,1-*d*]-1,3-oxazole (19)

4.13.1. Route 1. A mixture of acceptor **2** (100 mg, 241 μmol), donor **17** (175 mg, 290 μmol, 1.2 equiv), and powdered 4 Å MS (180 mg) in anhyd DCM (2.8 mL) was stirred at rt under an Ar atmosphere for 1 h, and then cooled to −60 °C. NIS (81 mg, 362 μmol, 1.5 equiv) and TfOH (5 μL, 29 μmol, 0.12 equiv) were added. The reaction was stopped after 30 min by adding Et_3N, while the temperature of the cooling bath had reached −40 °C and a TLC control (Tol/EtOAc 7:3) had indicated the presence of a major product (R_f 0.37). Solids were filtered, and the filtrate was concentrated to dryness. The residue was purified by flash chromatography (Tol/EtOAc 90:10 to 7:3) to give by order of elution, a mixture of oxazoline **19** and unreacted acceptor **2** (36 mg, molar ratio 1:1.3) and disaccharide **18** (151 mg, 69%), both as yellow foams.

4.13.2. Route 2. A mixture of acceptor **2** (5.70 g, 13.75 mmol), donor **17** (12.44 mg, 20.63 mmol, 1.5 equiv), and powdered 4 Å MS (10 g) in anhyd DCM (158 mL) was stirred at rt under an Ar atmosphere for 1 h, and then cooled to −65 °C. NIS (4.64 g, 20.63 mmol, 1.5 equiv) and TfOH (147 μL, 1.65 mmol, 0.12 equiv) were added, and stirring went on for 1 h while the cooling bath reached −40 °C. Since a TLC control (Tol/EtOAc 7:3) indicated the absence of any remaining acceptor (R_f 0.40) or donor (R_f 0.30), but the presence of a new product (R_f 0.37), the reaction was quenched by adding Et_3N. Solids were filtered, and the filtrate was concentrated to dryness. The residue was purified by flash chromatography (Tol/EtOAc 92:8 to 7:3) to give disaccharide **18** (10.33 g, 82%) as a yellow foam. The condensation product had $[\alpha]^{25}_D$ +29 (*c* 1.0). ^{1}H NMR ($CDCl_3$), δ 7.48–7.08 (m, 12H, H_{Ar}), 6.81 (d, 2H, *J*=8.6 Hz, H_{ArPMB}), 6.76 (d, 1H, $J_{NH,2}$=8.1 Hz, NH), 5.80 (m, 1H, CH=$_{All}$), 5.43 (s, 1H, CHPh), 5.17 (m, 1H, J_{trans}=17.2 Hz, J_{gem}=1.7 Hz, =CH_{2All}), 5.08 (m, 1H, J_{cis}=10.4 Hz, =CH_{2All}), 4.94 (dd, 1H, $J_{2,3}$=11.1 Hz, $J_{3,4}$=3.4 Hz, H-3_B), 4.83 (d, 1H, $J_{1,2}$=1.5 Hz, H-1_C), 4.80 (d, 1H, *J*=10.9 Hz, H_{Bn}), 4.70 (d, 1H, $J_{1,2}$=8.4 Hz, H-1_B), 4.62 (d, 1H, *J*=11.1 Hz, H_{Bn}), 4.51 (d, 1H, H_{Bn}), 4.47 (d, 1H, H_{Bn}), 4.28 (ptd, 1H, H-2_B), 4.19 (dd, 1H, $J_{5,6a}$=1.2 Hz, $J_{6a,6b}$=12.4 Hz, H-$6a_B$), 4.14 (d, 1H, H-4_B), 4.05 (m, 1H, H_{All}), 3.96 (dd, 1H, $J_{5,6b}$=1.5 Hz, H-$6b_B$), 3.93 (m, 1H, H-2_C), 3.85 (m, 1H, H_{All}), 3.80 (dd, 1H, $J_{2,3}$=3.1 Hz, $J_{3,4}$=9.3 Hz, H-3_C), 3.73 (s, 3H, CH_{3PMB}), 3.62 (dq, 1H, $J_{4,5}$=9.5 Hz, $J_{5,6}$=6.3 Hz, H-5_C), 3.35 (pt, 1H, H-4_C), 3.27 (br s, 1H, H-5_B), 2.74–2.41 (m, 4H, CH_{2Lev}), 1.92 (s, 3H, CH_{3Lev}), 1.24 (d, 3H, H-6_C). ^{13}C NMR ($CDCl_3$), δ 206.6 (CO_{Lev}), 172.1 (CO_{2Lev}), 161.7 (NHCO), 159.6 (C_{IVPMB}), 138.7, 137.5 (2C, C_{IVAr}), 133.9 (CH=$_{All}$), 130.5 (C_{IVAr}), 129.8–126.4 (12C, C_{Ar}), 117.1 (=CH_{2All}), 114.2 (2C, C_{ArPMB}), 101.3 (C-1_B, $^1J_{CH}$=161.5 Hz), 100.9 (CHPh), 98.5 (C-1_C, $^1J_{CH}$=174.4 Hz), 92.5 (CCl_3), 81.1 (C-4_C), 80.1 (C-3_C), 75.9 (C-2_C), 75.5, 73.3 (2C, C_{Bn}), 73.0 (C-4_B), 71.7 (C-3_B), 68.9 (C-6_B), 67.8 (2C, C-5_C, CH_{2All}), 66.6 (C-5_B), 55.3 (CH_{3PMB}), 52.4 (C-2_B), 37.7 (CH_{2Lev}), 29.7 (CH_{3Lev}), 28.2 (CH_{2Lev}), 17.9 (C-6_C). HRMS (ESI$^+$): *m/z* 928.2211 (calcd for $C_{44}H_{50}Cl_3NO_{13}Na$ [M+Na]$^+$: *m/z* 928.2245).

Oxazoline **19** had $[\alpha]^{25}_D$ +105 (*c* 1.0). ^{1}H NMR ($CDCl_3$), δ 7.52–7.50 (m, 2H, H_{Ar}), 7.43–7.39 (m, 3H, H_{Ar}), 6.60 (d, 1H, $J_{1,2}$=6.0 Hz, H-1), 5.58 (s, 1H, CHPh), 5.00 (dd, 1H, $J_{2,3}$=7.9 Hz, $J_{3,4}$=2.6 Hz, H-3), 4.56 (pt, 1H, $J_{4,5}$=2.4 Hz, H-4), 4.48 (dd, 1H, H-2), 4.43 (dd, 1H, $J_{5,6a}$=1.4 Hz, $J_{6a,6b}$=12.8 Hz, H-6a), 4.09 (dd, 1H, $J_{5,6b}$=1.8 Hz, H-6b), 3.95 (m, 1H, H-5), 2.81–2.76 (m, 2H, CH_{2Lev}), 2.73–2.68 (m, 2H, CH_{2Lev}), 2.15 (s, 3H, CH_{3Lev}). ^{13}C NMR ($CDCl_3$), δ 206.2 (CO_{Lev}), 172.3 (CO_{2Lev}), 163.2 (CN), 137.2 (C_{IVAr}), 129.3, 128.3, 126.1 (5C, C_{Ar}), 105.1 (C-1, $^1J_{CH}$=186.0 Hz), 100.7 (CHPh), 77.2 (CCl_3), 72.4 (C-3), 71.5 (C-4), 70.5 (C-5), 66.5 (C-6), 66.3 (C-2), 37.9 (CH_{2Lev}), 29.7 (CH_{3Lev}), 28.2 (CH_{2Lev}). HRMS (ESI$^+$): *m/z* 492.0412 (calcd for $C_{20}H_{21}Cl_3NO_7$ [M+H]$^+$: *m/z* 492.0384), *m/z* 514.0226 (calcd for $C_{20}H_{20}Cl_3NO_7Na$ [M+Na]$^+$: *m/z* 514.0203), and *m/z* 532.0306 (calcd for $C_{20}H_{22}Cl_3NO_8Na$ [M+H_2O+Na]$^+$: *m/z* 532.0309).

4.14. Allyl (4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-galactopyranosyl)-(1→2)-4-*O*-benzyl-3-*O*-*para*-methoxybenzyl-α-L-rhamnopyranoside (14)

4.14.1. Route 1. A solution of disaccharide **13** (4.59 g, 5.42 mmol) in anhyd MeOH (47 mL) was treated with 0.5 M methanolic NaOMe (0.5 mL, 1.08 mmol, 0.2 equiv). The mixture was stirred at rt under an Ar atmosphere for 1.5 h. When TLC (Tol/EtOAc, 7:3) showed the complete disappearance of the starting material (R_f 0.53) and the presence of a more polar product (R_f 0), the reaction mixture was neutralized with Dowex-H$^+$ resin and filtered. The filtrate was concentrated to give the corresponding crude triol as a white solid. Benzaldehyde dimethylacetal (3.2 mL, 21.68 mmol, 4.0 equiv) and CSA (63 mg, 271 μmol, 0.05 equiv) were added to a solution of the latter in MeCN (108 mL). The mixture was stirred for 2 h at rt under an Ar atmosphere, at which time a TLC control (Tol/EtOAc 4:6) indicated the conversion of the triol (R_f 0.06) into a major less polar compound (R_f 0.63). The reaction mixture was neutralized by addition of Et_3N and concentrated. The residue was purified by flash chromatography (Tol/EtOAc 8:2 to 7:3) to give acceptor **14** (3.50 g, 84%) as a white solid.

