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Stereospecific Domino Reaction

A Domino Epoxide Ring-Opening Xanthate Migration Reaction: An Alternative Entry to Thiosugars

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Abstract: A stereospecific and efficient synthesis of thiosugars derived from levoglucosenone and methyl α-D-glucopyranoside was developed by a domino epoxide ring opening-xanthate migration to afford 1,3-oxathiolane-2-thiones in high yields. The stereochemical outcome of the new C–S bond was defined by the configuration of the starting materials. The 1,3-oxathiolane-2-thiones were subsequently submitted to a second tandem reaction affording the corresponding 2,3-episulfide alcohols. The thiosugars obtained are useful building blocks for the synthesis of thiooligosaccharides with potential biological properties.

Introduction

Glycoconjugates play a valuable role in several biological processes, such as, inflammation, immune response, cancer metastasis, viral and bacterial infections, therefore, they offer a great opportunity for therapeutic drug development.[1] However, a drawback is the instability of glycosides toward chemical and enzymatic degradation due to the susceptibility of the glycosidic bond towards hydrolysis in *in vivo* applications. To address this issue, the synthesis of stable glycomimetics is a topic of current research interest.[2]

The replacement of an oxygen atom with a carbon, sulfur or nitrogen atoms modifies the biological properties of carbohydrate mimetics. These differences could be attributed to geometric, conformational and electronic factors. In particular sulfur containing carbohydrates or thiosugars possess uniques physicochemical properties, they have also provided crucial data on cellular recognition events and contributed to the rational design of new drugs. Natural free thiosugars are potential targets for the development of carbohydrate-based therapeutics. After the isolation of the first 5-thio-D-mannose from the marine sponge *Clathriapyramida* in 1987,[3] two other thiosugar families were found, corresponding to thioglycosides and 1,4-thioanhydrosugars.[1a] These discoveries along with the bioactivitives shown by these compounds, promoted many synthetic developments in carbohydrate chemistry, specially toward the synthesis of thiooligosaccharides, where the native *O*-glycosidic bond was replaced by a sulfur atom or a disulfide bond.[4] In many cases, these compounds act as glycosidases inhibitors in diseases like diabetes, bacterial or viral infections[4b,5] and lysosomal storage disorders.[6] The impact of these type of compounds in glycobiology and drug design has been widely reflected in literature.[7,8]

Among the different strategies to incorporate a sulfur functionality into a carbohydrate skeleton, anhydro sugar derivatives have demonstrated to be very useful building blocks to achieve this goal. We have recently reported the stereospecific synthesis of a 3-thiomannopyranoside starting from levoglucosenone (1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose) (**1**), A xanthate-thiocarbonate exchange under acidic conditions was the key step to build the C–S bond.[9]

Cyclic dithiocarbonates (1,3-oxathiolane-2-thiones) have received much attention due to their biological activities and in material science.[10] In addition, five-membered cyclic dithiocarbonates have been reported to possess important radioprotective properties[11] and applications as monomers in polymer syntheses.[12]

This valuable type of compounds can be prepared by reaction of epoxides with carbon disulfide.[13] However, this transformation leads to a range of products including regioisomeric mixture of five-membered dithiocarbonate, trithiocarbonate and episulfide, depending on the catalyst and reaction conditions.[14] This lack of selectivity could be solved by inducing an intramolecular reaction of a xantate derivative to a neighboring electron-deficient carbon.

In view of this exciting background, we turned our attention to the use of sugar-derived epoxy alcohols as a way to synthesize cyclic thiocarbonates via the corresponding xanthate derivative, allowing a stereospecific C–S bond formation within a pyranose framework (Scheme 1).

There are only a few precedents regarding the intramolecular ring opening of an epoxide in linear chain by a xanthate anion to afford a 1,3-oxathiolane-2-thione.[15] Our interest in sugar epoxides lies both in the intrinsic reactivity of the oxirane ring and in the wide variety of methods for its generation (including

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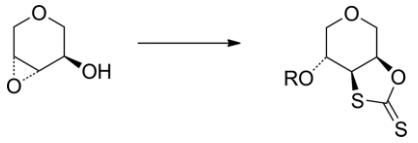


Scheme 1. General strategy.

intramolecular ring closing reactions and epoxidations of unsaturated sugars with peroxyacid derivatives). In addition, the conformational and stereoelectronic factors involved in the regio- and stereochemical outcome of epoxide opening reactions usually ensure high levels of selectivity.[16] The regio- and stereospecific ring opening of epoxides with a wide variety of nucleophiles, either intra- or intermolecularly, provides a useful entry towards other valuable functionalities.[17]

In the present work we report the stereospecific synthesis of novel thiosugars starting from the 2,3-epoxy alcohols derived from levoglucosenone (**1**) and methyl α-D-glucopyranoside (**2**) (Figure 1). The syntheses were made straightforward and in good yields. The thio-monosaccharides obtained are building blocks of interest in thiooligosaccharides synthesis for therapeutic applications.

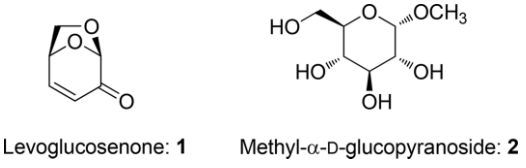


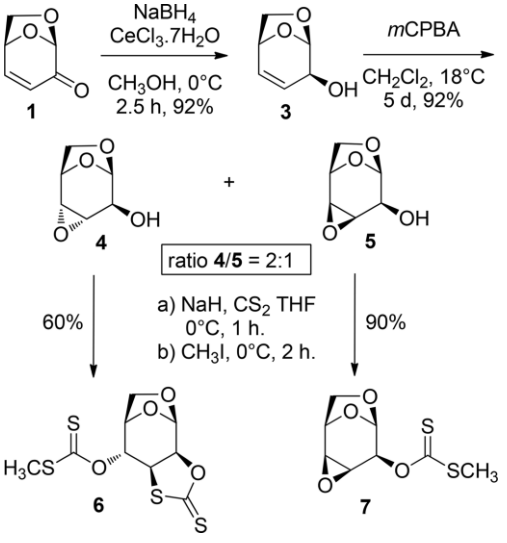
Figure 1. Levoglucosenone **1** and methyl α-D-glucopyranoside **2**.

Results and Discussion

Our strategy towards cyclic dithiocarbonates was based on the possibility to promote the epoxide ring opening by the intramolecular assistance of a xanthate anion derived from a 2,3-epoxy alcohol. In order to test our hypothesis, the epoxides derived from **1** and **2** were chosen as model compounds.

Levoglucosenone is a valuable chiral chemical platform easily obtained from pyrolysis of cellulosic residues,[18,19] whose epoxides derivatives have been successfully employed as starting materials for the synthesis of saccharides.[20] In addition, the anhydro bridge present in **1** avoids the need for protecting groups at the anomeric and C-6 carbons and fixes the conformation of the cyclic system which in turn makes the β-face sterically hindered. The structural singularities of this enone have already been exploited in the synthesis of several natural products and synthetic intermediates.[21,22]

To accomplish our purpose we relied on the stereoselective reduction of **1** under Luche conditions to give the allylic alcohol **3** (Scheme 2).[23] Epoxidation of **3** using *m*-chloroperbenzoic acid (*m*CPBA) afforded the two possible products **4** and **5** in a 2:1 ratio and very good yields,[20d] which could be easily separated by flash chromatography techniques. The steric restriction imposed by the 1,6-anhydro bridge in **3** resulted in the preferential formation of epoxide **4** although this structural factor does not completely overcome the directing ability of the hydroxyl group, obtaining significant quantities of **5** as well. Despite the α-epoxide could be obtained in a highly stereoselective manner by blocking the directing effect of the hydroxyl group by acetylation,[24] we envisaged the formation of the two isomers to explore the influence of the relative stereochemistry of the starting material in the reaction outcome.



Scheme 2. Synthesis of xanthates **6** and **7**.

In an effort to synthesize the corresponding xanthates, the 2,3-epoxy alcohols were treated with sodium hydride in a mixture of carbon disulfide and tetrahydrofuran at 0 °C, followed by the addition of methyl iodide. However, only in the case of *cis* epoxy-alcohol **5** the expected xanthate at C-2 was obtained (compound **7**, Scheme 1). Instead, a different reaction pathway took place from *trans* epoxy-alcohol **4**, yielding the 1,3-oxathiolane-2-thione ring with migration of the xanthate group at C-4 (compound **6**). The structure of **6** was made evident by the appearance of two distinctive signals in the ^{13}C NMR spectrum (215.1 and 209.0 ppm) assigned to thiocarbonyl groups while the IR spectrum showed no absorption bands for carbonyl groups in the region of 1700 cm^{-1}. A singlet peak at δ = 2.61 ppm in the ^{1}H NMR is also characteristic of a xanthate's methyl group. The structures of **6** and **7** were further confirmed after exhaustive 1D and 2D NMR studies.

The different outcome observed upon changing the relative orientation between the oxirane ring and the hydroxyl group at C-2 in precursors **4** and **5** could be rationalized according to the Fürst-Plattner rule,[25] which state the preference of epoxide ring opening by nucleophilic attack through an S_N2 *trans* diaxial approach. Taking into account this evidence, the formation of **6** could be explained through a domino mechanism depicted in Scheme 3.

