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Synthesis of linear β-(1→4)-*galacto*-hexa- and heptasaccharides and studies directed towards cyclogalactans

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Dedicated to Professor Derek Horton on the occasion of his 70th birthday

Abstract

Synthesis of an exclusively β-(1→4)-linked galactohexa- and heptasaccharide is described by coupling a 2-*O*-pivaloyl-3,6-*O*-allyl-protected thiogalactobioside donor with an equally protected, yet terminally 4-OH-free galactopentaoside. The same approach though failed to elaborate cyclic oligomers, as neither cyclodimerization of the correspondingly protected thiogalactotriosides with a 4″-OH could be effected, nor intramolecular glycosidation of the respective hexa- and heptagalactosides with an unprotected 4-OH at one, and phenylthio or sulfoxido groups at the reducing end. The causative factors underlying this are attributed to an inadequate predisposition of the linear β-(1→4)-galactan chains to adopt the tightly coiled molecular geometry necessary for cyclization—at least at the hexa- and heptasaccharide stage. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: β-(1→4)-*galacto*-Oligosaccharides; Galactosylations; Thioglycosides; Galactosyl phenylsulfoxides

1. Introduction

Linear chains of β-(1→4)-linked galactopyranose residues of varying lengths are the major carbohydrate components of pectins, either as part of arabinogalactans or galactans.[1] The chain length of these galactans appears to depend on the source, as well as the isolation procedure, with the number of galactose units varying from four (wood,[2] willow bark,[3] citrus fruits[4]), six (soy bean[5]), 28 (aloe[6]) to 33 (citrus pectin,[4] garlic[7]).

The conformational similarity of a β-(1→4)-D-galactan to its amylose α-(1→4)-D-glucan analog, is striking (Fig. 1), as only the orientation of the intersaccharidic linkages—axial at one side of the pyranoid ring and equatorial at the other—is interchanged, entailing kinks at every glycosidic bond in both cases, as well as 2-O···HO-3′ hydrogen bonds between contiguous residues. Thus, both have a pronounced predisposition for coiling toward a helical molecular geometry.

This analogy, which has been corroborated by simple calculations,[8] can be carried even further. Amylose, due to the six glucose units per helix turn, forms a distinctly hydrophobic channel of about 5.4 Å in diameter[9]—dimensions that are similar to those found for the cavity of α-cyclodextrin (**1**) (Fig. 2).[10] Molecular modelings on the hexameric β-(1→4)-cyclogalactan (**2**) revealed similar cavity dimensions,[11,12] yet the distribution of hydrophobic and hydrophilic surface regions is different, such that the hydrophobic areas extend significantly over the cavities narrower rim toward the outside (Fig. 2, bottom entries). Accordingly, the inclusion complexation behavior of **2** is expected to be quite different from that of its glucose analog (Fig. 2, bottom entries). Similar differences are to be inferred for a β-(1→4)-galactan, as it may be considered a tubular-extended analog of **2**.

We surmise that further insights into the molecular architecture of β-(1→4)-D-galactans would result from study of pure oligomers, but their isolation from pectic cell-wall material has proved exceedingly cumbersome and has not provided well-defined products larger than

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tetrasaccharide. Generation of oligo-β-(1→4)-galactosides by β-galactosidase-induced galactosyl transfer has, despite its simplicity, not even passed the β-(1→4)-galactobiose level.[13] Chemical synthesis[14–16] has proved a formidable task also, since the axially disposed 4-OH of a galactosyl acceptor—a priori comparatively unreactive, and necessarily carrying blocking groups at *O*-6 and *O*-3—is sterically less accessible for glycosylation than primary or equatorial OHs. Most recently though, a straightforward, preparatively efficient methodology for construction of β-(1→4)-intergalactosidic linkages has been developed,[16] key elements being the use of phenylthio and/or phenyl sulfoxide donor functionalities for glycosylations and a judiciously designed blocking group pattern for donor and acceptor alike: pivaloyl protection at *O*-2 for securing β-selectivity, sterically undemanding allyl or benzyl groups at *O*-3 and *O*-6 to minimize the steric bulk around the unreactive galactosyl-4-OH, the *p*-methoxyphenyl moiety, readily replaceable by SPh, as an intermediate anomeric substituent, and an acetyl group for temporary protection of the terminal Gal-4-OH.[16] In this paper, we document the application of this strategy to the synthesis of linear β-(1→4)-*galacto*-heptaosides, and report on protocols designed to lead to cyclic hexa- and heptamers.

2. Results and discussion

A deceptively simple approach to a *cyclo*-β-(1→4)-galactohexaoside, such as **2**, comprises the cyclodimerization of a suitably blocked β-(1→4)-galactotrioside with a terminal 4-OH and a donor functionality at the reducing end. Two trisaccharides meeting these requirements, i.e., **5** and **6**, could readily be prepared in two respective three steps from the well accessible[17] *p*-methoxyphenyl galactotrioside **3**: replacement of the anomeric blocking group with a phenylthio residue by exposure to TMS–thiophenol/BF_3 (→**4**, 88%) and subsequent liberation of the terminal 4-OH (→**5**, 90%). Oxidation of **5** to the respective phenylsulfoxide derivative **6** was best effected (87% yield) by peracetic acid, generated in situ from acetic anhydride and hydrogen peroxide, inasmuch as employing the usually used *m*-chloroperbenzoic acid resulted in sluggish, incomplete conversion, with yields not exceeding 50% (Scheme 1).

The trimeric precursors **5** and **6** thus obtained were then submitted to cyclization experiments under a variety of conditions. In detail, thioglycoside **5** and sulfoxide **6** were activated using 1–5 M equiv of methyl triflate and triflic anhydride, respectively, while the dilution of the reaction mixture (0.1–0.001 M) and the mode of addition (normal: addition of activator to a diluted solution of **5** or **6**; inverse: addition of **5** or **6** to

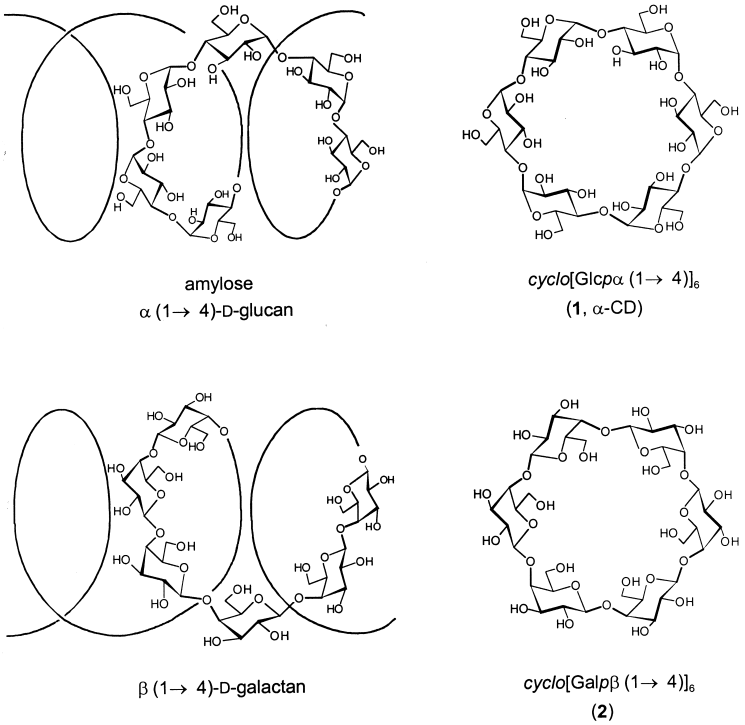


Fig. 1. Top: Sketch representation of a left-handed, single stranded helix of V_h-amylose (left), and of α-cyclodextrin (**1**) (right), which represents the excision of a single helix turn and its reconnection by CGTases. Bottom: depiction of a right-handed β-(1→4)-D-galactan helix (left), as predicted by early computational studies,[8] and its galactose analog **2**, a *cyclo*-β-(1→4)-D-galactohexaoside, as free of steric constraints as α-cyclodextrin (**1**).[10,11] Conversely, amylose and its β-(1→4)-D-galactan analog may be considered as tubular extensions of **1** and **2**.

