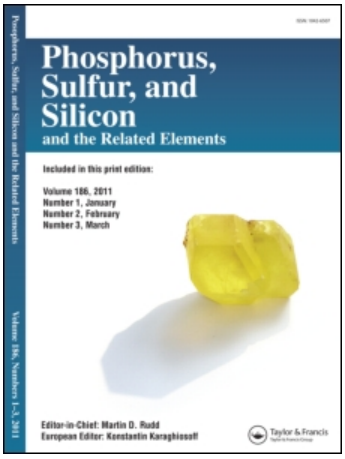

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Preparation of Anhydro-Thiohexopyranosides and -Thiohexofuranosides with D-*fructo*-, L-*sorbo*-, L-*psico*- and L-*tagato*-Configuration Starting from L-Sorbose

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Methyl α-L-sorbopyranoside is transformed into the bicyclic thiosugar methyl 1,5-anhydro-3,4-di-O-mesyl-1-thio-β-D-fructopyranoside in two steps, whereas the corresponding 3-O-benzoate is obtained from methyl 1,3-O-benzylidene-α-L-sorbopyranoside in three steps. 2,3-O-Isopropylidenesorbofuranosides, on the other hand, can be transformed into 6-S-thioacetates by use of the thio-Mitsunobu reaction. These are suitable precursors for the preparation of 1,6-anhydro-1-thiosorbofuranosides. Also, methyl 1-S-acetyl-1-thio-L-sorbofuranosides with mesylate leaving groups are available by the thio-Mitsunobu reaction. They yield 1,4-anhydro-1-thio-β-L-tagatofuranosides, 1,3-anhydro-α-L-psicofuranosides and 1,6-anhydro-1-thio-α-L-sorbofuranosides depending on the configuration of the starting compound. Attempts to prepare azido-thio-sugars by displacement of mesylate groups with alkali metal azides failed.

Keywords Anhydrothiosugars; intramolecular S_N2 reaction; methyl sorbopyranosides; methyl sorbofuranosides; thio-Mitsunobu reaction

INTRODUCTION

In a recent article in this journal,[3] we have described first results on the synthesis of anhydro-thio-furanosides starting from a ketose, namely from D-fructose. The key step in these syntheses, i.e., the introduction of sulfur into the carbohydrate molecule, was achieved by the thio-Mitsunobu reaction. This method had already turned out earlier to be

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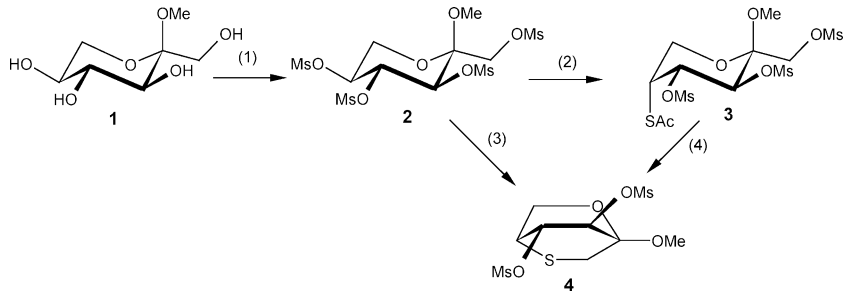
the method of choice in the pentofuranoside[4] and glucopyranoside[5] series. In particular, it was possible in most cases to prepare thioacetates directly from the corresponding methyl glycosides without protection of the hydroxy groups. We were, therefore, interested in an extension of the method to further ketoses and have explored its applicability in the sorbose series. In spite of the fact that L-sorbose is an inexpensive sugar because it is the intermediate in the most important process for the technical production of L-ascorbic acid,[6,7] its chemistry in general has been much less studied than that of other monosaccharides. In particular, thiosorbose derivatives are rather rare. In addition to the synthesis of compounds of this type, we also wanted to investigate the stereochemistry of the reactions and, furthermore, of follow-up reactions of suitably substituted thiosorbosides such as the nucleophilic substitution with azides.

