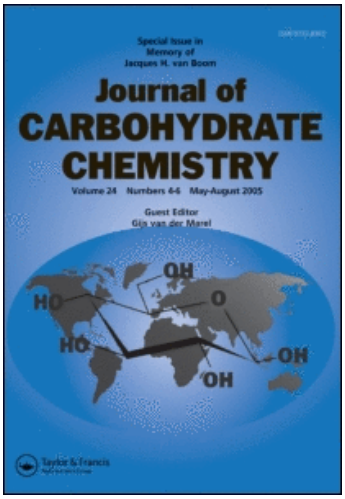

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Rhizobial Saccharides Part 3. Unexpected α-Selective Glycosylation During Synthesis of Pyruvated Tetrasaccharide Fragments Related to Exopolysaccharides of *Rhizobium Leguminosarum*

Thomas Ziegler[a]; Elisabeth Eckhardt[a]; Dirk Keller[a]
[a] Institute of Organic Chemistry, University of Cologne, Koeln, Germany

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RHIZOBIAL SACCHARIDES PART 3. UNEXPECTED α-SELECTIVE GLYCOSYLATION DURING SYNTHESIS OF PYRUVATED TETRASACCHARIDE FRAGMENTS RELATED TO EXOPOLYSACCHARIDES OF *RHIZOBIUM LEGUMINOSARUM*

Thomas Ziegler,* Elisabeth Eckhardt and Dirk Keller

Institute of Organic Chemistry, University of Cologne
Greinstraße 4, D-50939 Koeln, Germany

Dedicated to Professor Hans Paulsen on the occasion of his 75th birthday

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ABSTRACT

The two diastereomeric tetrasaccharide allyl glycosides 3,4-Py-β-D-Gal$_p$-(1→6)-β-D-Gal$_p$-(1→6)-β-D-Glc$_p$-(1→6)-α-D-Gal$_p$-(1→O-allyl) related to the exopolysaccharide of *Rhizobium leguminosarum* biovar *phaseoli* 127 K 87 having an (*R*)- and (*S*)-configurated pyruvic acid acetal, respectively at positions 3 and 4 of the galactopyranosyl residue of the non-reducing end, were prepared from two disaccharide blocks. The fully benzoylated diastereomeric disaccharide donors having the structure 3,4-Py-β-D-Gal$_p$-(1→6)-α-D-Gal$_p$-(1→X) with leaving groups X = bromide and trichloroacetimidate were synthesised by a stepwise approach from benzoylated 3,4-pyruvated galactosyl donors (chlorides, bromides, trichloroacetimidates) and benzyl and phenyl 1-thio- 2,3,4-tri-*O*-benzoyl-β-D-galactopyranosides, respectively. The disaccharide acceptors having the structure β-D-Glc$_p$-(1→6)-α-D-Gal$_p$-(1→O-allyl) were obtained by coupling allyl 2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside and its 6-*O*-trimethylsilyl ether with suitably protected glucosyl chlorides or fluorides. The coupling of the pyruvated disaccharide trichloroacetimidates with the disaccharide acceptors afforded the β-(1→6)-linked tetrasaccharides whereas the coupling of the pyruvated disaccharide bromide resulted in an α-(1→6)-selective glycosylation. The anomeric selectivity was attributed to a double diastereoselection caused by the configuration of the pyruvic acid acetal. Deblocking

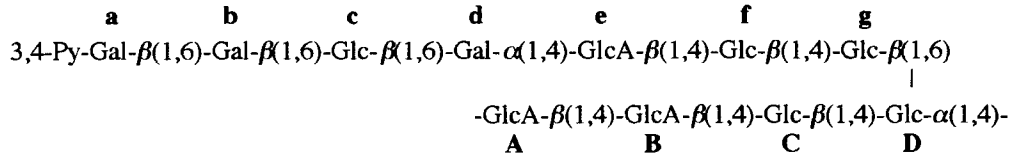


Figure 1. Repeating unit of the exopolysaccharide (EPS) of *Rhizobium leguminosarum* biovar *phaseoli* 127 K 87; residues **ABCD** = linear main chain, **a-g** = pyruvated side chain; Gal = D-galactopyranosyl, Glc = D-glucopyranosyl, GlcA = D-glucuronic acid, Py = pyruvic acid acetal.

of the three tetrasaccharides provided the corresponding tetrasaccharide allyl glycosides which are suitable for preparation of glycoconjugates.

INTRODUCTION

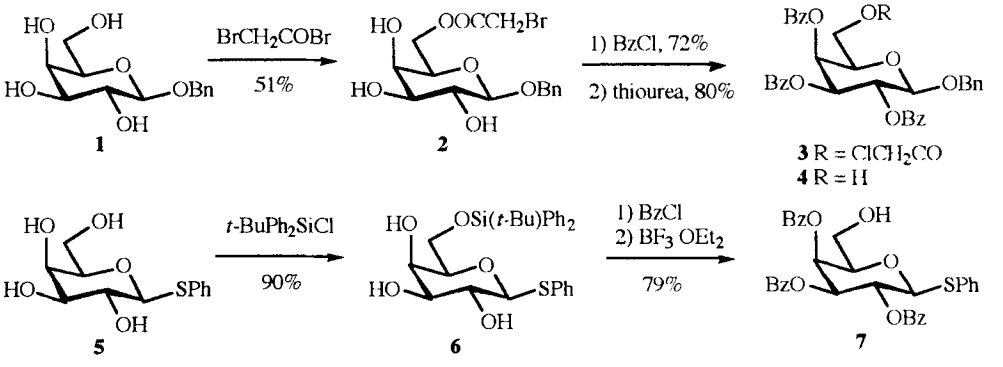
Ongoing efforts in our laboratory toward the efficient synthesis of pyruvated oligosaccharides related to exopolysaccharides (EPS) of *Rhizobium* bacteria[1] turned our interest to *Rhizobium leguminosarum* biovar *phaseoli* 127 K 87. The repeating unit of the EPS of the latter organism is represented by an undecasaccharide[2] (Fig. 1). The linear main chain **ABCD** of this repeating unit [β-D-GlcA$_p$-(1→4)-β-D-GlcA$_p$-(1→4)-β-D-Glc$_p$-(1→4)-α-D-Glc$_p$-(1→4)-] has been identified as a common motif of several EPS biovars of *R. leguminosarum*. Depending on the biovar, side chains of different length are β-glycosidically bound to position 6 of the α-D-Glc$_p$-residue (*i.e.*, site **D** of the main chain). All these side chains have one or two pyruvated sugar residues in common. For example, 4,6-pyruvated β-D-galactopyranosyl residues at the non-reducing end of the side chain are found in EPS of biovars *trifolii* 843,[3] *viciae*,[4] and *phaseoli* 127 K 44.[2] Furthermore, 4,6-pyruvated β-D-galactopyranosyl residues are also present in biovars *phaseoli* CIAT 899[5] and AHU 1133,[6] *trifolii* AHU 1134[6] and *lupini* KLU,[6] however, bound to another main chain. Similarly, 4,6-pyruvated β-D-glucopyranosyl residues are found in biovar *phaseoli* 127 K 36[2] (with the main chain **ABCD** as in Fig. 1) and in EPS I of *R. meliloti* YE-27[7] (with a different main chain). In this respect, the EPS of *R. leguminosarum* biovar *phaseoli* 127 K 87, as described here, is quite unique among pyruvated rhizobial EPS since it contains a 3,4-pyruvated β-D-galactopyranosyl residue **a** at the non-reducing end of its side chain **a-g** (Fig. 1).

The distinct biological function of the EPS of *Rhizobium* bacteria is not yet fully understood. For example, the EPS of these symbiotic bacteria are thought to be essential determinants and signal factors for the specific interaction of these organisms with their host plants (leguminoses).[8-11] However, much controversy is found in the literature about the in-

volvement of EPS in plant infections by *Rhizobium* bacteria.[10,12] Therefore, synthetic oligosaccharide fragments related to the EPS of *Rhizobium* bacteria are useful tools for studying these cell-cell interactions. Here, we describe the synthesis of tetrasaccharide fragments **a-d** (Fig. 1) of the pyruvated side chain of the EPS of *R. leguminosarum* biovar *phaseoli* 127 K 87.

