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Synthesis of Branched Dithiotrisaccharides via Ring-Opening Reaction of Sugar Thiiranes

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Supporting Information

ABSTRACT: Satisfactory procedures are described for the synthesis of 5,6- and 3,4-thiirane derivatives from the respective hexofuranose or hexopyranose epoxide precursors. The controlled ring-opening reaction of thiiranes by 1-thioaldoses was successfully accomplished to afford, regio- and stereoselectively, *β*-*S*-(1→4)-3,4-dithiodisaccharides. For instance, the regioselective attack of per-*O*-acetyl-1-thioglucose (**16**) to C-4 of 2-propyl 2,6-di-*O*-acetyl-3,4-epithio-*α*-D-galactopyranoside (**14**) gave the derivative of Glc*p*-*β*-*S*-(1→4)-3,4-dithioGlc*p*-*O*-*i*Pr (**17**). This thiodisaccharide was accompanied by the (1→3)-disulfide **18**, formed between **16** and **17**, and the symmetric (3→3)-disulfide **19**, which resulted from the oxidative dimerization of **17**. However, the *S*-acetyl derivative of **17** could be obtained in good yield (62%) by $LiAlH_4$ reduction of the crude mixture **17**−**19**, followed by acetylation. The same sequence of reactions starting from **14** and the 1-thiolate of Gal*p* afforded the per-*O*,*S*-acetyl derivative of Gal*p*-*β*-*S*-(1→4)-3,4-dithio-*α*-D-Glc*p*-*O*-*i*Pr (**23**), which was selectively *S*-deacetylated to give **25**. The dithiosaccharides **17** and **25** are 3,4-di-*S*-analogues of derivatives of the natural disaccharides cellobiose and lactose, respectively. The ring-opening reaction of 5,6-epithiohexofuranoses of D-*galacto* (**8**) or L-*altro* (**11**) configuration with 1-thioaldoses was also regio- and stereoselective to give the respective *β*-*S*-(1→6)-linked 5,6-dithiodisaccharides **26** or **29** in excellent yields. Glycosylation of the free thiol group of **17**, **25**, or **26**, using trichloroacetimidates as glycosyl donors, led to the corresponding branched dithiotrisaccharides. Some of them are sulfur analogues of derivatives of branched trisaccharides found in natural polysaccharides.

INTRODUCTION

Oligosaccharides are rarely considered for drug discovery due, among other reasons, to the lability of the glycosidic bond. To address the issue of the enzyme degradation of oligosaccharides in organisms, the preparation of stable mimetics is a topic of current interest.[1] Thus, oligosaccharide analogues with the glycosidic oxygen atom substituted by sulfur or other heteroatoms have been synthesized.[2,3] The thioglycosidic linkage is usually stable to enzymatic processes, and the thiooligosaccharides may display inhibitory activity against glycosidases. These glycomimetics are also useful tools for structural biology, as the sulfur atom may act as hydrogen bond acceptor and the thiolinkage provides a higher degree of flexibility between glycosyl units.[4] Therefore, thiooligosaccharides can change more easily their conformation, with respect to their natural counterparts, to enable a better fit in the catalytic site of enzymes. For all these reasons they are frequently employed to study protein−carbohydrate interactions, as binding and recognition events initiate immunological responses to infections and signaling processes that occur in inflammation and cancer metastasis.[5]

In the last years, we have been involved in a project on the synthesis of thiooligosaccharides as potential enzyme inhibitors,[6] and we have recently reported the diastereoselective synthesis of thiodisaccharides based on the ring-opening of sugar epoxides with 1-thioaldoses.[7] The advantage of this procedure relies upon the regio- and stereocontrol due to the steric and electronic effects operating during the ring-opening reaction.[8] These effects have been well established for reactions of oxirane derivatives of sugars with nucleophiles.[9] However, the analogous opening of episulfides by nucleophiles has been less studied. In this type of reactions, the thiol group released after the thiirane ring-opening competes with the attacking nucleophile leading to polymerizations and other side reactions.[10] Thiiranes can also react with electrophiles and are able to undergo oxidation or reduction at sulfur, and thermal and photochemical reactions have also been reported.[11] In the field of carbohydrates, some examples of ring-opening of sugar thiiranes by nucleophiles have been reported. For instance, the $LiAlH_4$ reduction of a 5,6-epithio derivative of *α*-D-glucofuranose afforded the expected 6-deoxy-5-thiofuranose, which upon attack to the unreacted thiirane, led to *S*-(5→6)-linked oligomers as by products.[12] A 1,2-episulfide has been proposed as the intermediate formed by treatment of phenyl 1,2-dithio-*α*-D-mannopyranoside with alkali. The 1,2-episulfide underwent ring-opening oligomerization to afford a family of (1→2)-linked thiooligo-*α*-D-mannopyranosides.[13] Derivatives of 1,2:5,6-diepithio-D-alditols have been employed as monomeric precursors of thiosugar polymers that contain thiofuranose, thiopyranose, and open-chain residues.[14]

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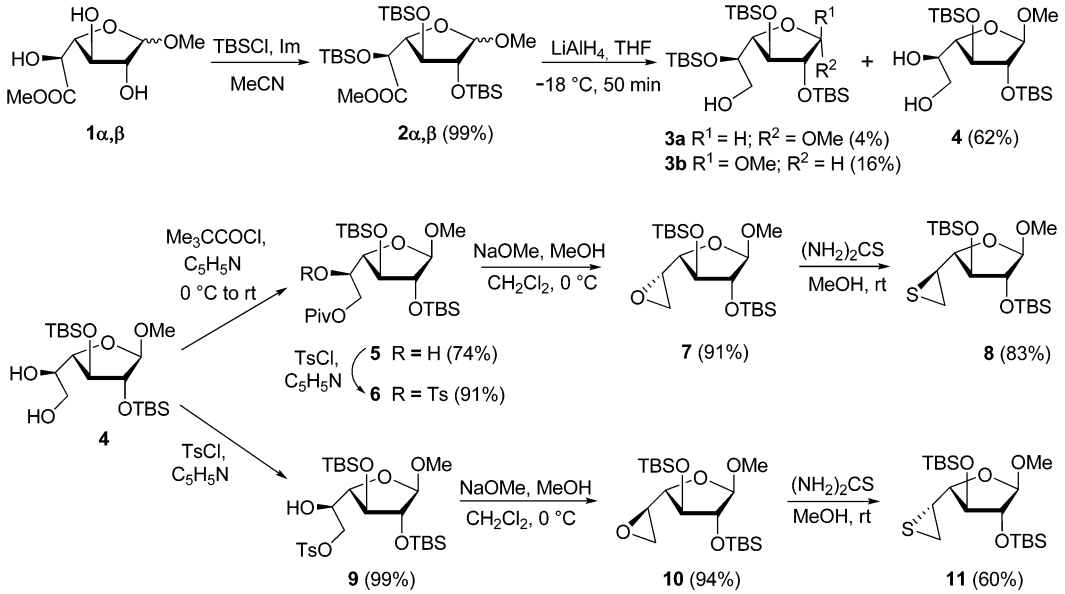
Scheme 1. Synthesis of Thiirane Derivatives 8 and 11



We assumed that the controlled ring-opening of a sugar thiirane by a 1-thiosugar nucleophile would allow the installation of two contiguous sulfur-containing stereocenters in a pyranose or furanose unit. The thiol group formed as result of the opening of the episulfide may be glycosylated by standard procedures to afford a branched dithiotrisaccharide. In contrast to this rather direct methodology, the classical approach for the synthesis of branched *S*,*S*-trisaccharides based on standard S_N2 displacement reaction,[1−3] has been limited to just a few examples because of its multistep nature.[15,16]

Here we describe convenient procedures for the synthesis of 5,6-thiirane derivatives of furanoses and a 3,4-thiirane derivative of a pyranose from the corresponding epoxide precursors. The controlled ring-opening reaction of episulfides with 1-thioaldoses was employed as key step for the preparation of the *S*-glycosidic linkage with the concomitant release of a thiol group in the vicinal carbon atom. The resulting products are useful precursors for the synthesis of branched dithiotrisaccharides.

RESULTS AND DISCUSSION

To explore the strategy proposed for the synthesis of branched dithiotrisaccharides, selectively protected sugar episulfides were required. These key intermediates are usually obtained from sugar epoxides, compounds that have been already prepared in our laboratory.[7] We considered that, similar to the 5,6-epoxides of a hexofuranose, the 5,6-thiirane analogues are expected to undergo regioselective ring-opening by attack of the nucleophile to the less substituted C-6 position. For this reason, and taking also into account the participation of galactofuranose (Gal*f*) in many biological processes in microorganisms,[17] we selected this sugar as starting compound. Conveniently protected derivatives of Gal*f* were prepared starting from methyl (methyl-α,β-D-galactofuranosid)uronate (**1α,β**),[18] the product of methanolysis of D-galacturonic acid (Scheme 1). Silylation of **1α,β** with an excess of *tert*-butyldimethylsilyl chloride (TBSCl) afforded the anomeric mixture (β/α ~9:1) of the 2,3,5-tri-*O*-silyl derivatives (**2α,β**) in almost quantitative yield. Reduction of the ester function of **2α,β** with $LiAlH_4$ in THF gave a product distribution that showed to be highly dependent on the reaction conditions. Thus, reduction of **2α,β** with a slight excess (1.3 molar equiv) of $LiAlH_4$ at low temperature (−18 °C) for short periods (30 min) afforded the expected product **3a** and **3b** (major). Under the same conditions but using longer reaction times (50 min), **2α,β** underwent removal of the silyl ether at C-5 to give the 2,3-di-*O*-silyl derivative **4** as the major product. This compound was envisioned as an useful precursor for the stereoselective synthesis of epoxides and thiiranes that belong to the D- or L-series, as described below. Additionally, it was observed that when the reaction was conducted at room temperature, the 5-*O* → 6-*O* migration of the TBS group in **3a,b** occurred to give the respective products having HO-5 free, although in a low isolated yield. The migration of ester groups from 5-*O* to 6-*O* is rather common in Gal*f* derivatives[19] and migrations of silyl ethers in carbohydrates have also been reported.[20]

To obtain the 5,6-thiirane of *galacto* configuration from **4**, a double inversion of the C-5 configuration was required. Therefore, the primary hydroxyl group of the diol **4** was selectively pivaloylated to the 6-*O*-pivaloyl derivative **5**. Further tosylation of HO-5 afforded the 5-*O*-sulfonyl derivative **6**, which on treatment with 2 M NaOMe in MeOH at 0 °C led to the epoxide **7** (α-L-*altro* configuration). The ^1H NMR spectrum of **7** showed characteristic signals of the oxirane ring protons protected at 3.07 (H-5), 2.81 (H-6a), and 2.73 ppm (H-6b). The ^{13}C NMR spectrum of **7** exhibited the resonances of the carbons, involved in the oxirane ring (C-5 and C-6), at relatively high fields, in the region of 52−44 ppm. Epoxides are usually converted into thiiranes by reaction with thiourea.[21] Thus, treatment of **7** with thiourea in methanol at room temperature afforded the episulfide **8** (D-*galacto* configuration). The replacement of the oxygen atom by the sulfur atom in the three-membered ring produces a further upfield shifting for the signals of the protons and carbons involved in the thiirane, with respect to those of the oxirane.

For the preparation of the 5,6-episulfide **11**, that belongs to the α-L-*altro* series, was needed retention of the C-5 configuration in the epoxide precursor. Hence, the selective tosylation of HO-6 in **4** led to the 6-*O*-tosyl derivative **9**. On

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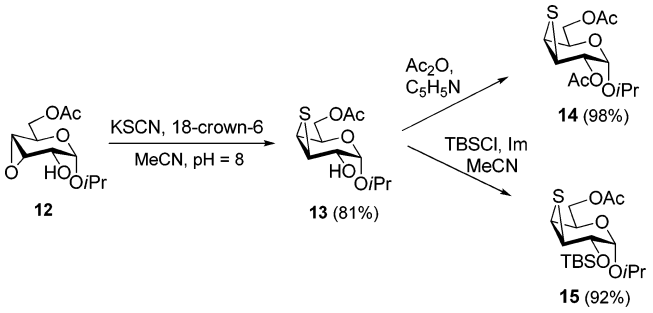
treatment with 2 M NaOMe/MeOH, compound **9** was converted into the epoxide **10**. Reaction of **10** with thiourea in MeOH afforded the 5,6-episulfide **11**. In the ^{13}C NMR spectrum of epoxides **7**, **10** and episulfides **8** and **11** the change of configuration at C-5 from D-*galacto* to L-*altro* produced a downfield shifting for the signal of the vicinal carbon atoms C-4 and C-6. In particular, the C-4 signal in the altrofuranoside **11** is strongly deshielded (89.9 ppm).

The epoxide **12** was employed as key precursor for the synthesis of a thiirane derivative fused to a pyranose ring (Scheme 2). Compound **12** has been readily prepared starting

Scheme 2. Synthesis of Thiirane Derivatives 13−15

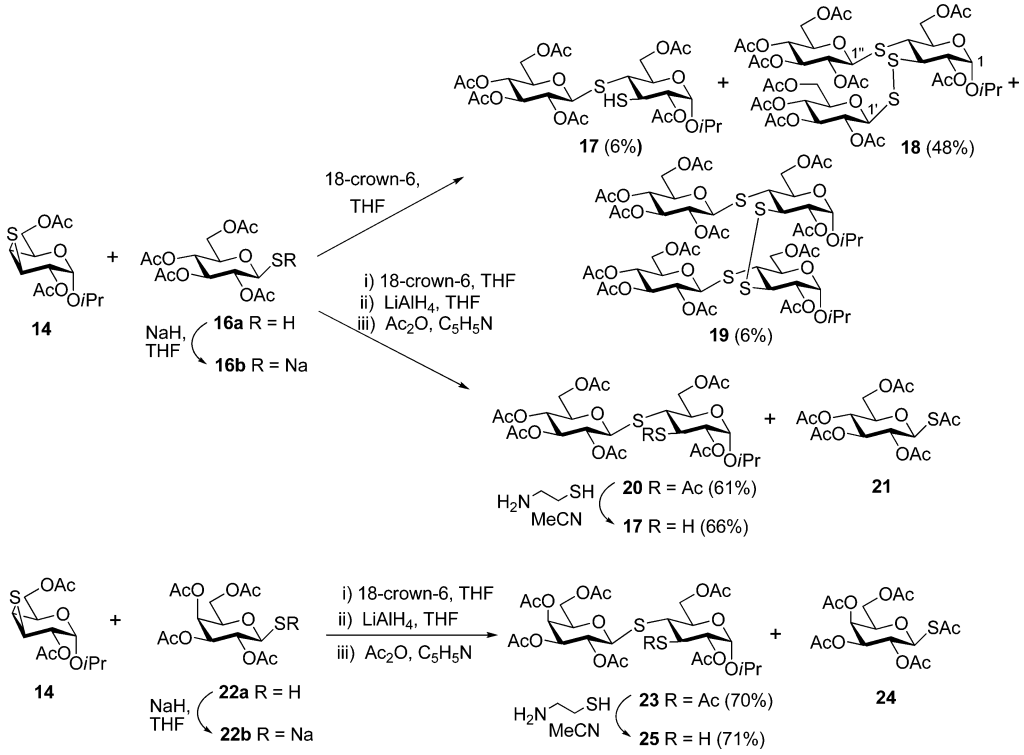


from a 2-acetoxy-per-*O*-acetyl-D-galactal.[7] We have selected the *galacto* configuration for the epithio pyranoside derivative as, similar to the analogous epoxide, the controlled ring-opening reaction with a 1-thioaldopyranose is expected to take place by attack to C-4 to produce a 3,4-dithioglucose derivative.[7] Glucose is a common component of polysaccharides and glycoconjugates, whereas gulose is a rather rare sugar. The 3,4-dithio derivative of gulose should be the result of the same attack to the thiirane of opposite D-*allo* configuration.