RESULTS AND DISCUSSION

Pyranoses

In contrast to the difficulties which one is faced to with the preparation of methyl fructosides exhibiting a definite structure and configuration,[3,8] methyl α-L-sorbopyranoside **1** is easily available with good yield.[9] Our attempts to introduce an acetylthio group directly into the primary 1-position of **1** by a thio-Mitsunobu reaction failed, however. Although we tried various solvents and applied reaction temperatures between 0°C and 130°C, only the starting material **1** was recovered. Obviously, steric hindrance (the "neopentyl effect") prevents an attack of the bulky reagent, which is involved in the Mitsunobu reaction, at the primary hydroxy group in the 1-position of **1**. We have observed the same effect in the fructose series, where the 1-position is very resistant to nucleophilic reactions too.[3] Therefore, we prepared the tetramesylate **2** as a starting compound, which gave the thioacetate **3** on reaction with potassium thioacetate in DMF (Scheme 1).

Again, the 1-position was not attacked by the nucleophile but instead the reaction took place at the least hindered secondary 5-position under inversion. The structure and the resulting β-D-*fructo*-configuration of **3** were confirmed by its NMR spectra. The structure of a 1-thioacetate can be excluded on account of the chemical shifts $\delta = 4.30/4.42$ for the protons at C-1 which agree with the corresponding values (4.33/4.44) in the precursor **1** in contrast to δ(1-H) = 3.33 in the related 1,6-di-*S*-acetyl-1,6-dithio-β-D-fructofuranoside.[3] Furthermore, the *trans*-diaxial coupling $^3J_{H3,H4} = 10.6$ Hz and the low vicinal couplings $^3J_{H5,H6/H5,H6'} =$ 1.5/2.3 Hz are indicative of the D-*fructo*-configuration of **3** and exclude



SCHEME 1 (1): MsCl, pyridine; (2): AcSK, DMF, 153 °C; (3): AcSK, $MeOCH_2CH_2OH$, 125 °C; (4): $Na_2S{\cdot}9H_2O$, DMSO, 100°C.

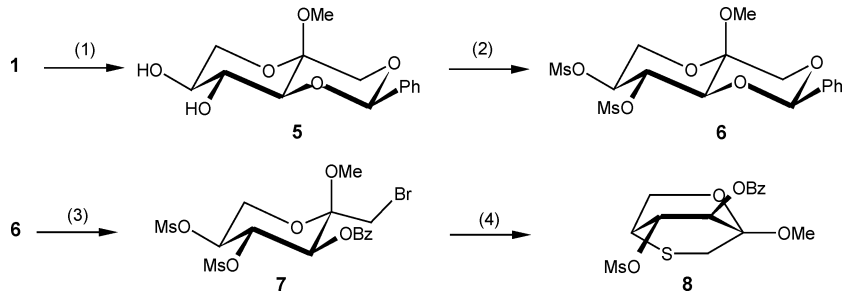
the alternative S_N2 substitution at the 4-position, which would have led to a 4-thioacetate with D-*tagato*-configuration.

The intramolecular cyclization of **3** was achieved by reaction with sodium sulfide. Not unexpectedly, it took place under formation of the 1,5-anhydro-thiosugar **4** since nucleophilic displacement of the mesylate group at the primary 1-position is strongly favored over the much less reactive 3-mesylate group neighboring the anomeric center. Compound **4** can also be obtained directly from **2** and potassium thioacetate on prolonged refluxing in 2-methoxyethanol. In fact, it is difficult to isolate the intermediate **3** from reaction mixtures of **2** with potassium thioacetate (Scheme 1). Unfortunately, the yields are low in both cases but anyway the one-step procedure starting from **2** is, of course, more advantageous for the preparation of **4**.