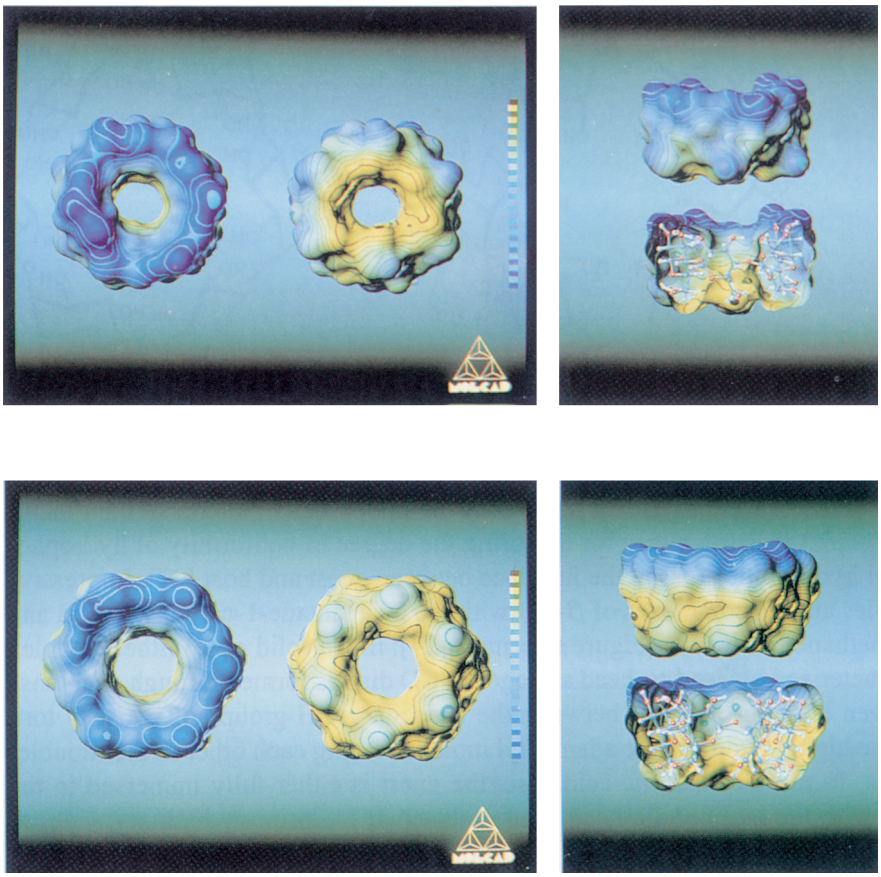


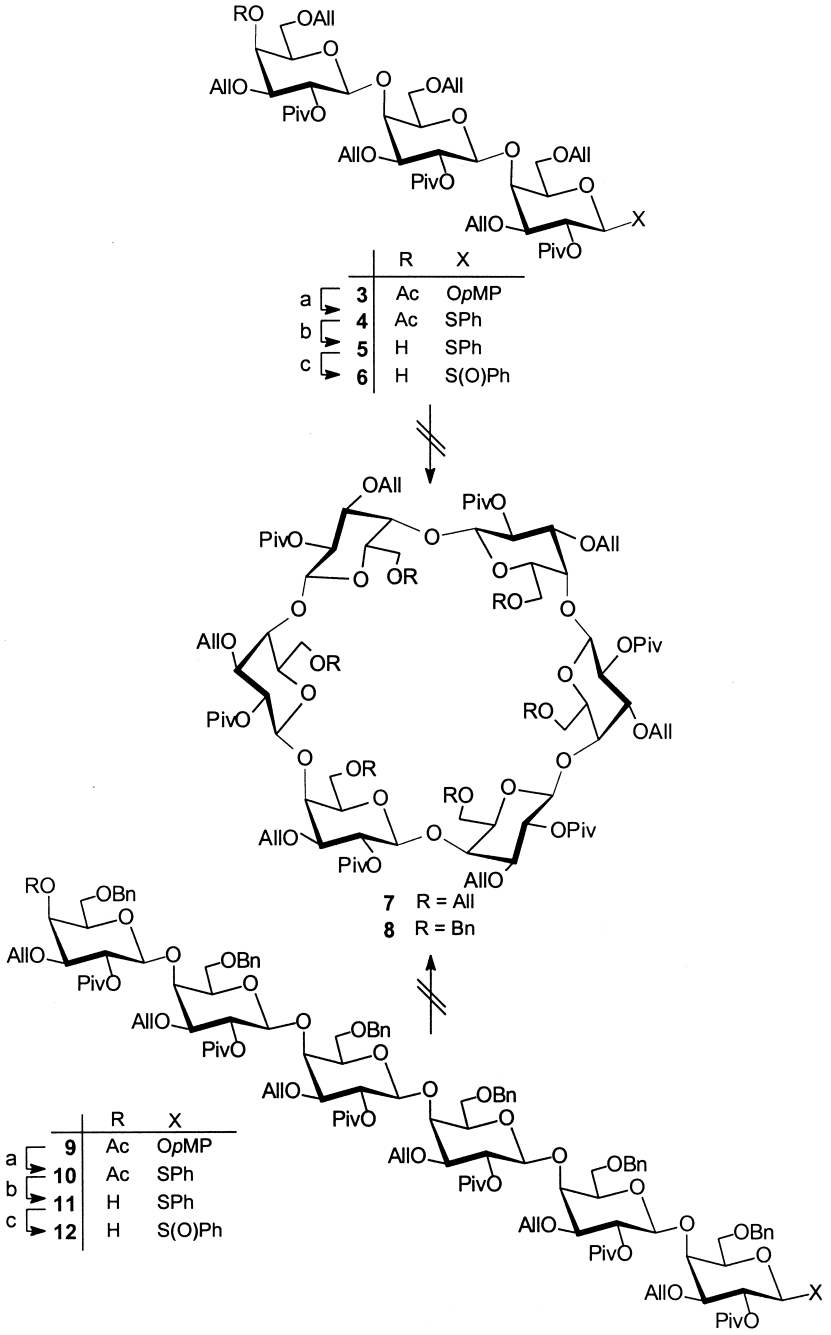
Fig. 2. MOLCAD program-generated molecular lipophilicity patterns (MLPs), projected onto the respective contact surfaces of α-cyclodextrin (**1**, top entry) and the respective *cyclo*-β-(1→4)-D-galactohexaoside (**2**, bottom).[11,12] The pictures on the left are viewed through the larger openings of the conically shaped molecules exposing the intensively hydrophilic (blue) 2-OH/3-OH side, whereas the representations in the middle depict the opposite, smaller aperture with the 6-CH_2OH groups facing the viewer, thereby clearly revealing the hydrophobic (yellow) surface areas. The side view MLPs on the right, in closed and bisected form each, are oriented in such a way that the 2-OH/3-OH side is aligned upward (larger opening of the torus) with the 6-CH_2OH groups pointing down. The substantially enlarged hydrophobic surface area in the cyclogalactoside **2** as compared to α-CD is clearly apparent.

a solution of activating agent) was systematically varied. The reactions were then monitored by TLC, and the mixture was quenched when no further change of product distribution could be detected. Whereas both **5** and **6** partly dimerized to linear hexamers (as judged by TLC using reference compounds, and NMR spectra of fractions obtained after column chromatography), and may also contain higher oligomers, no cyclic product such as **7** was detectable.