Unfortunately, the reaction with thiourea that successfully converted epoxides **7** or **10** into the corresponding thiiranes **8** or **11** failed when applied to **12**, and no reaction took place either under more drastic conditions. It is known that epoxides with high S_N2 reactivity produce thiiranes when treated with potassium or ammonium thiocyanates.[22,23] Under standard conditions, the reaction of **12** with KSCN was unsuccessful, and at higher temperatures the conversion of the epoxide into the corresponding alkene was observed. However, the synthesis of thiirane **13** could be successfully accomplished (81% yield) by reaction of **12** with KSCN at pH = 8, in the presence of 18-crown-6. Similar conditions have been employed by Bellomo and Gonzalez[24] for the conversion of epoxide derivatives of inositols into episulfides. The absolute configuration for the C-3 and C-4 stereocenters in **13** was confirmed by means of the NOESY spectrum. The NOE contacts between H-3 and H-5, and those of one methyl group of the isopropyl substituent with H-3 and H-4 are indicative that the thiirane ring was located in the β face of the molecule (D-*galacto* configuration). A 3,4-thiirane derivative analogue of **13**, methyl 2-*O*-acetyl-6-deoxy-3,4-epithio-α-D-galactopyranoside, has been obtained as a minor product by KSCN ring-opening reaction from a 3,4-epoxide precursor.[25]

In compound **13**, the free hydroxyl group at C-2 is conveniently disposed with respect to the vicinal 3,4-thiirane ring for the intramolecular nucleophilic attack to C-3, as observed for analogous epoxide systems.[7,9] Therefore, the alcohol function of **13** was acetylated or silylated under standard conditions to afford, respectively, the 2-*O*-acetyl (**14**) or 2-*O*-TBS (**15**) derivatives. It is worth mentioning that the synthesis of thiiranes **14** or **15** starting from the 2-*O*-acetyl or 2-*O*-TBS derivatives of the epoxide **12**, under the above-mentioned conditions, produced only very low yield of such

Scheme 3. Ring-Opening Reaction of Thiirane 14 by 1-Thioaldoses



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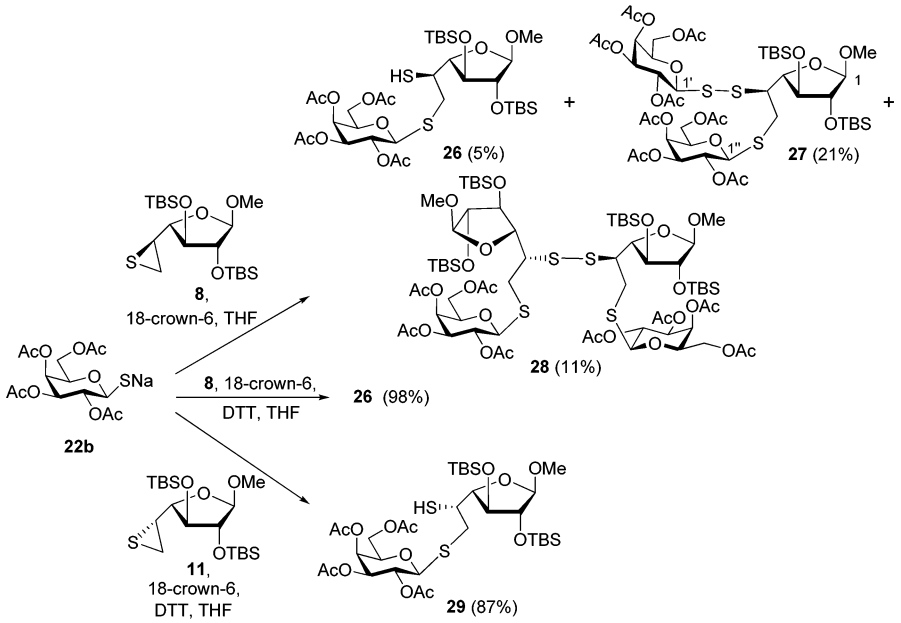
Scheme 4. Ring-Opening Reaction of Thiirane 8 and 11



products, indicating the strong effect of the substitution of the HO-2 in the course of the reaction.

Having the thiiranes **8**, **11**, and **13**−**15** in hand, the episulfide-opening reaction was studied. We expected that the nucleophilic opening of the thiirane ring in the pyranose derivatives **13**−**15** should be more difficult than that in the analogue furanoses (**8** and **11**), as the latter involves a terminal methylene carbon in the ring. Therefore, we explored first the reaction with the pyranose-derived thiirane **14** (Scheme 3). Under the conditions optimized for the oxirane-ring-opening of pyranoses with 1-thioaldoses (LiOMe−MeOH at 60 °C, followed by acetylation),[7] the reaction of the thiirane **15** with the 1-thioglucose derivative **16a** afforded unreacted material together with the per-*O*-acetyl derivative of Glc-*S*-(1→1)-*S*-Glc[26] (the symmetric disulfide of **16**) and 2-propyl 6-*O*-acetyl-2-*O*-*tert*-butyldimethylsilyl-3,4-dideoxy-α-D-*erythro*-hex-3-eno-pyranoside,[7] the product of eliminative desulfuration of **15**. This one was the main product when the temperature of the reaction was increased, in agreement with the fact that unsaturated derivatives are usually obtained upon heating alkaline solutions of episulfides.[27] The opening of the thiirane was also unsuccessful using acid catalysis[28] (AcOH in DMF or TMSI in CH_2Cl_2) as unreacted starting material was recovered. However, attack to the episulfide ring of **14** took place using as nucleophile the sodium thiolate **16b** (prepared by reaction of **16a** with NaH) in the presence of 18-crown-6. Column chromatography of the reaction mixture afforded three products; the first one was the expected thiodisaccharide **17**, which was isolated in low yield (6%). From the following fractions of the column were obtained the disulfides **18** and **19**, in 48% and 6% yield, respectively.

The structures of **17**−**19** were established on the basis of their NMR spectra. Thus, the ^{1}H NMR spectrum of **17** showed at high fields (3.99 and 2.91 ppm) the signals of the protons linked to sulfur (H-3 and H-4, respectively). The large values (>11 Hz) for the coupling constant associated to these signals ($J_{2,3}$, $J_{3,4}$, and $J_{4,5}$) were indicative of a *gluco* configuration for the reducing-end of the thiodisaccharide **17**. Furthermore, the *HS* signal appeared as a doublet because of the coupling with H-3 ($J_{3,HS}$ = 3.9 Hz). The $J_{1',2'}$ value (10.2 Hz) confirmed that the β anomeric configuration was maintained for the 1-thioaldose moiety, which showed the resonance of the anomeric proton shifted upfield ($\delta_{H\text{-}1'}$ = 4.65) with respect to that of the *O*-glycoside ($\delta_{H\text{-}1}$ = 5.09) because of the shielding effect of sulfur. Similarly, the ^{13}C NMR spectrum of **17** exhibited the C-1 signal of the *S*-glycoside at higher field ($\delta_{C\text{-}1'}$ = 82.3) than that of the *O*-glycoside ($\delta_{C\text{-}1}$ = 93.8). The HRMS of **17** was in agreement with the structure proposed; whereas that of **18** was indicative of the incorporation of an additional molecule of 1-thioaldose into the molecule. The presence of three sulfur atoms suggested the formation of a disulfide bond from **17**. The ^{1}H and ^{13}C NMR spectra confirmed this assumption, as **18** showed three anomeric signals, two of them [^{1}H: 5.09 ($J_{1,2}$ = 3.7 Hz) and 4.63 ppm ($J_{1'',2''}$ = 10.2 Hz); ^{13}C: 94.2 (C-1) and 81.3 ppm (C-1″)] similar to those observed for **17**. The additional signal detected in the respective spectra, at 4.51 ppm (J = 10.2 Hz) and 89.5 ppm, were assigned to the H and C of the anomeric center bonded to the disulfide. Thus, the anomeric carbon atom signal is shifted downfield (~8 ppm) with respect to the same signal of the thioglycoside, and the resonance of C-3 is also deshielded (~9 ppm) with respect to that of C-3 in **17**, linked to the free thiol group. In contrast, the signal of the β carbon bonded to sulfur (C-4) was shielded (~5 ppm) in comparison to same signal in **17**.

Compound **18** should be produced by disulfide bond formation between the free thiol groups of **17** and **16b**, whereas the oxidative dimerization of **17** would explain the formation of the symmetric disulfide **19**. The formation of disulfides in ring-opening reactions of thiiranes with common nucleophiles has been reported.[10] The structure of **18** was also confirmed as this disulfide was alternatively obtained by reaction of **16b** and **17**, under the conditions employed for the ring-opening reaction. Significantly, the dithiohexopyranose unit of compounds **17**−**19** has the same *gluco* configuration. This stereochemistry results from the regioselective attack of **16b** to C-4 of the episulfide **17**, with *trans*-opening of the ring. The approach of the nucleophile to C-3 should experience

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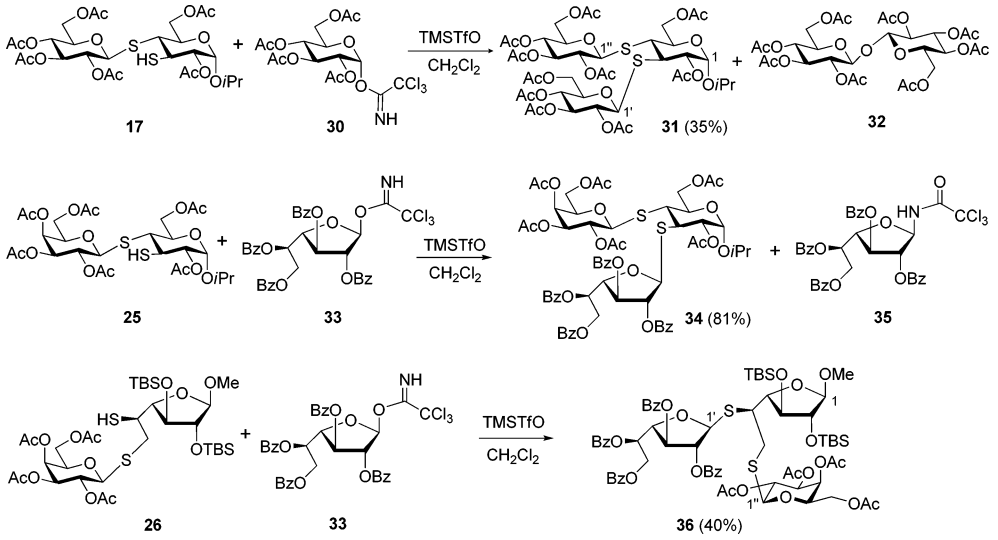
Scheme 5. Synthesis of Branched Dithiotrisaccharides 31, 34, and 36



gauche and 1,3-diaxial interactions with the respective vicinal acetoxy group and 2-propyloxy group at C-1. The approach of **16b** to C-4 of the thiirane **14** is free of such repulsive interactions.

The optimization of the conditions for the reaction between **14** and **16b** was attempted, in order to avoid the formation of the disulfides **18** and **19**. The change of the solvent (acetonitrile instead of THF) or a lowering in the temperature (−18 °C) did not produce a decrease of such byproducts. Although dithiothreitol (DTT) is usually employed to reduce the formation of disulfide linkages,[2,29] the incorporation of this reagent to the reaction medium did not have any effect. However, taking into account that compounds **18** and **19** can be seen as derivatives of the thiodisaccharide **17**, we considered that the disulfide reduction of compounds **17**−**19** will produce **17** as main product. Although reductions with sodium borohydride, Zn/AcOH, or Zn/Ac_2O were unsuccessfully attempted, we found that treatment of the crude mixture **17**−**19** with $LiAlH_4$ and further acetylation afforded **20**, the *S*-acetyl derivative of **17**, in 62% yield. As byproduct was isolated 2,3,4,6-tetra-*O*-acetyl-1-*S*-acetyl-1-thio-*β*-D-glucopyranose (**21**),[30] which may be formed from **18**, and also by acetylation of the excess of **16b** employed for the ring-opening of thiirane **14**.

Compound **14** was also allowed to react with the sodium salt of per-*O*-acetyl-1-thio-*β*-D-galactopyranose (**22b**). Further $LiAlH_4$ reduction of the reaction mixture, followed by acetylation, led to thiodisaccharide **23** (70% yield). This product was accompanied with **24**,[31] the *S*-acetyl derivative of **22a**. Selective removal of the thioacetyl group of **20** or **23** with cysteamine[29b,32] afforded, respectively, the thiodisaccharides **17** or **25**. Interestingly, compounds **17** and **25** are the respective 3,4-dithio analogues of the natural disaccharides cellobiose and lactose. Furthermore, an analogue of **17**, a derivative of 3-*S*-glycosyl-3,4-dithioglucose, has been previously synthesized as the dithiodisaccharide precursor of the thio-linked sialyl Lewis X.[16]

The reaction of the thiirane **8** with the sodium salt of per-*O*-acetyl-1-thio-*β*-D-galactopyranose (**22b**) was studied (Scheme 4). Under the same conditions employed for the ring-opening of **14**, compound **8** afforded the mixture of thiodisaccharide **26** (5%) and the disulfides **27** and **28** (21% and 11%, respectively). The thiodisaccharide **26** results, as expected, from the attack of the nucleophile **22b** to the less substituted ring carbon of the episulfide **8**. The ^1H NMR spectrum of **26** confirmed that the free thiol group was substituting C-5, as it was detected a coupling between H-5 and the *HS* (1.92 ppm, $J_{5,HS}$ = 9.4 Hz). Furthermore, in the ^{13}C NMR spectrum of **26** the chemical shift of the anomeric carbon of the furanose appeared, as expected, downfield (109.0 ppm) with respect to that of the 1-thiopyranose (83.7 ppm). The structure of the disulfide **27** was confirmed on the basis of the ^{13}C NMR data, which showed clearly the additional signal for the anomeric carbon bonded to the disulfide group, with a chemical shift value (91.4 ppm) intermediate between those of the furanose (109.7 ppm) and the 1-thiogalactopyranose units (84.5 ppm). As observed for the analogue **18**, the signal of the *α* carbon bonded to the disulfide group was shifted downfield (∼13 ppm) and that of the *β* carbon bonded to sulfur was shifted upfield (∼3 ppm), with respect to the same signals in **26**. Similar displacements were detected for the C-5 and C-6 signals in **28** (C-5 downfield 12 ppm, and C-6 upfield 4 ppm). The molecular weights of **26**−**28**, determined by HRMS, confirmed the structures proposed for these compounds. Libraries of glycosyldisulfides have been prepared using dynamic combinatorial chemistry, exploiting the ready thiol-disulfide conversion.[33] Evidence was presented that the disulfides are biologically active ligands for lectins. For instance, the dithiogalactosyldisulfide is an inhibitor of human lectins and a plant A,B-type toxin.[34]

The reaction conditions for the synthesis of the dithiosaccharide **26** were optimized. Thus, the ring-opening of thiirane **8** with the thiolate **22b** was conducted in the presence of 18-crown-6 and DTT. In contrast to the analogous reaction of the pyranose episulfide **14** with **16b**, in this case DTT prevented efficiently the formation of **27** and **28**, and the thiodisaccharide **26** was obtained in 98% yield. Under identical conditions, the reaction of episulfide **11** with the thiolate **22b**, in the presence of 18-crown-6 and DTT, afforded the thiodisaccharide **29** in 87% yield. The structure of **29** was confirmed from the NMR spectra, which was similar to that of the analogue **26**.