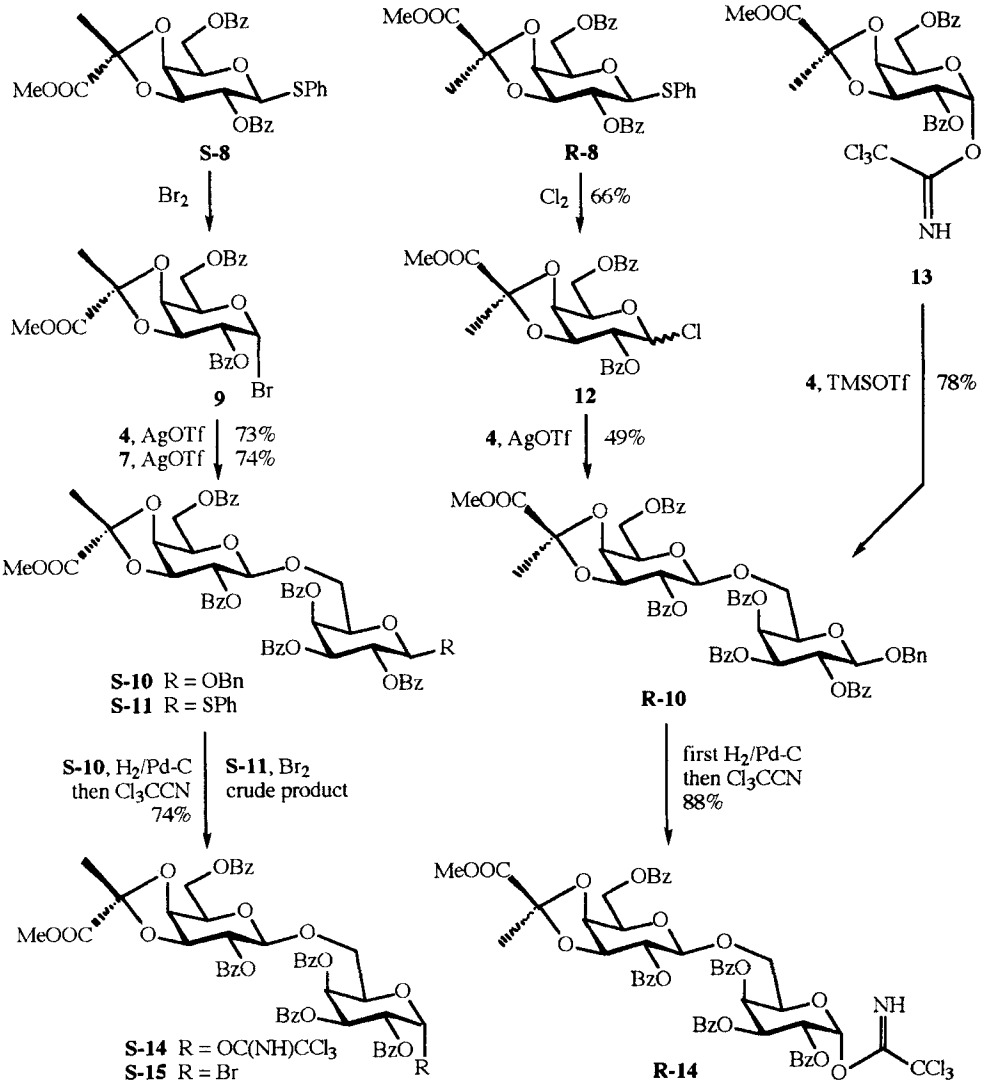
RESULTS AND DISCUSSION

Unfortunately, the configuration of the 3,4-linked pyruvic acid acetal carbon of the *R. leguminosarum* EPS has not been determined and NMR data which could help to do this are not available.[2,13] From 4,6-pyruvated pyranosyl residues it is known that the carboxylic function always adopts a thermodynamically favoured axial position [*i.e.* (*S*)-configuration of the acetal carbon in 4,6-pyruvated D-gluco- and mannopyranosyl residues and (*R*)-configuration in D-galactopyranosyl residues, respectively). This stable configuration is realised without any exception in all naturally occurring oligosaccharide structures of this type.[14-16] An argument by analogy is, however, not possible for 3,4-pyruvated D-galactopyranosyl residues. Although, merely all known 3,4-pyruvic acid acetals of D-galactopyranosyl residues in naturally occurring saccharides exhibit an *endo*-oriented methyl group,[14,17,18] the pyruvated galactan from the snail *Pomacea lineata* has undoubtly an *exo*-oriented methyl group of the acetal function.[19] Therefore, it could not be deduced for the title *R. leguminosarum* EPS which configuration of the pyruvic acid acetal carbon would be most likely and thus, both diastereomers have to be prepared.

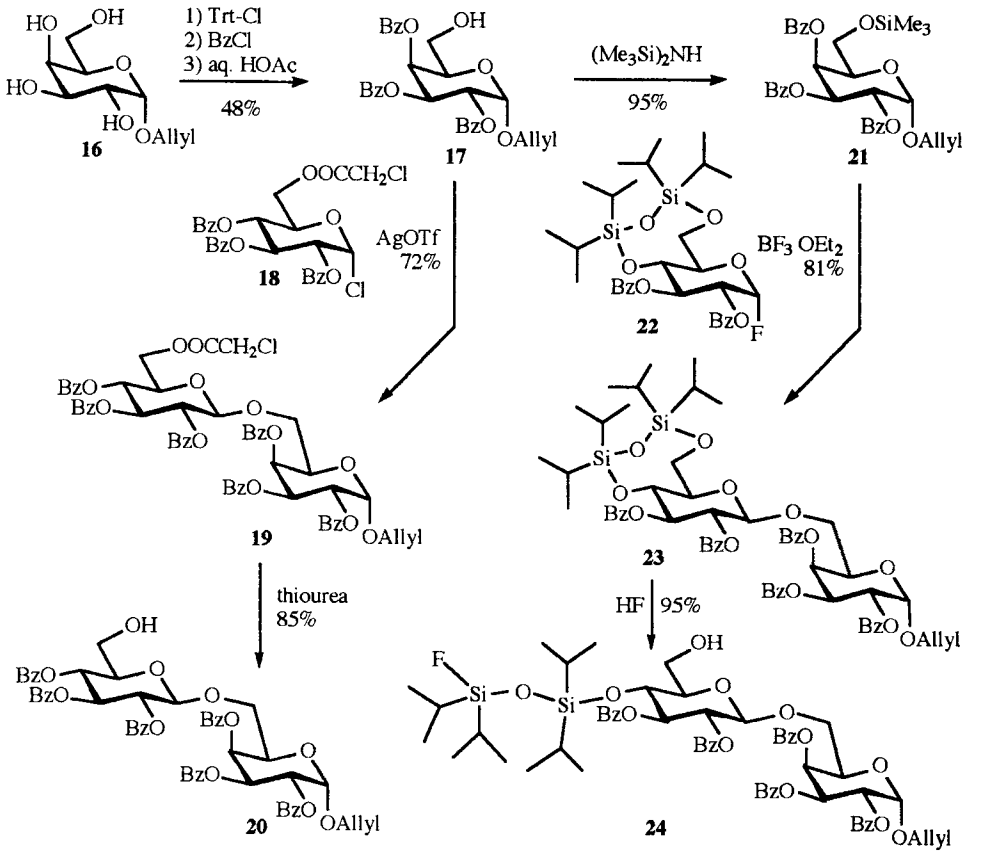


For the synthesis of the two diastereomeric tetrasaccharides related to the sequence **abcd** (Fig. 1) a blockwise approach was chosen that uses disaccharide donors related to the sequence **ab** and disaccharide allyl glycosides related to sequence **cd** as acceptors. As donors,

trichloroacetimidates (prepared from the corresponding benzyl and allyl glycosides) as well as halogenoses (prepared from the corresponding 1-thioglycosides) were planned to be used. Therefore, benzyl β-D-galactopyranoside[20] **1** was first selectively bromoacetylated[21] at position 6, to give crystalline intermediate **2** (51%). Treatment of the latter with a mixture of pyridine and benzoyl chloride in acetonitrile[21] afforded the chloroacetylated galactoside **3** (72%) that was finally converted with thiourea into crystalline acceptor **4** (80%). Similarly, phenyl 1-thio-β-D-galactopyranoside[22] **5** was regioselectively *t*-butyl diphenylsilylated[23] to afford first **6** (90%) which was subsequently benzoylated and desilylated[24] to give the acceptor **7** in 79% overall yield.



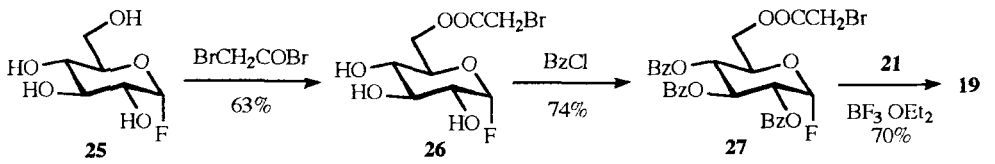
The pyruvated monosaccharide donors were obtained from the easily accessible[17] galactopyranosides **S-8**, **R-8**, respectively. The pyruvated phenyl 1-thio-β-D-galactopyranoside **S-8** was converted with bromine into the corresponding crude α-bromide **9** and coupled with silver trifluoromethanesulfonate (AgOTf) with acceptors **4** and **7** to give the disaccharides **S-10** (73%) and **S-11** (74%), respectively. Similarly, **R-8** was first converted with chlorine into the chlorides **12** isolated as a 1:1 mixture of anomers in 66% yield. However, coupling of the latter with acceptor **4** under promotion of AgOTf afforded disaccharide **R-10** in poor 49% yield. Therefore, a more efficient approach starting from the previously described[17] galactosyl imidate **13** was chosen. Trimethylsilyl trifluoromethanesulfonate (TMSOTf) catalysed condensation of **13** with **4** afforded **R-10** in 78% yield. To this end, the benzyl aglycon of disaccharides **S-10** and **R-10** were cleaved off and the intermediates were treated with trichloroacetonitrile to give the desired imidates **S-14** (74%) and **R-14** (88%), respectively. In addition, disaccharide 1-thioglycoside **S-11** was used for the preparation of crude bromide **S-15**.