4.14.2. Route 2. To a solution of disaccharide **18** (10.33 g, 11.37 mmol) in anhyd pyridine (95 mL) stirred at 0 °C under an Ar atmosphere were added AcOH (64 mL, dropwise) and hydrazine monohydrate (2.8 mL, 56.93 mmol, 5 equiv). The reaction mixture was stirred for 1 h, while the cooling bath reached rt. At this time,

follow up by TLC (Tol/EtOAc 7:3) showed the total conversion of the starting material (R_f 0.33) into a more polar product (R_f 0.21). Following addition of DCM and ice cold water, the two layers were separated and the aq phase was re-extracted twice with DCM. The combined organic phases were washed with brine, dried by passing through a phase separator filter, and concentrated to dryness. The residue was purified by flash chromatography (Tol/EtOAc 8:2 to 7:3) to give acceptor **14** (7.94 g, 86%) as a white foam. Alcohol **14** had $[\alpha]^{25}_D$ +6 (*c* 1.0). ^{1}H NMR ($CDCl_3$), δ 7.54–7.31 (m, 10H, H_{Ar}), 7.22 (m, 3H, 2H_{ArPMB}, NH), 6.88 (m, 2H, H_{ArPMB}), 5.92 (m, 1H, CH=$_{All}$), 5.59 (s, 1H, CHPh), 5.29 (m, 1H, J_{trans}=17.2 Hz, J_{gem}=1.5 Hz, =CH_{2All}), 5.20 (m, 1H, J_{cis}=10.4 Hz, =CH_{2All}), 4.95 (d_o, 1H, H-1$_C$), 4.93 (d_{po}, 1H, *J*=10.9 Hz, H_{Bn}), 4.75 (d, 1H, *J*=10.9 Hz, H_{Bn}), 4.65 (d, 1H, *J*=10.9 Hz, H_{Bn}), 4.60 (d_{po}, 1H, $J_{1,2}$=8.5 Hz, H-1$_B$), 4.59 (d_{po}, 1H, H_{Bn}), 4.32 (dd, 1H, $J_{5,6a}$=1.3 Hz, $J_{6a,6b}$=12.4 Hz, H-6a$_B$), 4.22–4.14 (m, 3H, H-2$_B$, H-4$_B$, H_{All}), 4.10 (dd, 1H, $J_{5,6a}$=1.7 Hz, H-6b$_B$) 4.00 (m, 1H, H-2$_C$), 3.97 (m_{po}, 1H, H_{All}), 3.93 (dd_{po}, 1H, $J_{2,3}$=3.1 Hz, H-3$_C$), 3.83 (s, 3H, CH_{3PMB}), 3.74 (dq, 1H, $J_{4,5}$=9.3 Hz, H-5$_C$), 3.66 (dd, 1H, $J_{2,3}$=10.6 Hz, $J_{3,4}$=3.5 Hz, H-3$_B$), 3.48 (pt, 1H, $J_{3,4}$=9.5 Hz, H-4$_C$), 3.37 (br s, 1H, H-5$_B$), 2.38 (s, 1H, OH-3$_B$), 1.35 (d, 3H, $J_{5,6}$=6.2 Hz, H-6$_C$). ^{13}C NMR ($CDCl_3$), δ 163.7 (NHCO), 159.7 (C_{IVPMB}), 138.6, 137.4 (2C, C_{IVAr}), 133.9 (CH=$_{All}$), 130.2 (C_{IVAr}), 129.8, 129.2, 128.5, 128.2, 127.7, 127.4, 126.3 (12C, C_{Ar}), 117.2 (=CH_{2All}), 114.2 (2C, C_{ArPMB}), 101.7 (C-1$_B$, $^1J_{CH}$=161.5 Hz), 101.2 (CHPh), 98.4 (C-1$_C$, $^1J_{CH}$=173.5 Hz), 92.3 (CCl_3), 81.2 (C-4$_C$), 80.2 (C-3$_C$), 76.7 (C-2$_C$), 75.5 (C_{Bn}), 75.1 (C-4$_B$), 73.7 (C_{Bn}), 73.5 (C-3$_B$), 68.9 (C-6$_B$), 67.8 (CH_{2All}), 67.6 (C-5$_C$), 67.0 (C-5$_B$), 55.6 (C-2$_B$), 55.4 (CH_{3PMB}), 17.9 (C-6$_C$). HRMS (ESI$^+$): *m*/*z* 830.1845 (calcd for $C_{39}H_{44}Cl_3NO_{11}Na$ [M+Na]$^+$: *m*/*z* 830.1877).

4.15. Allyl (2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→3)-(4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-galacto-pyranosyl)-(1→2)-4-*O*-benzyl-3-*O*-*para*-methoxybenzyl-α-L-rhamnopyranoside (21)

A mixture of acceptor **14** (100 mg, 0.12 mmol), donor[30] **20** (73 mg, 0.16 mmol, 1.2 equiv), and powdered MS 4 Å (200 mg) in anhyd Tol (1.2 mL) was stirred at rt under an Ar atmosphere for 1 h. The reaction mixture was cooled to −10 °C, then TMSOTf (2 μL, 12 μmol, 0.1 equiv) was added. After 20 min, a TLC control (Tol/EtOAc 9:1) showed the absence of both donor (R_f 0.32) and acceptor (R_f 0.15) and the presence of a new major product (R_f 0.26). The reaction was quenched with Et_3N, filtered, and concentrated. The residue was purified by flash chromatography (Tol/acetone 99:1 to 95:5) to give trisaccharide **21** (102 mg, 72%), as a white foam. The condensation product had $[\alpha]^{25}_D$ +3 (*c* 1.0). ^{1}H NMR ($CDCl_3$), δ 7.61–7.18 (m, 12H, H_{Ar}), 7.17 (d_{po}, 1H, $J_{NH,2}$=6.8 Hz, NH), 6.85 (d, 2H, *J*=8.6 Hz, H_{ArPMB}), 5.87 (m, 1H, CH=), 5.60 (s, 1H, CHPh), 5.38 (d, 1H, H-4$_A$), 5.30 (d, 1H, $J_{1,2}$=8.4 Hz, H-1$_B$), 5.28–5.20 (m, 2H, =CH_{2All}, H-2$_A$), 5.16 (m, 1H, J_{cis}=10.4 Hz, J_{gem}=1.4 Hz, =CH_{2All}), 4.96 (dd_{po}, 1H, $J_{2,3}$=10.4 Hz, $J_{3,4}$=3.3 Hz, H-3$_A$), 4.93–4.86 (m, 2H, H_{Bn}, H-1$_A$), 4.86 (d, 1H, $J_{1,2}$=1.5 Hz, H-1$_C$), 4.66 (dd, 1H, $J_{2,3}$=11.2 Hz, $J_{3,4}$=3.2 Hz, H-3$_B$), 4.65 (d, 1H, *J*=12.0 Hz, H_{Bn}), 4.61 (d, 1H, *J*=12.1 Hz, H_{Bn}), 4.57 (d, 1H, *J*=10.9 Hz, H_{Bn}), 4.31 (d, 1H, H-4$_B$), 4.27 (d_{po}, 1H, $J_{6a,6b}$=11.9 Hz, H-6a$_B$), 4.24 (dd_{po}, 1H, $J_{5,6a}$=6.9 Hz, $J_{6a,6b}$=11.3 Hz, H-6a$_A$), 4.15 (dd_{po}, 1H, $J_{5,6b}$=6.0 Hz, H-6b$_A$), 4.11 (m_o, 1H, H_{All}), 4.07 (d_o, 1H, H-6b$_B$), 4.04 (dd, 1H, $J_{2,3}$=2.8 Hz, H-2$_C$), 3.95–3.83 (m, 4H, H_{All}, H-5$_A$, H-2$_B$, H-3$_C$), 3.81 (s, 3H, CH_{3PMB}), 3.70 (dq, 1H, $J_{4,5}$=9.6 Hz, $J_{5,6}$=6.1 Hz, H-5$_C$), 3.46 (pt, 1H, $J_{3,4}$=9.4 Hz, H-4$_C$), 3.33 (br s, 1H, H-5$_B$), 2.18–1.96 (4s, 12H, CH_{3Ac}), 1.30 (d, 3H, H-6$_C$). ^{13}C NMR ($CDCl_3$), δ 170.3, 170.2, 170.1, 169.2 (4C, CO_{Ac}), 161.7 (NHCO), 159.6 (C_{IVPMB}), 138.6, 137.8 (2C, C_{IVAr}), 134.0 (CH=$_{All}$), 130.8 (C_{IVAr}), 129.6–126.1 (12C, C_{Ar}), 116.7 (=CH_{2All}), 113.9 (2C, C_{ArPMB}), 100.7 (C-1$_A$, $^1J_{CH}$=163.6 Hz), 100.4 (CHPh), 99.0 (C-1$_B$, $^1J_{CH}$=162.4 Hz), 98.8 (C-1$_C$, $^1J_{CH}$=173.4 Hz), 92.7 (CCl_3), 80.7 (C-4$_C$), 79.3 (C-3$_C$), 76.1 (C-4$_B$), 75.5 (C_{Bn}), 74.3 (C-2$_C$), 73.2 (C-3$_B$), 72.0 (C_{Bn}), 71.1 (C-5$_A$), 70.9 (C-3$_A$), 69.0 (C-6$_B$), 68.9 (C-2$_A$), 67.9 (C-5$_C$), 67.7 (CH_{2All}), 67.2 (C-4$_A$), 66.5 (C-5$_B$), 61.4 (C-6$_A$), 55.5 (C-2$_B$), 55.3 (CH_{3PMB}), 20.9, 20.8, 20.7, 20.4 (4C, C_{Ac}), 18.1 (C-6$_C$). HRMS (ESI$^+$): *m*/*z* 1160.2833 (calcd for $C_{53}H_{62}Cl_3NO_{20}Na$ [M+Na]$^+$: *m*/*z* 1160.2828).