As expected, **4** retains the β-D-*fructo*-configuration of **3** and exhibits a boat-conformation of the hexose ring, i.e., a bicyclo[2.2.2]octane type skeleton. This can be clearly deduced from its NMR spectra. The small coupling constant $^3J_{H3,H4} = 3.5$ Hz, in contrast to $^3J_{H3,H4} = 10.6$ Hz in **3**, is characteristic of a *gauche*-conformation of the two protons. The ^{13}C chemical shifts $\delta = 29.6$, $\delta = 37.5$, and $\delta = 96.1$ for C-1, C-5, and C-2, respectively, are in agreement with the structure of **4** too.

In a second reaction sequence, we have prepared the related benzoate **8** starting again with **1** (Scheme 2).

The benzylidene derivative **5** and the related dimesylate **6** are described in the literature.[10] The work-up procedure for **5** is, however, laborious and involves heavy losses. Large amounts of inorganic salts have to be removed, since an excess of zinc chloride is used as a catalyst and condensating agent. We preferred, therefore, to prepare **5** by use of 1,1-dimethoxytoluene with catalytic amounts of camphorsulfonic acid instead of benzaldehyde. Cleavage of **6** with *N*-bromosuccinimide[11] led to the 1-bromo derivative **7** with 80% yield. Finally, the reaction with



SCHEME 2 (1): $PhCH(OMe)_2$, DMF, H^+; (2): MsCl, pyridine; (3): NBS, CCl_4; (4): AcSK, DMF, 153°C.

potassium thioacetate gave the 3-*O*-benzoyl-anhydrothiosugar **8** in a nucleophilic substitution and concomitant base-promoted intramolecular cyclization (Scheme 2). The moderate yield of 26% is due to the several steps involved in the transformation of **7** to **8**. In this case, none of the expected intermediates, the 1-thioacetate or the 5-thioacetate, could be detected.

The ^{1}H NMR spectrum of **7** closely resembles that of the related **2**. Only the signals of 1-H, 1′-H and 3-H in **7** are shifted downfield as compared with **2** due to the 1-bromo substituent and the anisotropic effect of the 3-benzoyl group, whereas all coupling constants are nearly identical. The same holds for **8,** which even more resembles its analog **4**. The expected downfield shift of the signal of 3-H from $\delta = 4.93$ (**4**) to $\delta = 5.53$ (**8**) is the only significant difference observed (Table I). The structural assignments of **7** and **8** are also corroborated by the

TABLE I Relevant Chemical Shifts δ [ppm] and Vicinal Coupling Constants ^3J [Hz] in the ^{1}H NMR Spectra of Thioanhydrosugars

Compound	1-H/1′-H	3-H	$J_{3H,4H}$	4-H	$J_{4H,5H}$	5-H	$J_{5H,6H}$	$J_{5H,6'H}$	6-H/6′-H
4	2.71/3.48	4.93	3.6	5.17	3.4	3.08	1.6	3.0	4.47/4.50
8	2.82/3.45	5.53	3.4	5.26	3.4	3.11	1.7	3.0	4.52/4.56
13	2.42/3.31	5.05	1.8	5.15	6.9	5.1	0.7	3.2	2.36/3.03
14	2.36/3.02	4.65	3.1	4.94	7.3	4.7	1.0	3.2	2.28/2.87
15	2.25/3.35	4.76	3.1	4.99	7.2	4.8	1.0	3.1	2.35/2.94
16	2.25/3.36	4.28	2.3	4.41	7.4	4.70	2.2	2.8	2.34/2.91
17	2.48/3.05	3.63[a]	3.1	3.71[a]	3.1	4.51	1.8	3.2	2.30/3.15
23	3.02/3.02	4.44	2.5	3.26	0.0	4.61	5.7	5.0	4.22/4.23
26	3.10/3.14	3.53	2.5	5.25	0.0	4.69	4.6	4.2	4.23/4.32
27	2.25/3.36	4.77	3.1	5.00	7.2	4.84	1.0	3.1	2.35/2.95

[a]An unequivocal assignment to 3-H or 4-H is not possible

TABLE II Chemical Shifts δ [ppm] of Relevant Carbon Atoms in the ^{13}C NMR Spectra of Thioanhydrosugars