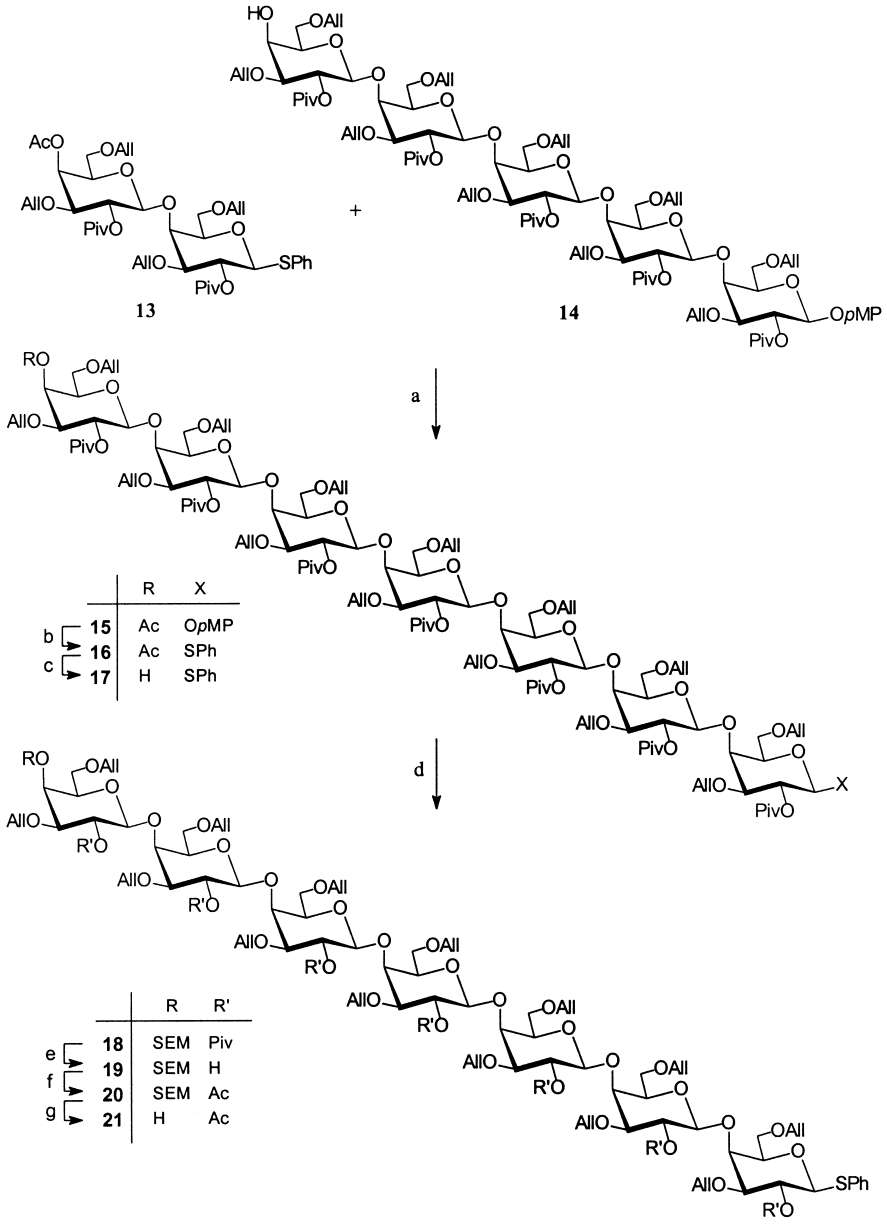
As an alternate approach to cyclic galacto-oligosaccharides, the cyclization of a suitably functionalized β-(1→4)-galactohexaoside was attempted next. Starting with hexagalactoside **9**, readily accessible from β-(1→4)-galactobioside building blocks by iterative extension,[16] the required hexameric precursors **11** and **12** were obtained using the reaction sequence elaborated at the trisaccharide stage for **3**→**5** and **3**→**6**, respectively. Thus, exposure of the hexameric *p*-methoxyphenyl glycoside **9** to TMS-protected thiophenol under BF_3-catalysis gave thioglycoside **10** (84%), and the removal of the terminal 4-OAc with sodium methoxide–methanol smoothly led to **11** (91%). The oxidation of the phenylthio to the phenylsulfoxido group, i.e., **10**→**11**, was again best performed using in situ generated peracetic acid (89%). Both thioglycoside **11** and sulfoxide **12** were activated under the same set of reaction conditions as outlined for trisaccharides **5** and **6**. Distinctly fewer side-products were observed in these reactions, yet here too, no cyclization products could be detected by either TLC or NMR. In the case of thioglycoside **11**, monitoring the reactions by TLC revealed the slow appearance of the corresponding lactol when 10 equiv of methyl triflate were used, yet no spot attributable to cyclization product **8**. Whereas the formation of the lactol proved that activation at the anomeric center had taken place, albeit rather slow, it obviously was not followed by intramolecular glycosidation of the terminal 4-OH. Sulfoxide **12**, on the other hand, disappeared nearly completely after activation with 5–10 equiv of triflic anhydride under a range of concentrations (0.1–

0.002 M), yet again furnished exclusively, the lactol upon aqueous work-up. In fact, in high dilution, both donor types turned out to be essentially inert, even when using 10 equiv of activating agent.

The reluctance of hexamers **11** and **12** to cyclize could be due to steric constraints of the comparatively bulky pivaloyl ester groups, one of which is situated next to the anomeric center to be activated, thereby obstructing the adoption of the pre-coiled shape required for joining terminal ends. Thus, an attempt was made towards lowering the steric bulk by two means: enlargement of ring size to be generated by using galactoheptaoside precursors and exchange of the bulky 2-*O*-pivaloyl groups by acetyl residues, despite their greater propensity to form orthoester side-products.[16,17] Accordingly, the respective β-(1→4)-galactoheptaoside **21** was synthesized using various standard methodologies. At first, the pivaloylated *p*-methoxyphenyl hep-



Scheme 1. Galacto-oligosaccharides used for cyclization experiments. Reagents and conditions: (a) $PhSSiMe_3$, $BF_3{\cdot}OEt_2$, $ClCH_2CH_2Cl$, 50 °C, 3 h; (b) NaOMe, $MeOH–CH_2Cl_2$, 25 °C, 16 h: (c) Ac_2O, H_2O_2, SiO_2, CH_2Cl_2, 25 °C, 16 h. Yields throughout were in the 90% range.



Scheme 2. Generation of galactoheptaosides and exchange of the bulky 2-OPiv for 2-OAc. Reagents and conditions: (a) MeOTf, 2,6-di-*t*Bu-pyridine, mol. sieve 4 Å, CH_2Cl_2, 25 °C, 16 h, 72%; (b) $PhSSiMe_3$, $BF_3{\cdot}OEt_2$, $ClCH_2CH_2Cl$, 50 °C, 3 h, 72%; (c) NaOMe, MeOH–CH_2Cl_2, 25 °C, 16 h, 86%; (d) SEMCl, iPr_2NEt, CH_2Cl_2, 25 °C, 24 h, 86%; (e) LiOH, MeOH, reflux, 12 h, 70%; (f) Ac_2O, DMAP, pyridine, 25 °C, 16 h, 77%; (g) HF–pyridine, THF, 25 °C, 30 min, 77%. SEM = $Me_3Si(CH_2)_2OCH_2$.

tasaccharide **15** was prepared by methyl triflate-promoted coupling of the readily accessible[17] disaccharide thiophenyl donor **13** and galactopentaoside acceptor **14** (72%), followed by exchange of the anomeric substituent for a phenylthio group (→**16**, 72%) and de-*O*-acetylation (→**17**, 86%). Replacement of the 2-*O*-pivaloyl blocking groups for the less bulky acetyl residue was then effected in a four-step sequence: temporary protection of the terminal 4-OH position with the (trimethylsilyl)ethoxymethyl (SEM) group[18] by exposure to SEM chloride (**17**→**18**, 86%), removal of the pivaloates by use of lithium hydroxide in refluxing methanol (→**19**, 70%), acetylation (→**20**, 77%) and cleavage of the SEM-group using hydrogen fluoride–pyridine[19] (→**21**, 77%) (Scheme 2).

Numerous experiments to induce the heptameric thiogalactosides **17** (with its bulky 2-*O*-pivaloyl ester groups) and the sterically less demanding 2-*O*-acetylated analog **21** to cyclization were not met with success, despite extensive variation of reaction conditions (methyl triflate activation, 5–10 equiv; dilution, 0.1–0.001 M; temperature, 20–40 °C).