To accomplish the synthesis of the branched dithiotrisaccharides, the glycosylation of the free thiol group in **17** was attempted (Scheme 5). For this purpose, several glycosyl donors were employed. The reaction of **17** with penta-*O*-acetyl-

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β-D-glucopyranose in the presence of $SnCl_4$ as Lewis acid,[35] or under neutral conditions using MoO_2Cl_2 as catalyst,[36] were unsuccessful. The glycosylation of **17** with per-*O*-acetyl glucopyranosyl iodide[37] in $Et_3N-CH_2Cl_2$ led mostly to decomposition. More satisfactory results were obtained using the trichloroacetimidate **30**[38] as glycosyl donor. The reaction between **17** and **30**, under strictly dry conditions and catalysis with trimethylsilyl triflate (TMSOTf), afforded the expected branched dithiotrisaccharide **31**, although in a moderate yield (35%). The thiol group in **17** seems to be hindered by the vicinal, *gauche*-disposed *S*-glucopyranose moiety at C-4 and the acetoxy group at C-2. Probably because of the low reactivity of HS-3, part of **30** is consumed in the formation of the (1→1)-*O*-linked disaccharide **32**, which was isolated from the reaction mixture and showed properties coincident with those described in the literature.[39] The fact that disulfides **18** and **19** are formed during the ring-opening reaction of episulfide **14**, supports the sterical hindrance to the HS group in **17**, as **18** and **19**, which have longer *S*−*S* linkages than that of the thioglycoside in **31**, are more readily formed. Hence, the glycosylation was conducted with a furanose derivative as less bulky glycosyl donor, compared to the analogous pyranose. To have the 3,4-dithiopyranose core substituted by two sugars sharing the same configuration, and as the trichloroacetimidate of Gal*f* **33** is readily accessible from galactose,[40] we studied the glycosylation of **25** with **33**. Under the conditions employed for the synthesis of **31**, the analogous dithiotrisaccharide **34** was obtained in 66% yield (or 81%, if corrected with respect to the recovered unreacted **25**). The *N*-glycosyl trichloroacetamide **35**[41] was isolated as a byproduct, which results from the rearrangement of the trichloroacetimidate group of **33**.

The glycosylation of the thiol group at C-5 of **26** was also conducted. Such a thiol group is expected to be difficult to substitute as it is hindered by the vicinal furanose ring and the 1-*S*-galactopyranose at C-6. However, the dithiotrisaccharide **36** could be obtained, in a moderate yield (40%), by the TMSOTf-catalyzed reaction between **26** and the galactofuranose trichloroacetimidate **33**.

The structure of the dithiotrisaccharides **31**, **34**, and **36** were confirmed by means of NMR spectroscopy and HRMS. The ^{1}H NMR spectra were fully assigned using 2D-experiments; and the coupling constants measured for the anomeric protons of the thioglycosides confirmed the β configuration for both the pyranose ($J_{1',2'} \sim J_{1'',2''} \sim 10$ Hz) and the furanose ($J_{1',2'}$ or $J_{1'',2''} < 1.0$ Hz) units. The ^{13}C NMR spectra showed also the characteristic chemical shifts for the anomeric carbons bonded to sulfur. For example, the C-1′, C-1″ signals in **31** appeared at 81.8, 80.7 ppm; in contrast with the analogue disulfide **19**, that exhibited the resonance of the anomeric carbon bonded to *S*-*S* at 89.5 ppm. In addition, the spectra of the dithiotrisaccharides **34** and **36** exhibited the respective C-1 signals of the *S*-linked furanose (88.5 and 88.2 ppm) and pyranose (82.1 and 83.3 ppm) moieties. To identify the signals of each thioglucopyranosyl residue in **31** (one bonded to C-3 and the other to C-4 of the reducing end) a NOESY-GPPH experiment was conducted. The H-1′ and H-1″ signals were assigned according to their respective NOE contacts with H-3 and H-4.

CONCLUSIONS

The ring-opening reaction of sugar thiiranes by 1-thioaldoses afforded diverse glycomimetics, with different stereochemistries and presentation modes. Under optimized conditions, the ring-opening of 5,6-thiirane derivatives of furanoses proved to be highly regio and stereselectively to afford glycosyl β-(1→6)-5,6-dithiofuranosides in excellent yields. The same reaction applied to a 3,4-thiirane-D-galactopyranoside analogue, was also regio and stereselective to give the corresponding (1→4)-dithiodisaccharides, having a 3,4-dithio-D-glucopyranose as reducing end. The dithiodisaccharides possess a thiol group free, and hence they can serve as building blocks for the synthesis of sugar disulfides, as potential biologically active molecules.[33,34] Moreover, thiol-containing compounds have an essential role in many biochemical reactions due to their ability to be readily oxidized and then regenerated.[42] Thiols can also act as radical-trapping antioxidants.[43] In this work, the free thiol group of the thiodisaccharides, derived from thiiranes of pyranoses or furanoses, could be successfully glycosylated using trichloroacetimidates as glycosyl donors, to afford the corresponding branched dithiotrisaccharides. Thus, diglycosyl-*S*,*S*-(1→3,4)-3,4-dithio-D-glucopyranose and diglycosyl-*S*,*S*-(1→5,6)-5,6-dithio-D-galactofuranose have been prepared. The β-D-glucosyl (1→3)- and (1→4)-linkages are common in linear polysaccharides present in the cell walls of cereal endosperm,[44] and a branched trisaccharide with glucosyl residues (1→3)- and (1→4)-linked to a Glc*p* core has been found as a constituent of the glucan isolated from the mushroom *Calocybe indica*.[45] A per-*O*-acetyl derivative 3,4-di-*S*-analogue of this trisaccharide has been prepared. A similar pattern of a glucose core with glycosyl residues at HO-3 and HO-4 is also found in the sialyl Lewis X epitope.[46]

With regard to the branched dithiotrisaccharides with a 5,6-dithio-Gal*f* residue as reducing end, a compound of this kind was synthesized as sulfur analogue of the motif β-D-Gal*p*-(1→6)-[β-D-Gal*f*-(1→5)]-D-Gal*f*, the repeating unit of the cell-wall galactan of *Bifidobacterium catenulatum* YIT 4016.[47] Other 5,6-branched galacto-oligosaccharides have been reported in structures isolated from natural sources.[48]

EXPERIMENTAL SECTION

Methyl (Methyl 2,3,5-tri-*O*-*tert*-butyldimethylsilyl-α,β-D-galactofuranosid)uronate (2α,β). Methyl (methyl α,β-D-galactofuranosid)uronate (**1α,β**) was synthesized as already described.[18] To a solution of **1α,β** (885 mg, 3.99 mmol) in dry MeCN (12 mL), TBSCl (2 g, 13.27 mmol), and imidazole (1.80 g, 2.43 mmol) were added, and the suspension was stirred at room temperature (rt) for 24 h. Evaporation of the solvent afforded a syrup that was dissolved in CH_2Cl_2 (50 mL) and washed with water (2 × 25 mL). The organic extract was dried ($MgSO_4$) and concentrated. Crude compound **2α,β** (2.23 g, 99%, β:α 9:1) showed by TLC a single spot (R_f 0.58, hexane/EtOAc, 10:1), and it was pure enough for the next step of the reaction. An analytical sample showed the following ^{1}H NMR ($CDCl_3$, 500 MHz) for the β anomer: δ 4.75 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 4.34 (d, 1H, $J_{4,5}$ = 3.1 Hz, H-5), 4.19 (dd, 1H, $J_{2,3}$ = 2.6, $J_{3,4}$ = 5.6 Hz, H-3), 4.16 (dd, 1H, $J_{3,4}$ = 5.6, $J_{4,5}$ = 3.1 Hz, H-4), 3.99 (dd, 1H, $J_{1,2}$ = 1.8, $J_{2,3}$ = 2.6 Hz, H-2), 3.75 (s, 3H, CH_3CO_2), 3.32 (s, 3H, CH_3O), 0.93, 0.88, 0.87 (3s, 27H, $(CH_3)_3CSiMe_2$), 0.13, 0.09 (×2), 0.08, 0.07, 0.06 (5 s, 18H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 172.0 (C-6), 109.5 (C-1), 85.4 (C-4), 84.3 (C-2), 79.2 (C-3), 72.1 (C-5), 55.0 (CH_3O), 51.9 (CH_3CO_2) 25.9, 25.7 (×2) [$(CH_3)_3CSiMe_2$], 18.5, 17.9, 17.8 [$(CH_3)_3CSiMe_2$], −4.1, −4.4, −4.5 (×2), −4.9, −5.1 [$(CH_3)_2SiBu^t$]. Anal. Calcd for $C_{26}H_{56}O_7Si_3$: C, 55.27; H, 9.99. Found: C, 55.39; H, 10.02.

Methyl 2,3,5-Tri-*O*-*tert*-butyldimethylsilyl-α-D-galactofuranoside (3a), Methyl 2,3,5-Tri-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranoside (3b), and Methyl 2,3-Di-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranoside (4). A solution of uronate **2** (564 mg, 1.00 mmol) in dry THF (15 mL) was cooled to −18 °C and $LiAlH_4$ (50 mg, 1.30 mmol) was added. The reaction mixture was stirred for

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50 min, and then EtOAc (15 mL), MeOH (15 mL), and AcOH (to pH 7) were added in sequence, and finally the mixture was concentrated. The solid obtained was suspended in CH_2Cl_2 and centrifuged (4−5 times) to eliminate Li and Al salts. Evaporation of the solvent afforded a residue that showed by TLC (hexane/EtOAc, 10:1) spots corresponding to **3a** (R_f 0.47), **3b** (R_f 0.43), and **4** (R_f 0.00) that were isolated by column chromatography (toluene/EtOAc 60:1→EtOAc). The yields and physical data are reported as follows. Compound **3a**: 21 mg, 4%; $[\alpha]^{25}_D$ +42.2 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.77 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1), 4.19 (t, 1H, $J_{2,3}$ = $J_{3,4}$ = 4.8 Hz, H-3), 3.94 (dd, 1H, $J_{1,2}$ = 3.8, $J_{2,3}$ = 4.8 Hz, H-2), 3.85 (ddd, 1H, $J_{4,5}$ = 4.8 Hz, H-5), 3.83 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 4.8 Hz, H-4), 3.69 (dddd, 1H, $J_{5,6a}$ = 4.8, $J_{6a,HO}$ = 6.4, $J_{6a,6b}$ = 11.2 Hz, H-6a), 3.62 (dddd, 1H, $J_{5,6b}$ = 4.8, $J_{6a,HO}$ = 6.4, $J_{6a,6b}$ = 11.2 Hz, H-6b), 3.40 (s, 3H, CH_3O), 2.34 (t, 1H, $J_{6b,HO}$ = $J_{6b,HO}$ = 6.4 Hz, *HO*), 0.92, 0.90, 0.87 (3s, 27H, $(CH_3)_3CSiMe_2$), 0.14, 0.12, 0.11, 0.10, 0.07, 0.06 (6s, 18H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 103.5 (C-1), 85.4 (C-4), 78.6 (C-2), 76.6 (C-3), 72.8 (C-5), 64.5 (C-6), 55.9 (CH_3O), 25.9 (×2), 25.7 [$(CH_3)_3CSiMe_2$], 18.3, 18.2, 17.9 [$(CH_3)_3CSiMe_2$], −3.8, −4.2, −4.5, −4.6, −4.7, −4.8 [$(CH_3)_2SiBu^t$]. Anal. Calcd for $C_{25}H_{56}O_6Si_3$: C, 55.92; H, 10.51. Found: C, 55.76; H, 10.59.

Compound ***3b****:* 86 mg, 16%; $[\alpha]^{25}_D$ −19.1 (*c* 1.1, $CHCl_3$); ^{1}H NMR (CDCl3, 500 MHz) δ 4.74 (br s, 1H, H-1), 4.09 (dd, 1H, $J_{2,3}$ = 2.0, $J_{3,4}$ = 4.9 Hz, H-3), 4.01 (dd, 1H, $J_{1,2}$ = 1.2, $J_{2,3}$ = 2.0 Hz, H-2), 3.98 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 4.9 Hz, H-4), 3.89 (c, 1H, $J_{4,5}$ = $J_{5,6a}$ = $J_{5,6b}$ = 4.9 Hz, H-5), 3.71 (ddd, 1H, $J_{5,6a}$ = 4.9, $J_{6a,HO}$ = 6.3, $J_{6a,6b}$ = 11.3 Hz H-6a), 3.66 (ddd, 1H, $J_{5,6b}$ = 4.9, $J_{6b,HO}$ = 6.3, $J_{6a,6b}$ = 11.3 Hz H-6b), 3.36 (s, 3H, CH_3O), 2.35 (br s, 1H, *HO*), 0.94, 0.92, 0.90 (3s, 27H, $(CH_3)_3CSiMe_2$), 0.16, 0.15, 0.13, 0.12, 0.11 (×2) (5s, 18H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 109.2 (C-1), 86.8 (C-4), 83.7 (C-2), 79.4 (C-3), 72.5 (C-5), 64.5 (C-6), 54.8 (CH_3O), 26.0, 25.7 (×2) [$(CH_3)_3CSiMe_2$], 18.4, 17.9, 17.8 [$(CH_3)_3CSiMe_2$], −4.1, −4.4 (×2), −4.5, −4.6, −4.8 [$(CH_3)_2SiBu^t$]. Anal. Calcd for $C_{25}H_{56}O_6Si_3$: C, 55.92; H, 10.51. Found: C, 55.52; H, 10.89.

Compound ***4****:* 262 mg, 62%; $[\alpha]^{25}_D$ −11.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.72 (d, 1H, $J_{1,2}$ = 1.4 Hz, H-1), 4.13 (dd, 1H, $J_{2,3}$ = 3.1, $J_{3,4}$ = 5.7 Hz, H-3), 3.99 (dd, 1H, $J_{1,2}$ = 1.4, $J_{2,3}$ = 3,1 Hz, H-2), 3.94 (dd, 1H, $J_{3,4}$ = 5.7, $J_{4,5}$ = 1.7 Hz, H-4), 3.76−3.68 (m, 3H, H-5, H-6a, H-6b), 3.35 (s, 3H, CH_3O), 2.62, 2.23 (2d, 2H, *J* ∼ 7.7 Hz, *HO*-5 y *HO*-6), 0.90, 0.88 (2s, 27H, $(CH_3)_3CSiMe_2$), 0.11, 0.10, 0.90 (×2) (3s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 109.7 (C-1), 84.9 (C-4), 83.1 (C-2), 79.1 (C-3), 69.8 (C-5), 65.3 (C-6), 55.1 (CH_3O), 25.7 (×2) [$(CH_3)_3CSiMe_2$], 17.9, 17.8 [$(CH_3)_3CSiMe_2$], −4.3, −4.7 (×2), −4.9 [$(CH_3)_2SiBu^t$]. Anal. Calcd for $C_{19}H_{42}O_6Si_2$: C, 53.99; H, 10.01. Found: C, 53.68; H, 10.10.