4.16. Allyl (2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→3)-(4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-galacto-pyranosyl)-(1→2)-3-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranoside (22)

4.16.1. Route 1. Water (1.3 mL) and CAN (733 mg, 1.33 mmol, 4.0 equiv) were added to a solution of the fully protected **21** (380 mg, 0.33 mmol) in MeCN (13.4 mL) and the reaction mixture was stirred for 30 min at rt. A TLC control (Tol/EtOAc 6:4) indicated the complete disappearance of the starting material (R_f 0.56) and the presence of a major more polar product (R_f 0.26). The reaction was quenched with satd aq $NaHCO_3$. The reaction mixture was diluted with water and extracted three times with DCM. The combined extracts were washed with brine, dried by passing through a phase separator filter, and condensed to dryness. The crude oil was dissolved in pyridine (16.7 mL), excess acetic anhydride (3.16 mL) and DMAP (41 mg, 0.33 mmol, 1.0 equiv) were added at rt and the reaction mixture was stirred for 2 h at this temperature. At this time, a TLC control (Tol/EtOAc 6:4) showed the conversion of the intermediate alcohol into a less polar product (R_f 0.48). Volatiles were evaporated and co-evaporated three times with Tol. The residue was purified by flash chromatography (Tol/EtOAc 8:2 to 75:25) to give pentaacetate **22** (290 mg, 82%) as a white foam.

4.16.2. Route 2. A mixture of acceptor **14** (895 mg, 1.11 mmol), donor **20** (708 mg, 1.44 mmol, 1.3 equiv), and powdered MS 4 Å (1.8 g) in anhyd Tol (11.1 mL) was stirred at rt under an Ar atmosphere for 1 h. The reaction mixture was cooled to −10 °C, and TMSOTf (10 μL, 55 μmol, 0.05 equiv) was added. After 20 min, a TLC control (Tol/EtOAc 9:1) showed the absence of both donor (R_f 0.32) and acceptor (R_f 0.15) and the presence of a new major product (R_f 0.26). The reaction was quenched with Et_3N, and the reaction mixture was filtered and concentrated to dryness. The residue was purified by flash chromatography (Tol/EtOAc 98:2 to 9:1) to give slightly contaminated trisaccharide **21** as a white foam. This contaminated product was dissolved in MeCN (37 mL). Water (3.8 mL) and CAN (2.43 g, 4.42 mmol, 4.0 equiv) were added. The reaction mixture was stirred for 30 min, at which time a TLC control (Tol/EtOAc 6:4) showed the complete disappearance of the starting material (R_f 0.56) and the presence of a major more polar product (R_f 0.26). The reaction was quenched with satd aq $NaHCO_3$. The reaction mixture was diluted with water and extracted three times with DCM. The combined extracts were washed with brine, dried by passing through a phase separator filter, and condensed to dryness. The crude oil was dissolved in pyridine (58 mL), excess acetic anhydride (3.12 mL) and DMAP (135 mg, 1.11 mmol, 1.0 equiv) were added at rt and the reaction mixture was stirred for 2 h. At this time, a TLC control (Tol/EtOAc 6:4) showed the conversion of the intermediate alcohol into a less polar product (R_f 0.48). Volatiles were evaporated and co-evaporated three times with Tol. The residue was purified by flash chromatography (Tol/EtOAc 8:2 to 65:35) to give pentaacetate **22** (870 mg, 74%, three steps) as a white foam. Pentaacetate **22** had $[\alpha]^{25}_D$ +14 (*c* 1.0). ^{1}H NMR ($CDCl_3$), δ 7.60–7.15 (m, 11H, 10H_{Ar}, NH), 5.91 (m, 1H, CH=$_{All}$), 5.63 (s, 1H, CHPh), 5.37 (d, 1H, H-4$_A$), 5.34–5.16 (m, 5H, H-1$_B$, H-2$_A$, H-3$_C$, 2=CH_{2All}), 5.01 (d, 1H, $J_{1,2}$=7.9 Hz, H-1$_A$), 4.95 (dd, 1H, $J_{2,3}$=10.3 Hz, $J_{3,4}$=3.2 Hz, H-3$_A$), 4.91 (d, 1H, $J_{1,2}$=1.6 Hz, H-1$_C$), 4.75 (dd, 1H, $J_{2,3}$=11.4 Hz, $J_{3,4}$=3.3 Hz, H-3$_B$), 4.69 (d, 1H, *J*=11.2 Hz, H_{Bn}), 4.59 (d, 1H, H_{Bn}), 4.38 (d, 1H, H-4$_B$), 4.29 (d, 1H, $J_{6a,6b}$=12.7 Hz, H-6a$_B$), 4.27-4.22 (m, 2H, H-6a$_A$, H-2$_C$), 4.18–4.07 (m, 3H, H_{All}, H-6b$_B$, H-6b$_A$),

3.99 (m, 1H, H_{All}), 3.86–3.77 (m, 3H, H-5_A, H-5_C, H-2_B), 3.54 (pt, 1H, $J_{3,4}$=$J_{4,5}$=9.6 Hz, H-4_C), 3.47 (br s, 1H, H-5_B), 2.20–1.98 (5s, 15H, H_{Ac}), 1.33 (d, 3H, $J_{5,6}$=6.2 Hz, H-6_C). ^{13}C NMR ($CDCl_3$), δ 171.0, 170.5, 170.2, 170.0, 169.1 (5C, CO_{Ac}), 161.6 (NHCO), 138.3, 137.8 (2C, C_{IVAr}), 133.9 (CH=$_{All}$), 129.7–125.9 (10C, C_{Ar}), 117.1 (=CH_{2All}), 100.4 (CHPh), 100.3 (C-1_A), 98.9 (C-1_B), 98.8 (C-1_C), 92.7 (CCl_3), 79.5 (C-4_C), 76.4 (C-4_B), 75.2 (C_{Bn}), 75.0 (C-2_C), 73.6 (C-3_C), 72.3 (C-3_B), 71.3 (C-5_A), 71.0 (C-3_A), 69.1 (C-6_B), 69.0 (C-2_A), 68.0 (CH_{2All}), 67.2 (C-5_C), 67.1 (C-4_A), 66.6 (C-5_B), 61.5 (C-6_A), 55.7 (C-2_B), 21.2, 20.9, 20.8, 20.7, 20.5 (5C, C_{Ac}), 18.0 (C-6_C). HRMS (ESI$^+$): *m*/*z* 1082.2361 (calcd for $C_{47}H_{56}Cl_3NO_{20}Na$ [M+Na]$^+$: *m*/*z* 1082.2358).

4.17. Allyl β-D-galactopyranosyl-(1→3)-(4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-galactopyranosyl)-(1→2)-3-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranoside (23)

A solution of trisaccharide **22** (179 mg, 0.17 mmol) in anhyd MeOH (10 mL) was treated by 0.5 M methanolic NaOMe (51 μL, 25 μmol, 0.15 equiv) at 0 °C. The mixture was stirred under an Ar atmosphere at this temperature for 2.5 h. Follow up by TLC (DCM/MeOH, 9:1) showed the conversion of the starting material (R_f 0.97) into a major more polar product (R_f 0.35), the reaction mixture was neutralized with Dowex-H$^+$ resin. The suspension was filtered and volatiles were evaporated. The residue was purified by flash chromatography (DCM/MeOH 98:2 to 9:1) to give first tetraol **23** (105 mg, 70%) as a white foam. Pentaol **24** (20 mg, 14%) was isolated as the second eluting product, resulting from over trans-esterification. Tetraol **23** had $[\alpha]^{25}_D$ +17 (*c* 1.0, MeOH). ^{1}H NMR (MeOD), δ 7.58–7.52 (m, 2H, H_{Ar}), 7.40–7.24 (m, 8H, H_{Ar}), 5.95 (m, 1H, CH=$_{All}$), 5.63 (s, 1H, CHPh), 5.32 (m, 1H, J_{trans}=17.1 Hz, J_{gem}=1.5 Hz, =CH_{2All}), 5.22 (dd$_{po}$, 1H, $J_{2,3}$=3.4 Hz, $J_{3,4}$=9.6 Hz, H-3_C), 5.19 (m$_{po}$, 1H, J_{cis}=10.5 Hz, =CH_{2All}), 5.05 (d, 1H, $J_{1,2}$=1.6 Hz, H-1_C), 4.94 (d, 1H, $J_{1,2}$=8.2 Hz, H-1_B), 4.65 (br s, 2H, H_{Bn}), 4.49 (d, 1H, $J_{3,4}$=3.3 Hz, H-4_B), 4.42 (dd$_{po}$, 1H, $J_{2,3}$=10.8 Hz, H-3_B), 4.43 (d$_{po}$, 1H, $J_{1,2}$=7.7 Hz, H-1_A), 4.22–4.15 (m, 3H, H-6a$_B$, H-6b$_B$, H_{All}), 4.14 (dd, 1H, H-2_C), 4.11–4.00 (m, 2H, H-2_B, H_{All}), 3.84–3.72 (m, 4H, H-6a$_A$, H-6b$_A$, H-4_A, H-5_C), 3.61 (br s, 1H, H-5_B), 3.60 (pt$_{po}$, 1H, $J_{4,5}$=9.2 Hz, H-4_C), 3.56 (dd, 1H, H-2_A), 3.52 (pt, 1H, H-5_A), 3.42 (dd, 1H, $J_{2,3}$=9.8 Hz, $J_{3,4}$=3.4 Hz, H-3_A), 2.09 (s, 3H, CH_{3Ac}), 1.29 (d, 3H, $J_{5,6}$=6.2 Hz, H-6_C). ^{13}C NMR (MeOD), δ 171.2 (CO_{Ac}), 162.6 (NHCO), 138.5, 138.3 (2C, C_{IVAr}), 133.9 (CH=$_{All}$), 129.6–126.3 (10C, C_{Ar}), 116.0 (=CH_{2All}), 104.7 (C-1_A), 100.9 (CHPh), 100.7 (C-1_B), 98.7 (C-1_C), 92.8 (CCl_3), 79.4 (C-4_C), 75.9 (C-4_B), 75.8 (C-2_C), 75.7 (C-5_A), 74.9 (C_{Bn}), 74.4 (C-3_B), 73.3, 73.2 (2C, C-3_C, C-3_A), 71.0 (C-2_A), 69.0 (C-4_A), 68.7 (C-6_B), 67.9 (C-5_C), 67.7 (CH_{2All}), 66.6 (C-5_B), 61.3 (C-6_A), 54.5 (C-2_B), 20.1 (CH_{3Ac}), 16.8 (C-6_C). HRMS (ESI$^+$): *m*/*z* 914.1931 (calcd for $C_{39}H_{48}Cl_3NO_{16}Na$ [M+Na]$^+$: *m*/*z* 914.1937).