Hence, the alkoxide **8** (formed by deprotonation of **4** with NaH) may react with CS_2 present in excess to produce the sodium S-xanthate **9**. This intermediate is a well suited nucleophile that could make an intramolecular S_N2 attack on the adjacent carbon to produce the epoxide ring opening. This process is possible because the two groups are in a *trans* relationship,

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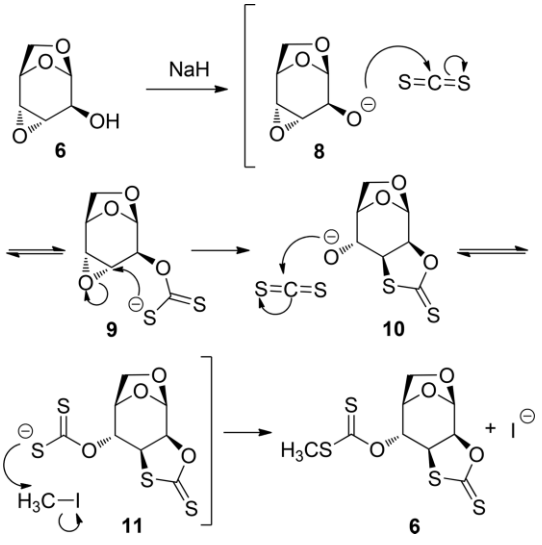
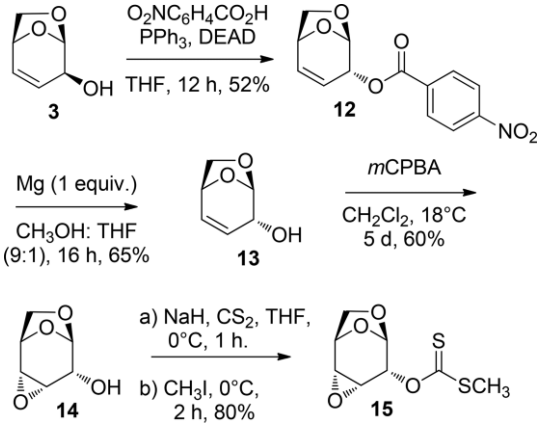


Scheme 3. Proposed mechanism for the epoxide ring opening-xanthate migration.

therefore the entering and leaving anions could adopt the adequate trajectory.[16a] In a later stage, the alkoxide **10** reacts again with CS_2 yielding the sulfur anion **11** which is finally trapped with methyl iodide to form **6**.

On the other hand, the hydroxyl epoxide **5** has both groups in a *cis* relationship which preclude an intramolecular attack when it is submitted to the same reaction conditions, affording only the product with a xanthate group at C-2. It is noteworthy to mention that the reaction pathway followed by compound **4** depends on the time elapsed between the additions. If the methyl iodide is added soon after the addition of CS_2, a certain amount of the epoxy-xanthate diastereomeric of **7** at C-3 and C-4 could be trapped and isolated. However, when the alkoxide was allowed to react with CS_2 for longer time, only the product of the domino reaction was formed.

According to the experimental evidence and our mechanistic proposal, the configuration of the hydroxyl group at C-2, and its relative orientation with the epoxide, dictate the chemo- and stereospecificity of the reaction. Hence, in order to explore the scope of the domino process towards cyclic dithiocarbonates, we envisaged the synthesis and evaluation of the corresponding epimers of **4** and **5** at C-2, which in turn could be prepared from allylic alcohol **13** (Scheme 4). Given the difficulty to obtain **13** by direct reduction of levoglucosenone as a result of the high steric hindrance of the β-face of the molecule, we achieved our goal by inverting the configuration of **3** through a Mitsunobu reaction.[26] The *p*-nitrobenzoate derivative **12** was readily synthesized under standard conditions, however the hydrolysis was not a trivial step. Different conditions were assayed in order to avoid the formation of a by-product arising from the attack of the hydroxide at C-4 with concomitant rearrangement of the double bond. Magnesium methoxide was the reagent that afforded the desired **13** with the best yields.[27] Finally, the allylic alcohol was treated with *m*CPBA to obtain the corresponding oxirane ring. However, in this case we observed that the directing effect of the hydroxyl group in addition to the steric hindrance of the 1,6-anhydro bridge promoted exclusively the formation of the α-epoxide **14**, with the functional groups in a *cis* relationship. Synthetic attempts to obtain the β-epoxide were unsuccessful, even when the hydroxyl group was protected with bulky substituents such as *tert*-butyl dimethylsilyl or *tert*-butyl diphenylsilyl, nor when the epoxidation was performed with **12**. In all cases, the *cis* α-epoxy alcohol **14** was exclusively obtained, suggesting that the steric hindrance of the 1,6-anhydro bridge dominates the facial selectivity. Compound **14** was submitted to the reaction conditions previously described for the formation of the xanthate group. As expected, the xanthate **15** was obtained in high yields, confirming that the intramolecular reaction does not take place for a precursor with a *cis* relationship between both functional groups, like in the case of **5**.



Scheme 4. Synthesis of allylic alcohol **13** and xanthate **15**.

The difficulty to synthesize the β-epoxide derived from **13** prompted us to study others epoxide sugar derivatives with less marked steric preferences towards one of the faces of the molecule. For this reason, we considered those obtained from methyl α-D-glucopyranoside **2**, a commercial and inexpensive starting material which has been extensively used in the synthesis of optically pure compounds.[28]

In order to achieve our targets it was necessary to protect the C-4 and C-6 hydroxyl groups. Benzylidene acetal is a commonly used protecting group for 1,3-diols and it has the advantage that can be removed under neutral hydrogenolysis conditions or by acid hydrolysis.[29] Based on our previous work,[30] **2** was transformed into the corresponding benzylidene acetal derivative **16**[31] (Scheme 5). Taking advantage of the slight reactivity difference between the C-2 and C-3 hydroxyl groups it is possible to manipulate them to obtain the α or β epoxides.

Diol **16** was treated under two different reaction conditions to afford the α and β-2,3-anhydro sugars **17** and **18**, respectively. The epoxides **17** and **18** showed different reactivity during the deprotection step; therefore different reaction conditions had to be applied in each case. The primary alcohols at C-6 were subsequently and selectively protected with trityl chloride yielding the expected 2,3-epoxy alcohols **19b** and **20b**.[32]

In complete agreement with our previous hypothesis, treatment of **19b** with NaH and CS_2 and trapping the anion with methyl iodide following the procedure previously applied to

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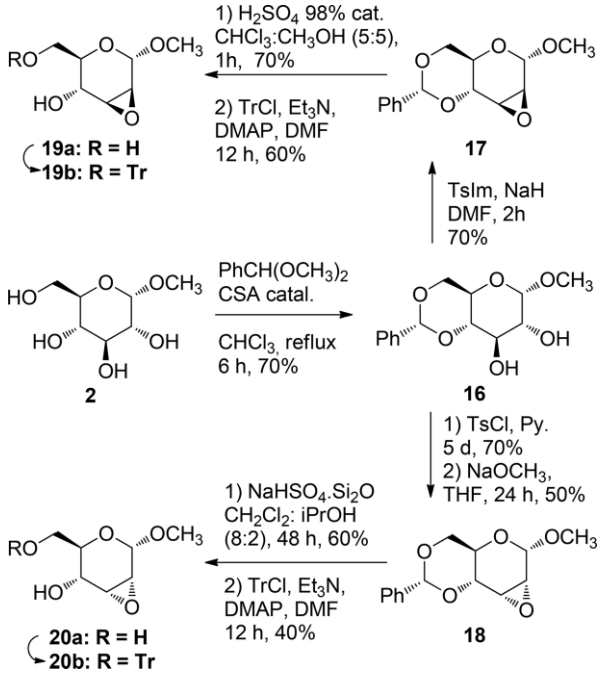
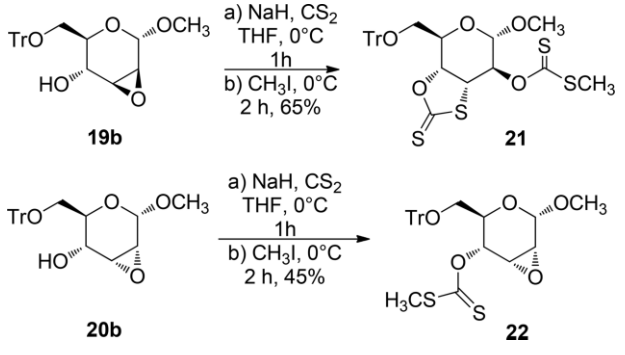


Scheme 5. Synthesis of epoxides **19** and **20**.

compound **4** afforded exclusively the cyclic xanthate **21**. The *trans* disposition of the hydroxyl group and the oxirane ring allowed the domino reaction to take place. Alternatively, similar procedure with the epoxy alcohol **20b** resulted in the predictable xanthate **22** (Scheme 6).

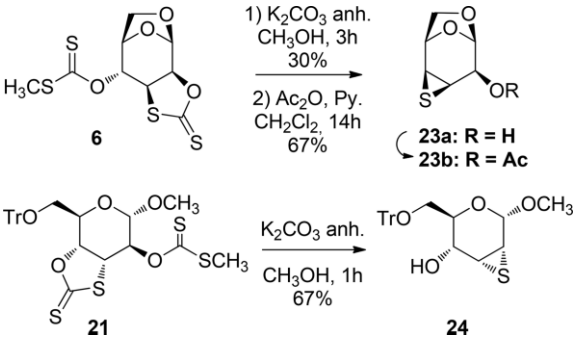


Scheme 6. Synthesis of the xanthates **21** and **22**.