Methyl 2,3-Di-*O*-*tert*-butyldimethylsilyl-6-*O*-pivaloyl-*β*-D-galactofuranoside (5). To a solution of the diol **4** (210 mg, 0.50 mmol) in dry pyridine (3.6 mL) was added pivaloyl chloride (135 μL, 1.10 mmol). The mixture was stirred at 0 °C for 3 h and then at rt for 1 h; TLC (toluene/EtOAc, 5:1) showed a main spot of R_f 0.66. The mixture was poured into ice/water, extracted with CH_2Cl_2, and washed with HCl 5%, water, and satd aq $NaCO_3H$. The extract was dried ($MgSO_4$) concentrated, and the residue was purified by column chromatography (toluene/EtOAc, 20:1) to afford **5** (185 mg, 74%): $[\alpha]^{25}_D$ −30.0 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.72 (d, 1H, $J_{1,2}$ = 1.0 Hz, H-1), 4.23 (dd, 1H, $J_{5,6a}$ = 6.5, $J_{6a,6b}$ = 11.0 Hz, H-6a), 4.10 (dd, 1H, $J_{3,4}$ = 5.6, $J_{4,5}$ = 2.4 Hz, H-4), 4.09 (dd, 1H, $J_{5,6b}$ = 6.5, $J_{6a,6b}$ = 11.0 Hz, H-6b), 4.00 (dd, 1H, $J_{1,2}$ = 1.0, $J_{2,3}$ = 1.8 Hz, H-2), 3.94 (dd, 1H, $J_{2,3}$ = 1.8, $J_{3,4}$ = 5.6 Hz, H-3), 3.88 (m, 1H, $J_{5,6a}$ = $J_{5,6b}$ ∼ 6.5, $J_{5,HO}$ = 8.0 Hz, H-5), 3.34 (s, 3H, CH_3O), 2.52 (d, 1H, $J_{5,HO}$ = 8.0 Hz, *HO*), 1.22 (s, 9H, $COC(CH_3)_3$), 0.90, 0.88 (2s, 18H, $(CH_3)_3CSiMe_2$), 0.11, 0.09 (×2), 0.08 (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 178.3 ($COC(CH_3)_3$), 109.5 (C-1), 83.4 (C-3), 83.2 (C-2), 79.1 (C-4), 67.9 (C-5), 65.3 (C-6), 54.9 (CH_3O), 38.8 ($COC(CH_3)_3$), 27.2 ($COC(CH_3)_3$), 25.8, 25.7 [$(CH_3)_3CSiMe_2$], 17.9, 17.8 [$(CH_3)_3CSiMe_2$], −4.3, −4.6, −4.7, −4.9 [$(CH_3)_2SiBu^t$]. Anal. Calcd for $C_{24}H_{50}O_7Si_2$: C, 56.88; H, 9.94. Found: C, 56.93; H, 10.22.

Methyl 2,3-Di-*O*-*tert*-butyldimethylsilyl-6-*O*-pivaloyl-5-*O*-tosyl-*β*-D-galactofuranoside (6). Compound **5** (350 mg, 0.69 mmol) dissolved in dry pyridine (20 mL) was treated with tosyl chloride (1.24 g, 6.48 mmol). The reaction mixture was stirred at rt for 3 days, and then MeOH (10 mL) was added. The syrup obtained after evaporation of the solvent was dissolved in CH_2Cl_2, and the organic layer was washed with water (20 mL), dried ($MgSO_4$), and concentrated. Analysis by TLC (toluene/EtOAc, 9:1) showed a major product of R_f 0.71, which was purified by column chromatography (toluene/EtOAc, 60:1) to afford **6** (415 mg, 91%): $[\alpha]^{25}_D$ −12.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.83, 7.36 (2d, 4H, *J* ∼ 8.2 Hz, H-aromatic), 4.97 (dddd, 1H, $J_{4,5}$ = 3.9, $J_{5,6a}$ = 5.3, $J_{5,6b}$ = 6.6 Hz H-5), 4.58 (d, 1H, $J_{1,2}$ = 1.2 Hz, H-1), 4.37 (dd, 1H, $J_{5,6a}$ = 5.3, $J_{6a,6b}$ = 11.9 Hz, H-6a), 4.15 (dd, 1H, $J_{5,6b}$ = 6.6, $J_{6a,6b}$ = 11.9 Hz, H-6b), 4.04 (dd, 1H, $J_{2,3}$ = 2.2, $J_{3,4}$ = 5.5 Hz, H-3), 4.02 (dd, 1H, $J_{3,4}$ = 5.5, $J_{4,5}$ = 3.9 Hz, H-4), 3.97 (dd, 1H, $J_{1,2}$ = 1.2, $J_{2,3}$ = 2.2 Hz, H-2), 3.26 (s, 3H, CH_3O), 2.43 (s, 3H, CH_3Ph), 1.21 (s, 9H, $COC(CH_3)_3$), 0.91, 0.88 (2s, 18H, $(CH_3)_3CSiMe_2$), 0.11 (×2), 0.10, 0.08 (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 177.9 ($COC(CH_3)_3$), 144.9, 144.6, 129.9, 129.6, 128.1, 127.9 (C-aromatic), 109.5 (C-1), 83.9 (C-3), 82.5 (C-2), 79.4 (C-4), 77.5 (C-5), 62.4 (C-6), 56.2 ($COC(CH_3)_3$), 54.9 (CH_3O), 27.1 ($COC(CH_3)_3$), 25.8, 25.7 [$(CH_3)_3CSiMe_2$], 21.6 (CH_3Ph), 17.9, 17.8 [$(CH_3)_3CSiMe_2$], −4.3, −4.5, −4.8, −4.9 [$(CH_3)_2SiBu^t$]; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{56}NaO_9SSi_2$ 683.3076, found 683.3088.

Methyl 5,6-Anhydro-2,3-di-*O*-*tert*-butyldimethylsilyl-*α*-L-altrofuranoside (7). A solution of **6** (148 mg, 0.24 mmol) in CH_2Cl_2 (6 mL) was cooled at 0 °C, and 1.3 mL of 2 M NaOMe/MeOH solution was added. The mixture was stirred for 2 h at 0 °C; TLC (hexane/EtOAc, 10:1) showed a main spot of R_f 0.48. The reaction was diluted with CH_2Cl_2 (30 mL) and washed with water (2 × 25 mL). The organic phase was dried and concentrated and the residue was purified by column chromatography (hexane/EtOAc, 40:1) to afford **7** (80 mg, 83% from **6a**; 88 mg, 91% from **6b**): $[\alpha]^{25}_D$ −40.1 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.74 (br s, 1H, H-1), 4.03 (dd, 1H, $J_{2,3}$ = 2.4, $J_{3,4}$ = 4.4 Hz, H-3), 4.01 (dd, 1H, $J_{1,2}$ ∼ 1.0, $J_{2,3}$ = 2.4 Hz, H-2), 3.77 (dd, 1H, $J_{3,4}$ = 4.4, $J_{4,5}$ = 5.6 Hz, H-4), 3.35 (s, 3H, CH_3O), 3.07 (dddd, 1H, $J_{4,5}$ = 5.7, $J_{5,6a}$ = 3.9, $J_{5,6b}$ = 2.7 Hz, H-5), 2.81 (dd, 1H, $J_{5,6a}$ = 3.9, $J_{6a,6b}$ = 5.2 Hz, H-6a), 2.73 (dd, 1H, $J_{5,6b}$ = 2.7, $J_{6a,6b}$ = 5.2 Hz, H-6b), 0.89 (×2) (2s, 18H, $(CH_3)_3CSiMe_2$), 0.11, 0.10 (×2), 0.09 (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 110.1 (C-1), 84.7 (C-4), 83.4 (C-2), 81.2 (C-3), 55.0 (CH_3O), 52.0 (C-5), 45.4 (C-6), 25.7 (×2) [$(CH_3)_3CSiMe_2$], 17.9 (×2) [$(CH_3)_3CSiMe_2$], −4.4, −4.7, −4.8, −4.9 [$(CH_3)_2SiBu^t$]. Anal. Calcd for $C_{19}H_{40}O_5Si_2$: C, 56.39; H, 9.96. Found: C, 56.69; H, 10.26.

Methyl 2,3-Di-*O*-*tert*-butyldimethylsilyl-5,6-epithio-*β*-D-galactofuranoside (8). To a solution of the epoxide **7** (85 mg, 0.21 mmol) in dry MeOH (3 mL) was added thiourea (42 mg, 0.55 mmol), and the mixture was stirred at rt for 48 h. Upon concentration, the residue was dissolved in CH_2Cl_2 (25 mL), washed with water (2 × 25 mL), dried ($MgSO_4$), and concentrated. Analysis by TLC (hexane/EtOAc, 10:1) showed a main compound of R_f 0.68, which was purified by column chromatography (hexane/EtOAc, 70:1) to afford **8** (73 mg, 83%): $[\alpha]^{25}_D$ −41.2 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.69 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 4.00 (dd, 1H, $J_{1,2}$ = 1.8, $J_{2,3}$ = 4.1 Hz, H-2), 3.90 (dd, 1H, $J_{2,3}$ = 4.1, $J_{3,4}$ = 7.0 Hz, H-3), 3.55 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 7.0 Hz, H-4), 3.34 (s, 3H, CH_3O), 3.04 (ddd, 1H, $J_{4,5}$ = 7.0, $J_{5,6a}$ = 6.5, $J_{5,6b}$ = 5.4 Hz, H-5), 2.49 (dd, 1H, $J_{5,6a}$ = 6.5, $J_{6a,6b}$ = 1.1 Hz, H-6a), 2.37 (dd, 1H, $J_{5,6b}$ = 5.4, $J_{6a,6b}$ = 1.1 Hz, H-6b), 0.90, 0.89 (2s, 18H, $(CH_3)_3CSiMe_2$), 0.11, 0.10, 0.09, 0.08 (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 109.2 (C-1), 85.6 (C-4), 84.4 (C-2), 82.9 (C-3), 55.1 (CH_3O), 35.3 (C-5), 25.8, 25.7 [$(CH_3)_3CSiMe_2$], 21.8 (C-6), 17.9, 17.8 [$(CH_3)_3CSiMe_2$], −4.1, −4.6 (×2), −4.9 [$(CH_3)_2SiBu^t$]; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{40}NaO_4SSi_2$ 443.2084, found 443.2083. Anal. Calcd for $C_{19}H_{40}O_4SSi_2$: C, 54.24; H, 9.58. Found: C, 54.50; H, 9.65.

Methyl 2,3-Di-*O*-*tert*-butyldimethylsilyl-6-*O*-tosyl-*β*-D-galactofuranoside (9). To a solution of **4** (250 mg, 0.59 mmol) in dry pyridine (6 mL) was added tosyl chloride (226 mg, 1.18 mmol) at 0 °C. The mixture was stirred for 10 h at that temperature and then at rt for additional 50 h. The workup described for the tosylation of **5** was followed to give **9** (337 mg, 99%). This compound showed to be pure

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enough for the next step (R_f 0.47, hexane/EtOAc, 4:1). An analytical sample of **9** obtained by column chromatography gave $[\alpha]^{25}_D$ −25.5 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.81, 7.34 (2d, 4H, J ∼ 8.2 Hz, H-aromatic), 4.67 (br s, 1H, H-1), 4.08 (d, 2H, $J_{5,6a} = J_{5,6b}$ = 6.4 Hz, H-6a, H-6b), 4.05 (dddd, 1H, $J_{2,3}$ = 2.6, $J_{3,4}$ = 5.1 Hz, H-3), 3.96 (dd, 1H, $J_{1,2}$ = 1.1, $J_{2,3}$ = 2.6 Hz, H-2), 3.94 (dd, 1H, $J_{3,4}$ = 5.1, $J_{4,5}$ = 1.6 Hz, H-4), 3.89 (dddd, 1H, $J_{4,5}$ = 1.6, $J_{5,6a} = J_{5,6b}$ = 6.4, $J_{5,HO}$ = 7.3 Hz, H-5), 3.29 (s, 3H, CH_3O), 2.64 (d, 1H, $J_{5,HO}$ = 7.3 Hz, *H*O), 2.44 (s, 3H, CH_3Ph), 0.87 (×2) (2s, 18H, $(CH_3)_3CSiMe_2$), 0.09, 0.07 (×2), 0.05 (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz,) δ 144.8, 132.9, 129.8, 128.0 (C-aromatic), 109.5 (C-1), 83.4 (C-4), 82.7 (C-2), 79.0 (C-3), 70.7 (C-6), 67.8 (C-5), 54.9 (CH_3O), 25.7 (×2) [$(CH_3)_3CSiMe_2$], 21.6 (CH_3Ph), 17.8 (×2) [$(CH_3)_3CSiMe_2$], −4.4, −4.7, −4.8, −5.0 [$(CH_3)_2SiBu^t$]. Anal. Calcd for $C_{26}H_{48}O_8SSi_2$: C, 54.13; H, 8.39. Found: C, 54.03; H, 8.43.

Methyl 5,6-Anhydro-2,3-di-*O*-*tert*-butyldimethylsilyl-β-D-galactofuranoside (10). A solution of crude **9** (337 mg, 0.58 mmol) in CH_2Cl_2 (14 mL) was treated with 2 M NaOMe/MeOH (3 mL) at 0 °C for 1 h; monitoring by TLC (toluene) showed a main spot of R_f 0.40. The mixture was diluted with CH_2Cl_2 (25 mL), extracted with water (2 × 15 mL), dried, and concentrated to afford crude **10** (221 mg, 94%) with a high degree of purity. An analytical sample was obtained by column chromatography: $[\alpha]^{25}_D$ −10.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.68 (d, 1H, $J_{1,2}$ = 2.0 Hz, H-1), 4.01 (dd, 1H, $J_{1,2}$ = 2.0, $J_{2,3}$ = 4.4 Hz, H-2), 3.98 (dd, 1H, $J_{2,3}$ = 4.4, $J_{3,4}$ = 7.3 Hz, H-3), 3.62 (dd, 1H, $J_{3,4}$ = 7.3, $J_{4,5}$ = 6.0 Hz, H-4), 3.36 (s, 3H, CH_3O), 3.09 (dddd, 1H, $J_{4,5}$ = 6.0, $J_{5,6a}$ = 4.3, $J_{5,6b}$ = 2.7 Hz, H-5), 2.83 (dd, 1H, $J_{5,6a}$ = 4.3, $J_{6a,6b}$ = 5.2 Hz, H-6a), 2.75 (dd, 1H, $J_{5,6b}$ = 2.7, $J_{6a,6b}$ = 5.2 Hz, H-6b), 0.90, 0.88 (2s, 18H, $(CH_3)_3CSiMe_2$), 0.10, 0.09, 0.08, 0.07 (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 109.4 (C-1), 84.3 (C-2), 82.4 (C-4), 80.1 (C-3), 55.3 (CH_3O), 51.7 (C-5), 44.2 (C-6), 25.8, 25.6 [$(CH_3)_3CSiMe_2$], 17.9 (×2) [$(CH_3)_3CSiMe_2$], −4.2, −4.6, −4.9 (×2) [$(CH_3)_2SiBu^t$]; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{40}NaO_5Si_2$ 427.2307, found 427.2320.