4.18. Allyl β-D-galactopyranosyl-(1→3)-(4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-galactopyranosyl)-(1→2)-4-*O*-benzyl-α-L-rhamnopyranoside (24)

A solution of trisaccharide **22** (1.07 g, 1.01 mmol) in anhyd MeOH (15 mL) was treated with 0.5 M methanolic NaOMe (1.0 mL, 0.50 mmol, 0.5 equiv) at rt. The mixture was stirred at this temperature under an Ar atmosphere for 2 h. Follow up by TLC (DCM/MeOH, 9:1) showed the conversion of the starting material (R_f 0.97) into a major more polar product (R_f 0.32), the reaction mixture was neutralized with Dowex-H$^+$ resin. The suspension was filtered and volatiles were evaporated. The residue was purified by flash chromatography (DCM/MeOH 92:8 to 85:15) to give pentaol **24** (786 mg, 92%) as a white foam. Pentaol **24** had $[\alpha]^{25}_D$ +8 (*c* 1.0). ^{1}H NMR (MeOD), δ 7.58–7.55 (m, 2H, H_{Ar}), 7.41–7.22 (m, 8H, H_{Ar}), 5.94 (m, 1H, CH=$_{All}$), 5.63 (s, 1H, CHPh), 5.30 (m, 1H, J_{trans}=17.3 Hz, J_{gem}=1.6 Hz, =CH_{2All}), 5.18 (m, 1H, J_{cis}=10.5 Hz, =CH_{2All}), 5.09 (d, 1H, $J_{1,2}$=8.0 Hz, H-1_B), 5.01 (d, 1H, $J_{1,2}$=1.6 Hz, H-1_C), 4.92 (d, 1H, *J*=11.2 Hz, H_{Bn}), 4.61 (d, 1H, H_{Bn}), 4.49 (d, 1H, $J_{3,4}$=3.2 Hz, H-4_B), 4.44 (d, 1H, $J_{1,2}$=7.6 Hz, H-1_A), 4.31 (dd, 1H, $J_{2,3}$=11.0 Hz, H-3_B), 4.27–4.13 (m, 4H, H-6a$_B$, H-6b$_B$, H-2_B, H_{All}), 4.03–3.97 (m, 2H, H_{All}, H-2_C), 3.96 (dd$_{po}$, 1H, $J_{2,3}$=3.3 Hz, $J_{3,4}$=9.3 Hz, H-3_C), 3.82 (dd$_{po}$, 1H, $J_{5,6a}$=7.2 Hz, $J_{6a,6b}$=11.4 Hz, H-6a$_A$), 3.81 (dd$_o$, 1H, $J_{4,5}$=0.8 Hz, H-4_A), 3.76 (dd, 1H, $J_{5,6b}$=4.7 Hz, H-6b$_A$), 3.64 (m$_o$, 1H, $J_{4,5}$=9.5 Hz, $J_{5,6}$=6.2 Hz, H-5_C), 3.64 (br s$_o$, 1H, H-5_B), 3.56 (dd$_{po}$, 1H, $J_{2,3}$=9.8 Hz, H-2_A), 3.53 (ddd$_o$, 1H, H-5_A), 3.43 (dd$_{po}$, 1H, $J_{3,4}$=3.2 Hz, H-3_A), 3.42 (pt$_{po}$, 1H, H-4_C), 1.25 (d, 3H, H-6_C). ^{13}C NMR (MeOD), δ 163.0 (NHCO), 138.8, 138.3 (2C, C_{IVAr}), 134.1 (CH=$_{All}$), 128.6–126.1 (10C, C_{Ar}), 115.8 (=CH_{2All}), 104.8 (C-1_A), 101.5 (C-1_B), 101.0 (CHPh), 98.7 (C-1_C), 92.8 (CCl_3), 81.8 (C-4_C), 78.5 (C-2_C), 75.9 (C-4_B), 75.7 (2C, C-3_B, C-5_A), 75.0 (C_{Bn}), 73.2 (C-3_A), 71.1 (C-3_C), 71.0 (C-2_A), 69.0 (C-4_A), 68.8 (C-6_B), 67.6 (2C, C-5_C, CH_{2All}), 66.8 (C-5_B), 61.4 (C-6_A), 54.1 (C-2_B), 16.9 (C-6_C). HRMS (ESI$^+$): *m*/*z* 872.1804 (calcd for $C_{37}H_{46}Cl_3NO_{15}Na$ [M+Na]$^+$: *m*/*z* 872.1830).

4.19. Allyl β-D-galactopyranosyluronic acid-(1→3)-(4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-galactopyranos-yl)-(1→2)-3-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranoside (25)

To a solution of tetraol **23** (100 mg, 112 μmol) in MeCN/0.67 M phosphate buffer (1:1, 2.6 mL) were added successively $NaClO_2$ (16 mg, 0.22 mmol, 2.0 equiv), TEMPO (5.2 mg, 34 μmol, 0.3 equiv), and a commercially available NaOCl solution (available chlorine 4%, 22 μL, 11 μmol, 0.1 equiv), resulting in a brown coloration of the reaction mixture. The reaction mixture was stirred at 45 °C for 24 h, while more NaOCl (22 μL, 11 μmol, 0.1 equiv) was added after 5 h, 7 h, and 10 h. A TLC control (DCM/MeOH 8:2+a drop of water+a drop of AcOH) indicated the total conversion of the starting **23** (R_f 0.73) into a more polar product (R_f 0.20). The reaction was quenched by addition of few drops of EtOH and volatiles were evaporated. The residue was suspended in MeOH, triturated, and filtered. The filtrate was concentrated and the residue was purified by flash chromatography (DCM/MeOH/H_2O/AcOH 425:75:10:4 to 400:80:10:4) to give uronic acid **25** (92 mg, 90%) as a white solid, following evaporation and repeated co-evaporations with MeOH and Tol. The oxidation product **25** had $[\alpha]^{25}_D$ +7 (*c* 1.0). ^{1}H NMR (MeOD), δ 7.62–7.54 (m, 2H, H_{Ar}), 7.42–7.24 (m, 8H, H_{Ar}), 5.96 (m, 1H, CH=$_{All}$), 5.72 (s, 1H, CHPh), 5.32 (m, 1H, J_{trans}=17.3 Hz, J_{gem}=1.5 Hz, =CH_{2All}), 5.22 (dd$_{po}$, 1H, $J_{2,3}$=3.2 Hz, $J_{3,4}$=9.8 Hz, H-3_C), 5.19 (m$_{po}$, 1H, =CH_{2All}), 5.07 (d, 1H, $J_{1,2}$=1.5 Hz, H-1_C), 4.85 (d, 1H, $J_{1,2}$=8.8 Hz, H-1_B), 4.66 (d, 1H, $J_{3,4}$=3.1 Hz, H-4_B), 4.64 (br s, 2H, H_{Bn}), 4.45 (d$_{po}$, 1H, $J_{1,2}$=7.7 Hz, H-1_A), 4.43 (dd$_{po}$, 1H, $J_{2,3}$=11.0 Hz, H-3_B), 4.23–4.16 (m, 4H, H-6a$_B$, H-6b$_B$, H-2_B, H_{All}), 4.14 (d, 1H, $J_{3,4}$=3.2 Hz, H-4_A), 4.13 (dd, 1H, H-2_C), 4.04 (m, 1H, H_{All}), 3.88 (s, 1H, H-5_A), 3.76 (dq, 1H, $J_{4,5}$=9.4 Hz, $J_{5,6}$=6.2 Hz, H-5_C), 3.63 (br s, 1H, H-5_B), 3.60 (pt$_{po}$, 1H, H-4_C), 3.57 (dd, 1H, H-2_A), 3.42 (dd, 1H, $J_{2,3}$=9.6 Hz, H-3_A), 2.08 (s, 3H, CH_{3Ac}), 1.29 (d, 3H, H-6_C). ^{13}C RMN (MeOD), δ 173.8 (C-6_A), 171.1 (CO_{Ac}), 162.7 (NHCO), 138.5, 138.3 (2C, C_{IVAr}), 133.9 (CH=$_{All}$), 128.6–126.4 (10C, C_{Ar}), 116.0 (=CH_{2All}), 104.0 (C-1_A), 101.1 (C-1_B), 100.9 (CHPh), 98.7 (C-1_C), 92.8 (CCl_3), 79.4 (C-4_C), 76.1 (C-5_A), 76.0 (C-2_C), 75.5 (C-4_B), 74.9 (C_{Bn}), 74.0 (C-3_B), 73.3, 73.2 (2C, C-3_C, C-3_A), 70.7 (C-2_A), 70.5 (C-4_A), 68.7 (C-6_B), 67.9 (C-5_C), 67.7 (CH_{2All}), 66.6 (C-5_B), 54.3 (C-2_B), 20.1 (CH_{3Ac}), 16.8 (C-6_C). HRMS (ESI$^+$): *m*/*z* 928.1711 (calcd for $C_{39}H_{46}Cl_3NO_{17}Na$ [M+Na]$^+$: *m*/*z* 928.1729).