3. Conclusions

The previously developed strategy for the construction of β-(1→4)-intergalactosidic linkages[16] can readily be applied to the generation of linear heptasaccharides, e.g., coupling of a 2-*O*-pivaloyl-3,6-di-*O*-allyl protected thiogalactobioside donor with a terminally 4-OH-free galactopentaoside proceeded efficiently (72% yield). However, the same approach failed to produce cyclic oligomers and cyclodimerization could not be induced with trigalactosides carrying an unprotected 4″-OH. In addition hexa- and heptasaccharides blocked respectively by phenylthio or sulfoxido groups at the reducing end and 4-OH at the other did not yield cycloglycosylation. The causative factors underlying this are multifaceted, but seem to narrow down to an inadequate predisposition to adopt the appropriate coiled geometry for effecting a head–tail reaction—at least at the hexa- and heptasaccharide stage. Preliminary molecular dynamics studies on "infinite" β-(1→4)-galactan polymers in periodic tetragonal boxes filled with water molecules show a pronounced tendency to elaborate right-handed helices with an average pitch per turn of about 15–17 Å.[20] Compared to the single-stranded, left-handed V_h-form of amylose (cf. Fig. 1, top left), which has a repeating height of only 8–9 Å, the sizably larger end-to-end distance of the β-(1→4)-galactose oligomers appears to indicate a substantially lower tendency for cyclization than in the respective α-(1→4)-glucose analogs. Accordingly, the unfeasibility of inducing a head-to-tail reaction in suitably blocked β-(1→4)-galactohexa- and heptaosides is likely to be due to coiling characteristics inherent in a β-(1→4)-galactan chain, rather than in insufficiently reactive donor substituents or too bulky blocking groups. Sizably higher oligogalactosides may in fact be required to chemically effect cyclization, despite the fact that the cyclohexamer, β-(1→4)-cyclogalactin **2**, can elaborate an essentially unstrained macrocycle with a cavity (cf. Fig. 2) somewhat wider than that of α-cyclodextrin.

4. Experimental

General.—Reactions were carried out under Ar. All solvents were of reagent grade and were further dried; reagents were used as received. Optical rotations were measured on a Perkin–Elmer 241 polarimeter at 20 °C using a cell of 1 dm path length. Mass spectra were recorded on Varian MAT 311 and MAT 212 spectrometers. Microanalyses were determined on a Perkin–Elmer 240 elemental analyzer. Analytical thin-layer chromatography (TLC) was performed on precoated Merck plastic sheets (0.2 mm Silica Gel 60 F_{254}) with detection by UV (254 nm) and/or spraying with H_2SO_4 (50%) and heating. Column chromatography was carried out on Fluka Silica Gel 60 (70–230 mesh); eluents are given in brackets. ^{1}H and ^{13}C NMR spectra were recorded on Bruker WM-300, AC-300, and Avance 500 spectrometers. The structures of all new compounds were confirmed by COSY, HETCOR, TOCSY, and decoupling experiments. Chemical shifts are reported relative to Me_4Si as an internal reference. Coupling constants are listed separately if an assignment was possible.

In the listings of ^{1}H and ^{13}C NMR data for the individual compounds, signals originating from blocking groups are omitted if well separated from the galactose–CH and CH_2 protons, i.e., pivaloyl groups (9 H-singlets between 1.18–1.26 ppm, carbon resonances at 27–28 ppm for CH_3, 38–39 ppm for CMe_3, 176–178 ppm for CO), the aromatic protons and carbons of phenyl, *p*-methoxyphenyl, and benzyl moieties, and most allyl resonances, i.e., All-H-2 multiplets (5.60–6.00 ppm), All-H-3 multiplets (5.00–5.40 ppm), All-C-2 signals (134–136 ppm) and All-C-3 signals (116–118 ppm). Protons and carbons of the galactose moieties are designated alphabetically starting from that containing the aglycon, i.e., 1-Ha, 1-Hb, …up to 1-Hf for ^{1}H NMR, C-1a, C-1b, etc. for ^{13}C NMR data.

*Phenyl (4-*O*-acetyl-3,6-di-*O*-allyl-2-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1→4)-(3,6-di-*O*-allyl-2-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1→4)-3,6-di-*O*-allyl-2-*O*-pivaloyl-1-thio-β-*D*-galactopyranoside* (**4**).—*p*-Methoxyphenyl galactotrioside **3**[16] (2.86 g, 2.5 mmol) in $ClCH_2CH_2Cl$ (30 mL) was exposed to $PhSSiMe_3$ (1.88 mL, 10 mmol) in the presence of $BF_3{\cdot}Et_2O$ (223 μL, 1.75 mmol) for 3 h at 50 °C. After diluting with CH_2Cl_2 (200 mL), the mixture was washed with satd aq $NaHCO_3$ (250 mL), and the $NaHCO_3$-layer was extracted with CH_2Cl_2 (100 mL), and the combined organic layers were dried ($MgSO_4$), filtered and evaporated in vacuo. Purification of the residue by elution from a silica gel column (8:1 toluene–EtOAc) gave **4** (2.5 g, 88%) as a syrup; R_f 0.42 (4:1 toluene–EtOAc); $[\alpha]_D^{20}$ −7.1° (*c* 0.96, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.12 (s, 3 H, AcCH_3), 3.44 (m, 6 H, H-3 (a–c), H-5c, 2 H-6), 3.59 (m, 2 H, H-5, H-6), 3.70 (m, 4 H, H-5a, 3 H-6), 3.83–4.17 (m, 12 H, 12 All-H-1), 4.32 (d, 1 H, H-4a), 4.42 (d, 1 H, H-4b), 4.62 (d, 1 H, H-1a), 4.90 (d, 1 H, H-1b), 4.98–5.11 (m, 4 H, H-1c, H-2 (a–c)), 5.42 (d, 1 H, H-4c), $J_{1a,2a}$ 10.0, $J_{3a,4a}$ 2.4, $J_{1b,2b}$ 7.9, $J_{3b,4b}$ 2.0, $J_{3c,4c}$ 2.9 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.8 (AcCH_3), 67.0 (C-4c), 67.5 (C-4b), 68.5 (C-6c), 69.1, 69.2, 69.3 (C-2a, C-4a, C-6), 70.1 (C-6), 70.7, 70.8 (C-2b,c), 71.0, 71.1 (All-C-1), 72.4, 72.5, 72.6 (C-5c, All-C-1), 73.7 (C-5b), 77.0 (C-3c), 78.4 (C-5a), 80.6 (C-3b), 81.2 (C-3a), 87.2 (C-1a), 99.1 (C-1c), 99.9 (C-1b), 170.2 (*C*OMe); MS (ESI): *m*/*z* 1153.6 $[M-H+Na]^+$. Anal. Calcd for $C_{59}H_{86}O_{19}S$ (1131.38): C, 62.64; H, 7.66. Found: C, 62.44; H, 7.46.

The use of thiophenol instead of its TMS-derivative gave considerably lower yields.

Phenyl (3,6-di-O-allyl-2-O-pivaloyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-O-allyl-2-O-pivaloyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-allyl-2-O-pivaloyl-1-thio-β-D-galactopyranoside (**5**).—Trisaccharide **4** (2.3 g, 2.0 mmol) was dissolved in 4:1 MeOH–CH_2Cl_2 (20 mL) and treated with NaOMe (0.5 M in MeOH, 1 mL) for 16 h. The solution was neutralized with Amberlite IR 120 (H^+ form), filtered and concentrated in vacuo. Purification of the residue by elution from a silica gel column (4:1 toluene–EtOAc) gave **5** (1.96 g, 90%) as a colorless foam; R_f 0.21 (4:1 toluene–EtOAc); $[\alpha]_D^{20}$ −13.5° (*c* 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.49 (bs, 1 H, 4c-OH), 3.45 (m, 3 H, H-3 (a–c)), 3.51–3.68 (m, 8 H, H-5 (a–c),5 H-6), 3.74 (dd, 1 H, H-6), 3.90–4.17 (m, 12 H, 12 All-H-1), 4.00 (m, 1 H, H-4c), 4.32 (d, 1 H, H-4a), 4.41 (d, 1 H, H-4b), 4.62 (d, 1 H, H-1a), 4.90 (d, 1 H, H-1b), 5.02–5.11 (m, 4 H, H-1c, H-2 (a–c)), $J_{1a,2a}$ 10.0, $J_{3a,4a}$ 2.4, $J_{1b,2b}$ 7.9, $J_{3b,4b}$ 1.9, $J_{5,6b}$ 5.9 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 66.5 (C-4c), 67.6 (C-4b), 69.0 (C-6c), 69.1, 69.4 (C-2a, C-4a), 69.6, 70.2 (C-6a,b), 70.6, 70.8 (C-2b,c), 71.0, 71.1, 72.4, 72.5 (6 All-C-1), 73.5, 74.0 (C-5b,c), 78.4 (C-5a), 78.9 (C-3c), 80.7 (C-3b), 81.2 (C-3a), 87.2 (C-1a), 99.0 (C-1c), 99.9 (C-1b); MS (ESI): *m*/*z* 1112.6 $[M+Na]^+$. Anal. Calcd for $C_{57}H_{84}O_{18}S$ (1089.34): C, 62.85; H, 7.77. Found: C, 62.90; H, 7.87.