For the synthesis of the acceptor blocks related to fragments **cd** (Fig. 1) three approaches were chosen and compared with each other: a "classical" approach using the chloroacetyl group[21] as temporary protection of position 6 (for residue **c**); an approach using the glycodesilylation protocol;[25] a combination of the aforementioned approaches. First, allyl α-D-galactopyranoside[26] **16** was conventionally converted by subsequent tritylation, benzoylation and detritylation into allyl 2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside **17** (48%). Next, **17** was coupled under promotion of AgOTf with 2,3,4-tri-*O*-benzoyl-6-*O*-choroacetyl-α-D-glucopyranosyl chloride[21] **18**, to afford the β-(1→6)-linked disaccharide **19** in 72% yield. Dechloroacetylation of the latter with thiourea then gave the disaccharide allyl glycoside **20** (85%).

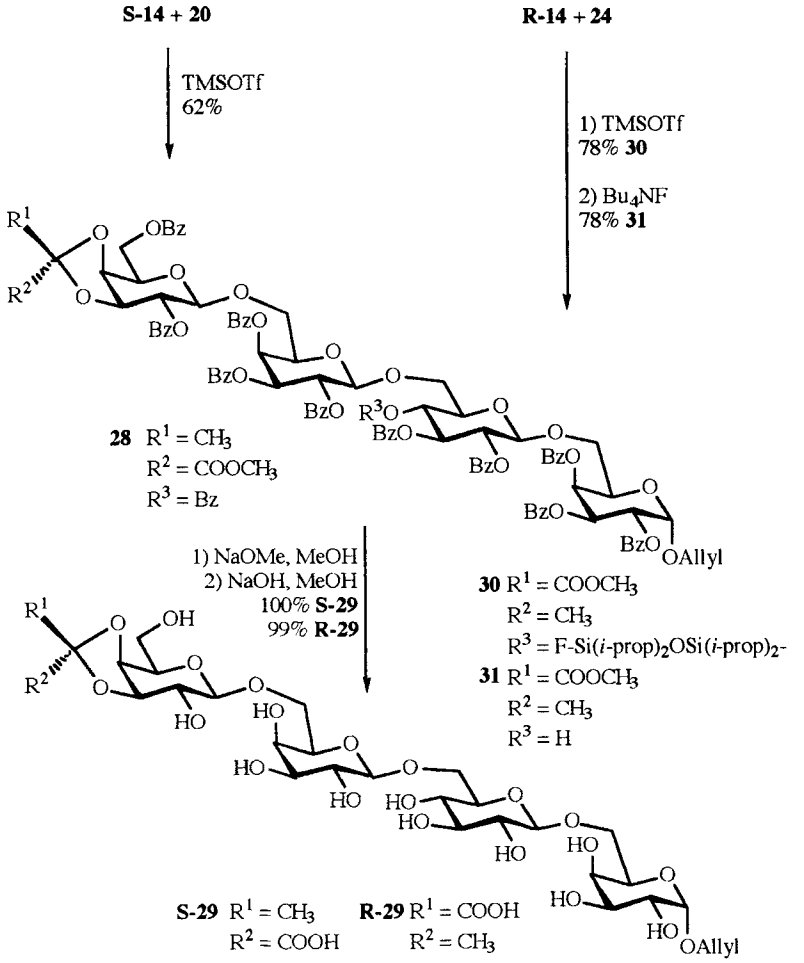
For the realisation of the glycodesilylation protocol, compound **17** was first trimethylsilylated at position 6 with hexamethyldisilazane, to give galactoside **21** (95%). Trimethylsilyl ethers are known to condense with glycosyl fluorides under Lewis acid catalysis, to give the corresponding glycosides with concomitant elimination of fluorotrimethylsilane.[27] Thus, treatment of **21** with 2,3-di-*O*-benzoyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-glucopyranosyl fluoride[25c] **22** and a catalytic amount of boron trifluoride diethyl ether complex resulted in a clean reaction and afforded disaccharide **23** in 81% yield. As was observed previously,[25c] no self condensation occurred with **22**. Finally, hydrofluoric acid was regioselectively[25c] added to the siloxane function of disaccharide **22**, to give the acceptor block **24** (95%) that allows the elongation of the sugar chain at position 6' with the above described donors **14** and **15**. Compared to the "classical" approach *via* chloride **18**, the latter approach *via* fluoride **22** appears to be more convenient from a practical standpoint and gives the desired acceptor in higher overall yield.

The third approach leading to disaccharide acceptor **20** used a combination of the two alternative procedures described above. α-D-Glucopyranosyl fluoride **25** was first bromoacetylated[21] to give intermediate **26** (63%) followed by benzoylation to afford donor **27** (74%). Lewis acid catalysed coupling of the latter with galactoside **21** then gave the chloroacetylated disaccharide **19** in 70% yield. Thus, this alternative does not provide any advantages with respect to the number of steps and overall yield compared to the glycodesilylation protocol using donor **22**.

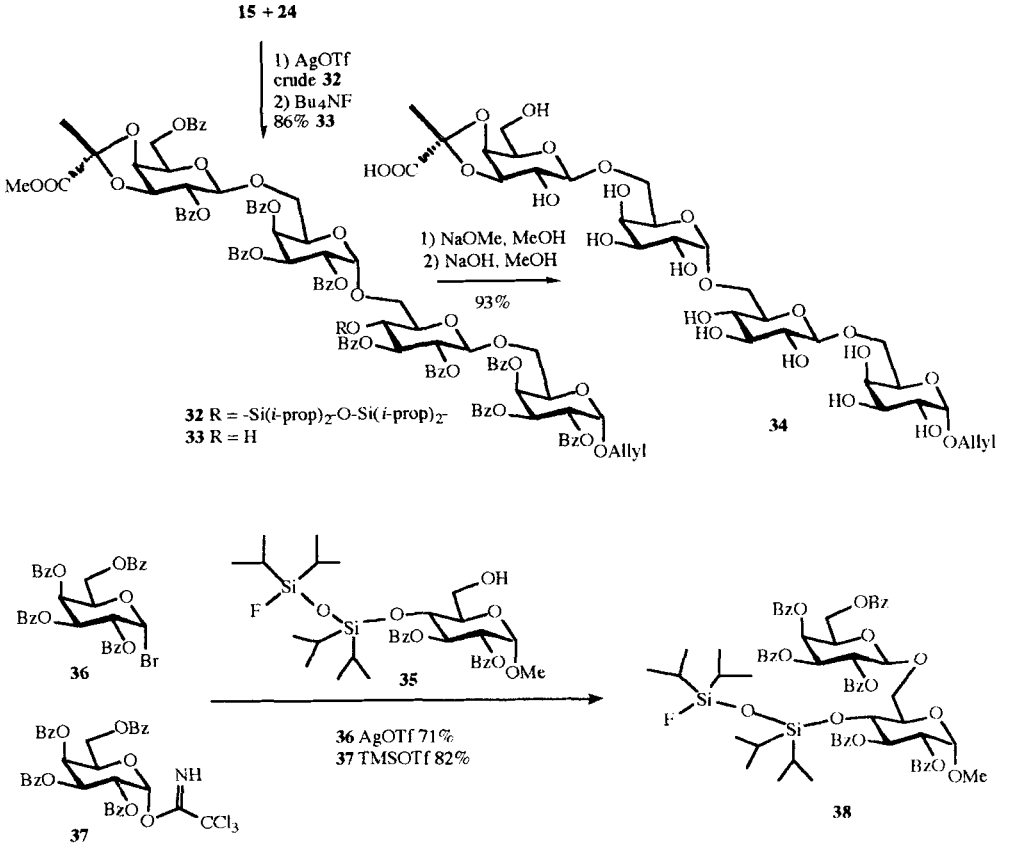


For the construction of the diastereomeric tetrasaccharides, the trichloroacetimidates **S-14** and **R-14** were coupled with the acceptors **20** and **24**, respectively. The TMSOTf cata-

lysed condensation of **S-14** with **20** proceeded smoothly although the resulting β-(1→6)-linked tetrasaccharide **28** could be isolated in moderate 62% yield only. This was due to some minor byproducts that were difficult to remove because they had similar mobilities as **28** during chromatographic purification of the crude reaction mixture. Final sequential deblocking of **28** (*i.e.*, Zemplén-debenzoylation and saponification of the methyl pyruvate acetal moiety) afforded **S-29** in quantitative yield. Similarly, **R-14** was condensed with acceptor block **24** to give crude tetrasaccharide **30**. Without purification of the intermediate, the siloxane residue was split off to afford **31** in 78% overall yield. The advantage of using acceptor **24** instead of **20** was evident from TLC inspection of the crude reaction mixture of the two couplings. No side products were formed in the second case. Final deblocking as described for **S-29** gave the tetrasaccharide **R-29** (99%).