Methyl 2,3-Di-*O*-*tert*-butyldimethylsilyl-5,6-epithio-α-L-altrofuranoside (11). Crude compound **10** (221 mg, 0.55 mmol) was treated with thiourea as described for the synthesis of **8**. The product which showed by TLC (toluene) R_f 0.57 was purified by column chromatography (hexane/EtOAc, 50:1) and identified as **11** (138 mg, 60%): $[\alpha]^{25}_D$ −17.3 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.78 (br s, 1H, H-1), 4.04 (dd, 1H, $J_{2,3}$ = 2.1, $J_{3,4}$ = 3.7 Hz, H-3), 3.99 (dd, 1H, $J_{1,2}$ = 0.8, $J_{2,3}$ = 2.1 Hz, H-2), 3.51 (dd, 1H, $J_{3,4}$ = 3.7, $J_{4,5}$ = 8.2 Hz, H-4), 3.34 (s, 3H, CH_3O), 3.04 (dddd, 1H, $J_{4,5}$ = 8.2, $J_{5,6a}$ = 6.1, $J_{5,6b}$ = 5.3 Hz, H-5), 2.53 (dd, 1H, $J_{5,6a}$ = 6.1, $J_{6a,6b}$ = 1.2 Hz, H-6a), 2.30 (dd, 1H, $J_{5,6b}$ = 5.3, $J_{6a,6b}$ = 1.2 Hz, H-6b), 0.90, 0.89 (2s, 18H, $(CH_3)_3CSiMe_2$), 0.11 (×2), 0.10 (×2) (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 110.4 (C-1), 89.9 (C-4), 83.2 (C-2), 82.6 (C-3), 54.9 (CH_3O), 34.5 (C-5), 25.8, 25.7 [$(CH_3)_3CSiMe_2$], 23.5 (C-6), 17.9 (×2) [$(CH_3)_3CSiMe_2$], −4.3, −4.5, −4.6, −4.8 [$(CH_3)_2SiBu^t$]; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{40}NaO_4SSi_2$ 443.2084, found 443.2083. Anal. Calcd for $C_{19}H_{40}O_4SSi_2$: C, 54.24; H, 9.58. Found: C, 54.07; H, 9.81.

2-Propyl 6-*O*-Acetyl-3,4-epithio-α-D-galactopyranoside (13). To a solution of **12**[7] (0.25 g, 1.01 mmol) in MeCN (9 mL) was added KSCN (345 mg, 3.55 mmol), and the pH was maintained alkaline (8−9) with Et_3N. After the addition of 18-crown-6 (62.5 mg, 0.24 mmol) the solution was stirred at 65 °C for 36 h, when TLC (hexane/EtOAc, 1:1.5) showed the conversion of **12** (R_f 0.53) into a less polar product (R_f 0.76). The solvent was evaporated, and the residue was dissolved in CH_2Cl_2 (15 mL) and extracted with H_2O (2 × 15 mL). The organic layer was dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (hexane/EtOAc, 6:1→2:1) to afford **13** (180 mg, 68%): $[\alpha]^{25}_D$ +29.5 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.89 (d, 1H, $J_{1,2}$ = 4.9 Hz, H-1), 4.60 (m, 1H, $J_{4,5}$ = 2.6, $J_{5,6a}$ = 4.5, $J_{5,6b}$ = 7.4 Hz, H-5), 4.27 (dd, 1H, $J_{5,6a}$ = 4.5, $J_{6a,6b}$ = 11.4 Hz, H-6a), 4.13 (dd, 1H, $J_{5,6b}$ = 7.4, $J_{6a,6b}$ = 11.4 Hz, H-6b), 4.09 (dd, 1H, $J_{1,2}$ = 4.9, $J_{2,OH}$ = 9.6 Hz, H-2), 3.97 (m, 1H, J = 6.2 Hz, Me_2CHO), 3.17 (dd, 1H, $J_{3,4}$ = 6.8, $J_{4,5}$ = 2.6 Hz, H-4), 3.14 (d, 1H, $J_{3,4}$ = 6.8 Hz, H-3), 2.84 (d, 1H, $J_{2,OH}$ = 9.6 Hz, HO), 2.10 (s, 3H, CH_3CO), 1.20, 1.29 (2d, each 3H, J = 6.2 Hz, $(CH_3)_2CHO$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.8 (CH_3CO), 93.4 (C-1), 71.3 (Me_2CHO), 66.7 (C-6), 65.4 (C-2), 64.1 (C-5), 35.2 (C-3), 35.0 (C-4), 23.0, 21.7 [$(CH_3)_2CHO$], 20.8 (CH_3CO); HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{18}NaO_5S$ 285.0773, found 285.0786. Anal. Calcd for $C_{11}H_{18}O_5S$: C, 50.36; H, 6.92. Found: C, 50.68; H, 7.09.

From further fractions of the column was recovered unreacted **12** (40 mg, 16%) and the corrected yield for **13** was 81%.

2-Propyl 2,6-Di-*O*-acetyl-3,4-epithio-α-D-galactopyranoside (14). Compound **13** (110 mg, 0.42 mmol) was acetylated with acetic anhydride (1.5 mL) and pyridine (1.5 mL) at rt for 16 h. Examination by TLC (hexane/EtOAc, 1:1) showed the complete conversion of **13** (R_f 0.59) into a faster moving product (R_f 0.74). The mixture was concentrated and subjected to column chromatography (hexane/EtOAc, 8.5:1.5) to give **14** (125 mg, 98%): $[\alpha]^{25}_D$ +71.4 (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.09 (d, 1H, $J_{1,2}$ = 4.7 Hz, H-1), 5.02 (dd, 1H, $J_{1,2}$ = 4.7, $J_{2,3}$ = 1.1 Hz, H-2), 4.67 (m, 1H, $J_{4,5}$ = 2.8, $J_{5,6a}$ = 4.5, $J_{5,6b}$ = 7.4 Hz, H-5), 4.30 (dd, 1H, $J_{5,6a}$ = 4.5, $J_{6a,6b}$ = 11.4 Hz, H-6a), 4.13 (dd, 1H, $J_{5,6b}$ = 7.4, $J_{6a,6b}$ = 11.4 Hz, H-6b), 3.86 (m, 1H, J = 6.2 Hz, Me_2CHO), 3.20 (dd, 1H, $J_{3,4}$ = 6.8, $J_{4,5}$ = 2.8 Hz, H-4), 3.15 (dd, 1H, $J_{2,3}$ = 1.1, $J_{3,4}$ = 6.8 Hz, H-3), 2.10, 2.13 (2s, each 3H, CH_3CO), 1.12, 1.27 (2d, each 3H, J = 6.2 Hz, $(CH_3)_2CHO$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.7, 170.0 (CH_3CO), 92.1 (C-1), 71.3 (Me_2CHO), 68.4 (C-2), 66.7 (C-6), 63.8 (C-5), 34.5 (C-4), 32.3 (C-3), 23.0, 21.7 [$(CH_3)_2CHO$], 20.8, 20.7 (CH_3CO); HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{20}NaO_6S$ 327.0872, found 327.0875. Anal. Calcd for $C_{13}H_{20}O_6S$: C, 51.30; H, 6.62. Found: C, 51.29; H, 6.54.

2-Propyl 6-*O*-Acetyl-2-*O*-*tert*-butyldimethylsilyl-3,4-epithio-α-D-galactopyranoside (15). The silylation of **13** (40 mg, 0.15 mmol) was performed with TBSCl (29 mg, 0.19 mmol) and imidazole (20 mg, 0.30 mmol) in MeCN (1 mL). After 4 h, TLC (hexane/EtOAc, 4:1) revealed the complete formation of a faster moving product (R_f 0.58). The reaction mixture was concentrated, and the residue was dissolved in CH_2Cl_2 (15 mL) and extracted with water (15 mL). The organic phase was dried ($MgSO_4$) and concentrated, and the resulting syrup was purified by column chromatography (hexane/EtOAc, 24:1) to afford **15** (52 mg, 92%): $[\alpha]^{25}_D$ +28.7 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.70 (d, 1H, $J_{1,2}$ = 4.4 Hz, H-1), 4.65 (m, 1H, $J_{4,5}$ = 3.3, $J_{5,6a}$ = 4.5, $J_{5,6b}$ = 7.6 Hz, H-5), 4.29 (dd, 1H, $J_{5,6a}$ = 4.5, $J_{6a,6b}$ = 11.3 Hz, H-6a), 4.11 (dd, 1H, $J_{5,6b}$ = 7.6, $J_{6a,6b}$ = 11.3 Hz, H-6b), 4.07 (dd, 1H, $J_{1,2}$ = 4.4, $J_{2,3}$ = 1.6 Hz, H-2), 3.89 (m, 1H, J = 6.2 Hz, Me_2CHO), 3.19 (dd, 1H, $J_{3,4}$ = 7.0, $J_{4,5}$ = 3.2 Hz, H-4), 3.09 (dd, 1H, $J_{3,4}$ = 7.0, $J_{2,3}$ = 1.6 Hz, H-3), 2.10 (s, 3H, CH_3CO), 1.19, 1.29 (2d, each 3H, J = 6.2 Hz, $(CH_3)_2CHO$), 0.94 (s, 9H, $(CH_3)_3CSiMe_2$), 0.12, 0.15 (2s, each 3H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.7 (CH_3CO), 95.1 (C-1), 71.2 (Me_2CHO), 69.5 (C-2), 66.9 (C-6), 64.2 (C-5), 36.6 (C-3), 35.5 (C-4), 25.8 [$(CH_3)_3CSiMe_2$], 23.0, 21.8 [$(CH_3)_2CHO$], 20.8 (CH_3CO), 18.2 [$(CH_3)_3CSiMe_2$], −4.7, −4.8 [$(CH_3)_2SiBu^t$]; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{32}NaO_5SSi$ 399.1635, found 399.1625. Anal. Calcd for $C_{17}H_{32}O_5SSi$: C, 54.22; H, 8.56. Found: C, 54.29; H, 8.49.

2-Propyl 2,6-Di-*O*-acetyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3,4-dithio-α-D-glucopyranoside (17), 2-Propyl 2,6-Di-*O*-acetyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)disulfide-3,4-dithio-α-D-glucopyranoside (18), and Bis[2-Propyl 2,6-Di-*O*-acetyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3,4-dithio-α-D-glucopyranos-3-yl]disulfide (19). A solution of the 1-thioaldose **16a**[30a,49] (76 mg, 0.21 mmol) and NaH (10 mg) in dry THF (3.5 mL) was stirred at rt under nitrogen until the evolution of gas ceased (∼1 h). The yellowish solution was concentrated, the resulting salt (**16b**) was dissolved in THF (1.0 mL) and cooled at −18 °C, and the thiirane **14** (50 mg, 0.16 mmol) dissolved in dry THF (1.0 mL) was added. The mixture was stirred at rt for 10 min, and 18-crown-6 (5 mg, 0.02 mmol) was added. After 30 min, an additional amount of 18-crown-6 (5 mg, 0.02 mmol) was incorporated, and the mixture was stirred at rt for 24 h. When TLC (toluene/EtOAc, 1:1) showed the complete conversion of **14** (R_f 0.72) into an elongated spot of R_f 0.23, the mixture was concentrated and purified by column chromatography. The faster moving component isolated was the starting thiirane **14** (18 mg). The next component that eluted from the

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column was identified as thiodisaccharide **17** (3.5 mg, 6%): $[\alpha]^{25}_{D}$ +38.4 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.21 (t, 1H, $J_{2',3'} = J_{3',4'}$ = 9.6 Hz, H-3′), 5.09 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 5.08 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 9.6 Hz, H-4′), 4.99 (dd, 1H, $J_{1',2'}$ = 10.2, $J_{2',3'}$ = 9.3 Hz, H-2′), 4.75 (dd, 1H, $J_{1,2}$ = 3.4, $J_{2,3}$ = 11.5 Hz, H-2), 4.65 (d, 1H, $J_{1',2'}$ = 10.2 Hz, H-1′), 4.48 (dd, 1H, $J_{5,6a}$ = 2.3, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.45 (dd, 1H, $J_{5,6b}$ = 3.8, $J_{6a,6b}$ = 12.0 Hz, H-6b), 4.16 (m, 2H, H-6′a, 6′b), 4.10 (ddd, $J_{4,5}$ = 11.5, $J_{5,6a}$ = 2.3, $J_{5,6b}$ = 3.8 Hz, H-5), 3.87 (m, 1H, *J* = 6.2 Hz, Me_2CHO), 3.67 (ddd, 1H, $J_{4',5'}$ = 9.6, $J_{5',6'a}$ = 3.0, $J_{5',6'b}$ = 4.8 Hz, H-5′), 3.99 (dt, 1H, $J_{2,3} = J_{3,4}$ = 11.5, $J_{3,HS}$ = 3.9 Hz, H-3), 2.91 (t, 1H, $J_{3,4} = J_{4,5}$ = 11.5 Hz, H-4), 2.32 (d, 1H, $J_{3,HS}$ = 3.9 Hz, *HS*), 2.14, 2.11, 2.10, 2.09, 2.04, 2.01 (6s, 18H, CH_3CO), 1.23, 1.12 (2d, each 3H, *J* = 6.2 Hz, $(CH_3)_2CHO$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.5−169.2 (CH_3CO), 93.8 (C-1), 82.3 (C-1′), 75.8, 74.8, 73.7, 71.0, 69.9, 69.6, 68.1 (C2, 5, 2′, 3′, 4′, 5′, Me_2CHO), 63.9 (C-6), 62.1 (C-6′), 50.2 (C-4), 40.2 (C-3), 23.2, 21.6 [$(CH_3)_2CHO$], 20.8−20.6 (CH_3CO); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{40}NaO_{15}S_2$ 691.1701, found 691.1717.