Phenyl (3,6-di-O-allyl-2-O-pivaloyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-O-allyl-2-O-pivaloyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-allyl-2-O-pivaloyl-β-D-galactopyranosyl sulfoxide (**6**).—To a solution of phenylthio galactotrioside **5** (610 mg, 0.56 mmol) in CH_2Cl_2 (3 mL) was added silica gel 60 (230–400 mesh, 110 mg), Ac_2O (59 μL, 0.62 mmol), and H_2O_2 (30% aq solution, 68 μL, 0.68 mmol). After 8 h of stirring at rt, the mixture was diluted with CH_2Cl_2 (100 mL), filtered through a sintered frit, washed with satd aq $KHSO_3$ (50 mL), satd aq $NaHCO_3$ (50 mL), and brine (50 mL) followed by drying ($MgSO_4$), and concentration in vacuo. The solid residue was subjected to column chromatography (7:4 toluene–EtOAc) to afford **6** (540 mg, 87%) as a colorless powder, comprising an approximate 1:1 mixture of the two sulfoxide diastereomers. Their separation may be achieved by another elution from a silica gel column (4:1 toluene–EtOAc).

Diastereomer **6 I**. R_f 0.28 (1:1 toluene–EtOAc); $[\alpha]_D^{20}$ −39.3° (*c* 0.82, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.45 (b, 1 H, 4c-OH), 3.36–3.57 (m, 8 H, H-3 (a–c), H-5 (a–c), 2 H-6), 3.60–3.76 (m, 4 H, 4 H-6), 3.81–4.19 (m, 12 H, 12 All-H-1), 4.00 (m, 1 H, H-4c), 4.08 (d, 1 H, H-1a), 4.18 (d, 1 H, H-4a), 4.40 (d, 1 H, H-4b), 4.71 (d, 1 H, H-1b), 4.91 (dd, 1 H, H-2b), 4.97–5.07 (m, 2 H, H-1c, H-2c), 5.37 (t, 1 H, H-2a), $J_{1a,2a}$ 9.4, $J_{2a,3a}$ 9.4, $J_{3a,4a}$ 1.8, $J_{1b,2b}$ 7.8, $J_{2b,3b}$ 10.1, $J_{3b,4b}$ 2.3 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 66.5 (C-4c), 67.2 (C-4b), 68.3 (C-2a), 69.0, 69.3 (C-6 (a–c)), 70.2 (C-4a), 70.6, 70.7 (C-2b,c), 70.9, 71.1, 71.6, 72.2, 72.5, 72.6 (6 All-C-1), 73.5, 73.8 (C-5b,c), 78.8 (C-3c), 79.2, 80.0 (C-3a, C-5a), 80.7 (C-3b), 94.1 (C-1a), 99.0 (C-1c), 100.6 (C-1b).

Diastereomer **6 II**. R_f 0.21 (1:1 toluene–EtOAc); $[\alpha]_D^{20}$ +11.6° (*c* 0.95, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.45 (bs, 1 H, 4c-OH), 3.41 (dd, 1 H, H-3b), 3.46–3.60 (m, 6 H, H-3c, H-5 (a–c), 2 H-6), 3.62–3.75 (m, 5 H, H-3a, 4 H-6), 3.78–4.15 (m, 12 H, 12 All-H-1), 4.00 (m, 1 H, H-4c), 4.16 (d, 1 H, H-1a), 4.30 (d, 1 H, H-4a), 4.38 (d, 1 H, H-4b), 4.83 (d, 1 H, H-1b), 4.97 (dd, 1 H, H-2b), 5.02 (m, 2 H, H-1c, H-2c), 5.09–5.35 (m, 13 H, H-2a, 12 All-H-3), $J_{1a,2a}$ 9.8, $J_{3a,4a}$ 2.3, $J_{1b,2b}$ 7.9, $J_{2b,3b}$ 10.1, $J_{3b,4b}$ 3.1, $J_{2c,3c}$ 10.2 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 66.5 (C-4c), 67.1 (C-2a), 67.8 (C-4b), 69.0 (C-6c), 69.3 (C-4a), 69.6, 69.8 (C-6a,b), 70.6, 70.7 (C-2b,c), 71.0, 71.1, 71.2, 72.5, 72.6 (6 All-C-1), 73.5, 74.0 (C-5b,c), 78.8 (C-3c), 80.0 (C-5a), 80.6 (C-3b), 80.7 (C-3a), 91.9 (C-1a), 99.0 (C-1c), 100.0 (C-1b); MS (FD): *m*/*z* 1129 $[M+H+Na]^+$. Anal. Calcd for $C_{57}H_{84}O_{19}S$ (1105.34): C, 61.94; H, 7.66. Found: C, 61.54; H, 7.55.

Phenyl (4-O-acetyl-3-O-allyl-6-O-benzyl-2-O-pivaloyl-β-D-galactopyranosyl)-(1→4)-[(3-O-allyl-6-O-benzyl-2-O-pivaloyl-β-D-galactopyranosyl)-(1→4)]$_4$-3-O-allyl-6-O-benzyl-2-O-pivaloyl-1-thio-β-D-galactopyranoside (**10**).—Galactohexaoside **9**[16] (970 mg, 0.4 mmol) was treated with $PhSSiMe_3$ (0.3 mL, 1.6 mmol) as described above for **3**→**4**. The resulting residue was subjected to chromatography on silica gel (10:1 toluene–EtOAc) to give thiogalactoside **10** (810 mg, 84%) as a colorless foam; R_f 0.56 (4:1 toluene–EtOAc); $[\alpha]_D^{20}$ +4.0° (*c* 0.65, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.00 (s, 3 H, AcCH_3), 3.38 (m, 5 H, 5 H-3), 3.47–3.78 (m, 19 H, H-3, H-5 (a–f), 2 H-6 (a–f)), 3.82–4.14 (m, 12 H, 12 All-H-1), 4.24, 4.30, 4.33 (3 bs, 5 H, H-4 (a–e)), 4.37–4.55 (m, 12 H, 6 CH_2Ph), 4.60 (d, 1 H, H-1a), 4.84 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 4.86 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.90 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 4.95–5.24 (m, 20 H, 2 H-1, H-2 (a–f), 12 All-H-3), 5.48 (d, 1 H, H-4f), $J_{1a,2a}$ 10.9 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.8 (AcCH_3), 66.6 (C-4f), 67.7, 68.1 (2 C-4), 68.1 (C-6f), 68.8, 69.0, 69.4 (3 C-4), 69.8, 70.5, 70.6, 70.7 (C-6 (a–e)), 70.8, 71.1, 71.3 (6 C-2, 6 All-C-1), 72.3 (C-5f), 73.4, 73.5, 73.6, 73.7 (6 CH_2Ph), 73.9, 74.3, 74.4, (C-5 (b–e)), 77.2 (C-3f), 78.5 (C-5a), 80.0, 80.1, 80.4, 81.0 (C-3 (a–e)), 87.2 (C-1a), 99.4, 99.8, 100.0 (C-1 (b–f)), 170.2 (*C*OMe); MS (ESI): *m*/*z* 2433.1 $[M+Na]^+$. Anal. Calcd for $C_{134}H_{176}O_{37}S$ (2410.91): C, 66.76; H, 7.36. Found: C, 66.66; H, 7.35.