Compound	C-1	C-2	C-3	C-4	C-5	C-6
4	29.6	96.1	83.3	83.6	37.5	70.9
8	29.7	96.4	76.7	82.8	37.3	70.8
13	30.6	110.4	86.4	82.2	81.0	24.1
14	33.4	99.7	75.8	87.1	75.8	23.9
15	30.4	102.4	76.6	86.0	76.9	23.8
16	30.0	100.7	81.0	80.8	78.0	24.2
17	30.1	101.6	52.8[a]	53.0[a]	74.3	25.7
23	33.0	111.8	70.3	48.1	82.6	69.1
26	34.1	110.2	45.5	74.8	84.0	68.2
27	30.4	100.4	76.6	86.1	76.9	23.8

[a]An unequivocal assignment to C-3 or C-4 is not possible.

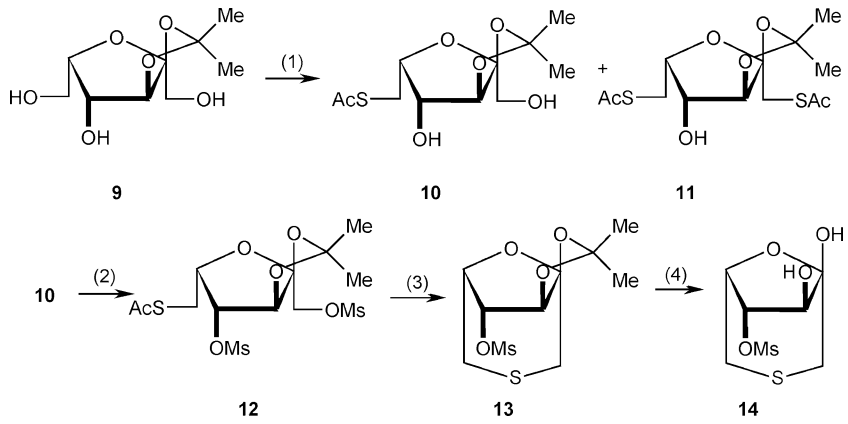
agreement of their ^{13}C NMR spectra with those of **2** and **4**, respectively. Only the C-1 signal of **7** at $\delta = 29.3$ appears with a considerable upfield shift as compared with $\delta = 66.0$ for **2** according to the bromo substituent. Also the C-3 signals at $\delta = 70.9$ (**7**) and $\delta = 76.7$ (**8**) are slightly but significantly shifted with respect to $\delta = 73.8$ (**2**) and $\delta = 83.3$ (**4**) (Table II).

Attempts to replace the mesylate group in **8** by an azido substituent failed. Debenzoylation of **8** with sodium methoxide and subsequent reaction with sodium azide and ammonium chloride led to decomposition without the formation of any azido derivative.

Furanoses

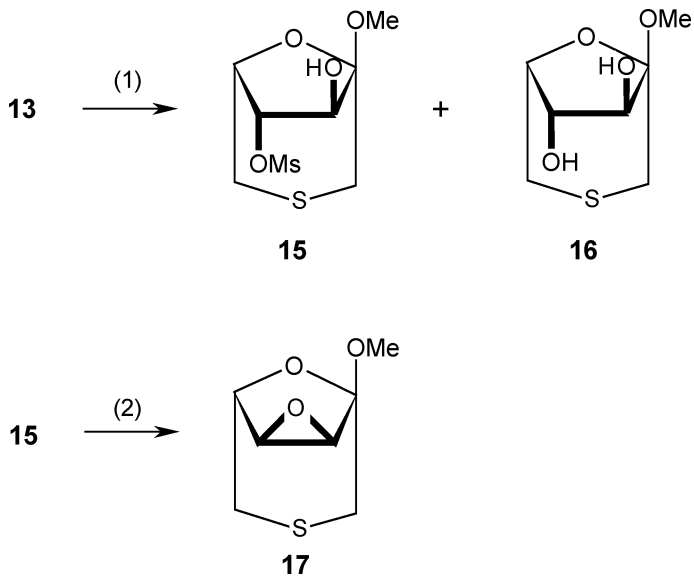
The preparation of sorbofuranosides is not as easy since the formation of the corresponding pyranosides is absolutely prevalent. Therefore, we started from 2,3-*O*-isopropylidene-α-L-sorbose **9** with a fixed furanose structure in order to synthesize anhydrothio-sorbofuranosides (Scheme 3).