These results confirm that the intramolecular domino reaction in a pyranoside ring is only feasible when the epoxide and the adjacent hydroxyl group are in a *trans* relationship and that under these reaction conditions other possible competing processes like the Payne rearrangement are disfavored.[33]

The generation of the 1,3-oxathiolane-2-thione is not only an effective strategy for the stereospecific construction of a C–S bond but also offers a paramount of possibilities for the syntheses of biological interesting products or its application in glycosylation reactions.[34]

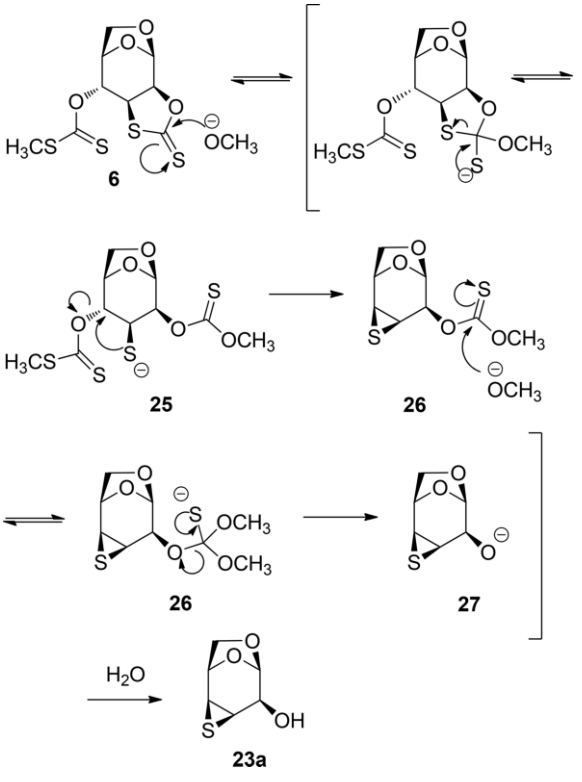
A useful synthetic application of this ring system was achieved when compounds **6** and **21** were treated with potassium carbonate in methanol and episulfides **23a** and **24** were obtained in moderated to good yields (Scheme 7). In order to characterized episulfide **23a** by mass spectroscopy, it was necessary to transform the alcohol into its acetate derivative **23b**.



Scheme 7. Synthesis of thiiranes **23** and **24**.

Thiiranes has been widely studied and their importance is due to its reactivity that turn them into suitable precursors for a variety of chemical transformations.[35, 36] In particular those derived from carbohydrates have been widely applied to the synthesis of oligosaccharides and other glycomimetics.[7a,34d,37]

Based on a mechanism proposed by Uenishi[15a,15b] the formation of the thiirane ring could be explained as another tandem reaction (Scheme 8). The nucleophilic attack of the methoxide anion occurs preferentially at the thione group affording the thiolate **25**. This anion is axial and *antiperiplanar* to the xanthate group which favors an intramolecular displacement with the concomitant ring closure of the thiirane and generation of the intermediate **26**. The remaining thiocarbonate suffers a second nucleophilic cleavage yielding the correspond-



Scheme 8. Proposed mechanim for the thiirane formation.

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ing alkoxide **27** which after the workup affords the 2,3-thiirane alcohol **23a**.

The same mechanistic proposal is applicable to xanthate **21** which complies with the configurational relationship between the functional groups involved.

We assumed that the difference in yields observed between the episulfides **23a** and **24** may be a consequence of the ring strain in each precursor, however no free thiols were observed in any case.

To the best of our knowledge, there are no reports in the literature describing the synthesis of carbohydrate derived thiiranes involving a xanthate group. This novel protocol allows the preparation of this type of compounds in a stereo- and enantiospecific manner without ambiguity. The importance of sugar episulfides relies on their applications in the syntheses of more complex carbohydrates structures through a ring-opening reaction with several nucleophiles, the ability to undergo oxidation or reduction processes at the sulfur atom, and thermal or photochemical reactions.[38]

Conclusions

We described a simple and efficient method to build a C–S bond into a pyranose ring in a stereospecific manner through a cascade xanthate formation-epoxide ring opening-1,3-oxathiolane-2-thione ring closure-xanthate migration. The procedure was applied to levoglucosenone and methyl α-D-glucopyranoside derivatives with different configurational relationships and ring strains. We demonstrated that the domino process is feasible only when the epoxide and the adjacent alcohol are in a *trans* relationship. No Payne rearrangement or other competing reactions were observed under the applied conditions.

The products of the domino migration were converted into episulfides in another stereocontrolled tandem process. The initial 2,3-epoxy alcohols were converted into a 2,3-thiirane alcohol within a rigid cyclic system with inversion of the configuration in the three membered heterocycle. Due to the role played by thiocompounds in many biochemical processes, enantiomerically pure sugar episulfides become attractive building blocks for the synthesis of oligosaccharides with potential biological activities.

Experimental Section

All reagents and solvents were used directly as purchased or purified according to standard procedures. Analytical thin layer chromatography was carried out using commercial silica gel plates (Merck, Silica Gel 60 F254) and visualization was effected with short wavelength UV light (254 nm) and *p*-anysaldehyde solution with subsequent heating. Flash column chromatography was performed with silica gel 60 H (Merck) using EtOAc/hexanes mixtures. NMR spectra were recorded at 300 MHz for ^{1}H, and 75 MHz for ^{13}C on a Bruker Avance-300 DPX spectrometer with $CDCl_3$ as solvent and $(CH_3)_4Si$ (^{1}H) as internal standard. Chemical shifts are reported in delta (δ) units in parts per million (ppm) and splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; and m, multiplet. Coupling constants are recorded in Hertz (Hz). The structure of the products were determined by a combination of spectroscopic methods such as IR, 1D and 2D NMR (including NOE, COSY, HSQC and HMBC experiments) and HRMS. Infrared spectra were recorded on a Shimadzu IR Prestige-21 spectrometer using sodium chloride plate pellets. Absorbance frequencies are recorded in reciprocal centimeters (cm^{-1}). High resolution mass spectra (HRMS) were obtained on a Bruker micrOTOF Q II (Q-TOF), nebulizer pressure 0.4 Bar, dry gas 4.0 l/min at 180 °C, source ESI positive mode, capillary voltaje 4500V, scan 50–1500 *m/z*. Optical rotations were determined using a JASCO DIP-1000 digital polarimeter in 100 mm cells and the sodium D line (589 nm) at room temperature in the solvent and concentration indicated. The melting points were taken on a Leitz Wetzlar Microscope Heating Stage Model 350 apparatus and are uncorrected. Levoglucosenone was obtained according to the procedure previously described.[18]

Synthesis of Allylic Alcohol 3: Levoglucosenone (5.94 g, 47.13 mmol) was dissolved in CH_3OH (32 mL) and cooled to 0 °C. $CeCl_3{\cdot}7H_2O$ (17.56 g, 47.13 mmol) and $NaBH_4$ (1.42 g, 37.7 mmol) were added and stirred for 2.5 h. The solution was neutralized with HCl 0.1 N to reach pH = 7. The mixture was diluted with water (5 mL) and extracted several times with 50 mL portions of EtOAc. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography to afford **3** (5.59 g, 43.60 mmol, 92 %) as a white crystalline solid; m.p. 67–68 °C (ethyl ether). $[\alpha]_D^{25}$ = –32.2 (*c* = 0.99, $CHCl_3$); δ_H (300 MHz $CDCl_3$) 6.12 (dd, 1 H, $^{3}J_{4,3}$ = 9.8, $^{3}J_{4,5}$ = 4.3 Hz, H-4), 5.70 (ddd, 1 H, $^{3}J_{3,4}$ = 9.8, $^{3}J_{3,2}$ = 2.4, $^{4}J_{3,1}$ = 2.2 Hz, H-3), 5.51 (dd, 1 H, $^{3}J_{1,2}$ = 2.7, $^{3}J_{1,3}$ = 2.2 Hz, H-1), 4.66 (dd, 1 H, $^{3}J_{5,4}$ = 4.3, $^{3}J_{5,6exo}$ = 4.2 Hz, H-5), 4.33 (s, 1 H, H-2), 3.84 (d, 1 H, $^{2}J_{gem}$ = 6.6 Hz, H-6*endo*), 3.75 (dd, 1 H, $^{2}J_{gem}$ = 6.6, $^{3}J_{6exo,5}$ = 4.2 Hz, H-6*exo*), 2.15 (s, 1 H, OH); δ_C (75 MHz $CDCl_3$) 130.6 (C-4), 129.0 (C-3), 101.1 (C-1), 71.1 (C-2), 70.5 (C-6), 68.6 (C-5).[23]

Synthesis of Epoxy Alcohols 4 and 5: Compound **3** (1.19 g, 5.45 mmol) was dissolved in anhydrous CH_2Cl_2 (80 mL), *m*-CPBA (3.76 g, 21.8 mmol) was added and it was stirred during 5 days at 18 °C. The reaction mixture was then treated with diazomethane and finally concentrated under reduced pressure. The crude was purified by flash chromatography to afford **4** and **5** (720 mg, 92 %, ratio 4:5 = 2:1) as white solids. **4**: m.p. 158–160 °C (CH_2Cl_2/hexane). $[\alpha]_D^{20}$ = –129 C (*c* 0.5, CH_3OH); δ_H (300 MHz $CDCl_3$) 5.32 (1 H, m, H-1), 4.73 (1 H, d, $^{3}J_{5,4}$ = 3.9 Hz, H-5), 4.05 (1 H, d, $^{2}J_{gem}$ = 7.3 Hz, H-6), 3.87–3.83 (2H, m, H-6, H-2), 3.13 (1 H, d, $^{3}J_{4,5}$ = 3.9 Hz, H-4), 3.00 (1 H, m, H-3); δ_C (75 MHz $CDCl_3$) 99.1 (C-1), 69.8 (C-5), 67.3 (C-6), 65.0 (C-2), 51.0 (C-3), 50.0 (C-4). **5**: m.p. 71–73 °C (CH_2Cl_2/hexane). $[\alpha]_D^{20}$ = +56 C, (*c* 0.5, CH_3OH); δ_H (300 MHz $CDCl_3$) 5.29 (d, 1 H, $^{3}J_{1,2}$ = 3.4 Hz, H-1), 4.81 (t, 1 H, $^{3}J_{5,4}$ = $^{3}J_{5,6}$ = 4.9 Hz, H-5), 3.99 (d, 1 H, $^{2}J_{gem}$ = 6.9, H-6), 3.78 (m, 2 H, H-2, H-4), 3.55 (m, 1 H, H-6), 3.33 (m, 1 H, H-3); δ_C (75 MHz $CDCl_3$) 97.8 (C-1), 71.7 (C-5), 66.5 (C-2), 63.9 (C-6), 57.3 (C-4), 50.2 (C-3).[24]