Unexpectedly, when crude bromide **15** having an *endo*-oriented methyl group at the pyruvic acid acetal moiety (*i.e.*, (*S*)-configuration) was condensed with acceptor **24** under promotion of AgOTf followed by flouride catalysed desilylation of the intermediate **32**, solely the α-(1→6)-linked tetrasaccharide **33** (86%) was obtained. No trace of the expected β-(1→6)-linked saccharide could be detected on TLC of the crude reaction mixture. The α-linkage was evident from the carbon NMR spectra of the blocked compound that showed a chemical shift for the newly formed glycosidic bond at C-1" of 96.1 ppm for **33**. The β-linked tetrasaccharides **28** and **31** showed chemical shifts for the corresponding carbon of 100.2 and 100.7 ppm, respectively. In addition, deblocking of **33** resulted in tetrasaccharide **34** (93%) which gave a signal at 100.5 ppm for C-1" (typical for α-linked galactosyl residues) compared to 105.1 and 105.2 ppm for tetrasaccharides **29** (typical for β-linked galactosyl residues).



Since apart from the configuration of the pyruvate acetal carbon, the most significant differences between the β-selective coupling of **R-14** and **24** and the α-selective one between **15** and **24** were the applied donors (*i.e.*, imidate *vs.* bromide) and the glycosylation protocol, it was originally speculated that these differences could be responsible for the unexpected

anomeric selectivity in case of compound **33**. In order to justify if this is the case, more "simple" substrates were tested under identical conditions. Thus, the previously described[25c] glucoside **35** was chosen as the acceptor. It contained a 3-fluoro-1,1,3,3-tetraisopropyl-1,3-disiloxane-1-yl residue at position 4 (adjacent to the reacting OH-6) similar to the glucosyl residue in acceptor **24** and α-configuration similar to the galactosyl residue in **24**. However, coupling of **35** with benzobromogalactose **36** (AgOTf as the promotor) and 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl trichloroacetimidate **37** (TMSOTf as the catalyst), respectively gave exclusively the corresponding β-linked disaccharide **38** in 71% and 82% yield, respectively. Therefore, it appears to be likely that in fact the configuration of the pyruvate acetal at the distant galactosyl residue in **14** and **15** is involved in a rather subtle way in the anomeric outcome of the above described couplings. Similar unexpected α-selective galactosylations have been described for pyruvated[28] and non-pyruvated[29] galactosyl donors and have been attributed to a double diastereoselection during these glycosylations.

If such a double diastereoselection may be operative here as well has to be investigated in greater detail and further examples are under investigation (for example, condensation of copmounds **S-14** and **24**). Nevertheless, in addition to the diastereomeric tetrasaccharides **R-29** and **S-29**, the α-linked tetrasaccharide allyl glycoside **34** provides a useful probe for the investigation of the possible involvement of EPS in host specific infection mechanisms of *R. leguminosarum via* well established conjugation through its allyl group.[30]

EXPERIMENTAL

General Procedures. All glycosylations were performed with dried solvents under an atmosphere of Ar. Organic phases were dried with Na_2SO_4 and concentrated under reduced pressure at < 40 °C bath temperature. NMR Spectra were recorded at 25 °C (internal Me_4Si, δ = 0.00 ppm), using a Bruker AC 250 F spectrometer. Proton signals were assigned by first order analysis. Of the two magnetically nonequivalent geminal protons, the one resonating at lower field was designated as H^a and the one resonating at higher field H^b. TLC was performed on precoated plastic sheets, Polygram SIL G/UV_{254}, 40 X 80 mm (Macherey-Nagel). Spots were detected by UV light and by charring with 5% sulfuric acid in ethanol. Optical rotations were measured at 20 °C with a Perkin-Elmer automatic polarimeter, Model 241. Melting points were determined with a Büchi apparatus, Model SMP-20.

Benzyl 6-*O*-Bromoacetyl-β-D-galactopyranoside (2). A solution of bromoacetyl bromide (0.97 g, 4.8 mmol) in toluene (10 mL) was added dropwise during 15 min at -50 °C to a stirred solution of benzyl β-D-galactopyranoside[20] **1** (1.0 g, 3.7 mmol) and *sym*-collidine (0.63 g, 5.2 mmol) in DMF (50 mL). The mixture was gradually warmed during 0.5 h to room temperature, diluted with toluene (50 mL), filtered and the filtrate was concentrated. Chromatography (CH_2Cl_2/MeOH, 10:1) of the residue afforded **2** (0.74 g, 51%) as colourless

crystals: mp 176-178 °C (from EtOH/hexane); $[\alpha]_D$ +2.3° (*c* 0.5, MeOH); ^{13}C NMR δ (D_2O): 105.2 (C-1), 78.1, 76.3, 73.9, 73.0 (C-2,3,4,5), 71.7 (CH_2Ph), 63.9 (C-6), 27.6 (CH_2Br).

Anal. Calcd for $C_{15}H_{19}BrO_7$: C, 46.07; H, 4.90; Br 20.43. Found: C, 45.99; H, 5.03; Br, 20.70.

Benzyl 2,3,4-Tri-*O*-benzoyl-6-*O*-chloroacetyl-β-D-galactopyranoside (3). A freshly prepared solution of benzoyl chloride (1.12 g, 7.9 mmol) and pyridine (0.59 g, 7.5 mmol) in acetonitrile (10 mL) was added at once at room temperature to a solution of **2** (0.69 g, 1.76 mmol) in acetonitrile (10 mL) and the mixture was stirred for 1 h at 50 °C. The mixture was poured into H_2O and extracted with CH_2Cl_2. The combined extracts were subsequently washed with aqueous HCl and $NaHCO_3$ solution, dried and concentrated to afford crude **3** (0.83 g, 72%) as a colourless foam. The material appeared to be homogeneous on TLC and was used for the next step without further purification.

Benzyl 2,3,4-Tri-*O*-benzoyl-β-D-galactopyranoside (4). A solution of crude **3** (0.83 g, 1.26 mmol) and thiourea (0.23 g, 3.0 mmol) in MeOH (5 mL) was stirred for 4 h at 50 °C, cooled to room temperature, diluted with CH_2Cl_2 (50 mL), washed with H_2O, dried and concentrated. Chromatography (CCl_4/acetone, 5:1) of the residue afforded **4** (0.59 g, 80%) as colourless crystals: mp 72-74 °C (from ethyl acetate/hexane); $[\alpha]_D$ +163.3° (*c* 0.3, $CHCl_3$); ^1H NMR δ ($CDCl_3$): 5.92 (dd, 1 H, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 10.4 Hz, H-2), 5.81 (br.d, 1 H, $J_{3,4}$ = 3.4 Hz, $J_{4,5}$ < 1.0 Hz, H-4), 5.54 (dd, 1 H, H-3), 4.94 (d, 1 H, *J* = -12.6 Hz, CH_2Ph), 4.83 (d, 1 H, H-1), 4.75 (d, 1 H, CH_2Ph), 4.00 (br.t, 1 H, $J_{5,6a}$ = 6.7 Hz, $J_{5,6b}$ = 6.8 Hz, H-5), 3.85 (dd, 1 H, $J_{6a,6b}$ = -11.8 Hz, H-6a), 3.67 (dd, 1 H, H-6b); ^{13}C NMR δ ($CDCl_3$): 99.9 (C-1), 74.0, 71.8, 70.9, 68.9 (C-2,3,4,5), 69.9 (CH_2Ph), 60.6 (C-6).

Anal. Calcd for $C_{34}H_{30}O_9$: C, 70.09; H, 5.19. Found: C, 69.93; H, 5.10.

Phenyl 6-*O*-(*t*-Butyldiphenylsilyl)-1-thio-β-D-galactopyranoside (6). *t*-Butyldiphenyl chlorosilane (4.59 g, 16.7 mmol) was added dropwise at room temperature to a stirred solution of phenyl 1-thio-β-D-galactopyranoside[22] **5** (4.13 g, 15.2 mmol) and imidazole (2.27 g, 33.4 mmol) in DMF (40 mL). The mixture was stirred for 5.5 h, poured into H_2O and extracted with CH_2Cl_2. The combined extracts were washed with H_2O, dried and concentrated. Chromatography (CCl_4/acetone, 2:1) of the residue afforded **6** (7.00 g, 90%) as a colourless foam; $[\alpha]_D$ -19.1° (*c* 1.2, $CHCl_3$); ^{13}C NMR δ ($CDCl_3$): 88.7 (C-1), 78.5, 75.0, 69.8, 69.5 (C-2,3,4,5), 63.8 (C-6).

Anal. Calcd for $C_{28}H_{34}O_5SSi$: C, 65.85; H, 6.71; S, 6.28. Found: C, 65.88; H, 6.75; S, 6.17.

Phenyl 2,3,4-Tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (7). Benzoyl chloride (0.98 g, 7.0 mmol) was added dropwise at 0 °C to a stirred solution of **6** (0.7 g, 1.37 mmol) in pyridine (20 mL) and the mixture was stirred at room temperature for 10 h. H_2O was added dropwise with cooling in order to destroy the excess of benzoyl chloride. The mixture was

poured into H_2O and extracted with CH_2Cl_2. The combined extracts were subsequently washed with aqueous HCl and $NaHCO_3$ solution, dried and concentrated to give a colourless foam (1.13 g) which was dissolved in MeOH/CH_2Cl_2 (2:1, 100 mL). BF_3 diethyl ether complex (0.25 mL, 2.0 mmol) was added at room temperature to this solution and the mixture was stirred for 24 h. The mixture was diluted with CH_2Cl_2, washed with aqueous $NaHCO_3$ solution, dried and concentrated. Chromatography (CCl_4/acetone, 5:1) of the residue afforded **7** (0.63 g, 79%); identical in all physical properties to the previously described[31] compound.