4.20. Allyl β-D-galactopyranosyluronic acid-(1→3)-(4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-galactopyranos-yl)-(1→2)-4-*O*-benzyl-α-L-rhamnopyranoside (26)

To a solution of pentaol **24** (250 mg, 0.112 mmol) in MeCN/0.67 M phosphate buffer (1:1, 7.0 mL) were added $NaClO_2$ (43 mg, 0.59 mmol, 2.0 equiv), TEMPO (14 mg, 88 μmol, 0.3 equiv), and

a commercially available NaOCl solution (available chlorine 4%, 69 μL, 0.029 mmol, 0.1 equiv), causing a brown coloration. The reaction mixture was stirred at 45 °C for 24 h, while more NaOCl (44 μL, 11 μmol, 0.1 equiv) was added after 5 h, 6 h, and 10 h. A TLC control (DCM/MeOH 8:2+a drop of water+a drop of AcOH) showed the total conversion of the starting material (R_f 0.73) into a more polar product (R_f 0.15). The reaction was quenched by adding few drops of EtOH and volatiles were evaporated. The residue was suspended in MeOH, triturated, and filtered. The filtrate was concentrated and the residue was purified by flash chromatography (DCM/MeOH/H_2O/AcOH 425:75:10:4 to 400:80:10:4) to give uronic acid **26** (218 mg, 86%) as a white solid, following evaporation and repeated co-evaporation with MeOH and Tol. The oxidation product **26** had $[\alpha]^{25}_D$ +4 (*c* 1.0). ^{1}H NMR (MeOD), δ 7.62–7.57 (m, 2H, H_{Ar}), 7.43–7.25 (m, 8H, H_{Ar}), 5.94 (m, 1H, CH=$_{All}$), 5.72 (s, 1H, CHPh), 5.30 (m, 1H, J_{trans}=17.3 Hz, J_{gem}=1.5 Hz, =CH_{2All}), 5.18 (m, 1H, J_{cis}=10.4 Hz, =CH_{2All}), 5.04 (d, 1H, $J_{1,2}$=7.7 Hz, H-1_B), 5.02 (d, 1H, $J_{1,2}$=1.3 Hz, H-1_C), 4.92 (d, 1H, *J*=11.2 Hz, H_{Bn}), 4.66 (d, 1H, $J_{3,4}$=1.7 Hz, H-4_B), 4.61 (d, 1H, H_{Bn}), 4.46 (d, 1H, $J_{1,2}$=7.6 Hz, H-1_A), 4.37–4.28 (m, 2H, H-2_B, H-3_B), 4.26–4.12 (m, 4H, H-$6a_B$, H-$6b_B$, H_{All}, H-4_A), 4.04–3.98 (m, 2H, H-2_C, H_{All}), 3.96 (dd_{po}, 1H, $J_{2,3}$=3.3 Hz, $J_{3,4}$=9.3 Hz, H-3_C), 3.90 (s, 1H, H-5_A), 3.66 (br s_o, 1H, H-5_B), 3.64 (dq_{po}, 1H, $J_{4,5}$=9.5 Hz, $J_{5,6}$=6.2 Hz, H-5_C), 3.56 (dd, 1H, H-2_A), 3.47 (dd, 1H, $J_{2,3}$=9.7 Hz, $J_{3,4}$=3.3 Hz, H-3_A), 3.60 (pt_{po}, 1H, H-4_C), 1.25 (d, 3H, H-6_C). ^{13}C NMR (MeOD), δ 174.1 (C-6_A), 163.1 (NHCO), 138.7, 138.3 (2C, C_{IVAr}), 134.1 (CH=$_{All}$), 128.7–126.4 (10C, C_{Ar}), 115.8 (=CH_{2All}), 104.1 (C-1_A), 101.7 (C-1_B), 101.0 (CHPh), 98.7 (C-1_C), 92.8 (CCl_3), 81.7 (C-4_C), 78.7 (C-2_C), 76.1 (C-5_A), 75.5 (C-3_B), 75.2 (C-4_B), 75.0 (C_{Bn}), 73.3 (C-3_A), 71.1 (C-4_A), 70.7 (C-3_C), 70.4 (C-2_A), 68.8 (C-6_B), 67.6 (2C, C-5_C, CH_{2All}), 66.8 (C-5_B), 54.0 (C-2_B), 16.9 (C-6_C). HRMS (ESI$^+$): *m*/*z* 886.1591 (calcd for $C_{37}H_{44}Cl_3NO_{16}Na$ [M+Na]$^+$: *m*/*z* 886.1624).

4.21. Propyl β-D-galactopyranosyl-(1→3)-(2-acetamido-deoxy-β-D-galactopyranosyl)-(1→2)-3-*O*-acetyl-α-L-rhamnopyranoside (27) and propyl β-D-galactopyranosyl-(1→3)-(2-acetamido-deoxy-β-D-galactopyranosyl)-(1→2)-4-*O*-acetyl-α-L-rhamno-pyranoside (28)