Phenyl [(3-O-allyl-6-O-benzyl-2-O-pivaloyl-β-D-galactopyranosyl)-(1→4)]$_5$-3-O-allyl-6-O-benzyl-2-O-pivaloyl-1-thio-β-D-galactopyranoside (**11**).—Thiogalactoside **10** (600 mg, 0.25 mmol) was de-*O*-acetylated as described above for **4**→**5**. Purification of the residue by elution from a silica gel column (6:1 tolu-

ene–EtOAc) gave **11** (536 mg, 91%) as a colorless syrup; R_f 0.36 (4:1 toluene–EtOAc); $[\alpha]_D^{20}$ −1.6° (*c* 0.82, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 2.44 (bs, 1 H, 4f-OH), 3.33–3.47 (m, 6 H, H-3 (a–f)), 3.51 (m, 4 H, 4 H-5), 3.56–3.67 (m, 6 H, 2 H-5, 4 H-6), 3.68–3.79 (m, 8 H, 8 H-6), 3.81–4.14 (m, 12 H, 12 All-H-1), 4.05 (m, 1 H, H-4f), 4.24 (d, 1 H, $J_{3,4}$ 2.3 Hz, H-4), 4.30 (m, 4 H, 4 H-4), 4.40–4.56 (m, 12 H, 6 CH_2Ph), 4.60 (d, 1 H, H-1a), 4.82–4.97 (m, 5 H, H-1 (b–f)), 5.09–5.30 (m, 18 H, H-2 (a-f), 12 All-H-3), $J_{1a,2a}$ 10.0 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 66.3 (C-4f), 67.8, 68.4, 69.0, 69.3, 69.4 (C-4 (a–e)), 70.0, 70.1, 70.3, 70.6, 70.7, 70.8, 71.0, 71.1, 71.3 (C-2 (a–f), C-6 (a–f), 6 All-C-1), 73.6, 73.7, 73.8 (6 *C*H_2Ph), 74.1, 74.2, 74.4, 74.6 (C-5 (b–f)), 78.8 (C-5a), 79.1, 80.3, 80.5, 81.3 (C-3 (a–f)), 87.3 (C-1a), 99.6, 100.0, 100.2 (C-1 (b–f)); MS (ESI): *m*/*z* 2391.4 $[M + Na]^+$. Anal. Calcd for $C_{132}H_{174}O_{36}S$ (2368.87): C, 66.93; H, 7.40. Found: C, 66.52; H, 7.50.

*Phenyl [(3-*O*-allyl-6-*O*-benzyl-2-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1→4)]$_5$-3-*O*-allyl-6-*O*-benzyl-2-*O*-pivaloyl-β-*D*-galactopyranosyl sulfoxide* (**12**).—Phenyl galactohexaoside **11** (543 mg, 0.23 mmol) in CH_2Cl_2 (2 mL) was treated with Ac_2O (24 μL, 0.25 mmol) and H_2O_2 (30%, 28 μL, 0.28 mmol) in the presence of silica gel (230–400 mesh, 50 mg) for 24 h, followed by workup as described above for **5**→**6**. The resulting syrup was subjected to chromatography on silica gel (3:1 toluene–EtOAc) to give sulfoxide **12** (485 mg, 89%) as a single diastereomer; R_f 0.19 (4:1 toluene–EtOAc); $[\alpha]_D^{20}$ +6.0° (*c* 1.51, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 2.20–2.50 (b, 1 H, 4f-OH), 3.35 (m, 4 H, H-3 (b–e)), 3.43–3.58 (m, 10 H, H-3a,f, H-5 (a–f), 2 H-6), 3.60–3.73 (m, 10 H, 10 H-6), 3.76–3.97 (m, 6 H, 6 All-H-1), 4.05 (m, 7 H, H-4f, 6 All-H-1), 4.08 (d, 1 H, H-1a), 4.13 (b, 1 H, H-4), 4.24 (d, 1 H, $J_{3,4}$ 2.6 Hz, H-4), 4.29 (m, 3 H, 3 H-4), 4.32–4.56 (m, 12 H, 6 CH_2Ph), 4.71 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.82 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.86–4.98 (m, 3 H, 3 H-1), 4.90–5.10 (m, 5 H, H-2 (b–f)), 5.00–5.28 (m, 12 H, 12 All-H-3), 5.37 (t, 1 H, H-2a), $J_{1a,2a}$ 9.3, $J_{2a,3a}$ 9.2 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 66.4 (C-4f), 67.3, 68.3, 68.8, 69.0 (C-4 (b–e)), 70.2 (C-6), 70.4 (C-4a), 70.6, 70.7 (5 C-6), 70.8, 71.0, 71.1, 71.2 (C-2 (a–f)), 71.3, 71.4 (6 All-C-1), 73.7, 73.8, 73.9 (6 *C*H_2Ph), 74.0, 74.1, 74.2, 74.5 (C-5 (b–f)), 77.2, 79.0, 79.3, 80.0, 80.2, 80.5 (C-3 (a–f), C-5a), 94.0 (C-1a), 99.4, 99.6, 99.8, 100.1, 100.5 (C-1 (b–f)); MS (ESI): *m*/*z* 2407.5 $[M + Na]^+$. Anal. Calcd for $C_{132}H_{174}O_{37}S$ (2384.87): C, 66.48; H, 7.35. Found: C, 66.32; H, 7.53.

*4-Methoxyphenyl (4-*O*-acetyl-3,6-di-*O*-allyl-2-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1→4)-[(3,6-di-*O*-allyl-2-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1→4)-]$_5$-3,6-di-*O*-allyl-2-*O*-pivaloyl-β-*D*-galactopyranoside* (**15**).—A solution of pentasaccharide acceptor **14**[16] (3.10 g, 1.9 mmol), galactobioside donor **13**[14] (2.80 g, 3.4 mmol), and 2,6-di-tbutylpyridine (2.05 mL, 8.7 mmol) in CH_2Cl_2 (20 mL) was stirred with freshly activated molecular sieve (4 Å) for 15 min. Then, MeOTf (0.78 mL, 6.9 mmol) was added and the mixture was stirred at rt for 16 h, diluted with CH_2Cl_2 (250 mL), washed with satd aq $NaHCO_3$ (250 mL), which after separation was reextracted with CH_2Cl_2 (250 mL). The combined organic layers were then dried ($MgSO_4$), filtered and concentrated to a syrup which was purified by elution from a silica gel column (10:1 toluene–EtOAc) to afford heptasaccharide **15** (3.35 g, 72%) as a colorless foam; R_f 0.52 (4:1 toluene–EtOAc); $[\alpha]_D^{20}$ −6.0° (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 2.11 (s, 3 H, AcCH_3), 3.34–3.71 (m, 28 H, H-3 (a–g), H-5 (a–g), 2 H-6 (a–g)), 3.74 (s, 3 H, OCH_3), 3.82–4.22 (m, 28 H, 28 All-H-1), 4.23–4.35 (m, 6 H, H-4 (a–f)), 4.74 (d, 1 H, H-1a), 4.82–5.04 (m, 12 H, H-1 (b–g), H-2 (b–g)), 5.09–5.35 (m, 29 H, H-2a, 28 All-H-3), 5.42 (d, 1 H, H-4g), $J_{1a,2a}$ 7.9, $J_{3g,4g}$ 3.1 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.8 (Ac*C*H_3), 55.6 (OCH_3), 67.0 (C-4g), 68.5, 68.9, 70.7, 70.8, 71.0, 73.9, 74.2, 74.5, 75.0, 77.3, 80.5 (C-2 (a–g), C-3 (a–g), C-5 (a–g), C-4 (a–f)), 68.6, 69.5, 70.0, 70.3, 70.4, 70.5, 71.1, 71.2, 71.3, 71.4, 72.6, 72.7 (C-6 (a–g), 14 All-C-1), 99.6, 99.9 (C-1 (b–g)), 101.2 (C-1a), 170.3 (*C*OMe); MS (ESI): *m*/*z* 2473.7 $[M + Na]^+$. Anal. Calcd for $C_{128}H_{192}O_{45}$ (2450.90): C, 62.73; H, 7.90. Found: C, 63.07; H, 7.95.