Synthesis of Cyclic Xanthate 6: To a solution of compound **4** (286 mg, 1.99 mmol) in 10 mL of anhydrous THF was added a suspension of NaH (60 % dispersion in mineral oil) (95 mg, 3.98 mmol) in 30 mL of anhydrous THF. The mixture was cooled to 0 °C and CS_2 (0.32 mL, 5.57 mmol) was added. After 1 h, CH_3I (0.43 mL, 6.97 mmol) was added. The mixture was stirred during 2 more hours and then a solution of NH_4Cl (sat) (0.5 mL) was added. The solution was extracted with EtOAc (30 mL) and then washed with 2 mL of brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography to afford **6** (380 mg, 1.17 mmol, 60 %) as a yellow solid; R_f (60 % hexane/EtOAc) 0.7; m.p. 136–137 °C (CH_2Cl_2/hexane). $[\alpha]_D^{29}$ = –64.98 (*c* = 1.075, $CHCl_3$); $\tilde{\nu}_{max}$ = (KBr) 2918, 1315, 1196 (C=S), 1150, 1064 cm^{-1}; δ_H (300 MHz $CDCl_3$) 5.68 (d, 1 H, $^{3}J_{1,2}$ = 2.7 Hz, H-1),

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5.65 (s, 1 H, H-4), 5.17 (dd, 1 H, $^3J_{2,3}$ = 8.8, $^3J_{2,1}$ = 2.7 Hz, H-2), 4.87 (d, 1 H, $^3J_{5,6exo}$ = 5.8 Hz, H-5), 4.58 (d, 1 H, $^3J_{3,2}$ = 8.8 Hz, H-3), 4.30 (d, 1 H, $^2J_{gem}$ = 8.3 Hz, H-6*endo*), 3.96 (dd, 1 H, $^2J_{gem}$ = 8.3, $^3J_{6exo,5}$ = 5.8 Hz, H-6*exo*), 2.61 (s, 3 H, SCH_3); δ_C (75 MHz $CDCl_3$) 215.1 (C=S), 209.0 (C=S), 97.6 (C-1), 83.8 (C-2), 77.0 (C-4), 74.2 (C-5), 66.4 (C-6), 48.3 (C-3), 19.6 (SCH_3). HRMS (EI, MNa^+) MNa^+ found 332.93692, $C_9H_{10}NaO_4S_4^+$ calcd. 332.93541.

Synthesis of Xanthate 7: To a solution of compound **5** (60 mg, 0.42 mmol) in 3 mL of anhydrous THF was added a suspension of NaH (60 % dispersion in mineral oil) (20 mg, 0.832 mmol) in 7 mL of anhydrous THF. The mixture was cooled to 0 °C and CS_2 (0.068 mL, 1.16 mmol) was added. After 1 h, CH_3I (0.091 mL, 1.46 mmol) was added. The mixture was stirred during 2 more hours and then a solution of NH_4Cl (sat) (0.3 mL) was added. The solution was extracted with EtOAc (6 mL) and then washed with 1 mL of brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography to afford **7** (90 mg, 0.38 mmol, 90 %) as a yellow oil; R_f (60 % hexane/EtOAc) 0.76. $[\alpha]_D^{29}$ = –11.38 (*c* = 0.305, $CHCl_3$); $\tilde{\nu}_{max}$ = (KBr) 2918, 2848, 1203 (C=S), 1147, 1060 cm^{-1}; δ_H (300 MHz $CDCl_3$) 5.79 (t, 1 H, $^3J_{2,1}$ = 3.5 Hz, H-2), 5.54 (d, 1 H, $^3J_{1,2}$ = 3.5 Hz, H-1), 4.85 (t, 1 H, $^3J_{5,4}$ = $^3J_{5,6exo}$ = 4.6 Hz, H-5), 4.10 (d, 1 H, $^2J_{gem}$ = 6.7 Hz, H-6*endo*), 3.79 (t, 1 H, $^3J_{4,3}$ = $^3J_{4,5}$ = 4.6 Hz, H-4), 3.62 (dd, 1 H, $^2J_{gem}$ = 6.7, $^3J_{6exo-5}$ = 4.6 Hz, H-6*exo*), 3.82 (m, 1 H, H-3), 2.60 (s, 3 H, SCH_3); δ_C (75 MHz $CDCl_3$) 216.3 (C=S), 95.6 (C-1), 76.7 (C-2), 72.1 (C-5), 64.7 (C-6), 56.4 (C-4), 47.6 (C-3), 19.4 (SCH_3). HRMS (EI, MNa^+) MNa^+ found 256.99024, $C_8H_{10}NaO_4S_2^+$ calcd. 256.99127.

Synthesis of *p*-Nitrobenzoate Derivative 12: Compound **3** (130.3 mg, 1.01 mmol) was dissolved in THF (7.5 mL). At room temperature and under argon atmosphere, *p*-nitrobenzoic acid (643.3 mg, 3.85 mmol) and triphenylphosphine (1.01 g, 3.85 mmol) were added. The mixture was cooled to 0 °C in an ice bath and diethyl azodicarboxylate (670 mg, 3.85 mmol) was added dropwise. The mixture was stirred during 12 h at room temperature. After that, it was diluted with ethyl ether (25 mL) and was washed with aqueous $NaHCO_3$ (2 × 7 mL). The organic layer was then dried with Na_2SO_4 anh. The solvent was evaporated under reduced pressure. The residue was purified by flash chromatography to afford compound **12** (146 mg, 0.52 mmol, 52 %) as white crystalline solid. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.37–8.20 (m, 4 H, aromatics); 6.42 (dd, 1 H, $^3J_{4,3}$ = 9.9, $^3J_{4,2}$ = 4.2 Hz, H-4); 5.90 (dd, 1 H, $^3J_{3,4}$ = 9.9, $^3J_{3,2}$ = 4.3 Hz, H-3); 5.68 (s, 1 H, H-1); 5.01 (d, 1 H, $^3J_{5,6}$ = 3.9 Hz, H-5); 4.83 (dd, 1 H, $^3J_{2,3}$ = 4.3, $^3J_{2,4}$ = 4.2 Hz, H-2); 3.82–3.72 (m, 2 H, H-6). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.7 (C-7); 150.6 (C-11), 135.0 (C-8); 133.3 (C-4); 130.3 (C-9); 123.5 (C-10); 122.1 (C-3); 100.0 (C-1); 70.4 (C-2); 69.1 (C-6); 67.5 (C-5).[39]

Synthesis of Allylic Alcohol 13: Compound **12** (64 mg, 0.23mmol) was dissolved in a mixture of anhydrous CH_3OH/THF (19:1) (5 mL) and magnesium metal (6 mg, 0.23 mmol) was added. The mixture was stirred for 16 h at room temperature under argon atmosphere. After completion (according to TLC analysis) the solvent was evaporated and the reaction mixture was dissolved in HCl 1 N (3 mL) and extracted with CH_2Cl_2 (2 × 15 mL). The combined organic layers were dried (Na_2SO_4 anh.) and concentrated under reduce pressure. The resulting residue was purified by flash chromatography to afford compound **13** (20 mg, 0.15 mmol, 65 %) as a white solid. R_f (60 % hexane/EtOAc) 0.24. $[\alpha]_D^{28}$ = –132 (*c* = 1.790, $CDCl_3$); m.p. 50.5–52.5 °C (EtOH/H_2O); $\tilde{\nu}_{max}$ = (KBr) 3595, 3433, 3057, 1606 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.18 (dd, 1 H, $^3J_{4,3}$ = 9.7, $^3J_{4,5}$ = 4.7 Hz, H-4); 5.90 (dd, 1 H, $^3J_{3,4}$ = 9.7, $^3J_{3,2}$ = 3.9, $^4J_{3,1}$ = 1.9 Hz, H-3); 5.53 (sa, 1 H, H-1); 4.68 (ddd, 1 H, $^3J_{5,4}$ = 4.7, $^3J_{5,6}$ = 3.6, $^3J_{5,6}$ = 1.4 Hz, H-5); 3,73–3.66 (m, 2 H, H-6*endo*, H-6*exo*); 3.63 (d, 1 H, $^3J_{2,3}$ = 3.9 Hz, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 131.0 (CH, C-4); 126.3 (CH, C-3); 100.2 (CH, C-1); 70.5 (CH, C-2); 68.8 (CH_2, C-6); 65.7 (CH, C-5).[40]

Synthesis of Epoxy Alcohol 14: Compound **13** (40 mg, 0.18 mmol) was dissolved in anhydrous CH_2Cl_2 (5 mL), *m*-CPBA (126.6 mg, 0.734 mmol) was added and it was stirred at 18 °C during 5 days. The reaction mixture was then treated with diazomethane and finally concentrated under reduced pressure. The crude was purified by flash chromatography to afford **14** (20 mg, 60 %) as white crystalline solid. R_f (100 % EtOAc) 0.43; m.p. 158–160 °C (CH_2Cl_2/hexane). $[\alpha]_D^{23}$ = –32.91 (*c* = 0.2, $CHCl_3$); $\tilde{\nu}_{max}$ = (KBr) 3400 (OH), 2920, 2850, 1462, 1462, 1138, 1053 cm^{-1}; δ_H (300 MHz $CDCl_3$) 5.20 (1 H, s, H-1), 4.69 (1 H, dd, $^3J_{5,6exo}$ = 4.5, $^3J_{5,4}$ = 1.5 Hz, H-5), 3.97 (1 H, d, $^2J_{gem}$ = 7.5 Hz, H-6*endo*), 3.79 (1 H, dd, $^2J_{gem}$ = 7.5, $^3J_{6exo,5}$ = 4.5 Hz, H-6*exo*), 3.59 (1 H, m, H-2), 3.34 (1 H, m, H-3), 3.24 (1 H, dd, $^3J_{4,3}$ = 4.0, $^3J_{4,5}$ = 1.5 Hz, H-4), 2.36 (1 H, d, *J* 10.5 Hz, OH); δ_C (75 MHz $CDCl_3$) 102.3 (C-1), 69.4 (C-5), 65.8 (C-6), 65.5 (C-2), 50.6 (C-4), 49.3 (C-3). HRMS (EI MNa^+) found 167.03140. $C_6H_8O_4Na^+$ calcd. 167.03148.