A solution of trisaccharide **23** (152 mg, 170 μmol) in MeOH (10 mL) was passed through a 10% Pd/C cartridge (CatCart® 30) using an H-Cube™ continuous flow hydrogenation system ('full H_2' mode, 30 °C, 1 mL min flow rate) until MS analysis of the crude reaction mixture indicated the presence of essentially two compounds, with molecular weights corresponding to that of the target trisaccharide **27** and of the *N*-chloroacetyl analog. Et_3N (71 μL, 0.51 mmol, 3 equiv) was added and the reaction mixture was passed through the same cartridge using the same parameters. As the system did not evolve according to MS follow up, the pressure was set up to 10 bar. Additional runs through the same cartridge allowed full conversion as indicated by MS analysis. Purification of the crude material by RP-MPLC (C18 2x20 cm, linear gradient of MeOH/H_2O 100:0 to 70:30, 50 min at a flow rate of 10 mL min^{-1}) gave a 5:1 mixture of trisaccharides **27** and **28** (76 mg, 73%) as a white solid following repeated freeze-drying. The separation of the two regioisomers was successful when eluting the material (70 mg) from a C18 column (3.1×30 cm, 215 nm, 0–80% linear gradient of MeCN/0.08% aq TFA 80:20 in 0.08% aq TFA over 60 min, 20 mL min^{-1}), which provided first compound **27** (38.5 mg), then regioisomer **28** (4.5 mg). The 3-*O*-acetyl trisaccharide **27** had $[\alpha]^{25}_D$ +13 (*c* 1.0, water). ^{1}H NMR (D_2O), δ 5.03 (dd, 1H, $J_{1,2}$=3.0 Hz, $J_{1,2}$=10.0 Hz, H-3_C), 4.96 (br s, 1H, H-1_C), 4.49 (d, 1H, $J_{1,2}$=8.1 Hz, H-1_B), 4.47 (d, 1H, $J_{1,2}$=7.7 Hz, H-1_A), 4.15 (d, 1H, $J_{3,4}$=2.6 Hz, H-4_B), 4.11 (dd, 1H, H-2_C), 3.98 (dd, 1H, $J_{2,3}$=10.9 Hz, H-2_B), 3.90 (dd_{po}, 1H, H-3_B), 3.89 (d_o, 1H, H-4_A), 3.80–3.71 (m, 5H, H-3_A, H-$6a_B$, H-$6b_B$, H-$6a_A$, H-$6b_A$), 3.70–3.57 (m, 4H, H-5_A, H-5_B, H-5_C, OCH_{2Pr}), 3.55–3.47 (m, 3H, H-2_A, OCH_{2Pr}, H-4_C), 2.18 (s, 3H, CH_{3Ac}), 2.06 (s, 3H, CH_{3NHAc}), 1.60 (m, 2H, CH_{2Pr}), 1.28 (d, 3H, $J_{5,6}$=6.2 Hz, H-6_C), 0.90 (t, 3H, *J*=7.4 Hz, CH_{3Pr}). ^{13}C NMR (D_2O), δ 177.2 (NHCO), 176.2 (CO_{Ac}), 107.3 (C-1_A), 105.3 (C-1_B), 101.2 (C-1_C), 81.8 (C-3_B), 79.1 (C-2_C), 77.7 (C-5_A), 77.1 (C-5_B), 75.6 (C-3_C), 75.1 (C-3_A), 73.3 (C-2_A), 72.8 (C-4_C), 72.3 (OCH_{2Pr}), 71.4, 71.3 (2C, C-5_C, C-4_A), 70.5 (C-4_B), 63.7, 63.5 (2C, C-6_B, C-6_A), 54.2 (C-2_B), 25.0 (CH_{3NHAc}), 24.6 (CH_{2Pr}), 23.2 (CH_{3Ac}), 19.2 (C-6_C), 12.5 (CH_{3Pr}). HRMS (ESI$^+$): *m*/*z* 636.2473 (calcd for $C_{25}H_{43}NO_{16}Na$ [M+Na]$^+$: *m*/*z* 636.2479). RP-HPLC (215 nm): t_R=12.5 min, RP-HPLC (215 nm, Aeris Peptide Phenomenex 3.6 μm C_{18} 100 Å 2.1×100 mm analytical column, 0–20% linear gradient of MeCN in 0.08% aq TFA over 20 min at 0.3 mL min^{-1}): t_R=14.9 min. The 4-*O*-acetyl analog **28** had ^{1}H NMR (D_2O, partial), δ 4.96 (br s_o, 1H, H-1_C), 4.79 (t_{po}, 1H, $J_{1,2}$=9.6 Hz, H-4_C), 4.73 (d_o, 1H, H-1_B), 4.43 (d, 1H, $J_{1,2}$=7.6 Hz, H-1_A), 4.15 (d_o, 1H, H-4_B), 4.08 (dd, 1H, H-2_C), 4.05–3.97 (m, 2H, H-3_C, H-2_B), 3.85 (m_{po}, 1H, H-5_C), 3.52 (dd_o, 1H, H-2_A), 2.13 (s, 3H, CH_{3Ac}), 2.02 (s, 3H, CH_{3NHAc}), 1.61–1.56 (m_o, 2H, CH_{2Pr}), 1.14 (d, 3H, $J_{5,6}$=6.2 Hz, H-6_C), 0.89 (t, 3H, *J*=7.4 Hz, CH_{3Pr}). HRMS (ESI$^+$): *m*/*z* 636.2474 (calcd for $C_{25}H_{43}NO_{16}Na$ [M+Na]$^+$: *m*/*z* 636.2479). RP-HPLC (215 nm): t_R=16.5 min, RP-HPLC (Aeris Peptide Phenomenex 3.6 μm C_{18} 100 Å 2.1×100 mm analytical column, 0–20% linear gradient of MeCN in 0.08% aq TFA over 20 min at 0.3 mL min^{-1}): t_R=21.0 min.

4.22. Propyl β-D-galactopyranosyl-(1→3)-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-(1→2)-α-L-rhamnopyranoside (29)

To a stirred solution of trisaccharide **24** (143 mg, 170 μmol) in MeOH (4.1 mL), was added 10% Pd/C (115 mg). The suspension was stirred under a hydrogen atmosphere for a day. Additional 10% Pd/C (50 mg) and Et_3N (117 μL, 0.84 mmol, 4.0 equiv) were added and the suspension was stirred under a hydrogen atmosphere for 2 days. After this time, MS analysis of the crude reaction mixture indicated the presence of a single compound, with a molecular weight corresponding to that of the target **29**. The reaction mixture was filtered over a pad of Celite®. Evaporation of the volatiles, freeze-drying, and purification of the crude material by RP-HPLC (215 nm, 0–30% linear gradient of MeCN in 0.08% aq TFA over 20 min, 5.5 mL min^{-1}) gave trisaccharide **29** (48.4 mg, 51%) as a white solid following repeated freeze-drying. Trisaccharide **29** had $[\alpha]^{25}_D$ −4 (*c* 1.0, water). ^{1}H NMR (D_2O), δ 4.85 (d, 1H, $J_{1,2}$=1.6 Hz, H-1_C), 4.57 (d, 1H, $J_{1,2}$=8.4 Hz, H-1_B), 4.33 (d, 1H, $J_{1,2}$=7.7 Hz, H-1_A), 4.05 (d, 1H, $J_{3,4}$=3.1 Hz, H-4_B), 3.93–3.87 (m, 2H, H-2_B, H-2_C), 3.78 (d_o, 1H, $J_{3,4}$=3.2 Hz, H-4_A), 3.77 (dd_{po}, 1H, $J_{2,3}$=11.0 Hz, H-3_B), 3.72–3.59 (m, 5H, H-3_C, H-$6a_B$, H-$6b_B$, H-$6a_A$, H-$6b_A$), 3.59–3.48 (m, 5H, H-5_A, H-5_B, H-5_C, H-3_A, OCH_{2Pr}), 3.41 (dd_{po}, 1H, $J_{2,3}$=10.1 Hz, H-2_A), 3.37 (dt_{po}, 1H, *J*=6.3 Hz, *J*=9.8 Hz, OCH_{2Pr}), 3.21 (pt, 1H, $J_{3,4}$=$J_{4,5}$=9.7 Hz, H-4_C), 1.92 (s, 3H, CH_{3NHAc}), 1.48 (m, 2H, CH_{2Pr}), 1.15 (d, 3H, $J_{5,6}$=6.2 Hz, H-6_C), 0.79 (t, 3H, *J*=7.4 Hz, CH_{3Pr}). ^{13}C NMR (D_2O), δ 177.5 (NHCO), 107.4 (C-1_A, $^1J_{CH}$=162.9 Hz), 105.3 (C-1_B, $^1J_{CH}$=163.7 Hz), 101.1 (C-1_C, $^1J_{CH}$=172.8 Hz), 82.1 (C-3_B), 81.0 (C-2_C), 77.5 (C-5_B*), 77.2 (C-5_A*), 75.0 (C-3_A), 74.9 (C-4_C), 73.1 (C-2_A), 72.6 (C-3_C), 72.2 (OCH_{2Pr}), 71.1 (2C, C-5_C, C-4_A), 70.5 (C-4_B), 63.5, 63.4 (2C, C-6_B, C-6_A), 54.1 (C-2_B), 24.9 (CH_{3NHAc}), 24.5 (CH_{2Pr}), 19.1 (C-6_C), 12.4 (CH_{3Pr}). HRMS (ESI$^+$): *m*/*z* 594.2369 (calcd for $C_{23}H_{41}NO_{15}Na$ [M+Na]$^+$: *m*/*z* 594.2374). RP-HPLC (215 nm): t_R=10.3 min.

4.23. Propyl β-D-galactopyranosyluronic acid-(1→3)-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-(1→2)-3-*O*-acetyl-α-L-rhamnopyranoside (30) and propyl β-D-galactopyranosyl-uronic acid-(1→3)-(2-acetamido-2-deoxy-β-D-galactopyranos-yl)-(1→2)-4-*O*-acetyl-α-L-rhamnopyranoside (31)

To a stirred solution of trisaccharide **25** (81 mg, 89 μmol) in THF/H_2O (2:1, 4.0 mL) was added 10% Pd/C (80 mg). The suspension was