*Phenyl (4-*O*-acetyl-3,6-di-*O*-allyl-2-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1→4)-[(3,6-di-*O*-allyl-2-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1→4)-]$_5$-3,6-di-*O*-allyl-2-*O*-pivaloyl-1-thio-β-*D*-galactopyranoside* (**16**).—*p*-Methoxyphenyl galactoheptaoside **15** (2.46 g, 1.0 mmol) in $ClCH_2CH_2Cl$ (30 mL) was treated with $PhSSiMe_3$ (0.76 mL, 4.0 mmol) in the presence of $BF_3{\cdot}Et_2O$ (90 μL, 0.7 mmol) as described above for **3**→**4**. Purification of the residue by chromatography on silica gel (6:1 toluene–EtOAc) gave **16** (1.76 g, 72%) as a colorless syrup; R_f 0.49 (4:1 toluene–EtOAc); $[\alpha]_D^{20}$ −3.5° (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.19, 1.20, 1.22, 1.24, 1.26 (5 s, 63 H, 7 C(CH_3)$_3$), 2.11 (s, 3 H, AcCH_3), 3.35–3.70 (m, 28 H, H-3 (a–g), H-5 (a–g), 2 H-6 (a–g)), 3.83–4.15 (m, 28 H, 28 All-H-1), 4.25 (bd, 1 H, H-4), 4.32 (m, 5 H, H-4 (a–f)), 4.61 (d, 1 H, H-1a), 4.82–5.02 (m, 12 H, H-1 (b–g), H-2 (b–g)), 5.09–5.35 (m, 29 H, H-2a, 28 All-H-3), 5.42 (d, 1 H, H-4g), $J_{1a,2a}$ 9.9, $J_{3g,4g}$ 3.4 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.9 (Ac*C*H_3), 67.1 (C-4g), 68.1, 68.5, 69.0, 69.3, 70.8, 71.0, 71.1, 73.9, 74.2, 74.5, 74.6, 77.3, 78.8, 80.3, 80.4, 80.5, 81.3 (C-2 (a–g), C-3 (a–g), C-5 (a–g), C-4 (a–f)), 68.6, 69.4, 70.0, 70.3, 70.4, 70.5, 71.2, 71.3, 71.4, 72.5, 72.7 (C-6 (a–g), 14 All-C-1), 87.3 (C-1a), 99.7, 100.1 (C-1 (b–g)), 170.3 (*C*OMe); MS (ESI): *m*/*z* 2459.4 $[M + Na]^+$. Anal. Calcd for $C_{127}H_{190}O_{43}S$ (2436.93): C, 62.59; H, 7.86. Found: C, 62.60; H, 7.84.

*Phenyl [(3,6-di-*O*-allyl-2-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1→4)-]$_6$-3,6-di-*O*-allyl-2-*O*-pivaloyl-1-thio-*

β-D-*galactopyranoside* (**17**).—Galactoheptaoside **16** (1.71 g, 0.7 mmol) was de-*O*-acetylated as described above for **4**→**5**. The resulting residue was subjected to column chromatography (3:1 toluene–EtOAc) to give **17** (1.43 g, 86%) as a colorless syrup; R_f 0.47 (2:1 toluene–EtOAc); $[\alpha]_D^{20}$ −8.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 2.20–2.50 (bs, 1 H, 4g-OH), 3.35–3.75 (m, 28 H, H-3 (a–g), H-5 (a–g), 2 H-6 (a–g)), 3.86–4.16 (m, 29 H, H-4g, 28 All-H-1), 4.23–4.35 (m, 6 H, H-4 (a–f)), 4.61 (d, 1 H, H-1a), 4.81–5.09 (m, 13 H, H-1 (b–g), H-2 (a–g)), $J_{1a,2a}$ 10.0 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): *δ* 66.6 (C-4g), 68.1, 68.6, 69.0, 69.3, 69.5 (C-4 (a–f)), 69.1, 69.8, 70.1, 70.4, 70.5, 71.1, 71.2, 71.3, 71.5, 72.7 (C-6 (a–g), 14 All-C-1), 70.7, 71.1 (C-2 (a–g)), 73.6, 74.2, 74.3, 74.5 (C-5 (a–g)), 78.8, 79.1, 80.3, 80.5, 81.3 (C-3 (a–g)), 99.5, 99.6, 100.0, 100.1 (C-1 (b–g)); MS (ESI): *m*/*z* 2417.2 $[M+Na]^+$. Anal. Calcd for $C_{126}H_{188}O_{42}S$ (2394.90): C, 62.69; H, 7.91. Found C, 62.28; H, 7.60.

Phenyl (3,6-di-O-*allyl-2*-O-*pivaloyl-4*-O-*trimethylsilylethoxymethyl-β*-D-*galactopyranosyl)-(1→4)-[(3,6-di*-O-*allyl-2*-O-*pivaloyl-β*-D-*galactopyranosyl)-(1→4)-]$_5$-*3,6-di*-O-*allyl-2*-O-*pivaloyl-1-thio-β*-D-*galactopyranoside* (**18**).—A solution of 4g-OH free heptaoside **17** (1.36 g, 0.57 mmol), EtN(*i*Pr)$_2$ (0.17 mL, 1.0 mmol) and 2-(trimethylsilyl)ethoxymethyl chloride (0.12 mL, 0.68 mmol) in CH_2Cl_2 (1 mL) was stirred at rt for 24 h. After dilution with CH_2Cl_2 (250 mL), the mixture was washed with 2 N HCl (250 mL) and satd aq $NaHCO_3$ (250 mL), dried ($MgSO_4$), filtered, and concentrated to a syrup. Chromatography on silica gel (5:1 toluene–EtOAc) afforded, after the evaporation of the appropriate fractions, **18** (1.23 g, 86%) as a colorless syrup; R_f 0.80 (2:1 toluene–EtOAc); $[\alpha]_D^{20}$ −11.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): *δ* −0.01 (s, 9 H, Si(CH_3)$_3$), 0.90 (m, 2 H, SiCH_2), 3.33–3.73 (m, 30 H, H-3 (a–g), H-5 (a–g), 2 H-6 (a–g), OCH_2), 3.85–4.14 (m, 29 H, H-4g, 28 All-H-1), 4.29 (m, 6 H, H-4 (a–f)), 4.59 (d, 1 H, H-1a), 4.72 (d, 1 H, J_{OCH_2O} 6.8 Hz, 0.5 OCH_aH$_b$O), 4.81–5.00 (m, 13 H, H-1 (b–g), H-2 (b–g), 0.5 OCH$_a$$H_b$O), 5.04–5.34 (m, 29 H, H-2a, 28 All-H-3), $J_{1a,2a}$ 9.8 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): *δ* −1.4 (Si(*C*H$_3$)$_3$), 17.8 (Si*C*H$_2$), 65.7 (O*C*H$_2$), 67.8, 68.0, 68.3, 68.7, 69.0, 69.2 (C-4 (a–g)), 70.8 (C-2 (a–g)), 69.5, 69.9, 70.2, 70.3, 70.9, 71.0, 71.3, 72.4 (C-6 (a–g), 14 All-C-1), 73.9, 74.1, 74.2, 74.3 (C-5 (a–g)), 78.5, 79.8, 80.0, 80.3, 81.0 (C-3 (a–g)), 87.1 (C-1a), 95.6 (O*C*H$_2$O), 99.4, 99.5, 99.8 (C-1 (b–g)); MS (ESI): *m*/*z* 2548.2 $[M+Na]^+$. Anal. Calcd for $C_{131}H_{202}O_{43}SSi$ (2525.16): C, 62.31; H, 8.06. Found: C, 62.45; H, 7.94.