Synthesis of Xanthate 15: To a solution of compound **14** (42 mg, 0.29 mmol) in 2 mL of anhydrous THF was added a suspension of NaH (60 % dispersion in mineral oil) (14 mg, 0.58 mmol) in 5 mL of anhydrous THF. The mixture was cooled to 0 °C and CS_2 (0.048 mL, 0.812 mmol) was then added. After 1 h, CH_3I (0.063 mL, 1.05 mmol) was added. The mixture was stirred during 2 more hours and then a solution of NH_4Cl (sat) (0.2 mL) was added. The solution was extracted with EtOAc (4 mL) and then washed with 0.8 mL of brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography to afford **15** (54 mg, 0.23 mmol, 80 %) as a yellow oil; R_f (60 % hexane/EtOAc) 0.76. $[\alpha]_D^{30}$ = –120.02 (*c* = 0.6, $CHCl_3$); $\tilde{\nu}_{max}$ = (KBr) 1747, 1213 (C=S), 1141, 1072 cm^{-1}; δ_H (300 MHz $CDCl_3$) 5.46 (dd, 1 H, $^3J_{2,3}$ = 4.2, $^4J_{2,4}$ = 0.6 Hz, H-2), 5.42 (d, 1 H, $^4J_{1,3}$ = 2 Hz, H-1), 4.81 (dd, 1 H, $^3J_{5,6exo}$ = 4.5, $^3J_{5,4}$ = 1.4 Hz, H-5), 4.02 (d, 1 H, $^2J_{gem}$ = 7.5 Hz, H-6*endo*), 3.81 (dd, 1 H, $^2J_{gem}$ = 7.5, $^3J_{6exo,5}$ = 4.5 Hz, H-6*exo*), 3.57 (m, 1 H, H-3), 3.23 (dd, 1 H, $^3J_{4,3}$ = 4.2, $^3J_{4,5}$ = 1.4 Hz, H-4), 2.61 (s, 3 H, SCH_3); δ_C (75 MHz $CDCl_3$) 215.6 (C=S), 99.7 (C-1), 76.6 (C-2), 69.4 (C-5), 65.5 (C-6), 49.1 (C-4), 46.1 (C-3), 19.5 (SCH_3). HRMS (EI, MNa^+) MNa^+ found 256.99024, $C_8H_{10}O_4S_2Na^+$ calcd. 256.99127.

Synthesis of Methyl *4,6-O*-benzylidene-α-*D*-glucopyranoside (16):[31] The benzylidene dimethyl acetal (1.3 mL, 1.7 mmol) was dissolved in chloroform (25 mL) and camphorsulfonic acid monohydrate (31 mg, 0.26 mmol) and methy α-D-glucopyranoside (1 g, 5.2 mmol) were sequentially added. A Dean Stark trap for solvents heavier than water and loaded with 4 A molecular sieves (activated at 350 °C for 3 h) was fitted into the flask and the reaction mixture was stirred and heated under reflux during 6 h. After that, K_2CO_3 was added and the solution was stirred and heated for 30 more minutes. Then, the heated mixture was filtered in order to eliminate the carbonate and concentrated. The resulting solid was washed with hexane and purified by recrystallization with 2-propanol to afford the protected product as white solid (1.2 g, 3.6 mmol, 70 %). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.48 (m, 2 H, aromatics), 7.35 (m, 3 H, aromatics), 5.50 (s, 1 H, H-7), 4.76 (d, 1 H, $^3J_{1,2}$ = 3.8 Hz, H-1), 4.28 (dd, 1 H, $^2J_{gem}$ = 9.2, $^3J_{6,5}$ = 3.3 Hz, H-6), 3.89 (dd, 1 H, $^2J_{gem}$ = 9.2 Hz, H-6), 3,40–3.82 (m, 4 H, H-2, H-3, H-4, H-5), 3.42 (s, 3 H, $COCH_3$), 2.89 (1 H, sa, OH), 2.40 (1 H, sa, *J* = 9.3 Hz, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.9 (C-aromatic), 128.9 (C-aromatic), 128.0 (2C, C-aromatics), 126.2 (2C, C-aromatics), 101.6 (C-7), 99.7 (C-1), 80.7 (C-4), 72.5 (C-2), 70.9 (C-3), 68.9 (C-6), 62.2 (C-5), 55.2 (OCH_3).

Synthesis of Methyl *2,3*-Anhydro-*4,6-O*-benzylidene-α-*D*-mannopyranoside (17): To a solution of compound **16** (250 mg, 0.89 mmol) in 5 mL of anhydrous DMF was added a suspension of

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NaH (60 % dispersion in mineral oil) (49 mg, 2.07 mmol) in 10 mL of anhydrous DMF. The mixture was stirred during 45 minutes. Then, a solution of TsIm in 7 mL of DMF was added drop by drop during 1h. After 2h of reaction, the mixture was flipped over H_2O:ice (4:1) and the resulting white solid was filtered. The product **17** was purified by recrystallization from CH_3OH (165 mg, 0.62 mmol, 70 %). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.50 (m, 2 H, aromatics), 7.37 (m, 3 H, aromatics), 5.57 (s, 1 H, H-7), 4.90 (s, 1 H, H-1), 4.25 (m, 1 H, H-6), 3.70 (m, 3 H, H-4, H-5, H-6), 3.46 (d, 1 H, $^3J_{2,3}$ = 3.7 Hz, H-5), 3.45 (s, 3 H, COCH_3), 3.15 (d, 1 H, $^3J_{3,2}$ = 3.7 Hz, H-3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.9 (C-aromatic), 128.9 (C-aromatic), 128.0 (2C, C-aromatics), 125.9 (2C, C-aromatics), 102.0 (C-7), 96.6 (C-1), 74.6 (C-4), 69.1 (C-6), 61.4 (C-5), 55.4 (OCH_3), 53.5 (C-2), 50.2 (C-3).[30a]

Synthesis of Methyl *2,3*-Anhydro-*4,6*-*O*-benzylidene-α-*D*-allopyranoside (18): Compound **16** (330 mg, 1.17 mmol) was dissolved in 2.9 mL of pyridine and the solution was cooled to 0 °C. Then, TsCl (356.5 mg, 1.87 mmol) was added. After stirring the mixture during 5 days, it was diluted with $CHCl_3$ and was poured over H_2O/ice (4:1). The product was extracted with $CHCl_3$ and the organic phase was washed with solutions of H_2SO_4 5 %, $NaHCO_3$ 5 %, KOH 2 % and saturated NaCl. The combined organic phase was dried (Na_2SO_4), concentrated and used in the next step without purification.[30c] The di-*O*-tosyl derivative (489 mg, 0.83 mmol) was dissolved in THF (5 mL) and it was cooled to 0 °C, $NaOCH_3$ (171 mg, 3.16 mmol) was then added. The mixture was stirred during 24 h. After stirring, the product was extracted with $CHCl_3$ and the organic phase was washed with distilled H_2O. The solid product obtained was dried (Na_2SO_4) and concentrated to afford compound **18** as a white solid (109 mg, 0.42 mmol, 50 %). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.52 (m, 5 H, aromatics), 5.57 (s, 1 H, H-7), 4.89 (d, 1 H, $^3J_{1,2}$ = 1.8 Hz, H-1), 4.24 (dd, 1 H, $^2J_{gem}$ = 9.8, $^3J_{6,5}$ = 4.8 Hz, H-6), 4.09 (1, m, H-4, H-5), 3.95 (d, 1 H, $^3J_{4,5}$ = 8.9 Hz, H-4), 3.68 (dd, 1 H, $^3J_{6,5}$ = $^2J_{gem}$ = 9.8 Hz, H-6), 3.49–3.65 (m, 2 H, H-2, H-3), 3.47 (s, 3 H, COCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.1 (C-aromatic), 129.1 (C-aromatic), 128.2 (2C, C-aromatics), 126.2 (2C, C-aromatics), 102.7 (C-7), 95.2 (C-1), 77.8 (C-4), 68.8 (C-6), 59.9 (C-5), 55.7 (OCH_3), 53.0 (C-3), 50.2 (C-2).[30c]

Synthesis of Methyl *2,3*-Anhydro-α-*D*-mannopyranoside (19a): Compound ***17*** (30 mg, 0.11 mmol) was dissolved in CH_3OH/$CHCl_3$ (50:50) mixture (4 mL). Then, 2 drops of H_2SO_4 98 % were added. The mixture was stirred during 30 minutes. After that, it was diluted with AcOEt and the organic phase was washed with with 5 % aqueous $NaHCO_3$ (5 mL), brine (5 mL), and dried (Na_2SO_4 anh.) and concentrated to afford compound **19a** as a colorless oil (14 mg, 0.08 mmol, 70 %). R_f (20 % hexane/EtOAc) 0.32. $[\alpha]_D^{24}$ = +82 (*c* = 0.88, $CHCl_3$); $\tilde{\nu}_{max}$ = (KBr) 3404 (OH), 2920, 1448, 1377, 1114, 1076, 1028 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.89 (s, 1 H, H-1), 3.87 (d, 1 H, $^3J_{4,5}$ = 9.2 Hz, H-4), 3.78 (m, 2 H, H-6, H-6), 3.50–3.65 (m, 1 H, H-5), 3.46 (s, 3 H, OCH_3), 3.32 (d, 1 H, $^3J_{2,3}$ = 3.7 Hz, H-2), 3.13 (d, 1 H, $^3J_{3,2}$ = 3.7 Hz, H-3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 96.0 (C-1), 68.9 (C-5), 62.9 (C-6), 62.7 (C-4), 55.7 (OCH_3), 55.3 (C-3), 48.9 (C-3). HRMS (EI, MNa^+) MNa^+ found 199.05866, $C_7H_{12}O_5Na^+$. Calcd 199.05769.