Further fractions from the column afforded **18** (54 mg, 48%): $[\alpha]^{25}_{D}$ −15.9 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.23 (t, 1H, $J_{2'',3''} = J_{3'',4''}$ = 9.7 Hz, H-3″), 5.21 (t, 1H, $J_{2',3'} = J_{3',4'}$ = 9.6 Hz, H-3′), 5.14 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 9.6 Hz, H-4′), 5.09 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 5.08 (t, 1H, $J_{3'',4''} = J_{4'',5''}$ = 9.7 Hz, H-4″), 5.02 (t, 1H, $J_{1',2'} = J_{2',3'}$ = 9.6 Hz, H-2′), 4.96 (dd, 1H, $J_{1'',2''}$ = 10.2, $J_{2'',3''}$ = 9.7 Hz, H-2″), 4.90 (dd, 1H, $J_{1,2}$ = 3.7, $J_{2,3}$ = 10.3 Hz, H-2), 4.63 (d, 1H, $J_{1'',2''}$ = 10.2 Hz, H-1″), 4.61 (dd, 1H, $J_{5,6a}$ = 1.8, $J_{6a,6b}$ = 11.8 Hz, H-6a), 4.51 (d, 1H, $J_{1',2'}$ = 9.6 Hz, H-1′), 4.44 (dd, 1H, $J_{5,6b}$ = 5.3, $J_{6a,6b}$ = 11.8 Hz, H-6b), 4.39 (dd, 1H, $J_{5',6'a}$ = 4.2, $J_{6'a,6'b}$ = 12.5 Hz, H-6′a), 4.24 (ddd, $J_{4,5}$ = 10.6, $J_{5,6a}$ = 1.8, $J_{5,6b}$ = 5.3 Hz, H-5), 4.20 (dd, 1H, $J_{5'',6''a}$ = 4.8, $J_{6''a,6''b}$ = 12.5 Hz, H-6″a), 4.13 (dd, 2H, $J_{5',6'b} = J_{5',6'b}$ = 2.4, $J_{6'a,6'b} = J_{6''a,6''b}$ = 12.5 Hz, H-6′b, H-6″b), 3.89 (m, 1H, *J* = 6.2 Hz, Me_2CHO), 3.71 (ddd, 1H, $J_{4',5'}$ = 9.6, $J_{5',6'a}$ = 4.2, $J_{5',6'b}$ = 2.4 Hz, H-5′), 3.65 (ddd, 1H, $J_{4'',5''}$ = 9.7, $J_{5'',6''a}$ = 4.8, $J_{5'',6''b}$ = 2.4 Hz, H-5″), 3.27 (dd, 1H, $J_{3,4}$ =11.3, $J_{4,5}$ = 10.6 Hz, H-4), 3.20 (dd, 1H, $J_{2,3}$ = 10.4, $J_{3,4}$ =11.3 Hz, H-3), 2.17, 2.11, 2.10, 2.09, 2.07 2.05, 2.04, 2.03, 2.02, 2.00 (10 s, 30H, CH_3CO), 1.25, 1.15 (2d, each 3H, *J* = 6.2 Hz, $(CH_3)_2CHO$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 193.7 (CH_3COS) 170.6−169.2 (CH_3CO), 94.2 (C-1), 89.5 (C-1′ observed by HMQC), 81.3 (C-1″), 76.5 (C-5′), 75.7 (C-5″), 74.0 (C-3′), 73.6 (C-3″), 70.9 (C-2), 70.6 (Me_2CHO), 69.9 (C-2″), 69.6 (C-2′), 69.0 (C-5), 68.0 (C-4″), 67.6 (C-4′), 64.1 (C-6), 62.0 (C-6″), 61.6 (C-6′), 48.5 (C-3), 44.3 (C-4), 23.2, 21.6 [$(CH_3)_2CHO$], 20.8−20.7 (CH_3CO); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{41}H_{58}NaO_{24}S_3$ 1053.2372, found 1053.2340. Anal. Calcd for $C_{41}H_{58}O_{24}S_3$: C, 47.76; H, 5.67. Found: C, 48.02; H, 5.60.

Finally, it was isolated the symmetric disulfide **19** (8 mg, 6%): $[\alpha]^{25}_{D}$ +17.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.23 (t, 1H, $J_{2',3'} = J_{3',4'}$ = 9.3 Hz, H-3′), 5.08 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 5.08 (dd, 1H, $J_{3',4'}$ = 9.3, $J_{4',5'}$ = 10.0 Hz, H-4′), 4.97 (dd, 1H, $J_{1',2'}$ = 10.1, $J_{2',3'}$ = 9.3 Hz, H-2′), 4.88 (dd, 1H, $J_{1,2}$ = 3.4, $J_{2,3}$ = 11.4 Hz, H-2), 4.69 (d, 1H, $J_{1',2'}$ = 10.1 Hz, H-1′), 4.57 (dd, 1H, $J_{5,6a}$ = 1.9, $J_{6a,6b}$ = 11.9 Hz, H-6a), 4.39 (dd, 1H, $J_{5,6b}$ = 5.4, $J_{6a,6b}$ = 11.9 Hz, H-6b), 4.21 (dd, 1H, $J_{5',6'a}$ = 4.6, $J_{6'a,6'b}$ = 12.4 Hz, H-6′a), 4.18 (ddd, $J_{4,5}$ = 11.4, $J_{5,6a}$ = 1.9, $J_{5,6b}$ = 5.4 Hz, H-5), 4.14 (dd, 1H, $J_{5',6'b}$ = 2.5, $J_{6'a,6'b}$ = 12.4 Hz, H-6′b), 3.87 (m, 1H, *J* = 6.2 Hz, Me_2CHO), 3.67 (ddd, 1H, $J_{4',5'}$ = 10.0, $J_{5',6'a}$ = 4.6, $J_{5',6'b}$ = 2.5 Hz, H-5′), 3.20 (t, 1H, $J_{2,3} = J_{3,4}$ = 11.4 Hz, H-3), 3.00 (t, 1H, $J_{3,4} = J_{4,5}$ = 11.4 Hz, H-4), 2.16, 2.10 (×2), 2.09, 2.03, 2.00 (6 s, 18H, CH_3CO), 1.25, 1.13 (2d, each 3H, *J* = 6.2 Hz, $(CH_3)_2CHO$); ^{13}C NMR ($CDCl_3$, 50,3 MHz) δ 170.5−169.2 (CH_3CO), 94.0 (C-1), 82.2 (C-1′), 75.8, 73.8, 71.2, 70.9, 70.1, 69.8, 68.0 (C-2, 5, 2′, 3′, 4′, 5′, Me_2CHO), 64.3 (C-6), 61.9 (C-6′), 51.4 (C-4), 46.7 (C-3), 23.2, 21.6 [$(CH_3)_2CHO$], 20.9−20.6 (CH_3CO); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{54}H_{78}NaO_{30}S_4$ 1357.3353, found 1357.3308. Anal. Calcd for $C_{54}H_{78}O_{30}S_4$: C, 48.57, H, 5.89. Found: C, 48.97, H, 5.86.

2-Propyl 2,6-Di-*O*-acetyl-3-*S*-acetyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl)-3,4-dithio-*α*-D-glucopyranoside (20) and Its Conversion into 17. The reaction of thiirane **14** (100 mg, 0.32 mmol) and the sodium thiolate **16b** (175 mg, 0.49 mmol) in THF (2 mL) was conducted in the presence of 18-crown-6 (20 mg total), as previously described. The crude mixture of **17**−**19** obtained upon evaporation of the solvent was dissolved in dry THF (22 mL) and cooled to 0 °C. To this stirred solution was added $LiAlH_4$ (160 mg, 4.20 mmol) in portions during 1 h. The solution was allowed to reach rt, and the stirring was continued for 6 h. The excess of reducing agent was destroyed by addition, at 0 °C, of EtOAc (10 mL) followed by MeOH (10 mL). Finally, the mixture was neutralized with AcOH, and the solvents were evaporated. The dry residue was treated with pyridine (4 mL) and Ac_2O (4 mL) for 12 h, when TLC (toluene/EtOAc, 1:1) showed two main spots of R_f 0.65 and 0.55. The mixture was concentrated and the residue extracted with CH_2Cl_2 (2 × 20 mL). The organic layer was washed with H_2O (2 × 20 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was subjected to column chromatography (hexane/EtOAc, 9:1→2:1).

The first compound isolated was the byproduct 2,3,4,6-tetra-*O*-acetyl-1-*S*-acetyl-1-thio-*β*-D-glucopyranose (**21**, 66 mg) which showed properties identical to those described in the literature.[30] From following fractions from the column was obtained compound **20** (142 mg, 61%): $[\alpha]^{25}_{D}$ +16.2 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.20 (t, 1H, $J_{2',3'} = J_{3',4'}$ = 9.4 Hz, H-3′), 5.08 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 9.4 Hz, H-4′), 5.07 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.95 (dd, 1H, $J_{1',2'}$ = 10.0, $J_{2',3'}$ = 9.4 Hz, H-2′), 4.92 (dd, 1H, $J_{1,2}$ = 3.7, $J_{2,3}$ = 11.3 Hz, H-2), 4.69 (d, 1H, $J_{1',2'}$ = 10.0 Hz, H-1′), 4.50 (dd, 1H, $J_{5,6a}$ = 2.1, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.44 (dd, 1H, $J_{5,6b}$ = 4.1, $J_{6a,6b}$ = 12.0 Hz, H-6b), 4.26 (ddd, $J_{4,5}$ = 11.1, $J_{5,6a}$ = 2.1, $J_{5,6b}$ = 4.0 Hz, H-5), 4.23 (dd, 1H, $J_{5',6'a}$ = 4.4, $J_{6'a,6'b}$ = 12.5 Hz, H-6′a), 4.17 (dd, 1H, $J_{5',6'b}$ = 2.5, $J_{6'a,6'b}$ = 12.5 Hz, H-6′b), 3.99 (dd, 1H, $J_{2,3}$ = 11.3, $J_{3,4}$ = 12.0 Hz, H-3), 3.87 (m, 1H, *J* = 6.2 Hz, Me_2CHO), 3.71 (ddd, 1H, $J_{4',5'}$ = 9.4, $J_{5',6'a}$ = 4.4, $J_{5',6'b}$ = 2.5 Hz, H-5′), 3.12 (dd, 1H, $J_{3,4}$ = 12.0, $J_{4,5}$ = 11.1 Hz, H-4), 2.34 (s, 3H, CH_3COS), 2.11, 2.10, 2.05, 2.03 (×2), 1.99 (5s, 18H, CH_3CO), 1.25, 1.13 (2d, each 3H, *J* = 6.2 Hz, $(CH_3)_2CHO$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 193.8 (CH_3COS) 170.6, 170.5, 170.1, 170.0, 169.3, 169.2 (CH_3CO), 94.1 (C-1), 81.7 (C-1′), 75.6 (C-5′), 73.9 (C-3′), 71.1 (Me_2CHO), 71.0 (C-5), 70.2 (C-2), 70.0 (C-2′), 68.0 (C-4′), 64.2 (C-6), 61.8 (C-6′), 45.9 (C-4), 44.4 (C-3), 30.6 (CH_3COS), 23.1, 21.6 [$(CH_3)_2CHO$], 20.8−20.6 (CH_3CO). Anal. Calcd for $C_{29}H_{42}O_{16}S_2$: C, 49.01; H, 5.96. Found: C, 49.15; H, 5.74.

Compound **20** (76 mg, 0.11 mmol) was *S*-deacetylated by stirring with 2-aminoethanethiol (10 mg, 0.13 mmol) in MeCN (0.3 mL) at 65 °C for 1 h. Analysis by TLC (toluene/EtOAc, 1:1) showed the complete conversion of **20** (R_f 0.52) into the less polar product **17** (R_f 0.60). The mixture was concentrated, the residue dissolved in CH_2Cl_2 (20 mL) and washed in water (2 × 15 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated. The resulting syrup was purified by column chromatography (hexane/EtOAc, 4:1→2.3:1) to afford **17** (47 mg, 66%). This product showed properties identical to those of the one obtained from the reaction between **14** and **16b**.

2-Propyl 2,6-Di-*O*-acetyl-3-*S*-acetyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl)-3,4-dithio-*α*-D-glucopyranoside (23). Tetra-*O*-acetyl-1-thio-*β*-D-galactopyranose **22a**[50] (175 mg, 0.49 mmol) was converted into the sodium salt **22b**, as previously described for **16a**. The reaction of **22b** with the episulfide **14** (100 mg, 0.32 mmol) was performed under the conditions employed for the analogous reaction with **16b**. The crude mixture obtained was dissolved in dry THF (22 mL) and treated with $LiAlH_4$ (160 mg, 4.19 mmol) as described for the preparation of **17**. After the same workup and acetylation, the mixture showed by TLC (toluene/EtOAc, 1:1) two main spots of R_f 0.67 and 0.51. Purification by column chromatography (hexane/EtOAc, 4:1 → 1.5:1) afforded first 2,3,4,6-tetra-*O*-acetyl-1-*S*-acetyl-1-thio-*β*-D-galactopyranose **24**, which showed the same properties as the product already reported.[31]

Further fractions of the column afforded **23** as a syrup (R_f 0.51, 160 mg, 70% for the three steps of reaction): $[\alpha]^{25}_{D}$ +15.7 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.43 (dd, 1H, $J_{3',4'}$ = 3.4, $J_{4',5'}$= 1.0 Hz,

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H-4′), 5.13 (t, 1H, $J_{1',2'} = J_{2',3'}$ =10.0 Hz, H-2′), 5.07 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 5.02 (dd, 1H, $J_{2',3'}$ = 10.0, $J_{3',4'}$ = 3.4 Hz, H-3′), 4.93 (dd, 1H, $J_{1,2}$ = 3.6, $J_{2,3}$ = 11.2 Hz, H-2), 4.68 (d, 1H, $J_{1',2'}$ = 10.0 Hz, H-1′), 4.50 (dd, 1H, $J_{5,6a}$ = 4.1, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.46 (dd, 1H, $J_{5,6b}$ = 2.4, $J_{6a,6b}$ = 12.0 Hz, H-6b), 4.25 (ddd, $J_{4,5}$ = 11.0, $J_{5,6a}$ = 4.1, $J_{5,6b}$ = 2.4 Hz, H-5), 4.09 (dd, 1H, $J_{5',6'a}$ = 6.7, $J_{6'a,6'b}$ = 11.2 Hz, H-6′a), 4.08 (dd, 1H, $J_{5',6'b}$ = 6.7, $J_{6'a,6'b}$ = 11.2 Hz, H-6′b), 3.99 (dd, 1H, $J_{2,3}$ = 11.2, $J_{3,4}$ = 12.1 Hz, H-3), 3.92 (ddd, 1H, $J_{4',5'}$ = 1.0, $J_{5',6'a} = J_{5',6'b}$ = 6.7 Hz, H-5′), 3.87 (m, 1H, J = 6.2 Hz, Me_2CHO), 3.12 (dd, 1H, $J_{3,4}$ = 12.1, $J_{4,5}$ = 11.0 Hz, H-4), 2.33 (s, 3H, CH_3COS), 2.16, 2.09, 2.05, 2.04, 2.03, 1.96 (6s, 18H, CH_3CO), 1.26, 1.13 (2d, each 3H, J = 6.2 Hz, $(CH_3)_2CHO$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 193.7 (CH_3COS) 170.5, 170.2, 170.1, 170.0, 169.9, 169.4, 169.3 (CH_3CO), 94.0 (C-1), 82.2 (C-1′), 74.1 (C-5′), 71.8 (C-3′), 71.1 (C-2), 70.9 (Me_2CHO), 70.1 (C-5), 67.1 (C-2′), 67.0 (C-4′), 64.2 (C-6), 61.1 (C-6′), 45.9 (C-4), 44.5 (C-3), 30.7 (CH_3COS), 23.1, 21.5 [$(CH_3)_2CHO$], 20.8–20.5 (CH_3CO); HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{29}H_{42}NaO_{16}S_2$ 733.1807, found 733.1806.