Phenyl (3,6-di-O-*allyl-4*-O-*trimethylsilylethoxymethyl-β*-D-*galactopyranosyl)-(1→4)-[(3,6-di*-O-*allyl-β*-D-*galactopyranosyl)-(1→4)-]$_5$-*3,6-di*-O-*allyl-1-thio-β*-D-*galactopyranoside* (**19**).—A suspension of **18** (1.19 g, 0.47 mmol) and LiOH·H_2O (1.38 g, 32.9 mmol) in MeOH (10 mL) was refluxed for 16 h. After cooling to rt, the mixture was filtered and the residue was thoroughly washed with MeOH (100 mL). The combined filtrates were neutralized with Amberlite IR 120 (H^+ form), filtered, and concentrated. The resulting syrup was subjected to a silica gel column (2:1 toluene–EtOAc) to give **19** (640 mg, 70%) as a colorless foam; R_f 0.34 (1:1 toluene–EtOAc); $[\alpha]_D^{20}$ +4.7° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 0.00 (s, 9 H, Si(CH_3)$_3$), 0.92 (m, 2 H, SiCH_2), 3.28–3.87 (m, 44 H, H-2 (a–g), H-3 (a–g), H-5 (a–g), 2 H-6 (a–g), OCH_2, 7 OH], 3.90–4.42 (m, 41 H, H-1 (b–g), H-4 (a–g), 28 All-H-1), 4.47 (d, 1 H, H-1a), 4.72, 4.96 (2d, 1 H each, J_{OCH_2O} 7.0 Hz, OCH_2O), $J_{1a,2a}$ 9.6 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): *δ* −1.4 (Si(CH_3)$_3$), 18.1 (Si*C*H$_2$), 65.7 (O*C*H$_2$), 68.8, 69.0, 69.2, 69.3, 69.7 (C-6 (a-g)), 70.4, 72.0, 72.1, 72.2, 72.3, 72.6 (14 All-C-1), 69.4, 72.8, 73.4, 73.6, 73.8, 74.2, 75.4, 76.8, 76.6, 76.7, 77.0, 77.5, 78.5, 80.3, 80.4, 80.6, 81.2, 81.8 (C-2 (a–g), C-3 (a–g), C-4 (a–g), C-5 (a–g)), 88.5 (C-1a), 95.6 (O*C*H$_2$O), 105.0, 105.4, 105.7, 105.78, 105.8, 107.0 (C-1 (b–g)); MS (ESI): *m*/*z* 1959.7 $[M+Na]^+$. Anal. Calcd for $C_{96}H_{146}O_{36}SSi$ (1936.33): C, 59.55; H, 7.60. Found: C, 59.15; H, 7.52.

Phenyl (2-O-*acetyl-3,6-di*-O-*allyl-4*-O-*trimethylsilylethoxymethyl-β*-D-*galactopyranosyl)-(1→4)-[(2*-O-*acetyl-3,6-di*-O-*allyl-β*-D-*galactopyranosyl)-(1→4)-]$_5$-*2*-O-*acetyl-3,6-di*-O-*allyl-1-thio-β*-D-*galactopyranoside* (**20**).—A solution of **19** (600 mg, 0.31 mmol), pyridine (0.78 mL, 9.8 mmol), Ac_2O (0.62 mL, 6.5 mmol), and a catalytic amount of DMAP in CH_2Cl_2 (4 mL) was stirred at rt for 16 h. CH_2Cl_2 (100 mL) was added and the mixture was washed with 2 N HCl (100 mL) and satd aq $NaHCO_3$ (100 mL), dried ($MgSO_4$), filtered, and evaporated in vacuo. The residue was purified by elution from a silica gel column (2:1 toluene–EtOAc) to give **20** (540 mg, 77%); R_f 0.79 (1:1 toluene–EtOAc); $[\alpha]_D^{20}$ −24.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): *δ* 0.00 (s, 9 H, Si(CH_3)$_3$), 0.91 (m, 2 H, SiCH_2), 2.04, 2.06, 2.14, 2.15, 2.15 (6s, 21 H, 7 AcCH_3), 3.35–3.73 (m, 30 H, H-3 (a–g), H-5 (a–g), 2 H-6 (a–g), OCH_2), 3.93–4.15 (m, 29 H, H-4, 28 All-H-1), 4.20 (m, 6 H, 6 H-4), 4.55 (d, 1 H, H-1a), 4.72 (d, 2 H, $J_{1,2}$ 7.2, J_{OCH_2O} 7.2 Hz, 1-H, OCH_aH$_b$O), 4.86 (m, 6 H, 5 H-1, OCH$_a$$H_b$O), 5.09–5.34 (m, 35 H, H-2 (a–g), 28 All-H-3), $J_{1a,2a}$ 10.0 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): *δ* −1.4 [Si(*C*H$_3$)$_3$], 18.1 (Si*C*H$_2$), 20.8, 20.9 (7 Ac*C*H$_3$), 65.7 (O*C*H$_2$), 68.7, 69.1, 69.3, 69.9, 70.2, 71.1, 71.6 (C-2 (a–g), C-4 (a–g)), 69.2, 69.4, 69.5, 69.6 (C-6 (a–g)), 70.8, 70.9, 71.0, 72.4, 72.5 (14 All-C-1), 73.8, 73.9, 78.2, 79.5, 79.7, 79.9, 80.0, 81.1 (C-3 (a–g), C-5 (a–g)), 86.4 (C-1a), 95.7 (O*C*H$_2$O), 99.5, 99.8, 100.2 (C-1 (b–g)), 169.3, 169.8, 169.9, 170.0 (7 *C*OMe); MS (ESI): *m*/*z* 2253.2 $[M+Na]^+$. Anal. Calcd for $C_{110}H_{160}O_{43}SSi$ (2230.59): C, 59.23; H, 7.23. Found: C, 59.09; H, 7.30.

Phenyl (2-O-acetyl-3,6-di-O-allyl-β-D-galactopyranosyl)-(1→4)-[(2-O-acetyl-3,6-di-O-allyl-β-D-galactopyranosyl)-(1→4)-]$_5$-2-O-acetyl-3,6-di-O-allyl-1-thio-β-D-galactopyranoside (**21**).—A mixture of galactoheptaoside **20** (450 mg, 0.2 mmol) in THF (0.5 mL) and freshly activated molecular sieve (4 Å) was treated with HF–pyridine (3 mL) at rt for 30 min. The resulting slurry was extracted with CH_2Cl_2 (100 mL), washed with satd aq $NaHCO_3$ (100 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate in vacuo and chromatography of the residue on a silica gel column (3:2 toluene–EtOAc) afforded **21** (350 mg, 77%) as a colorless foam; R_f 0.53 (1:1 toluene–EtOAc); $[\alpha]_D^{20}$ −19.0° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.06, 2.08, 2.16, 2.18, 2.19, 2.22 (6s, 21 H, 7 AcCH_3), 2.30 (bs, 1 H, 4g-OH), 3.36–3.79 (m, 28 H, H-3 (a–g), H-5 (a–g), 2 H-6 (a–g)), 3.95–4.18 (m, 29 H, H-4, 28 All-H-1), 4.19–4.24 (m, 6 H, 6 H-4), 4.56 (d, 1 H, H-1a), 4.75 (d, 1 H, H-1), 4.89 (m, 5 H, 5 H-1), 5.05 (m, 6 H, H-2 (b–g)), 5.11–5.34 (m, 29 H, H-2a, 28 All-H-3), $J_{1a,2a}$ 10.0, $J_{1,2}$ 7.8 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.0, 21.1, 21.2 (7 AcCH_3), 66.8, 68.9, 69.2, 69.5, 70.1, 70.3, 71.3 (C-2 (a–g), C-4 (a–g)), 69.1, 69.3, 69.5, 69.6, 69.8 (C-6 (a–g)), 71.0, 71.1, 71.2, 72.6, 72.7 (14 All-C-1), 73.6, 73.8, 73.9, 78.4, 78.6, 79.9, 80.0, 80.2, 81.3 (C-3 (a–g), C-5 (a–g)), 86.4 (C-1a), 99.7, 99.8, 99.9, 100.1, 100.4 (C-1 (b–g)), 169.5, 170.0, 170.1, 170.2 (7 *C*OMe); MS (ESI): *m/z* 2122.8 $[M-H+Na]^+$, 2123.7 $[M+Na]^+$. Anal. Calcd for $C_{104}H_{146}O_{42}S$ (2100.33): C, 59.47; H, 7.01. Found C, 59.23; H, 7.07.

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