Synthesis of Methyl *2,3*-Anhydro-*6*-trityl-α-*D*-mannopyranoside (19b): Compound ***19a*** (70 mg, 0.40 mmol) was dissolved in 2 mL of anhydrous DMF. Then, TrCl (122 mg, 0.44 mmol), DMAP (2.4 mg, 0.02 mmol) and finally, 100 µL of Et_3N were added. The mixture was stirred during 12 h. After that, it was poured over a H_2O/ice mixture and the organic phase was extracted with $CHCl_2$ and washed with saturated solution of NH_4Cl (2 mL), water (2 mL) dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography to afford compound **19b** (37mg, 0.09 mmol, 60 %) as white crystalline solid. R_f (60 % hexane/EtOAc) 0.69. $[\alpha]_D^{30}$ = +6.5 (*c* = 0.34, $CHCl_3$); m.p. 110–111 °C (CH_2Cl_2/hexane); $\tilde{\nu}_{max}$ = (KBr) 3491 (OH), 2926, 1448, 1076 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.26–7.43 (m, 15 H, aromatics), 4.81 (s, 1 H, H-1), 3.69 (dd, 1 H, $^3J_{5,4}$ = 9.2, $^3J_{4,3}$ = 3.5 Hz, H-4), 3.58 (m, 1 H, H-5), 3.44 (dd, 1 H, $^2J_{gem}$ = 9.6, $^3J_{6,5}$ = 5.1 Hz, H-6), 3.40 (s, 3 H, OCH_3), 3.24 (m, 2 H, H-2, H-6), 3.07 (d, 1 H, $^3J_{2,3}$ = 3.5 Hz, H-3), 2.72 (d, 1 H, *J* = 3.1 Hz5 Hz, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.3 (C-aromatics), 128.5 (C-aromatics), 128.0 (C-aromatics), 127.3 (C-aromatics), 95.9 (C-1), 87.6 (C-7), 67.1 (C-5), 65.8 (C-6), 65.5 (C-4), 55.6 (OCH_3), 54.9 (C-2), 49.7 (C-3). HRMS (EI, MNa^+) MNa^+ found 441.16689, $C_{26}H_{26}O_5Na^+$. Calcd 441.16725.

Synthesis of Methyl *2,3*-Anhydro-α-*D*-allopyranoside (20a): To a stirred solution of compound ***18*** (33 mg, 0.13 mmol) in CH_2Cl_2/*i*PrOH, 80:20 mixture (3.5 mL) activated $NaHSO_4$. Si_2O (33 mg, dried at 105 °C for 10 h prior to use) was added at room temperature. After 48 h, the mixture was filtered through a Celite bed and the filtrate was concentrated. The residue was purified by flash chromatography to afford compound ***20a*** as a white solid (13 mg, 0.07 mmol, 60 %). ^1H NMR (300 MHz, $CDCl_3$): δ = 4.91 (d, 1 H, $^3J_{1,2}$ = 3.1 Hz, H-1), 3.99 (d, 1 H, $^3J_{5,4}$ = 8.8 Hz, H-4), 3.86 (dd, 1 H, $^2J_{gem}$ = 11.7, $^3J_{6,5}$ = 3.9 Hz, H-6), 3.80 (dd, 1 H, $^2J_{gem}$ = 11.7, $^3J_{6,5}$ = 3.9 Hz, H-6), 3.60–3.70 (m, 1 H, H-5), 3.57 (dd, 1 H, $^3J_{2,1}$ = 3.1, $^3J_{2,3}$ = 4.2 Hz, H-2), 3.49 (dd, 1 H, $^3J_{3,2}$ = 4.2, $^4J_{3,1}$ = 3.9 Hz, H-3), 3.46 (s, 3 H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 94.6 (C-1), 87.6 (C-7), 69.0 (C-5), 65.9 (C-5), 62.2 (C-6), 55.8 (OCH_3), 55.6 (C-2), 54.0 (C-3).[41]

Synthesis of Methyl *2,3*-Anhidro-*6*-trityl-α-*D*-allopyranoside (20b): Compound **20a** (13 mg, 0.07 mmol) was dissolved in 1 mL of anhydrous DMF. Then, TrCl (22 mg, 0.08 mmol) and DMAP (0.4 mg, 0.004 mmol) and finally, 17 µL of Et_3N were added. The mixture was stirred during 12 h. After stirring, it was poured over a H_2O/ice mixture, the organic phase was extracted with $CHCl_2$ and washed with saturated solution of NH_4Cl (1 mL) and water (1 mL) and dried (Na_2SO_4 anh.). The residue was purified by flash chromatography to afford compound ***20b*** (10.9 mg, 0.03 mmol, 40 %) as white solid. R_f (60 % hexane/EtOAc) 0.69. $[\alpha]_D^{32}$ = +34.9 (*c* = 0.38, $CHCl_3$); m.p. 149–150 °C (CH_2Cl_2/hexane); $\tilde{\nu}_{max}$ = (KBr) 3479 (OH), 2920, 1448, 1062 cm^{-1}; δ_H = (300 MHz, $CDCl_3$) 7.22–7.47 (m, 15 H, aromatics), 4.91 (d, 1 H, $^3J_{1,2}$ = 3.2 Hz, H-1), 3.88 (m, 1 H, H-4), 3.78 (m, 1 H, H-5), 3.55 (dd, 1 H, $^3J_{2,3}$ = 4.2, $^3J_{2,1}$ = 3.2 Hz, H-2), 3.49 (s, 3 H, OCH_3), 3.39 (dd, 1 H, $^3J_{3,2}$ = 4.2, $^4J_{3,1}$ = 1.7 Hz, H-3), 3.32 (m, 2 H, H-6, H-6). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.7 (C-aromatics), 128.7 (C-aromatics), 127.9 (C-aromatics), 127, 1(C-aromatics), 94.4 (C-1), 87.0 (C-7), 67.9 (C-5), 67.2 (C-4), 64.0 (C-6), 55.6 (OCH_3), 55.4 (C-2), 53.8 (C-3). HRMS (EI, MNa^+) MNa^+ found 441.16776, $C_{26}H_{26}O_5Na^+$. Calcd 441.16725.

Synthesis of Cyclic Xanthate 21: To a solution of compound **19b** (45 mg, 0.11 mmol) in 2 mL of anhydrous THF was added a suspension of NaH (60 % dispersion in mineral oil) (5.2 mg, 0.22 mmol) in 3 mL of anhydrous THF. The mixture was cooled to 0 °C and CS_2 (18 µL, 0.30 mmol) was added. After 1 h, CH_3I (24 µL, 0.38 mmol) was added. The mixture was stirred for 2 more hours and then a solution of NH_4Cl (sat) (0.2 mL) was added. The solution was extracted with EtOAc (3 mL) and then washed with 1 mL of brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography to afford ***21*** (23.4 mg, 0.072 mmol, 65 %) as a yellow oil; R_f (60 % hexane/EtOAc) 0.6. $[\alpha]_D^{31}$ = +45.6 (*c* = 0.650, $CHCl_3$); $\tilde{\nu}_{max}$ = (KBr) 2920, 2850, 1194 (C=S), 1070 cm^{-1}; δ_H (300 MHz $CDCl_3$) 7.22–7.47 (m, 15 H, aromatics), 5.96 (dd, 1 H, $^3J_{2,3}$ = 5.4, $^3J_{2,1}$ = 2.7 Hz, H-2), 5.15 (dd, 1 H, $^3J_{5,4}$ = 8.8, $^3J_{4,3}$ = 6.7 Hz, H-4), 4.92 (d, 1 H, $^3J_{1,2}$ = 2.7 Hz, H-1), 4.46 (dd, 1 H, $^3J_{3,4}$ = 6.7, $^3J_{3,2}$ = 5.4 Hz, H-3), 4.32 (m, 1 H, H-5), 3.52 (dd, 1 H, $^2J_{gem}$ = 10.4, $^3J_{6,5}$ = 2.7 Hz, H-6), 3.49 (s, 3 H, OCH_3), 3.36 (dd, 1 H, $^2J_{gem}$ = 10.4, $^3J_{6,5}$ = 5.7 Hz, H-6), 2.60 (s, 3 H, SCH_3); δ_C (75 MHz

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$CDCl_3$) 214.8 (C=S), 209.19 (C=S), 143.6 (C-aromatics), 128.7 (C-aromatics), 127.9 (C-aromatics), 127, 1(C-aromatics), 98.9 (C-1), 87.0 (C-7), 83.5 (C-4), 72.1 (C-5), 75.6 (C-2), 66.4 (C-5), 63.4 (C-6), 55.8 (OCH_3), 19.4 (SCH_3), 49.9 (C-3). HRMS (EI, MNa^+) MNa^+ found 607.07061, $C_{29}H_{28}NaO_5S_4^+$ calcd. 607.07118.