Compound **9** is easily available from L-sorbose via the 2,3:4,6-di-*O*-isopropylidene-α-L-sorbose.[7,12–14] In contrast to **1**, the isopropylidene-sorbofuranose **9** formed a thioacetate **10** by a direct thio-Mitsunobu reaction with thioacetic acid in the presence of diisopropyl azodicarboxylate (DIAD) and triphenylphosphine. As expected, only the primary hydroxy group in the 6-position was attacked when equivalent amounts of the reagents were used. The yield of **10** was, however, low (26%). It could be considerably increased to 62% by applying the reagents in excess. Under these conditions, also 11% of the 1,6-bis-thioacetate **11** was



SCHEME 3 (1): Ph_3P, DIAD, AcSH, THF; (2): MsCl, pyridine; (3): $NaHCO_3$, $MeOCH_2CH_2OH$; (4): AcOH.

formed as by-product. The structures of the 6-thioacetate **10** and the 1,6-bis-thioacetate **11** are obvious from their ^1H and ^{13}C NMR spectra. Mesylation of **10** gave the dimesylate **12**. Cyclization of **12** with sodium hydrogencarbonate in boiling 2-methoxyethanol finally led to the 1,6-anhydro-thiosorbose **13** by cleavage of the thioacetate group and subsequent intramolecular nucleophilic attack of the thiolate at C-1 (Scheme 3).[15] Small amounts of diisopropyl hydrazodicarboxylate (DIHD) could not be completely removed from **10**, **12**, and **13** despite of repeated column chromatography. Irrespective of this contamination, **13** was deprotected with aqueous acetic acid to yield pure 1,6-anhydro-4-*O*-mesyl-1-thio-α-L-sorbofuranose **14** (Scheme 3). The interesting 1,6-anhydrothio (oxa-thia-bicyclo[3,2,1]octane) skeleton of **13** (and, consequently, of **14**) represents the only reasonable outcome of the cyclization of **12**, due to the stereochemical situation, i.e., the *syn*-configuration of the thioacetate substituent and the mesylate leaving group in the 4-position, the alternative formation of a 4,6-anhydrothio derivative through intramolecular S_N2 displacement is not possible. The structures are of course in agreement with the NMR spectra. The chemical shifts of 4-H in **12** and **13** are nearly identical, whereas the 1-H and 1-H signals of **13** are shifted up-field as one would expect (Table I). The only significant difference between the ^{13}C NMR spectra of **12** and **13** consists in a considerable shift of the C-1 signal from 67.5 ppm in **12** to 30.6 ppm in **13** (33.4 in **14**). Again, the chemical shifts of the C-4 signals are virtually the same for **12** (80.7 ppm) and **13** (81.2 ppm) (Table II).