stirred under a hydrogen atmosphere for a day. Additional 10% Pd/C (40 mg) and Et_3N (50 μL, 0.36 mmol, 4.0 equiv) were added and the suspension was stirred under a hydrogen atmosphere for 2 days. After this time, MS analysis of the crude reaction mixture indicated the presence of a single compound, with a molecular weight corresponding to that of the target trisaccharide. The reaction mixture was filtered over a pad of Celite®. Evaporation of the volatiles, freeze-drying, and purification of the crude material by semi-preparative RP-HPLC (215 nm, 0–35% linear gradient of MeCN in 0.08% aq TFA over 16 min, then 35–100% linear gradient of MeCN in 0.08% aq TFA over 4 min, 5.5 mL min^{-1}) gave by order of elution trisaccharides **30** (26.5 mg, 47%) and **31** (8.9 mg, 16%), both as a white solids, following extensive freeze-drying. The 3_C-*O*-acetyl trisaccharide **30** had $[\alpha]^{25}_D$ −9 (*c* 0.7, water). ^1H NMR (D_2O), δ 4.97 (dd, 1H, $J_{2,3}$=3.0 Hz, $J_{3,4}$=10.0 Hz, H-3_C), 4.90 (d, 1H, $J_{1,2}$=1.5 Hz, H-1_C), 4.46 (d, 1H, $J_{1,2}$=7.8 Hz, H-1_A), 4.43 (d, 1H, $J_{1,2}$=8.2 Hz, H-1_B), 4.29 (d, 1H, $J_{4,5}$=1.3 Hz, H-5_A), 4.18 (dd, 1H, $J_{3,4}$=3.4 Hz, H-4_A), 4.15 (d, 1H, $J_{3,4}$=2.8 Hz, H-4_B), 4.05 (dd, 1H, $J_{2,3}$=2.9 Hz, H-2_C), 3.92 (dd_{po}, 1H, $J_{2,3}$=10.9 Hz, H-2_B), 3.84 (dd, 1H, H-3_B), 3.74–3.66 (m, 3H, H-$6a_B$, H-$6b_B$, H-5_C), 3.64 (dd, 1H, $J_{2,3}$=10.0 Hz, H-3_A), 3.61–3.52 (m, 2H, H-5_B, OCH_{2Pr}), 3.48 (dd_{po}, 1H, H-2_A), 3.47–3.40 (m, 2H, H-4_C, OCH_{2Pr}), 2.11 (s, 3H, CH_{3Ac}), 1.99 (s, 3H, CH_{3NHAc}), 1.54 (m, 2H, *J*=7.0 Hz, CH_{2Pr}), 1.22 (d, 3H, $J_{5,6}$=6.2 Hz, H-6_C), 0.84 (t, 3H, *J*=7.4 Hz, CH_{3Pr}). ^{13}C NMR (D_2O), δ 177.1 (NHCO), 176.1 (CO_{Ac}), 174.6 (C-6_A), 106.7 (C-1_A, $^1J_{CH}$=161.9 Hz), 105.3 (C-1_B, $^1J_{CH}$=162.8 Hz), 101.2 (C-1_C, $^1J_{CH}$=175.3 Hz), 82.1 (C-3_B), 79.1 (C-2_C), 77.1 (C-5_B), 76.4 (C-5_A), 75.5 (C-3_C), 74.6 (C-3_A), 72.7 (C-4_C), 72.5 (C-2_A), 72.3(OCH_{2Pr}), 72.1 (C-4_A), 71.3 (C-5_C), 70.1 (C-4_B), 63.5 (C-6_B), 54.1 (C-2_B), 25.0 (CH_{3NHAc}), 24.6 (CH_{2Pr}), 23.1 (CH_{3NHAc}), 19.1 (C-6_C), 12.4 (CH_{3Pr}). HRMS (ESI^+): *m*/*z* 650.2252 (calcd for $C_{25}H_{41}NO_{17}Na$ $[M+Na]^+$: *m*/*z* 650.2272). RP-HPLC (215 nm): t_R=12.7 min.

The 4_C-*O*-acetyl analog **31** had $[\alpha]^{25}_D$ −25 (*c* 0.5, water). ^1H NMR (D_2O), δ 4.85 (d, 1H, $J_{1,2}$=1.6 Hz, H-1_C), 4.68 (pt, 1H, $J_{3,4}$=$J_{4,5}$=9.8 Hz, H-4_C), 4.60 (d, 1H, $J_{1,2}$=8.5 Hz, H-1_B), 4.37 (d, 1H, $J_{1,2}$=7.8 Hz, H-1_A), 4.21 (d, 1H, $J_{4,5}$=1.3 Hz, H-5_A), 4.12 (dd, 1H, $J_{3,4}$=3.4 Hz, H-4_A), 4.11 (d, 1H, $J_{3,4}$=2.8 Hz, H-4_B), 3.98 (dd, 1H, $J_{2,3}$=3.0 Hz, H-2_C), 3.95–3.89 (m, 2H, H-2_B, H-3_C), 3.78–3.61 (m, 4H, H-3_B, H-5_C, H-$6a_B$, H-$6b_B$), 3.60–3.49 (m, 3H, H-3_A, H-5_B, OCH_{2Pr}), 3.43 (dd, 1H, $J_{2,3}$=10.0 Hz, H-2_A), 3.38 (dt, 1H, *J*=6.4 Hz, *J*=9.7 Hz, OCH_{2Pr}), 2.02 (s, 3H, CH_{3Ac}), 1.90 (s, 3H, CH_{3NHAc}), 1.48 (m, 2H, CH_{2Pr}), 1.04 (d, 3H, $J_{5,6}$=6.2 Hz, H-6_C), 0.78 (t, 3H, *J*=7.4 Hz, CH_{3Pr}). ^{13}C NMR (D_2O), δ 177.6 (NHCO), 176.3 (CO_{Ac}), 174.8 (C-6_A), 106.9 (C-1_A, $^1J_{CH}$=161.9 Hz), 105.0 (C-1_B, $^1J_{CH}$=163.7 Hz), 101.3 (C-1_C, $^1J_{CH}$=174.4 Hz), 82.5 (C-3_B), 80.2 (C-2_C), 77.4 (C-5_B), 76.9 (C-4_C), 76.5 (C-5_A), 74.6 (C-3_A), 72.6 (C-2_A), 72.4 (OCH_{2Pr}), 72.2 (C-4_A), 71.0 (C-3_C), 70.4 (C-4_B), 69.1 (C-5_C), 63.6 (C-6_B), 54.2 (C-2_B), 24.9 (CH_{3NHAc}), 24.6 (CH_{2Pr}), 23.1 (CH_{3NHAc}), 19.1 (C-6_C), 12.4 (CH_{3Pr}). HRMS (ESI^+): *m*/*z* 650.2305 (calcd for $C_{25}H_{41}NO_{17}Na$ $[M+Na]^+$: *m*/*z* 650.2272). RP-HPLC (215 nm): t_R=16.4 min.

4.24. Propyl β-D-galactopyranosyluronic acid-(1→3)-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-(1→2)-α-L-rhamnopyranoside (32)

To a stirred solution of trisaccharide **26** (103 mg, 119 μmol) in MeOH (5.4 mL) was added 10% Pd/C (100 mg). The suspension was stirred under a hydrogen atmosphere for one day. Additional 10% Pd/C (50 mg) and Et_3N (83 μL, 0.59 mmol, 5.0 equiv) were added and the suspension was stirred under a hydrogen atmosphere for 2 days. After this time, MS analysis of the crude material indicated the presence of a single compound, with a molecular weight corresponding to that of the target **32**. The reaction mixture was filtered on a pad of Celite®. Evaporation of the volatiles, freeze-drying, and purification of the residue by semi-preparative RP-HPLC (215 nm, 0–30% linear gradient of MeCN in 0.08% aq TFA over 20 min, 5.5 mL min^{-1}) gave trisaccharide **32** (48.6 mg, 70%) as a white solid following repeated freeze-drying. Trisaccharide **32** had $[\alpha]^{25}_D$ −24 (*c* 0.9, water). ^1H NMR (D_2O), δ 4.85 (d, 1H, $J_{1,2}$=1.5 Hz, H-1_C), 4.57 (d, 1H, $J_{1,2}$=8.4 Hz, H-1_B), 4.38 (d, 1H, $J_{1,2}$=7.8 Hz, H-1_A), 4.25 (d, 1H, $J_{4,5}$=1.3 Hz, H-5_A), 4.14 (dd, 1H, $J_{3,4}$=3.4 Hz, H-4_A), 4.10 (d, 1H, $J_{3,4}$=3.1 Hz, H-4_B), 3.91 (dd_{po}, 1H, $J_{2,3}$=10.9 Hz, H-2_B), 3.89 (dd_{po}, 1H, $J_{2,3}$=3.2 Hz, H-2_C), 3.76 (dd, 1H, H-3_B), 3.70 (dd_{po}, 1H, $J_{3,4}$=9.8 Hz, H-3_C), 3.69–3.65 (m, 1H, H-$6a_B$), 3.63 (dd, 1H, $J_{5,6b}$=4.4 Hz, $J_{6a,6b}$=11.8 Hz, H-$6b_B$), 3.60–3.48 (m, 4H, H-3_A, H-5_C, H-5_B, OCH_{2Pr}), 3.43 (dd, 1H, $J_{2,3}$=10.0 Hz, H-2_A), 3.37 (dt, 1H, *J*=6.4 Hz, *J*=9.8 Hz, OCH_{2Pr}), 3.21 (pt, 1H, $J_{4,5}$=9.7 Hz, H-4_C), 1.91 (s, 3H, CH_{3NHAc}), 1.48 (m, 2H, CH_{2Pr}), 1.14 (d, 3H, $J_{5,6}$=6.2 Hz, H-6_C), 0.78 (t, 3H, *J*=7.4 Hz, CH_{3Pr}). ^{13}C NMR (D_2O), δ 177.5 (NHCO), 174.5 (C-6_A), 106.9 (C-1_A, $^1J_{CH}$=160.1 Hz), 105.3 (C-1_B, $^1J_{CH}$=162.5 Hz), 101.1 (C-1_C, $^1J_{CH}$=174.3 Hz), 82.5 (C-3_B), 81.1 (C-2_C), 77.3 (C-5_B), 76.3 (C-5_A), 74.9 (C-4_C), 74.5 (C-3_A), 72.6 (C-3_C), 72.4 (C-2_A), 72.2 (OCH_{2Pr}), 72.0 (C-4_A), 71.1 (C-5_C), 70.2 (C-4_B), 63.5 (C-6_B), 54.1 (C-2_B), 24.9 (CH_{3NHAc}), 24.5 (CH_{2Pr}), 19.1 (C-6_C), 12.4 (CH_{3Pr}). HRMS (ESI^+): *m*/*z* 608.2145 (calcd for $C_{23}H_{39}NO_{16}Na$ $[M+Na]^+$: *m*/*z* 608.2167). RP-HPLC (215 nm): t_R=10.5 min.