2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*S*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl Bromide (9). Phenyl 2,6-di-*O*-benzoyl-3,4-*O*-[1-(*S*)-(methoxycarbonyl)ethylidene]-1-thio-β-D-galactopyranoside[17] **S-8** (amount for preparation of **S-10** and **S-11** see below) was dissolved in a solution of Br_2 (10 mol-equivalents) in CCl_4. The mixture was stirred at room temperature for 45 min, concentrated and kept in vacuo for 5 h to afford crude **9** which was used without further purification.

Benzyl {2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*S*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (S-10). AgOTf (256.9 mg, 0.5 mmol) was added at once at 0 °C to a stirred suspension of crude **9** (freshly prepared from 205.8 mg, 0.37 mmol **S-8**, as described above), *sym*-collidine (30.0 mg, 0.25 mmol), molecular sieves (3 A, 0.5 g) and **4** (291.3 mg, 0.5 mmol) in CH_2Cl_2 (15 mL). The mixture was stirred for 0.5 h, neutralised by addition of *sym*-collidine and filtered through a layer of celite. Concentration of the filtrate and chromatography (CCl_4/acetone, 10:1) of the residue afforded **S-10** (277.7 mg, 73%) as a colourless foam; $[\alpha]_D$ +80.8° (*c* 0.4, $CHCl_3$); ^1H NMR δ ($CDCl_3$): 5.78 (br.d, 1 H, $J_{3,4}$ = 3.4 Hz, $J_{4,5}$ < 1.0 Hz, H-4), 5.75 (dd, 1 H, $J_{1,2}$ = 7.9 Hz, $J_{2,3}$ = 10.4 Hz, H-2), 5.40 (dd, 1 H, H-3), 5.28 (br.d, 1 H, $J_{1',2'}$ = 7.5 Hz, $J_{2',3'}$ = 7.2 Hz, H-2'), 4.67 (d, 1 H, H-1), 4.65 (d, 1 H, H-1'), 4.62-4.50 (m, 3 H, H-6a,6a',6b'), 4.57 (dd, 1 H, $J_{3',4'}$ = 3.3 Hz, H-3'), 4.38 (br.d, 2 H, CH_2Ph), 4.18 (ddd, 1 H, $J_{4',5'}$ = 2.4 Hz, $J_{5',6a'}$ = 5.1 Hz, H-5'), 4.12-4.08 (m, 1 H, H-5), 4.10 (dd, 1 H, H-4'), 3.78 (dd, 1 H, $J_{6a,6b}$ = -12.2 Hz, H-6b), 3.72 (s, 3 H, OCH_3), 1.80 (s, 3 H, CH_3); ^{13}C NMR δ ($CDCl_3$): 106.4 (C_{acetal}), 100.5 (C-1), 99.1 (C-1'), 77.5 (C-3'), 75.3 (C-4'), 73.3, 73.1, 71.7, 70.5 (C-2,2',3,4), 70.1 (CH_2Ph), 69.7 (C-5), 68.9 (C-5'), 68.3 (C-6), 63.1 (C-6'), 52.5 (OCH_3), 22.9 (CH_3).

Anal. Calcd for $C_{58}H_{52}O_{18}$: C, 67.18; H, 5.05. Found: C, 66.98; H, 5.12.

Benzyl {2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*R*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (R-10). (a) Treatment of AgOTf (300.0 mg, 1.2 mmol), **12** (330.0 mg, 0.67 mmol, see below), *sym*-collidine (60.6 mg, 0.5 mmol), molecular sieves (3 A, 0.5 g) and **4** (316.5 mg, 0.54 mmol) in CH_2Cl_2 (7 mL) for 0.5 h at room temperature and work up as described for the preparation of **S-10** afforded **R-10** (272.6 mg, 49%) as a colourless foam; $[\alpha]_D$ +91.5° (*c* 0.2, $CHCl_3$); ^1H NMR δ ($CDCl_3$): 5.78 (br.d, 1 H, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ < 1.0 Hz, H-4), 5.73 (dd, 1 H, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 10.4 Hz, H-2), 5.39 (dd, 1 H, H-3), 5.53 (br.t, 1 H, $J_{1',2'}$ = 7.8 Hz, $J_{2',3'}$ = 7.7 Hz, H-2'), 4.70 (dd, 1 H,

$J_{5,6a}$ = 4.9 Hz, $J_{5,6b}$ = 5.7 Hz, H-6a), 4.61 (d, 1 H, H-1), 4.58-4.50 (m, 2 H, H-6a',6b'), 4.57 (dd, 1 H, $J_{3',4'}$ = 3.5 Hz, H-3'), 4.35 (br.d, 2 H, CH_2Ph), 4.17 (ddd, 1 H, $J_{4',5'}$ = 2.1 Hz, $J_{5',6a'}$ = 5.0 Hz, H-5'), 4.38-4.33 (m, 1 H, H-5), 4.11 (dd, 1 H, H-4'), 4.09 (d, 1 H, H-1'), 3.76 (dd, 1 H, $J_{6a,6b}$ = -11.5 Hz, H-6b), 3.92 (s, 3 H, OCH_3), 1.58 (s, 3 H, CH_3); ^{13}C NMR δ ($CDCl_3$): 106.7 (C_{acetal}), 100.7 (C-1), 99.2 (C-1'), 78.3 (C-3'), 74.4 (C-4'), 73.5, 73.3, 71.7, 70.9 (C-2,2',3,4), 70.1 (CH_2Ph), 69.7 (C-5), 69.0 (C-5'), 68.2 (C-6), 63.4 (C-6'), 53.1 (OCH_3), 23.3 (CH_3).

Anal. Calcd for $C_{58}H_{52}O_{18}$: C, 67.18; H, 5.05. Found: C, 66.91; H, 5.03.

(b) A solution of 2,6-di-*O*-benzoyl-3,4-*O*-[1-(*R*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl trichloroacetimidate[17] **13** (230.0 mg, 0.38 mmol) in CH_2Cl_2 (2 mL) was added with a syringe at -20 °C to a stirred solution of **4** (262.2 mg, 0.45 mmol) and TMSOTf (7 μL, 40 μmol) in CH_2Cl_2 (4.5 mL) and the solution was stirred for 0.5 h. Pyridine (2 drops) was added and the mixture was concentrated. Chromatography (CCl_4/acetone, 10:1) afforded **R-10** (310.0 mg, 78%).

Phenyl {2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*S*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-2,3,4-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (S-11). Treatment of AgOTf (0.64 g, 2.5 mmol), crude **9** (freshly prepared from 0.67 g, 1.19 mmol **S-8**, as described above), *sym*-collidine (97.0 mg, 0.8 mmol), molecular sieves (3 A, 1.5 g) and **7** (0.56 g, 0.95 mmol) in CH_2Cl_2 (20 mL) for 45 min. at room temperature and work up as described for the preparation of **S-10** afforded **S-11** (0.73 g, 74%) as a colourless foam; $[\alpha]_D$ +87.1° (*c* 0.4, $CHCl_3$); ^1H NMR δ ($CDCl_3$): 5.67 (br.t, 1 H, $J_{1,2}$ = 9.9 Hz, $J_{2,3}$ = 9.8 Hz, H-2), 5.21 (br.t, 1 H, $J_{1',2'}$ = 7.1 Hz, $J_{2',3'}$ = 6.0 Hz, H-2'), 4.89 (d, 1 H, H-1), 4.74 (d, 1 H, H-1'), 4.67-4.60 (m, 2 H, H-3,3'), 4.59 (dd, 2 H, H-6a,6a'), 4.48 (dd, 2 H, H-6b,6b'), 4.22-4.13 (m, 4 H, H-4,4',5,5'), 3.72 (s, 3 H, OCH_3), 1.80 (s, 3 H, CH_3); ^{13}C NMR δ ($CDCl_3$): 106.4 (C_{acetal}), 100.6 (C-1'), 85.2 (C-1), 77.1 (C-3'), 75.2 (C-4'), 73.0 (2 C, C-2,2'), 70.5 (C-3), 68.7 (2 C, C-4,5), 68.0 (C-6), 67.9 (C-5'), 63.2 (C-6'), 52.6 (OCH_3), 22.8 (CH_3).

Anal. Calcd for $C_{57}H_{50}O_{17}S$: C, 65.89; H, 4.85; S, 3.09. Found: C, 65.93; H, 4.95; S, 2.35.