2-Propyl 2,6-Di-*O*-acetyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3,4-dithio-α-D-glucopyranoside (25). A solution of **23** (60 mg, 0.08 mmol) in MeCN (0.25 mL) was treated with 2-aminoethanethiol (8 mg, 0.10 mmol). The reaction was stirred at 65 °C for 1 h, until TLC (toluene/EtOAc, 1:1) showed the complete conversion of the initial compound (R_f 0.51) into **25** (R_f 0.48). The reaction mixture was concentrated and extracted with CH_2Cl_2/H_2O. The organic phase was dried with $MgSO_4$ and purified by column in silica gel (hexane/EtOAc, 4:1→2.3:1) to give **25** (40 mg, 71%): $[\alpha]^{25}_D$ +40.5 (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.43 (dd, 1H, $J_{3',4'}$ = 3.4, $J_{4',5'}$ = 1.0 Hz, H-4′), 5.17 (t, 1H, $J_{1',2'} = J_{2',3'}$ =10.0 Hz, H-2′), 5.09 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 5.04 (dd, 1H, $J_{2',3'}$ = 10.0, $J_{3',4'}$ = 3.4 Hz, H-3′), 4.76 (dd, 1H, $J_{1,2}$ = 3.5, $J_{2,3}$ = 10.9 Hz, H-2), 4.61 (d, 1H, $J_{1',2'}$ = 10.0 Hz, H-1′), 4.49 (dd, 1H, $J_{5,6a}$ = 4.0, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.45 (dd, 1H, $J_{5,6b}$ = 2.3, $J_{6a,6b}$ = 12.0 Hz, H-6b), 4.12 (dd, 1H, $J_{5',6'a}$ = 7.0, $J_{6'a,6'b}$ = 11.4 Hz, H-6′a), 4.10 (ddd, $J_{4,5}$ = 11.3, $J_{5,6a}$ = 4.0, $J_{5,6b}$ = 2.3 Hz, H-5), 4.08 (dd, 1H, $J_{5',6'b}$ = 6.2, $J_{6'a,6'b}$ = 11.4 Hz, H-6′b), 3.89 (ddd, 1H, $J_{4',5'}$ = 1.0, $J_{5',6'a}$ = 7.0, $J_{5',6'b}$ = 6.2 Hz, H-5′), 3.87 (m, 1H, J = 6.2 Hz, Me_2CHO), 3.51 (td, 1H, $J_{2,3}$ = 10.9, $J_{3,4}$ = 11.3, $J_{3,SH}$ = 3.8 Hz, H-3), 2.89 (t, 1H, $J_{3,4} = J_{4,5}$ = 11.3 Hz, H-4), 2.32 (d, 1H, $J_{3,SH}$ = 3.8 Hz, S*H*), 2.18, 2.14, 2.11 (x2), 2.05, 1.99 (5s, 18H, CH_3CO), 1.24, 1.13 (2d, each 3H, J = 6.2 Hz, $(CH_3)_2CHO$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.2, 170.0, 169.9, 169.4 (CH_3CO), 93.7 (C-1), 82.8 (C-1′), 74.8 (C-2), 74.4 (C-5′), 71.8 (C-3′), 70.9 (Me_2CHO), 69.6 (C-5), 67.0 (C-2′), 66.9 (C-4′), 63.9 (C-6), 61.5 (C-6′), 50.3 (C-4), 40.2 (C-3), 23.1, 21.6 [$(CH_3)_2CHO$], 20.8–20.6 (CH_3CO); HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{27}H_{40}NaO_{15}S_2$ 691.1701, found 691.1719.

Methyl 6-*S*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3-di-*O*-*tert*-butyldimethylsilyl-5,6-dithio-β-D-galactofuranoside (26), Methyl 6-*S*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-5-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-disulfide-2,3-di-*O*-*tert*-butyldimethylsilyl-5,6-dithio-β-D-galactofuranoside (27), and Bis[methyl 2,3-Di-*O*-*tert*-butyldimethylsilyl-6-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-5,6-dithio-β-D-galactofuranos-5-*S*-yl]disulfide (28). The sodium salt of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose (**22b**), prepared as described from **22a**[50] (90 mg, 0.25 mmol), was dissolved in THF (1 mL) and added to a solution of the episulfide **8** (52 mg, 0.12 mmol) in dry THF (2 mL) cooled at 0 °C. After 10 min, 18-crown-6 (26 mg, 0.10 mmol) was added, and the stirring was continued for 1 h, when TLC (toluene/EtOAc, 2:1) showed three main spots of R_f 0.72, 0.54, and 0.44. This mixture was fractionated by column chromatography (toluene/EtOAc, 7:1→EtOAc) which afforded first the less polar product, the thiodisaccharide **26** (7 mg, 5%): $[\alpha]^{25}_D$ −37.8 (c 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.43 (dd, 1H, $J_{4',5'}$ = 0.9, $J_{3',4'}$ = 3.3 Hz, H-4′), 5.24 (t, 1H, $J_{1',2'} = J_{2',3'}$ = 10.0 Hz, H-2′), 5.02 (dd, 1H, $J_{3',4'}$ = 3.3, $J_{2',3'}$ = 10.0 Hz, H-3′), 4.66 (d, 1H, $J_{1,2}$ = 2.0 Hz, H-1), 4.55(d, 1H, $J_{1',2'}$ = 10.0 Hz, H-1′), 4.21 (dd, 1H, $J_{2,3}$ = 3.9, $J_{3,4}$ = 7.4 Hz, H-3), 4.18 (dd, 1H, $J_{4,5}$ = 1.8, $J_{3,4}$ = 7.4 Hz, H-4), 4.15 (dd, 1H, $J_{5',6'a}$ = 6.7, $J_{6'a,6'b}$ = 11.3 Hz, H-6′a), 4.13 (dd, 1H, $J_{5',6'b}$ = 6.7, $J_{6'a,6'b}$ = 11.3 Hz, H-6′b), 4.01 (dd, 1H, $J_{1,2}$ = 2.0, $J_{2,3}$ = 3.9 Hz, H-2), 3.92 (ddd, 1H, $J_{4',5'}$ = 0.9, $J_{5',6'a} = J_{5',6'b}$ = 6.7 Hz, H-5′), 3.32 (s, 3H, CH_3O), 3.14 (dd, 1H, $J_{5,6a}$ = 5.5, $J_{6a,6b}$ = 12.5 Hz, H-6a), 3.04 (m, 1H, $J_{4,5}$ = 1.8, $J_{5,6a}$ = 5.5, $J_{5,6b}$ = 8.3, $J_{5,HS}$ = 9.4 Hz, H-5), 3.00 (dd, 1H, $J_{5,6b}$ = 8.3, $J_{6a,6b}$ = 12.5 Hz, H-6b), 2.16, 2.07, 2.06, 1.98 (4s, 12H, CH_3CO), 1.92 (d, 1H, $J_{5,HS}$ = 9.4 Hz, *HS*), 0.90, 0.89 (2s, 18H, $(CH_3)_3CSiMe_2$), 0.11, 0.10, 0.09, 0.08 (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.2 (×2), 170.0, 169.5 (CH_3CO), 109.0 (C-1), 84.3 (C-2), 83.7 (C-1′), 81.2 (C-4), 80.2 (C-3), 74.4 (C-5′), 71.8 (C-3′), 67.2 (C-2′), 67.1 (C-4′), 61.2 (C-6′), 55.0 (CH_3O), 41.7 (C-5), 36.7 (C-6), 25.8, 25.7 [$(CH_3)_3CSiMe_2$], 21.4, 20.7, 20.6, 20.5 (CH_3CO), 17.8 (×2) [$(CH_3)_3CSiMe_2$], −4.1, −4.3, −4.6, −4.9 [$(CH_3)_2SiBu^t$]; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{33}H_{60}NaO_{13}S_2Si_2$ 807.2906, found 807.2918. Anal. Calcd for $C_{33}H_{60}O_{13}S_2Si_2$: C, 50.48; H, 7.70. Found: C, 50.80; H, 7.46.

From the next fractions of the column was obtained the symmetric disulfide **28** (20 mg, 11%): $[\alpha]^{25}_D$ +12.3 (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.45 (dd, 1H, $J_{3',4'}$ = 3.4, $J_{4',5'}$ = 1.0 Hz, H-4′), 5.20 (t, 1H, $J_{1',2'} = J_{2',3'}$ = 10.0 Hz, H-2′), 5.07 (dd, 1H, $J_{2',3'}$ = 10.0, $J_{3',4'}$ = 3,4 Hz, H-3′), 4.65 (d, 1H, $J_{1,2}$ = 1.6 Hz, H-1), 4.58 (d, 1H, $J_{1',2'}$ = 10.0 Hz, H-1′), 4.30 (dd, 1H, $J_{3,4}$ = 6.7, $J_{4,5}$ = 2.3 Hz, H-4), 4.17 (m, 2H, H-6′a, H-6′b), 4.16 (dd, 1H, $J_{2,3}$ = 3.5, $J_{3,4}$ = 6.8 Hz, H-3), 3.99 (m, 1H, H-5′), 3.98 (dd, 1H, $J_{1,2}$ = 1.6, $J_{2,3}$ = 3.5 Hz, H-2), 3.32 (s, 3H, CH_3O), 3.21–3.09 (m, 3H, H-5, H-6a, H-6b), 2.16, 2.07, 2.04, 1.98 (4s, 12H, CH_3CO), 0.90, 0.89 (2s, 18H, $(CH_3)_3CSiMe_2$), 0.12 (×2), 0.09, 0.08 (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.3, 170.2, 170.0, 169.5 (CH_3CO), 109.0 (C-1), 84.5 (C-1′), 84.1 (C-2), 82.1 (C-4), 80.0 (C-3), 74.3 (C-5′), 71.8 (C-3′), 67.6 (C-2′), 67.1 (C-4′), 61.0 (C-6′), 55.1 (CH_3O), 54.0 (C-5), 32.6 (C-6), 25.8 (×2)[$(CH_3)_3CSiMe_2$], 20.8, 20.7 (×2), 20.6 (CH_3CO), 17.9, 17.8 [$(CH_3)_3CSiMe_2$], −4.0, −4.2, −4.5, −4.9 [$(CH_3)_2SiBu^t$]; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{66}H_{118}NaO_{26}S_4Si_4$ 1589.5763, found 1589.5712. Anal. Calcd for $C_{66}H_{118}O_{26}S_4Si_4$: C, 50.55; H, 7.58. Found: C, 50.52; H, 7.57.

The last component of the mixture isolated from the column was the disulfide **27** (30 mg, 21%): $[\alpha]^{25}_D$ −0.6 (c 1.0, $(CH_3)_2CO$); ^1H NMR [$(CD_3)_2CO$, 500 MHz] δ 5.47, 5.45 (2dd, 2H, H-4′, H-4″), 5.28–5.16 (m, 4H, H-2′, H-2″, H-3′, H-3″), 4.91 (d, 1H, $J_{1',2'}$ = 9.9 Hz, H-1′), 4.87 (d, 1H, $J_{1'',2''}$ = 9.7 Hz, H-1″), 4.72 (d, 1H, $J_{1,2}$ = 1.2 Hz, H-1), 4.43 (d, 2H, H-6″a, H-6″b), 4.42 (dd, 1H, $J_{3,4}$ = 6.8, $J_{4,5}$ ~ 3.0 Hz, H-4), 4.36 (ddd, 1H, $J_{4',5'}$ = 1.2, $J_{5',6'a}$ ~ $J_{5',6'b}$ ~ 6.6 Hz, H-5′), 4.28 (dd, 1H, $J_{2,3}$ = 3.0, $J_{3,4}$ = 6.8 Hz, H-3), 4.25–4.16 (m, 3H, H-5″, H-6′a, H-6′b), 4.07 (dd, 1H, $J_{1,2}$ = 1.2, $J_{2,3}$ = 3.0 Hz, H-2), 3.54 (dd, 1H, H-6a), 3.36 (s, 3H, CH_3O), 3.35 (m, 1H, H-5), 3.18 (dd, 1H, $J_{5,6b}$ = 8.7, $J_{6a,6b}$ = 13.4 Hz, H-6b), 2.17, 2.16, 2.07 (×2), 2.05, 2.03, 1.94 (×2) (8s, 24H, CH_3CO), 0.96, 0.95 (2s, 18H, $(CH_3)_3CSiMe_2$), 0.22, 0.20, 0.16, 0.15 (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR [$(CD_3)_2CO$, 125.7 MHz] δ 170.8 (×2), 170.6, 170.5, 170.1 (×2), 170.0, 169.8 (CH_3CO), 109.7 (C-1), 91.4 (C-1′), 85.5 (C-2), 84.6 (C-1″), 83.2 (C-4), 81.6 (C-3), 75.6 (C-5′), 75.1 (C-5″), 72.5, 72.4 (C-3′, 3″), 68.4, 68.3, 68.2 (×2) (C-2′, 2″, 4′, 4″), 62.2, 62.0, (C-6′, 6″), 55.5, 55.2 (C-5, CH_3O), 33.4 (C-6), 26.3 (× 3) [$(CH_3)_3CSiMe_2$], 20.8 (× 3), 20.7 (×2), 20.6, 20.5 (×2) (CH_3CO), 18.5 (×2) [$(CH_3)_3CSiMe_2$], −3.7, −3.8, −4.2, −4.6 [$(CH_3)_2SiBu^t$]; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{47}H_{78}NaO_{22}S_3Si_2$ 1169.3578, found 1169.3538. Anal. Calcd for $C_{47}H_{78}O_{22}S_3Si_2{\cdot}5H_2O$: C, 45.61; H, 7.17. Found: C, 45.42; H, 6.49.

Alternatively, the thiodisaccharide **26** was obtained under optimized conditions and in the presence of dihiothreitol (DTT) as follows. The salt **22b**, prepared from **22a** (142 mg, 0.39 mmol), was dissolved in THF (2 mL) and added to a cold solution (0 °C) of the episulfide **8** (82 mg, 0.19 mmol) and DTT (32 mg, 0.21 mmol) in dry THF (4 mL). After 10 min, 18-crown-6 (20 mg, 0.08 mmol) was added and the stirring was continued for 30 min, when an additional amount of 18-crown-6 (20 mg, 0.08 mmol) was added. After 30 min of stirring, TLC (toluene/EtOAc, 2:1) showed a main spot of R_f 0.72. Purification by column chromatography as above afforded the thiodisaccharide **26** (146 mg, 98%).

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Methyl 6-*S*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3-di-*O*-*tert*-butyldimethylsilyl-5,6-dithio-α-L-altrofuranoside (29). The optimized procedure described for the opening of episulfide **8** was applied to the thiirane **11** (100 mg, 0.24 mmol). However, in this case the total reaction time was 2.5 h. Examination of the reaction mixture by TLC (toluene) showed a main spots of R_f 0.67. Purification by column chromatography (toluene/EtOAc, 7:1→EtOAc) afforded the thiodisaccharide **29** (163 mg, 87%): $[\alpha]^{25}_D$ −29.5 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.43 (dd, 1H, $J_{3',4'}$ = 3.4, $J_{4',5'}$ = 0.9 Hz, H-4′), 5.23 (t, 1H, $J_{1',2'} = J_{2',3'}$ = 10.0 Hz, H-2′), 5.04 (dd, 1H, $J_{2',3'}$ = 10.0, $J_{3',4'}$ = 3.4 Hz, H-3′), 4.74 (s, 1H, H-1), 4.59 (d, 1H, $J_{1',2'}$ = 10.0 Hz, H-1′), 4.14 (d, 2H, H-6a, H-6b), 4.12 (dd, 1H, $J_{2,3}$ = 1.2, $J_{3,4}$ = 3.4 Hz, H-3), 3.98−3.92 (m, 3H, H-2, H-4, H-5′), 3.32 (s, 3H, CH_3O), 3.24 (dd, 1H, $J_{5,6a}$ = 4.0, $J_{6a,6b}$ = 13.4 Hz, H-6a), 3.19 (dddd, 1H, $J_{4,5} \sim J_{5,6a}$ = 4.0, $J_{5,6b}$ = 7.5 Hz, H-5), 2.97 (dd, 1H, $J_{5,6b}$ = 7.5, $J_{6a,6b}$ = 13.4 Hz, H-6b), 2.16, 2.08, 2.04, 1.99 (4s, 12H, CH_3CO), 0.89, 0.88 (2s, 18H, $(CH_3)_3CSiMe_2$), 0.12 (×2), 0.10, 0.09 (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.3, 170.2, 170.0, 169.5 (CH_3CO), 110.2 (C-1), 89.0(C-4), 85.0 (C-1′), 82.4 (C-2), 80.7 (C-3), 74.4 (C-5′), 71.9 (C-3′), 67.6 (C-2′), 67.1 (C-4′), 61.2 (C-6′), 54.7 (CH_3O), 43.0 (C-5), 36.6 (C-6), 25.7 (×2) [$(CH_3)_3CSiMe_2$], 20.8, 20.6 (× 3) (CH_3CO), 17.8 (×2) [$(CH_3)_3CSiMe_2$], −4.3, −4.4, −4.7, −4.8 [$(CH_3)_2SiBu^t$]; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{60}NaO_{13}S_2Si_2$ 807.2906, found 807.2916. Anal. Calcd for $C_{33}H_{60}O_{13}S_2Si_2$: C, 50.48; H, 7.70. Found: C, 50.81; H, 7.81.