Acknowledgements

We thank C. Ganneau (UCB) for analytical RP-HPLC, Y.M. Coïc and F. Baleux (UCB) for LC–MS analysis, and F. Bonhomme (CNRS UMR 3523) for HRMS recording and NMR processing. This work was supported by grants from the Institut Pasteur (Fellowship to L.R.), the Ministère de l'Education Nationale, de la Recherche et de la Technologie (MENRT) (PhD fellowship to P.C.). The research leading to these results, including a fellowship to P.C., has received funding from the European Commission Seventh Framework Program [FP7/2007-2013] under Grant agreement n° 261472-STOPENTERICS.

Supplementary data

1D and 2D NMR spectra, including ^1H, ^{13}C, DEPT, COSY, and HSQC of all new compounds are provided. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.10.011.

References and notes

1. Levine, M. M. *Vaccine* **2006**, *24*, 3865–3873.
2. von Seidlein, L.; Kim, D. R.; Ali, M.; Lee, H.; Wang, X.; Thiem, V. D.; Canh do, G.; Chaicumpa, W.; Agtini, M. D.; Hossain, A.; Bhutta, Z. A.; Mason, C.; Sethabutr, O.; Talukder, K.; Nair, G. B.; Deen, J. L.; Kotloff, K.; Clemens, J. *PLoS Med.* **2006**, *3*, 1556–1569.
3. Kotloff, K. L.; Winickoff, J. P.; Ivanoff, B.; Clemens, J. D.; Swerdlow, D. L.; Sansonetti, P. J.; Adak, G. K.; Levine, M. M. *Bull. World Health Organ.* **1999**, *77*, 651–666.
4. Levine, M. M.; Kotloff, K. L.; Barry, E. M.; Pasetti, M. F.; Sztein, M. B. *Nat. Rev. Microbiol.* **2007**, *5*, 540–553.
5. Kweon, M. N. *Curr. Opin. Infect. Dis.* **2008**, *21*, 313–318.
6. Passwell, J. H.; Ashkenzi, S.; Banet-Levi, Y.; Ramon-Saraf, R.; Farzam, N.; Lerner-Geva, L.; Even-Nir, H.; Yerushalmi, B.; Chu, C. Y.; Shiloach, J.; Robbins, J. B.; Schneerson, R.; Grp, I. S. S. *Vaccine* **2010**, *28*, 2231–2235.
7. Noriega, F. R.; Liao, F. M.; Maneval, D. R.; Ren, S.; Formal, S. B.; Levine, M. M. *Infect. Immun.* **1999**, *67*, 782–788.
8. Kubler-Kielb, J.; Vinogradov, E.; Mocca, C.; Pozsgay, V.; Coxon, B.; Robbins, J. B.; Schneerson, R. *Carbohydr. Res.* **2010**, *345*, 1600–1608.
9. Phalipon, A.; Tanguy, M.; Grandjean, C.; Guerreiro, C.; Belot, F.; Cohen, D.; Sansonetti, P. J.; Mulard, L. A. *J. Immunol.* **2009**, *182*, 2241–2247.
10. Phalipon, A.; Costachel, C.; Grandjean, C.; Thuizat, A.; Guerreiro, C.; Tanguy, M.; Nato, F.; Vulliez-Le Normand, B.; Belot, F.; Wright, K.; Marcel-Peyre, V.; Sansonetti, P. J.; Mulard, L. A. *J. Immunol.* **2006**, *176*, 1686–1694.
11. Mulard, L.; Phalipon, A. In *Carbohydrate-based Vaccines*; Roy, R., Ed.; American Chemical Society: Washington DC, 2008; Vol. 989, pp 105–136.
12. Perepelov, A. V.; Shekht, M. E.; Liu, B.; Shevelev, S. D.; Ledov, V. A.; Senchenkova, S. N.; L'vov, V. L.; Shashkov, A. S.; Feng, L.; Aparin, P. G.; Wang, L.; Knirel, Y. A. *FEMS Immunol. Med. Microbiol.* **2012**, *66*, 201–210.
13. Hygge Blakeman, K.; Weintraub, A.; Widmalm, G. *Eur. J. Biochem.* **1998**, *251*, 534–537.

14. Chassagne, P.; Fontana, C.; Guerreiro, C.; Gauthier, C.; Phalipon, A.; Widmalm, G.; Mulard, L. A. *Eur. J. Org. Chem.* **2013**, 4085–4106.
15. Boutet, J.; Guerreiro, C.; Mulard, L. A. *J. Org. Chem.* **2009**, *74*, 2651–2670.
16. Enugala, R.; Carvalho, L. C. R.; Pires, M. J. D.; Marques, M. M. B. *Chem.—Asian J.* **2012**, *7*, 2482–2501.
17. Boutet, J.; Mulard, L. A. *Eur. J. Org. Chem.* **2008**, 5526–5542.
18. Gigg, R.; Payne, S.; Conant, R. *J. Carbohydr. Chem.* **1983**, *2*, 207–223.
19. Gurjar, M. K.; Mainkar, A. S. *Tetrahedron* **1992**, *48*, 6729–6738.
20. Matsui, H.; Furukawa, J.; Awano, T.; Nishi, N.; Sakairi, N. *Chem. Lett.* **2000**, 326–327.
21. Kajimoto, T.; Ishioka, Y.; Katoh, T.; Node, M. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5736–5739.
22. Collot, M.; Savreux, J.; Mallet, J. M. *Tetrahedron* **2008**, *64*, 1523–1535.
23. Bartek, J.; Muller, R.; Kosma, P. *Carbohydr. Res.* **1998**, *308*, 259–273.
24. Belot, F.; Jacquinet, J. C. *Carbohydr. Res.* **2000**, *325*, 93–106.
25. Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015–9020.
26. van den Bos, L. J.; Codee, J. D. C.; Litjens, R. E. J. N.; Dinkelaar, J.; Overkleeft, H. S.; van der Marel, G. A. *Eur. J. Org. Chem.* **2007**, 3963–3976.
27. Vogel, C.; Steffan, W.; Ott, A. Y.; Betaneli, V. I. *Carbohydr. Res.* **1992**, *237*, 115–129.
28. Wu, X. Y.; Cui, L. N.; Lipinski, T.; Bundle, D. R. *Chem.—Eur. J.* **2010**, *16*, 3476–3488.
29. Haller, M.; Boons, G. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 814–822.
30. Ren, T.; Liu, D. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1247–1250.
31. Dmitriev, B. A.; Nikolaev, A. V.; Shashkov, A. S.; Kochetkov, N. K. *Carbohydr. Res.* **1982**, *100*, 195–206.
32. Szurmai, Z.; Liptak, A. *Carbohydr. Res.* **1982**, *107*, 33–41.
33. Szurmai, Z.; Liptak, A.; Snatzke, G. *Carbohydr. Res.* **1990**, *200*, 201–208.
34. Lubineau, A.; Basset-Carpentier, K.; Auge, C. *Carbohydr. Res.* **1997**, *300*, 161–167.
35. Boutet, J.; Guerreiro, C.; Mulard, L. A. *Tetrahedron* **2008**, *64*, 10558–10572.
36. Zhao, M. Z.; Li, J.; Mano, E.; Song, Z. G.; Tschaen, D. M.; Grabowski, E. J. J.; Reider, P. J. *J. Org. Chem.* **1999**, *64*, 2564–2566.
37. Davis, N. J.; Flitsch, S. L. *Tetrahedron Lett.* **1993**, *34*, 1181–1184.
38. Anelli, P. L.; Biffi, C.; Montanari, F.; Quici, S. *J. Org. Chem.* **1987**, *52*, 2559–2562.
39. De Nooy, A. E. J.; Besemer, A. C.; van Bekkum, H. *Tetrahedron* **1995**, *51*, 8023–8032.
40. Hanessian, S.; Mascitti, V.; Lu, P. P.; Ishida, H. *Synthesis* **2002**, 1959–1968.
41. Vermaas, D. J.. US 6,310,200 B1; (NL), A. N. N. V., Ed., 2001.
42. Xie, J. *Eur. J. Org. Chem.* **2002**, 3411–3418.
43. Huang, L. J.; Teumelsan, N.; Huang, X. F. *Chem.—Eur. J.* **2006**, *12*, 5246–5252.
44. van den Bos, L. J.; Codee, J. D. C.; van der Toorn, J. C.; Boltje, T. J.; van Boom, J. H.; Overkleeft, H. S.; van der Marel, G. A. *Org. Lett.* **2004**, *6*, 2165–2168.
45. Paterson, I.; Florence, G. J.; Gerlach, K.; Scott, J. P.; Sereinig, N. *J. Am. Chem. Soc.* **2001**, *123*, 9535–9544.
46. Chappell, M. D.; Harris, C. R.; Kuduk, S. D.; Balog, A.; Wu, Z.; Zhang, F.; Lee, C. B.; Stachel, S. J.; Danishefsky, S. J.; Chou, T. C.; Guan, Y. *J. Org. Chem.* **2002**, *67*, 7730–7736.
47. Barbier, M.; Breton, T.; Servat, K.; Grand, E.; Kokoh, B.; Kovensky, J. *J. Carbohydr. Chem.* **2006**, *25*, 253–266.
48. Ohara, K.; Lin, C. C.; Yang, P. J.; Hung, W. T.; Yang, W. B.; Cheng, T. J. R.; Fang, J. M.; Wong, C. H. *J. Org. Chem.* **2013**, *78*, 6390–6411.
49. Roslund, M. U.; Aitio, O.; Warna, J.; Maaheimo, H.; Murzin, D. Y.; Leino, R. *J. Am. Chem. Soc.* **2008**, *130*, 8769–8772.