2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*R*)-(methoxycarbonyl)ethylidene]-D-galactopyranosyl Chloride (12). A solution of phenyl 2,6-di-*O*-benzoyl-3,4-*O*-[1-(*R*)-(methoxycarbonyl)-ethylidene]-1-thio-β-D-galactopyranoside[17] **R-8** (1.2 g, 2.13 mmol) in CCl_4 (150 mL) was mixed at room temperature with a solution of Cl_2 in CCl_4 (15 mL, 0.57 M) and stirred for 24 h. The mixture was washed with aqueous $NaHCO_3$ and $Na_2S_2O_3$ solution, dried and concentrated. Chromatography (CCl_4/acetone, 10:1) of the residue afforded **12** (0.70 g, 66%) as a 1:1 mixture of the α/β-anomers; ^1H NMR δ (significant signals in $CDCl_3$): 6.33 (d, 1 H, $J_{1,2}$ = 3.9 Hz, H-1α), 5.34 (s, 1 H, $J_{1,2}$ = 8.8 Hz, H-1β), 5.60 (dd, 1 H, $J_{2,3}$ = 7.9 Hz, H-2α), 5.66 (dd, 1 H, $J_{2,3}$ = 7.1 Hz, H-2β); ^{13}C NMR δ ($CDCl_3$): 106.4 ($C_{acetal}\alpha$), 107.0 ($C_{acetal}\beta$), 90.4 (C-1α), 87.8 (C-1β).

Anal. Calcd for $C_{24}H_{23}ClO_9$: C, 58.72; H, 4.72; Cl, 7.22. Found: C, 58.88; H, 4.73; Cl, 7.19.

{2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*S*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl Trichloroacetimidate (S-14). A sus-pension of **S-10** (0.25 g, 0.24 mmol) and Pd 10% on charcoal (0.1 g) in acetic acid (20 mL) was stirred at room temperature under an atmosphere of H_2 for 24 h. The mixture was filtered, the filtrate was concentrated and the residue was redissolved in CH_2Cl_2 (20 mL). Trichloroacetonitrile (0.5 mL, 5.0 mmol) and K_2CO_3 (1.0 g, 7.2 mmol) was added to this solution, the resulting suspension was stirred at room temperature for 24 h, filtered and concentrated. Chromatography (CCl_4/acetone, 10:1) of the residue afforded **S-14** (0.21 g, 74%) as a mixture of anomers; ^{13}C NMR δ (signals of the predominant α-anomer in $CDCl_3$): 106.4 (C_{acetal}), 100.2 (C-1'), 93.6 (C-1), 90.7 (CCl_3), 75.2 (C-3'), 73.0 (C-4'), 71.3 (2 C, C-2,2'), 70.5 (C-3), 68.9, 68.2, 67.1 (C-4,5,5'), 68.0 (C-6), 63.1 (C-6'), 52.5 (OCH_3), 22.8 (CH_3).

Anal. Calcd for $C_{60}H_{52}Cl_3NO_{18}$: C, 61.00; H, 4.44; N, 1.18. Found: C, 60.79; H, 4.30; N, 0.98.

{2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*R*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl Trichloroacetimidate (R-14). Treatment of **R-10** (0.39 g, 0.38 mmol) with Pd 10% on charcoal (0.1 g) and H_2 in acetic acid (25 mL) followed by trichloroacetonitrile (0.5 mL, 5.0 mmol) and K_2CO_3 (1.0 g, 7.2 mmol) in CH_2Cl_2 (25 mL) as described for the preparation of **S-14** afforded **R-14** (0.39 g, 88%) as pure α-anomer; $[\alpha]_D$ +124.6° (*c* 0.5, $CHCl_3$); ^1H NMR δ (significant signals in $CDCl_3$): 6.72 (br.s, 1 H, H-1), 4.67 (d, 1 H, $J_{1',2'}$ = 8.1 Hz, H-1'); ^{13}C NMR δ ($CDCl_3$): 106.6 (C_{acetal}), 99.9 (C-1'), 93.6 (C-1), 90.7 (CCl_3), 78.3 (C-3'), 74.6 (C-4'), 71.5 (2 C, C-2,2'), 70.9 (C-3), 68.9, 68.2, 66.8 (C-4,5,5'), 68.0 (C-6), 63.3 (C-6'), 53.0 (OCH_3), 23.2 (CH_3).

Anal. Calcd for $C_{60}H_{52}Cl_3NO_{18}$: C, 61.00; H, 4.44; N, 1.18. Found: C, 60.91; H, 4.19; N, 1.17.

{2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*S*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl Bromide (S-15). S-11 (0.55 g, 0.53 mmol) was dissolved in a solution of Br_2 (0.5 mL, 9.8 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature for 3 h, washed with aqueous $NaHCO_3$ and $Na_2S_2O_3$ solution and dried. Concentration of the solution and keeping the residue in vacuo for 5 h afforded crude **S-15** which was used without further purification.

Allyl 2,3,4-Tri-*O*-benzoyl-α-D-galactopyranoside (17). A solution of allyl α-D-galactopyranoside[26] **16** (2.2 g, 10.0 mmol) and trityl chloride (3.35 g, 12.0 mmol) in pyridine (50 mL) was stirred at room temperature for 48 h and cooled to 0 °C. Benzoyl chloride (7.0 mL, 60.0 mmol) was added and the mixture was stirred at room temperature for 2 h. H_2O was added at 0 °C in order to destroy the excess of benzoyl chloride, the mixture was poured into H_2O and extracted with CH_2Cl_2. The combined extracts were concentrated, the residue was

dissolved in aqueous acetic acid (80%, 100 mL) and stirred at 85 °C for 6 h. Concentration of the mixture and chromatography (CCl_4/acetone, 5:1) of the residue afforded **17** (2.48 g, 48%) as a colourless foam; $[\alpha]_D$ +265.0° (*c* 0.6, $CHCl_3$); ^1H NMR δ ($CDCl_3$): 6.06 (dd, 1 H, $J_{2,3}$ = 10.7 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 5.95 (br.d, 1 H, $J_{4,5}$ < 1.0 Hz, H-4), 5.79 (dd, 1 H, $J_{1,2}$ = 3.6 Hz, H-2), 5.47 (d, 1 H, H-1), 4.40 (br.t, 1 H, H-5), 3.67-3.90 (m, 2 H, H-6a,6b); ^{13}C NMR δ ($CDCl_3$): 95.5 (C-1), 69.7, 69.4, 69.3, 68.5 (C-2,3,4,5), 68.6 (OCH_2), 60.7 (C-6).

Anal. Calcd for $C_{30}H_{28}O_9$: C, 67.66; H, 5.30. Found: C, 67.42; H, 5.24.

Allyl (2,3,4-Tri-*O*-benzoyl-6-*O*-chloroacetyl-β-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside (19). (a) Treatment of AgOTf (257 mg, 1.0 mmol), 2,3,4-tri-*O*-benzoyl-6-*O*-chloroacetyl-α-D-glucopyranosyl chloride[21] **18** (350 mg, 0.6 mmol), *sym*-collidine (54.5 mg, 0.45 mmol), molecular sieves (3 A, 0.5 g) and **17** (319.5 mg, 0.6 mmol) in CH_2Cl_2 (10 mL) for 1 h at 0 °C and work up as described for the preparation of **S-10** afforded **19** (470 mg, 72%) as a colourless foam; $[\alpha]_D$ +94.7° (*c* 0.4, $CHCl_3$); ^1H NMR δ (significant signals in $CDCl_3$): 5.20 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.82 (d, 1 H, $J_{1',2'}$ = 7.9 Hz, H-1'); ^{13}C NMR ($CDCl_3$): 101.5 (C-1'), 95.3 (C-1), 72.6 (C-4'), 71.9 (C-3'), 71.7 (C-5'), 69.8 (C-2'), 69.2, 69.1 (C-2,3), 68.5 (2 C, C-6, OCH_2), 68.1 (C-4), 64.0 (C-5), 63.7 (C-6'), 40.5 (CH_2Cl).

Anal. Calcd for $C_{59}H_{51}ClO_{18}$: C, 65.40; H, 4.74. Found: C, 65.50; H, 4.72.

(b) A solution of BF_3 diethyl ether complex (62 μL, 0.5 mmol), **21** (0.20 g, 0.33 mmol, see below) and **27** (0.23 g, 0.4 mmol, see below) in CH_2Cl_2 (5 mL) was stirred for 2 h at room temperature, diluted with CH_2Cl_2, washed with aqueous $NaHCO_3$ solution, dried and concentrated. Chromatography (CCl_4/acetone, 5:1) of the residue afforded **19** (255 mg, 70%).

Allyl (2,3,4-Tri-*O*-benzoyl-β-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside (20). Treatment of **19** (0.38 g, 0.35 mmol) with thiourea (0.12 g, 1.5 mmol) in MeOH (10 mL) as described for the preparation of compound **4** afforded **20** (0.30 g, 85%) as a colourless foam; $[\alpha]_D$ +101.4° (*c* 0.5, $CHCl_3$); ^1H NMR δ (significant signals in $CDCl_3$): 5.21 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.85 (d, 1 H, $J_{1',2'}$ = 7.9 Hz, H-1'); ^{13}C NMR δ ($CDCl_3$): 101.2 (C-1'), 95.4 (C-1), 74.6 (C-4'), 72.8 (C-3'), 71.9 (C-5'), 69.6 (C-2'), 69.2, 69.1 (C-2,3), 68.7 (OCH_2), 68.5 (C-4), 68.3 (C-6), 68.2 (C-5), 60.8 (C-6').

Anal. Calcd for $C_{57}H_{50}O_{17}$: C, 67.99; H, 5.00. Found: C, 67.63; H, 5.15.