2-Propyl 2,6-Di-*O*-acetyl-3,4-di-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3,4-dithio-α-D-glucopyranoside (31). A suspension of **17** (44 mg, 0.07 mmol), the trichloroacetimidate **30**[38] (65 mg, 0.13 mmol), and freshly activated powdered molecular sieves (4 Å) in CH_2Cl_2 (1.5 mL) was stirred at room temperature for 1.5 h. The mixture was cooled to −18 °C, and TMSOTf (3 μL, 0.02 mmol) was added. Monitoring by TLC (CH_2Cl_2/EtOAc, 3:1) showed gradual conversion of the starting compounds **17** (R_f 0.63) and **30** (R_f 0.73) into other two more polar products (R_f 0.40 and 0.28). After 4 h, Et_3N (5 μL, 0.03 mmol) was added and the mixture was concentrated. The residue was subjected to column chromatography using CH_2Cl_2/EtOAc, 9:1→4:1 as solvent. The first fractions of the column afforded unreacted **17** (18 mg), and from the next fractions was isolated 2,3,4,6-tetra-*O*-acetyl-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1-β-D-glucopyranoside (**32**, 23 mg), which showed spectroscopic and physical data in agreement with those described in the literature.[39]

The more polar product obtained from the column was identified as **31** (16 mg, 35%, corrected): $[\alpha]^{25}_D$ +28.3 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.14 (t, 1H, $J_{2',3'} = J_{3',4'}$ = 9.4 Hz, H-3′), 5.14 (t, 1H, $J_{2'',3''} = J_{3'',4''}$ = 9.4 Hz, H-3″), 5.04 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.99 (t, 2H, $J_{3',4'} = J_{4',5'} = J_{3'',4''} = J_{4'',5''}$ = 9.4 Hz, H-4′, 4″), 4.90 (dd, 1H, $J_{1',2'}$ = 10.2, $J_{2',3'}$ = 9.4 Hz, H-2′), 4.84 (dd, 1H, $J_{1'',2''}$ = 10.2, $J_{2'',3''}$ = 9.4 Hz, H-2″), 4.74 (dd, 1H, $J_{1,2}$ = 3.5, $J_{2,3}$ = 11.4 Hz, H-2), 4.69 (d, 1H, $J_{1'',2''}$ = 10.2 Hz, H-1″), 4.64 (d, 1H, $J_{1',2'}$ = 10.2 Hz, H-1′), 4.49 (dd, 1H, $J_{5,6a}$ = 4.3, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.42 (dd, 1H, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 12.0 Hz, H-6b), 4.23 (dd, 1H, $J_{5'',6''a}$ = 4.5, $J_{6''a,6''b}$ = 12.5 Hz, H-6″a), 4.14 (ddd, 1H, $J_{4,5}$ = 10.9, $J_{5,6a}$ = 4.3, $J_{5,6b}$ = 2.0 Hz, H-5), 4.10 (m, 3H, H-6′a,H-6′b, H-6″b), 3.82 (m, 1H, *J* = 6.2 Hz, Me_2CHO), 3.64 (ddd, 1H, $J_{4',5'}$ = 9.4, $J_{5',6'a}$ = 4.3, $J_{5',6'b}$ = 2.3 Hz, H-5′), 3.58 (ddd, 1H, $J_{4'',5''}$ = 9.4, $J_{5'',6''a}$ = 4.5, $J_{5'',6''b}$ = 2.9 Hz, H-5″), 3.31 (t, 1H, $J_{2,3} = J_{3,4}$ = 11.4 Hz, H-3), 2.77 (dd, 1H, $J_{3,4}$ = 11.4, $J_{4,5}$ = 10.9 Hz, H-4), 2.08, 2.05, 2.04, 2.03, 2.02, 1.97, 1.96, 1.95, 1.93 (×2) (9 s, 30H, CH_3CO), 1.17, 1.07 (2d, 3H each, *J* = 6.2 Hz, $(CH_3)_2CHO$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.6−169.5 (CH_3CO), 93.9 (C-1), 81.8 (C-1″), 80.7 (C-1′), 76.1 (C-5′), 75.6 (C-5″), 73.7, 73.6 (C-3′,3″), 73.3 (C-2), 70.8 (Me_2CHO), 69.9 (C-5), 69.6, 69.5 (C-2′,2″), 68.0, 67.8 (C-4′, 4″), 64.1 (C-6), 62.0, 61.7 (C-6′,6″), 45.0 (C-4), 44.2 (C-3), 23.2, 21.6 [$(CH_3)_2CHO$], 20.7−20.5 (CH_3CO); HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{41}H_{58}NaO_{24}S_2$ 1021.2652, found 1021.2671. Anal. Calcd for $C_{41}H_{58}O_{24}S_2$: C, 49.29; H, 5.85. Found: C, 49.48; H, 5.84.

2-Propyl 2,6-Di-*O*-acetyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-*S*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-3,4-dithio-α-D-glucopyranoside (34). The reaction between **25** (30 mg, 0.045 mmol) and **33**[40] (84 mg, 0.11 mmol), under catalysis with TMSOTf (2 μL) in CH_2Cl_2 (1.5 mL), was performed in the same conditions described above for the synthesis of **31**. When analysis by TLC (CH_2Cl_2/EtOAc, 3:1) showed complete conversion of the starting **25** and **33** (R_f 0.27 and 0.64) into two products of R_f 0.54 y 0.19, the mixture was processed and subjected to column chromatography as for the previous reaction. The first compound isolated from the column (R_f 0.54) was the *N*-glycosyltrichloroacetamide **35**[41] (50 mg).

Further fractions of the column afforded the starting compound **25** (5 mg), and then the product with R_f 0.19, which was UV active, was obtained. This compound was identified as **34** (38 mg, 66%, corrected yield 81%): $[\alpha]^{25}_D$ +0.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.10−7.15 (m, 20H, H-aromatic), 6.09 (m, $J_{4',5'}$ = 4.5, $J_{5',6'a}$ = 3.5, $J_{5',6'b}$ = 7.7 Hz, H-5′), 5.85 (s, 1H, H-1′), 5.66 (d, 1H, $J_{3',4'}$ = 4.5 Hz, H-3′), 5.42 (s, 1H, H-2′), 5.32 (dd, 1H, $J_{3'',4''}$ = 3.4, $J_{4'',5''}$ = 0.7 Hz, H-4″), 5.14 (t, 1H, $J_{1'',2''} = J_{2'',3''}$ = 10.0 Hz, H-2″), 4.97 (d, 1H, $J_{1,2}$ = 4.5 Hz, H-1), 4.96 (dd, 1H, $J_{2'',3''}$ = 10.0, $J_{3'',4''}$ = 3.4 Hz, H-3″), 4.89 (dd, 1H, $J_{1,2}$ =4.5, $J_{2,3}$ = 11.0 Hz, H-2), 4.88 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 4.5 Hz, H-4′), 4.80 (dd, 1H, $J_{5',6'a}$ = 3.2, $J_{6'a,6'b}$ = 12.1 Hz, H-6′a), 4.76 (d, 1H, $J_{1'',2''}$ = 10.0 Hz, H-1″), 4.68 (dd, 1H, $J_{5',6'b}$ = 8.0, $J_{6'a,6'b}$ = 12.1 Hz, H-6′b), 4.45 (dd, 1H, $J_{5,6a}$ = 2.1, $J_{6a,6b}$ = 11.9 Hz, H-6a), 4.40 (dd, 1H, $J_{5,6b}$ = 4.1, $J_{6a,6b}$ = 11.9 Hz, H-6b), 4.18 (ddd, 1H, $J_{4,5}$ = 11.0, $J_{5,6a}$ = 2.1, $J_{5,6b}$ = 4.1 Hz, H-5), 4.02 (dd, 1H, $J_{5'',6''a}$ = 6.4, $J_{6''a,6''b}$ = 11.3 Hz, H-6″a), 3.93 (dd, 1H, $J_{5'',6''b}$ = 7.2, $J_{6''a,6''b}$ = 11.3 Hz, H-6″b), 3.80 (ddd, $J_{4'',5''}$ = 0.7, $J_{5'',6''a}$ = 6.4, $J_{5'',6''b}$ = 7.2 Hz, H-5″), 3.77 (m, 1H, *J* = 6.2 Hz, Me_2CHO), 3.36 (dd, 1H, $J_{2,3}$ = 11.0, $J_{3,4}$ = 11.4 Hz, H-3), 3.03 (dd, 1H, $J_{3,4}$ =11.4, $J_{4,5}$ = 11.0 Hz, H-4), 2.01, 1.97, 1.95, 1.91, 1.87, 1.86 (6s, 18H, CH_3CO), 1.16, 1.03 (2d, 3H each, *J* = 6.2 Hz, $(CH_3)_2CHO$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.2−169.5 (CH_3CO), 166.1−165.3 (PhCO), 133.7−128.2 (C-aromatic), 93.8 (C-1), 88.5 (C-1′), 82.7 (C-2′), 82.1 (C-1″), 82.0 (C-4′), 77.8 (C-3′), 74.0 (C-5′), 73.9 (C-2), 71.9 (C-3″), 71.0 (Me_2CHO), 70.5 (C-5), 70.2 (C-5″), 67.2 (C-2″), 66.9 (C-4″), 64.2 (C-6), 61.4 (C-6′), 61.0 (C-6″), 45.3 (C-4), 44.7 (C-3), 23.1, 21.6 [$(CH_3)_2CHO$], 20.9−20.5 (CH_3CO); HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{61}H_{66}NaO_{24}S_2$ 1269.3278, found 1269.3246.

Methyl 6-*S*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-5-*S*-(2,3,5,6-tetra-*O*-benzoyl-β-D-galactofuranosyl)-2,3-di-*O*-*tert*-butyldimethylsilyl-5,6-dithio-β-D-galactofuranoside (36). The reaction of the trichloroacetimidate **33**[40] (195 mg, 0.26 mmol) with the thiodisaccharide **26** (82 mg, 0.10 mmol) was performed as in the two previous reactions, using catalysis with TMSOTf (12 μL, 0.07 mmol). After 2 h TLC (hexane/EtOAc, 2:1), showed the formation of a main spot of R_f 0.24. The usual workup and purification by column chromatography (hexane/EtOAc, 5:1→2:1) gave the branched dithiotrisaccharide **36** (55 mg, 40%): $[\alpha]^{25}_D$ −36.8 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.09−7.28 (H-aromatic), 6.10 (dddd, 1H, $J_{5',6'a}$ = 3.6, $J_{4',5'}$ = 4.6, $J_{5',6'b}$ = 7.3 Hz, H-5′), 5.95 (br s, 1H, H-1′), 5.73 (d, 1H, $J_{3',4'}$ = 4.7 Hz, H-3′), 5.58 (br s, 1H, H-2′), 5.39 (d, 1H, $J_{3'',4''}$ = 3.4 Hz, H-4″), 5.22 (t, 1H, $J_{1'',2''} = J_{2'',3''}$ = 10.0 Hz, H-2″), 5.07 (dd, 1H, $J_{3'',4''}$ = 3.4, $J_{2'',3''}$ = 10.0 Hz, H-3″), 4.86 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 4.6 Hz, H-4′), 4.82 (dd, 1H, $J_{5',6'a}$ = 3.6, $J_{6'a,6'b}$ = 12.1 Hz, H-6′a), 4.73 (dd, 1H, $J_{5',6'b}$ = 7.3, $J_{6'a,6'b}$ = 12.1 Hz, H-6′b), 4.68 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 4.63 (d, 1H, $J_{1'',2''}$ = 10.0 Hz, H-1″), 4.36 (dd, 1H, $J_{4,5}$ = 2.1, $J_{3,4}$ = 7.2 Hz, H-4), 4.22 (dd, 1H, $J_{2,3}$ = 4.0, $J_{3,4}$ = 7.2 Hz, H-3), 4.10 (m, 2H, H-6″a, H6″b), 4.00 (dd, 1H, $J_{1,2}$ = 1.8, $J_{2,3}$ = 4.0 Hz, H-2), 3.94 (t, 1H, H-5″), 3.33 (dd, 1H, $J_{5,6a}$ = 5.6, $J_{6a,6b}$ = 13.0 Hz, H-6a), 3.31 (s, 3H, CH_3O), 3.27 (ddd. 1H, $J_{4,5}$ = 1.9, $J_{5,6a}$ = 5.6, $J_{5,6b}$ = 8.3 Hz, H-5), 3.19 (dd, 1H, $J_{5,6b}$ = 8.3, $J_{6a,6b}$ = 13.0 Hz, H-6b), 2.09, 1.99, 1.96, 1.92 (4s, 12H, CH_3CO), 0.85, 0.84 (2s, 18H, $(CH_3)_3CSiMe_2$), 0.09, 0.07 (×2), 0.06 (4s, 12H, $(CH_3)_2SiBu^t$); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.2 (×2), 169.9, 169.5 (MeCO), 166.0, 165.6, 165.4, 165.2 (PhCO), 133.5−128.3 (C-aromatic), 108.9 (C-1), 88.2 (C-1′), 84.4 (C-2), 83.3 (C-1″), 83.1 (C-2′), 82.4 (C-4), 81.9 (C-4′), 80.1 (C-3), 77.7 (C-3′), 74.2 (C-5″), 71.8 (C-3″), 70.4 (C-5′), 67.5 (C-2″), 67.1 (C-4″), 63.7

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(C-6′), 61.0 (C-6″), 55.1 (CH_3O), 46.3 (C-5), 33.1 (C-6), 25.8, 25.7 [$(CH_3)_3CSiMe_2$], 20.6 (× 3), 20.5 (CH_3CO), 17.8, 17.7 [$(CH_3)_3CSiMe_2$], −4.2, −4.3, −4.5, −4.9 [$(CH_3)_2SiBu^t$]; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{67}H_{86}NaO_{22}S_2Si_2$ 1385.4483, found 1385.4498. Anal. Calcd for $C_{67}H_{86}O_{22}S_2Si_2$: C, 59.01; H, 6.36. Found: C, 58.73; H, 5.96.

■ ASSOCIATED CONTENT

Supporting Information

Details on general experimental methods; copies of ^1H and ^{13}C NMR spectra for all new compounds and selected COSY and HMQC. This material is available free of charge via the Internet at http://pubs.acs.org.

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