Synthesis of Xanthate 22: To a solution of compound ***20b*** (15 mg, 0.04 mmol) in 1 mL of anhydrous THF was added a suspension of NaH (60 % dispersion in mineral oil) (1.7 mg, 0.07 mmol) in 2 mL of anhydrous THF. The mixture was cooled to 0 °C and CS_2 (6 µL, 0.10 mmol) was added. After 1 h, CH_3I (8 µL, 0.13 mmol) was added. The mixture was stirred for 2 more hours and then a solution of NH_4Cl (sat) (0.15 mL) was added. The solution was extracted with EtOAc (3 mL) and then washed with 0.6 mL of brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography to afford **22** (8 mg, 0.02mmol, 45 %) as a yellow oil; R_f (60 % hexane/EtOAc) 0.72. $[\alpha]_D^{32}$ = +105.2 (*c* = 0.225, $CHCl_3$); $\tilde{\nu}_{max}$ = (KBr) 2920, 2848, 1209 (C=S), 1060 cm^{-1}; δ_H (300 MHz $CDCl_3$) 7.24–7.44 (m, 15 H, aromatics), 6.10 (dd, 1 H, $^3J_{4,5}$ = 9.9, $^3J_{4,3}$ = 1.7 Hz, H-4), 5.01 (d, 1 H, $^3J_{1,2}$ = 3.2 Hz, H-1), 4.57 (ddd, 1 H, $^3J_{5,4}$ = 9.9, $^3J_{5,6}$ = 4.7, $^3J_{5,6}$ = 1.6 Hz, H-5), 3.77 (dd, 1 H, $^3J_{3,2}$ = 4.1, $^3J_{3,4}$ = 1.7 Hz, H-3), 3.58 (dd, 1 H, $^3J_{2,3}$ = 4.1, $^3J_{2,1}$ = 3.2 Hz, H-2), 3.51 (s, 3 H, OCH_3), 3.27 (dd, 1 H, $^2J_{gem}$ = 10.5, $^3J_{6,5}$ = 1.6 Hz, H-6), 3.06 (dd, 1 H, $^2J_{gem}$ = 10.5, $^3J_{6,5}$ = 4.7 Hz, H-6), 2.38 (s, 3 H, SCH_3); δ_C (75 MHz $CDCl_3$) 143.7 (C-aromatics), 128.7 (C-aromatics), 127.9 (C-aromatics), 127. 6 (C-aromatics), 126.9 (C-aromatic), 214.9 (C=S), 95.5 (C-1), 86.4 (C-7), 76.6 (C-4), 65.8 (C-5), 62.0 (C-6), 55.7 (OCH_3), 55.1 (C-2), 50.8 (C-3), 18.8 (SCH_3). HRMS (EI, MNa^+) MNa^+ found 531.12728, $C_{28}H_{28}O_5S_2Na^+$ calcd. 531.12704.

Synthesis of Episulfide 23a: Compound ***6*** (70 mg, 0.23 mmol) was dissolved in 7 mL of anhydrous CH_3OH and anhydrous K_2CO_3 (47 mg, 0.34 mmol). The mixture was stirred during 3 h at room temperature under argon atmosphere. After completion (according to TLC analysis), the reaction mixture was filtered through a Celite pad and washed with aliquots of CH_3OH. The combine filtrates were concentrated under reduced pressure to afford compound ***23a*** (11 mg, 0.07 mmol, 30 %) as white solid; R_f (60 % hexane/EtOAc) 0.35. $[\alpha]_D^{29}$ = –43.75 (*c* = 0.525, $CHCl_3$); m.p. 149–150 °C (CH_2Cl_2/hexane); $\tilde{\nu}_{max}$ =(KBr) 3456 (OH), 2937, 1462, 1338, 1286, 1138, 1105, 1058, 910 cm^{-1}; δ_H (300 MHz $CDCl_3$) 5.22 (1 H, d, $^3J_{1,2}$ = 3.8 Hz, H-1), 5.03 (1 H, dd, $^3J_{5,4}$ = 6.6, $^3J_{5,6}$ = 4.4 Hz, H-5), 4.12 (1 H, m, H-2), 3.92 (1 H, d, $^2J_{gem}$ = 7.0 Hz, H-6endo), 3.84 (1 H, t, $^3J_{4,3}$ = $^3J_{4,5}$ = 6.6 Hz, H-4), 3.55 (1 H, dd, $^3J_{6exo,5}$ = 4.4, $^2J_{gem}$ = 7.0 Hz, H-6exo), 3.35 (1 H,t, $^3J_{3,2}$ = $^3J_{3,4}$ = 6.6 Hz, H-3); δ_C (75 MHz $CDCl_3$) 97.8 (C-1), 71.8 (C-5), 67.9 (C-6), 66.5 (C-2), 42.6 (C-4), 35.4 (C-3). The sample was unstable to mass studies and its *acetyl derivative* was analyzed as described below.

Synthesis of Acetylated Episulfide 23b: Compound **23a** (10 mg, 0.06 mmol) was dissolved in anhydrous CH_2Cl_2 (1 mL) and freshly distilled pyridine (0.2 mL) was added at room temperature. Ac_2O (0.4 mL, 3.57 mmol) was added and the solution was stirred overnight under argon atmosphere. The mixture was treated with HCl 50 % (0.5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduce pressure. The resulting residue was purified by flash chromatography to afford the acetyl derivative **23b** (7.7 mg, 0.04 mmol, 67 %) as a colorless oil. R_f (60 % hexane/EtOAc) 0.29. $[\alpha]_D^{24}$ = –10.27 (*c* = 0.23, $CHCl_3$); $\tilde{\nu}_{max}$ =(KBr) 2924, 2850, 1737 (C=O), 1371, 1232, 1139, 1049 (cm^{-1}); δ_H (300 MHz $CDCl_3$) 5.36 (1 H, d, $^3J_{1,2}$ = 3.6 Hz, H-1), 5.17 (1 H, dd, $^3J_{2,3}$ = 6.5, $^3J_{1,2}$ = 3.6 Hz, H-2), 5.04 (1 H, dd, $^3J_{5,4}$ = 6.5, $^3J_{5,6exo}$ = 4.3 Hz, H-5), 4.05 (1 H, d, $^2J_{gem}$ = 7.0 Hz, H-6endo), 3.65 (1 H, t, $^3J_{4,3,5}$ = 6.5 Hz, H-4), 3.59 (1 H, dd, $^2J_{gem}$ = 7.0, $^3J_{6exo,5}$ = 4.3 Hz, H-6exo), 3.33 (1 H, t, $^3J_{3,2}$ = $^3J_{3,4}$ = 6.5 Hz, H-3), 2.18 (3H, s, SCH_3); δ_C (75 MHz $CDCl_3$) 170.6 (C=O), 96.1 (C-1), 72.1 (C-5), 69.7 (C-2), 68.5 (C-6), 40.6 (C-4), 30.3 (C-3), 20.9 (SCH_3). HRMS (EI, MNa^+) MNa^+ found 225.02004, $C_8H_{10}NaO_4S^+$ calcd. 225.01920.

Synthesis of Episulfide 24: Compound ***21*** (26 mg, 0.05 mmol) was dissolved in 1.5 mL of anhydrous CH_3OH and anhydrous K_2CO_3 (9.2 mg, 0.07 mmol). The mixture was stirred during 1 h at room temperature under argon atmosphere. After completion (according to TLC analysis), the reaction mixture was filtered through a Celite pad and washed with aliquots of CH_3OH. The combine filtrates were concentrated under reduced pressure to afford compound **24** (18 mg, 0.03 mmol, 67 %) as white solid; R_f (70 % hexane/EtOAc) 0.42. $[\alpha]_D^{31}$ = –51.44 (*c* = 0.390, $CHCl_3$); m.p. 165–166 °C (CH_2Cl_2/hexane); $\tilde{\nu}_{max}$ =(KBr) 3441 (OH), 2916, 2848, 1446, 1058 cm^{-1}; δ_H (300 MHz $CDCl_3$) 7.21–7.46 (m, 15 H, aromatics), 5.17 (1 H, d, $^3J_{1,2}$ = 5.0 Hz, H-1), 4.10 (1 H, m, H-4), 3.68–3.61 (2H, m, H-2, H-5), 3.56 (1 H, dd, $^3J_{3,4}$ = 6.6, $^3J_{3,2}$ = 4.0 Hz, H-3), 3.48 (s, 3 H, OCH_3), 3.34 (1 H, dd, $^2J_{gem}$ = 10.0, $^3J_{6,5}$ = 3.5 Hz, H-6), 3.26 (1 H,dd, $^2J_{gem}$ = 10.0, $^3J_{6,5}$ = 5.8 Hz, H-6), 1.69 (1 H, d, $^3J_{OH,4}$ = 8.7 Hz, OH); δ_C (75 MHz $CDCl_3$) 143.8 (C-aromatics), 128.7 (C-aromatics), 127. 8 (C-aromatic), 127.1 (C-aromatic), 93.4 (C-1), 86.9 (C-7), 66.7 (C-5), 66.4 (C-4), 63.8 (C-6), 55.4 (OCH_3), 40.8 (C-3), 40.0 (C-2). HRMS (EI, MNa^+) MNa^+ found 457.14492, $C_{26}H_{26}NaO_4S^+$ calcd. 457.14440.

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[1] a) Z. J. Witczak, *Curr. Med. Chem.* **1999**, *6*, 165–178; b) Z. J. Witczak, J. M. Culhane, *Appl. Microbiol. Biotechnol.* **2005**, *69*, 237–244.
[2] B. Ernst, J. L. Magnani, *Nat. Rev. Drug Discovery* **2009**, *8*, 661–677.
[3] R. J. Capon, J. K. MacLeod, *J. Chem. Soc., Chem. Commun.* **1987**, 1200–1201.
[4] a) L. Szilágyi, T. Z. Illyés, P. Herczegh, *Tetrahedron Lett.* **2001**, *42*, 3901–3903; b) T. Z. Illyés, T. Szabó, L. Szilágyi, *Carbohydr. Res.* **2011**, *346*, 1622–1627.
[5] M. Korycka-Machala, A. Brzostek, B. Dziadek, M. Kawka, T. Poplawski, Z. J. Witczak, J. Dziadek, *Molecules* **2017**, *22*, 812–826.
[6] E. M. Sánchez-Fernández, J. M. García Fernández, C. Ortiz Mellet, *Chem. Commun.* **2016**, *52*, 5497–5515.
[7] a) L. Lázár, M. Csávás, M. Tóth, L. Somsák, A. Borbás, *Chem. Pap.* **2015**, *69*, 889–895; b) Z. J. Witczak, P. Kaplon, P. M. Dey, *Carbohydr. Res.* **2003**, *338*, 11–18; c) N. A. Raut, P. W. Dhore, S. D. Saoji, D. M. Kokare, in *Studies in Natural Products Chemistry, Vol 48* (Eds.: Atta-ur-Rahman), Elsevier, Amsterdam, **2016**, pp. 287–315.
[8] a) L. Liu, M. McKee, M. H. Postema, *Curr. Org. Chem.* **2001**, *5*, 1133–1167; b) L. Szilágyi, O. Varela, *Curr. Org. Chem.* **2006**, *10*, 1745–1770; c) Z. J. Witczak, D. Lorchak, N. Nguyen, *Carbohydr. Res.* **2007**, *342*, 1929–1931.
[9] M. B. Comba, A. G. Suárez, A. M. Sarotti, M. I. Mangione, R. A. Spanevello, E. D. V. Giordano, *Org. Lett.* **2016**, *18*, 1748–1751.
[10] a) B. Quiclet-Sire, S. Z. Zard, *Synlett* **2016**, *27*, 680–701; b) B. Vanhorenbeke, C. Vriamont, F. Pennetreau, M. Devillers, O. Riant, S. Hermans, *Chem. Eur. J.* **2013**, *19*, 852–856; c) S. Motokucho, A. Sudo, T. Endo, Y. Itagaki, R. Kaneko, K. Uenishi, *WO***2005**/016908, 2005.
[11] Y. Robbe, J. P. Fernández, R. Dubief, J.-P. Chapat, H. Sentenac-Roumanou, M. Fatome, J.-D. Laval, G. Subra, *Eur. J. Med. Chem.* **1982**, *17*, 235–240.