Allyl 2,3,4-Tri-*O*-benzoyl-6-*O*-trimethylsilyl-α-D-galactopyranoside (21). Trifluoroacetic acid (3 drops) was added to a solution of **17** (1.0 g, 1.9 mmol) and hexamethyldisilazane (0.5 mL, 2.4 mmol), the mixture was stirred for 1 h at room temperature, washed with aqueous $NaHCO_3$ solution, dried and concentrated. Chromatography (CCl_4/acetone, 20:1) of the residue afforded **21** (1.1 g, 95%) as a colourless oil; $[\alpha]_D$ +200.9° (*c* 1.8, $CHCl_3$); ^1H NMR δ ($CDCl_3$): 5.98-5.92 (m, 2 H, H-3,4), 5.61 (br.dd, 1 H, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 11.5 Hz, H-2), 5.39 (d, 1 H, H-1), 4.29 (br.dd, 1 H, $J_{5,6a}$ = 6.6 Hz, $J_{6a,6b}$ = -13.0 Hz, H-6a), 4.23

(dt, 1 H, $J_{5,6b}$ = 5.9 Hz, H-5), 4.06 (br.dd, 1 H, H-6b); ^{13}C NMR δ ($CDCl_3$): 96.4 (C-1), 70.3, 70.2, 69.8, 69.6 (C-2,3,4,5), 69.5 (OCH_2), 61.5 (C-6).

Anal. Calcd for $C_{33}H_{36}O_9Si$: C, 65.54; H, 6.00. Found: C, 65.23; H, 5.97.

Allyl [2,3-Di-*O*-benzoyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-β-D-glucopyranosyl]-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside (23). BF_3 diethyl ether complex (292 μL, 2.6 mmol) was added at room temperature to a solution of **21** (0.72 g, 1.2 mmol), 2,3-di-*O*-benzoyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-glucopyranosyl fluoride[25c] **22** (0.82 g, 1.3 mmol) and Et_3N (181 μL, 1.3 mmol) in CH_2Cl_2 (5 mL) and the solution was stirred for 0.5 h. The mixture was diluted with CH_2Cl_2, washed with aqueous $NaHCO_3$ solution, dried and concentrated. Chromatography (CCl_4/acetone, 15:1) of the residue afforded **23** (1.11 g, 81%) as a colourless foam; $[\alpha]_D$ +123.6° (*c* 0.8, $CHCl_3$); ^{1}H NMR δ (significant signals in $CDCl_3$): 5.15 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.73 (d, 1 H, $J_{1',2'}$ = 7.9 Hz, H-1'); ^{13}C NMR δ ($CDCl_3$): 101.8 (C-1'), 95.1 (C-1), 77.0 (C-4'), 75.1 (C-3'), 72.5 (C-5'), 70.0 (C-2'), 69.4, 69.3 (C-2,3), 68.7 (OCH_2), 68.5 (C-6), 67.9 (2 C, C-4,5), 60.7 (C-6').

Anal. Calcd for $C_{62}H_{72}O_{17}Si_2$: C, 65.01; H, 6.34. Found: C, 65.28; H, 6.22.

Allyl [2,3-Di-*O*-benzoyl-4-*O*-(3-fluoro-1,1,3,3-tetraisopropyl-1,3-disiloxane-1-yl)-β-D-glucopyranosyl]-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside (24). Pyridine polyhydrogene fluoride (70%, 0.2 mL) was added at room temperature to a solution of **23** (0.96 g, 0.85 mmol) in CH_2Cl_2 (10 mL) in a polyethylene bottle. The mixture was stirred for 10 min., diluted with CH_2Cl_2, washed with aqueous $NaHCO_3$ solution, dried and concentrated. Chromatography (CCl_4/acetone, 15:1) of the residue afforded **24** (0.83 g, 84%) as a colourless foam; $[\alpha]_D$ +4.5° (*c* 0.4, $CHCl_3$); ^{1}H NMR δ (significant signals in $CDCl_3$): 5.23 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1), 4.77 (d, 1 H, $J_{1',2'}$ = 7.8 Hz, H-1'); ^{13}C NMR δ ($CDCl_3$): 100.6 (C-1'), 95.4 (C-1), 75.7 (C-4'), 72.4 (2 C, C-3,5'), 69.4 (2 C, C-2,2'), 69.3 (C3'), 68.9 (C-4), 68.5 (C-6), 68.0 (OCH_2), 60.8 (C-6').

Anal. Calcd for $C_{62}H_{73}FO_{17}Si_2$: C, 63.90; H, 6.31. Found: C, 63.66; H, 6.37.

6-*O*-Bromoacetyl-α-D-glucopyranosyl Fluoride (26). Treatment of α-D-glucopyranosyl fluoride **25** (3.64 g, 20.0 mmol) and *sym*-collidine (3.64 g, 30.0 mmol) in DMF (100 mL) with bromoacetyl bromide (5.04 g, 25.0 mmol) in toluene (10 mL) as described for the preparation of compound **2** afforded **26** (3.82 g, 63%) as a colourless foam; $[\alpha]_D$ -3.0° (*c* 0.5 MeOH); ^{1}H NMR δ (significant signals in CD_3OD): 5.53 (dd, 1 H, $J_{1,2}$ = 2.7 Hz, $J_{1,F}$ = 50.8 Hz, H-1), 2.34 (s, 2 H, CH_2Br); ^{13}C NMR δ (d_6-acetone): 169.0 (CO), 108.9 ($J_{1,F}$ = 211.6 Hz, C-1), 74.3 (C-5), 73.6 ($J_{3,F}$ = 3.6 Hz, C-3), 73.2 ($J_{2,F}$ = 44.9 Hz, C-2), 70.7 (C-4), 65.8 (C-6), 30.8 (CH_2Br).

Anal. Calcd for $C_8H_{12}BrFO_6$: C, 31.70; H, 3.99; Br, 26.37. Found: C, 31.82; H, 4.10; Br, 25.97.

2,3,4-Tri-*O*-benzoyl-6-*O*-chloroacetyl-α-D-glucopyranosyl Fluoride (27). Treatment of a solution of **26** (3.4 g, 11.2 mmol) in acetonitrile (20 mL) with a freshly prepared solution of benzoyl chloride (7.08 g, 50.0 mmol) and pyridine (3.8 g, 48.0 mmol) in acetonitrile (20 mL) as described for the preparation of compound **3** afforded **27** (4.76 g, 74%) as a colourless foam; $[\alpha]_D$ +45.6° (*c* 0.3, $CHCl_3$); ^1H NMR δ (significant signals in $CDCl_3$): 6.19 (t, 1 H, $J_{2,3} = J_{3,4} = 10.3$ Hz, H-3), 6.02 (dd, 1 H, $J_{1,2} = 2.7$ Hz, $J_{1,F} = 52.8$ Hz, H-1), 5.70 (t, 1 H, $J_{4,5} = 10.3$ Hz, H-4), 5.41 (ddd, 1 H, $J_{2,F} = 16.4$ Hz, H-2), 2.16 (s, 2 H, CH_2Cl); ^{13}C NMR δ (significant signals in $CDCl_3$): 104.0 ($J_{1,F} = 230.1$ Hz, C-1), 63.1 (C-6), 40.7 (CH_2Cl).

Anal. Calcd for $C_{29}H_{24}ClFO_9$: C, 61.01; H, 4.24; Cl, 6.21. Found: C, 61.00; H, 4.30; Cl, 6.00.

Allyl {2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*S*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-(2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→6)-(2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside (28). Treatment of a solution of **20** (201.4 mg, 0.2 mmol) and TMSOTf (7 μL, 40 μmol) in CH_2Cl_2 (3 mL) for 0.5 h at -30 °C with a solution of **S-14** (189.1 mg, 0.16 mmol) in CH_2Cl_2 (2 mL) as described for the preparation of compound **R-10** (b) afforded **28** (204.7 mg, 62%) as a colourless foam; $[\alpha]_D$ +106.2° (*c* 0.1, $CHCl_3$); ^{13}C NMR δ (significant signals in $CDCl_3$): 106.3 (C_{acetal}), 101.4 (C-1'''), 101.0 (C-1'), 100.2 (C-1''), 95.1 (C-1), 77.0 (C-3'''), 53.4 (OCH_3), 23.8 (CH_3).

Anal. Calcd for $C_{118}H_{94}O_{34}$: C, 68.93; H, 4.61. Found: C, 68.78; H, 4.70.

Allyl {3,4-*O*-[1-(*S*)-(Hydroxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-(β-D-galactopyranosyl)-(1→6)-(β-D-glucopyranosyl)-(1→6)-α-D-galactopyranoside (S-29). A solution of **28** (200.0 mg, 97 μmol) and a catalytic amount of NaOMe in MeOH (20 mL) was stirred for 24 h at 40 °C. The solution was neutralised by addition of ion exchange resin (Lewatit, H^+ form), filtered and concentrated. The residue was stored for 24 h at 60 °C in vacuo and redissolved in MeOH (20 mL). Aqueous NaOH solution (0.1 M, 2 mL) was added, the mixture stirred for 5 h at room temperature, neutralised with ion exchange resin (Lewatit, H^+ form), filtered and concentrated. Chromatography (H_2O) of the residue on Bio Gel P2 and lyophilisation of the carbohydrate containing fractions afforded **S-29** (75.6 mg, 100%) as a colourless, hygroscopic foam; $[\alpha]_D$ +33.8° (*c* 0.4, H_2O); ^{13}C NMR δ (significant signals in D_2O): 108.9 (C_{acetal}), 106.2 (C-1'''), 105.6 (C-1'), 105.1 (C-1''), 100.4 (C-1), 78.3 (C-3'''), 25.7 (CH_3).

FAB-MS (pos.) Calcd for $C_{30}H_{47}O_{23}$: 776. Found: 777 ($M+H^+$).

Allyl {3,4-*O*-[1-(*R*)-(Hydroxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-(β-D-galactopyranosyl)-(1→6)-(β-D-glucopyranosyl)-(1→6)-α-D-galactopyranoside (R-29). Treatment of **31** (150.0 mg, 78 μmol, see below) with a catalytic amount of NaOMe in MeOH followed by aqueous NaOH solution in MeOH as described for the preparation of **S-**

29 afforded **R-29** (60.2 mg, 99%) as a colourless, hygroscopic foam; $[\alpha]_D$ +28.9° (*c* 0.2, H_2O); ^{13}C NMR δ (significant signals in D_2O): 110.6 (C_{acetal}), 106.4 (C-1'''), 105.8 (C-1'), 105.2 (C-1''), 100.6 (C-1), 78.6 (C-3'''), 26.4 (CH_3).

FAB-MS Calcd for $C_{30}H_{47}O_{23}$: 776. Found: FAB-MS (pos.) 777 ($M+H^+$); FAB-MS (neg.) 775 ($M-H^+$).

Allyl {2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*R*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-(2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→6)-[2,3-di-*O*-benzoyl-4-*O*-(3-fluoro-1,1,3,3-tetraisopropyl-1,3-disiloxane-1-yl)-β-D-glucopyranosyl]-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside (30). Treatment of a solution of **24** (249.4 mg, 0.21 mmol) and TMSOTf (7 μL, 40 μmol) in CH_2Cl_2 (3 mL) for 0.5 h at -20 °C with a solution of **R-14** (252.7 mg, 0.21 mmol) in CH_2Cl_2 (2 mL) as described for the preparation of compound **R-10** (b) afforded crude **28** (350.0 mg, 78%) as a colourless foam which was homogeneous by TLC analysis and used without further purification for the next step.

Allyl {2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*R*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-(2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→6)-(2,3-di-*O*-benzoyl-β-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside (31). A solution of crude **30** (350.0 mg, 0.17 mmol) and a catalytic amount of Bu_4NF 3 H_2O (ca. 100 mg) in THF (10 mL) was stirred for 0.5 h at room temperature, diluted with CH_2Cl_2, washed with aqueous $NaHCO_3$ solution, dried and concentrated. Chromatography (CCl_4/acetone, 10:1) of the residue afforded **31** (250.0 mg, 78%) as a colourless foam; $[\alpha]_D$ +181.8° (*c* 0.1, $CHCl_3$); ^{13}C NMR δ (significant signals in $CDCl_3$): 106.8 (C_{acetal}), 102.0 (C-1'''), 101.4 (C-1'), 100.7 (C-1''), 95.3 (C-1), 78.1 (C-3'''), 53.2 (OCH_3), 23.3 (CH_3).

Anal. Calcd for $C_{111}H_{90}O_{33}$: C, 68.30; H, 4.65. Found: C, 68.02; H, 4.55.

Allyl {2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*S*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-galactopyranosyl)-(1→6)-[2,3-di-*O*-benzoyl-4-*O*-(3-fluoro-1,1,3,3-tetraisopropyl-1,3-disiloxane-1-yl)-β-D-glucopyranosyl]-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside (32). Treatment of AgOTf (257 mg, 1.0 mmol), crude **S-15** (prepared from 0.55 g, 0.53 mmol **S-11** as described above), *sym*-collidine (48.0 mg, 0.4 mmol), molecular sieves (3 A, 0.2 g) and **24** (580.0 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) for 15 min. at 0 °C and work up as described for the preparation of **S-10** afforded crude **32** (800 mg, 76%) as a colourless foam which was homogeneous by TLC analysis and used without further purification for the next step.

Allyl {2,6-Di-*O*-benzoyl-3,4-*O*-[1-(*S*)-(methoxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-(2,3,4-tri-*O*-benzoyl-α-D-galactopyranosyl)-(1→6)-(2,3-di-*O*-benzoyl-β-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside (33). Treatment of crude **32** (800.0 mg, 0.38 mmol) with a catalytic amount of Bu_4NF 3 H_2O in THF (10 mL) as described for the preparation of compound **31** afforded **33** (640.0 mg, 86%) as a colourless foam; $[\alpha]_D$ +147.3° (*c* 0.4, $CHCl_3$); ^{13}C NMR δ (significant signals in $CDCl_3$):

106.0 (C_{acetal}), 101.9 (C-1'''), 101.2 (C-1'), 96.1 (C-1''), 95.3 (C-1), 77.0 (C-3'''), 52.6 (OCH_3), 23.3 (CH_3).

Anal. Calcd for $C_{111}H_{90}O_{33}$: C, 68.30; H, 4.65. Found: C, 68.41; H, 5.02.

Allyl {3,4-*O*-[1-(*S*)-(Hydroxycarbonyl)ethylidene]-β-D-galactopyranosyl}-(1→6)-(α-D-galactopyranosyl)-(1→6)-(β-D-glucopyranosyl)-(1→6)-α-D-galactopyranoside (34). Treatment of **33** (289.0 mg, 148 μmol) with a catalytic amount of NaOMe in MeOH followed by aqueous NaOH solution in MeOH as described for the preparation of **S-29** afforded **34** (106.8 mg, 93%) as a colourless, hygroscopic foam; $[\alpha]_D$ +70.8° (*c* 0.3, H_2O); ^{13}C NMR δ (significant signals in D_2O): 109.0 (C_{acetal}), 106.2 (C-1'''), 105.7 (C-1'), 100.5 (2 C, C-1,1''), 78.5 (C-3'''), 25.9 (CH_3).

FAB-MS (neg.) Calcd for $C_{30}H_{47}O_{23}$: 776. Found: 775 ($M-H^+$).

Methyl [2,3-Di-*O*-benzoyl-4-*O*-(3-fluoro-1,1,3,3-tetraisopropyl-1,3-disiloxane-1-yl)-β-D-glucopyranosyl]-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranoside (38). (a) Treatment of AgOTf (128.5 mg, 0.5 mmol), methyl 2,3-di-*O*-benzoyl-4-*O*-(3-fluoro-1,1,3,3-tetraisopropyl-1,3-disiloxane-1-yl)-β-D-glucopyranoside[25c] **35** (150.0 mg, 0.23 mmol), *sym*-collidine (20 mg, 0.15 mmol), molecular sieves (3 A, 0.1 g) and 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide **36** (197.9 mg, 0.3 mmol) in CH_2Cl_2 (11.5 mL) for 0.5 h at room temperature and work up as described for the preparation of **S-10** afforded **38** (180.0 mg, 71%) as a colourless foam; $[\alpha]_D$ +107.5° (*c* 0.5, $CHCl_3$); ^1H NMR δ ($CDCl_3$): 6.06 (br.d, 1 H, $J_{3',4'}$ = 3.5 Hz, $J_{4',5'}$ < 1.0 Hz, H-4'), 5.88 (dd, 1 H, $J_{1',2'}$ = 7.9 Hz, $J_{2',3'}$ = 10.1 Hz, H-2'), 5.88 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 10.1 Hz, H-3), 5.66 (dd, 1 H, H-3'), 5.01 (d, 1 H, H-1'), 5.00 (dd, 1 H, $J_{1,2}$ = 3.5 Hz, H-2), 4.85 (d, 1 H, H-1), 4.50-4.36 (m, 3 H, H-5,6a,6b), 4.69 (dd, 1 H, $J_{5',6a'}$ = 5.4 Hz, $J_{6a',6b'}$ = -10.9 Hz, H-6a'), 4.07 (br.dd, 1 H, $J_{5',6b'}$ = 8.4 Hz, H-5'), 3.81 (dd, 1 H, H-6b'), 3.10 (s, 3 H, OCH_3); ^{13}C NMR δ ($CDCl_3$): 102.4 (C-1'), 96.2 (C-1), 73.1 (C-5), 72.6 (C-3'), 71.7 (C-4), 71.2 (2 C, C-3,5'), 70.6 (C-6), 70.4 (C-2'), 69.9 (C-2), 68.1 (C-4'), 61.9 (C-6'), 54.8 (OCH_3).

Anal. Calcd for $C_{67}H_{75}FO_{18}Si_2$: C, 64.72; H, 6.08. Found: C, 65.02; H, 6.03.

(b) Treatment of a solution of **35** (150.0 mg, 0.23 mmol) and TMSOTf (7 μL, 40 μmol) in CH_2Cl_2 (6 mL) for 10 min. at -20 °C with a solution of 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl trichloroacetimidate **37** (222.3 mg, 0.3 mmol) in CH_2Cl_2 (2 mL) as described for the preparation of compound **R-10** (b) afforded **38** (230.0 mg, 82%).

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