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[12] S. Motokucho, Y. Itagaki, A. Sudo, T. Endo, *J. Polym. Sci., Part A J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 3711–3843.
[13] R. Maggi, C. Malmassari, C. Oro, R. Pela, G. Sartori, L. Soldi, *Synthesis* **2008**, 53–56.
[14] a) H. Wang, B. Li, X-B. Lu, **2009**, http://www.paper.edu.cn/lwzx/en_releasepaper/content/28362; b) M. North, P. Villuendas, *Synlett* **2010**, 623–0627; c) S. Hayashi, M. Furukawa, Y. Fujino, T. Nakao, K. Nagato, *Chem. Pharm. Bull.* **1971**, *19*, 1594–1597.
[15] a) J. Uenishi, M. Motoyama, Y. Nishiyama, S. Wakabayashi, *J. Chem. Soc., Chem. Commun.* **1991**, 1421–1422; b) J. Uenishi, M. Motoyama, Y. Nishiyama, Y. Hirota, Y. Kubo, *Heteroat. Chem.* **1994**, *5*, 51–60; c) J. Uenishi, Y. Kubo, *Tetrahedron Lett.* **1994**, *35*, 6697–6700; d) J. Uenishi, M. Motoyama, K. Takahashi, *Tetrahedron: Asymmetry* **1994**, *5*, 101–110.
[16] a) F. H. Newth, *Q. Rev. Chem. Soc.* **1959**, *13*, 30–47; b) K. Haraguchi, S. Takeda, Y. Kubota, H. Kumamoto, H. Tanka, T. Hamasaki, M. Baba, E. Paintsil, Y.-C. Cheng, *Curr. Pharm. Des.* **2013**, *19*, 1880–1897.
[17] P. C. A. Pena, S. M. Roberts, *Curr. Org. Chem.* **2003**, *7*, 555–571.
[18] a) C. Morin, *Levoglucosenone and Levoglucosans: Chemistry and Applications* (Ed.: Z. J. Witczak), ATL Press: Mount Prospect, **1994**, pp. 17–21; b) A. M. Sarotti, R. A. Spanevello, A. G. Suárez, *Green Chem.* **2007**, *9*, 1137–1140.
[19] G. F. Giri, G. Viarengo, R. L. E. Furlán, A. G. Suárez, E. Garcia Véscovi, R. A. Spanevello, *Ind. Crops Prod.* **2017**, *105*, 113–123.
[20] a) K. Matsumoto, T. Ebata, K. Koseki, K. Okano, H. Kawakami, H. Matsushita, *Heterocycles* **1992**, *34*, 1935–1947; b) K. Matsumoto, T. Ebata, K. Koseki, K. Okano, H. Kawakami, H. Matsushita, *Carbohydr. Res.* **1993**, *246*, 345–352; c) M. E. Jung, M. Kiankarimi, *J. Org. Chem.* **1998**, *63*, 8133–8144; d) T. T. Stevenson, M. G. Essig, F. Shafizadeh, *Carbohydr. Res.* **1983**, *118*, 261–268; e) M. Cerny in *Levoglucosenone and Levoglucosans: Chemistry and Applications* (Ed.: Z. J. Witczak), ATL Press: Mount Prospect, **1994**, pp. 121–146.
[21] a) D. Urabe, T. Nishikawa, M. Isobe, *Chem. Asian J.* **2006**, *1*, 125–135; b) Z J. Witczak in Carbohydrate Synthons in Natural Products Chemistry (Eds.: Z. J. Witczak, K. Tatsuta), *ACS Symposium Series*; American Chemical Society, Washington, DC, **2002**, Chap. 1; c) M. A. Zurita, A. Avila, R. A. Spanevello, A. G. Suárez, A. M. Sarotti, *Carbohydr. Res.* **2015**, *402*, 67–70.
[22] a) A. M. Sarotti, M. M. Zanardi, R. A. Spanevello, A. G. Suárez, *Curr. Org. Synth.* **2012**, *9*, 439–459; b) V. Corne, M. C. Botta, E. D. V. Giordano, G. F. Giri, D. F. Llompart, H. D. Biava, A. M. Sarotti, M. I. Mangione, E. G. Mata, A. G. Suárez, R. A. Spanevello, *Pure Appl. Chem.* **2013**, *85*, 1683–1692; c) M. B. Comba, Y.-H. Tsai, A. M. Sarotti, M. I. Mangione, A. G. Suárez, R. A. Spanevello, *Eur. J. Org. Chem.* **2018**, 590–604 and references cited therein.
[23] M. M. Zanardi, A. G. Suárez, *Tetrahedron Lett.* **2009**, *50*, 999–1002.
[24] X. Ma, N. Anderson, L. White, S. Bae, W. Raverty, A. C. Willis, M. G. Banwell, *J. Aust. Chem.* **2015**, *68*, 593–599.
[25] E. Elliel, S. H. Wilen, in *Stereochemistry of Organic Compounds* - J. Wiley and Sons, Inc., New York, **1994**, pp. 730.
[26] O. Mitsunobu, Y. Yamada, *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2380–2382.
[27] Y. C. Xu, E. Lebeau, C. Walker, *Tetrahedron Lett.* **1994**, *35*, 6207–6210.
[28] D. Horton in *Advances in Carbohydrate Chemistry and Biochemistry Vol. 60* (Eds.: J. Karban, J. Kroutil), Elsevier Inc. **2006**, pp. 1–392.
[29] P. G. M. Wuts, T. W. Greene in *Greene's protecting groups in organic chemistry*, Wiley and Sons, Inc. Hoboken, **2007**, pp. 321–323.
[30] a) R. A. Spanevello, S. C. Pellegrinet, *Synth. Commun.* **1995**, *25*, 3663–3670; b) S. C. Pellegrinet, R. A. Spanevello, *Tetrahedron Lett.* **1997**, *38*, 8623–8626; c) M. I. Mangione, A. G. Suárez, R. A. Spanevello, *Carbohydr. Res.* **2003**, *338*, 2177–2183.
[31] R. A. Spanevello, D. D. Saavedra, *Org. Prep. Proced. Int.* **1999**, *31*, 460–462.
[32] S. K. Chaudhary, O. Hernández, *Tetrahedron Lett.* **1979**, *20*, 95–98.
[33] A. Mubarak, B. Fraser-Reid, *J. Org. Chem.* **1982**, *47*, 4265–4268.
[34] a) K. V. Laak, H.-D. Scharf, *Tetrahedron Lett.* **1989**, *30*, 4505–4506; b) L. B. Marcaurelle, C. R. Bertozzi, *J. Am. Chem. Soc.* **2001**, *123*, 1587–1595; c) I. Izquierdo, M. T. Plaza, A. Ramírez, F. Aragón, *J. Heterocycl. Chem.* **1996**, *33*, 1239–1242; d) E. Repetto, V. E. Manzano, M. L. Uhrig, O. Varela, *J. Org. Chem.* **2001**, *77*, 253–265.
[35] U. Zoller, in *Chemistry of Heterocyclic Compounds: A Series of Monographs*, *Vol. 42* (Eds.: A. Weissberger, E. C. Taylor), Wiley and Sons Inc. New York, **1983**, pp. 334–335.
[36] a) N. Iranpoor, F. Kazemi, *Synthesis* **1996**, 821–822; b) K. Surendra, N. S. Krishnaveni, K. R. Rao, *Tetrahedron Lett.* **2004**, *45*, 6523–6526; c) F. Kazemi, A. R. Kiasat, *J. Chem. Res. Synop.* **2003**, 290–291.
[37] M. J. Lo Fiego, C. Marino, O. Varela, *RSC Adv.* **2015**, *5*, 45631–45640.
[38] a) J. Warkentin, D. Plażuk, in *Comprehensive Heterocyclic Chemistry III*; *Vol. 1* (Eds.: A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven, R. J. K. Taylor, A. Padwa), Pergamon: New York, **2008**, pp. 299–390; b) J. Warkentin, D. Plażuk, in *Comprehensive Heterocyclic Chemistry III*; *Vol. 1* (Eds.: A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven, R. J. K. Taylor, A. Padwa), Pergamon: New York, **2008**, pp. 391–431.
[39] K. Matsumoto, T. Ebata, K. Koseki, H. Kawakami, H. Matsushita, *Heterocycles* **1991**, *32*, 2225–2239.
[40] T. B. Grindley, G. J. Reimer, J. Kralovec, R. G. Brown, M. Anderson, *Can. J. Chem.* **1987**, *65*, 1065–1071.
[41] K. Michigami, T. Manami, H. Masahiko, *Synthesis* **2013**, *45*, 1519–1523.

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