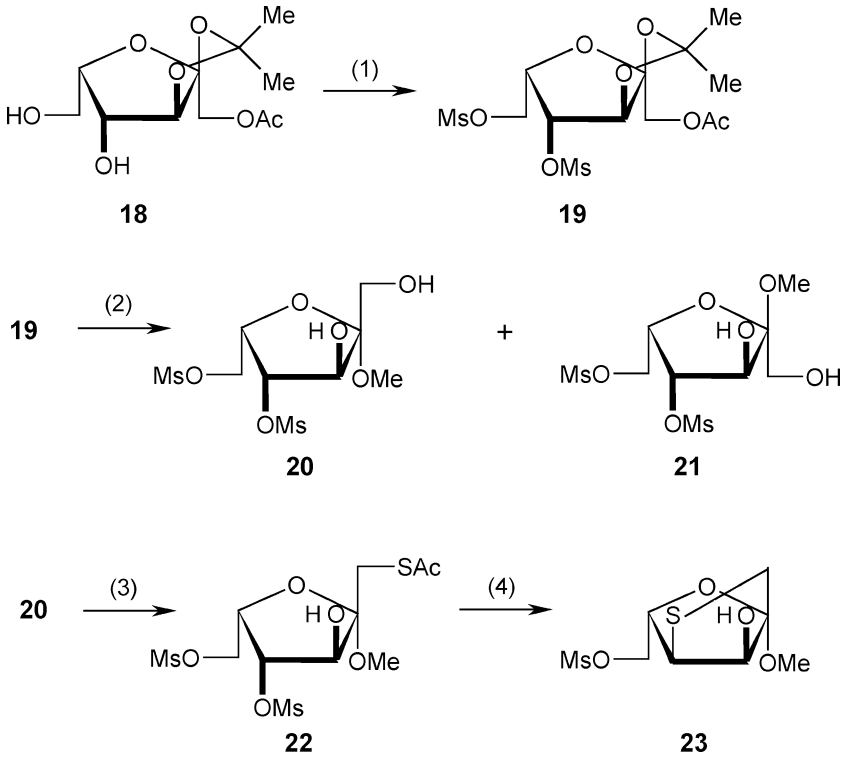


SCHEME 4 (1): HCl, MeOH; (2): LiN_3 (LiOH, cf. text), DMF.

The isopropylidene derivative **13** was glycosylated with methanolic hydrogen chloride. Besides a 61% yield of **15**, also 4% of the solvolysis product **16** was obtained (Scheme 4).

When we tried to replace the mesylate group of **15** by an azide substituent we failed again. Only the starting material was recovered after refluxing **15** with sodium azide in DMF for 22 h. The corresponding reaction with lithium azide, on the other hand, unexpectedly led to the 3,4-anhydro derivative **17** with 92% yield. Obviously, the reagent was contaminated with lithium hydroxide, which set off a base-catalyzed epoxide formation under elimination of the mesylate group (Scheme 4).

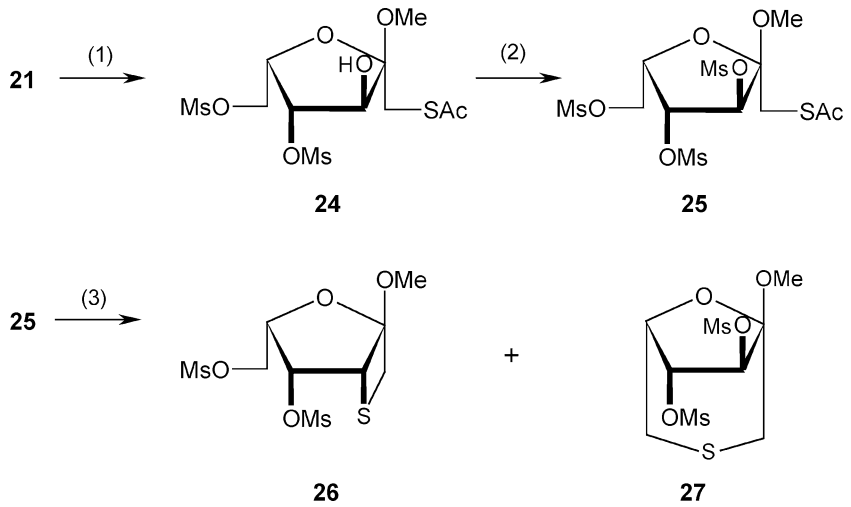
The NMR spectra of **15** and **16** are in agreement with their structures. The proton signals of 3-H and 4-H (3.63 and 3.71 ppm or *vice versa*) in **17** exhibit the typical high-field shifts as compared with 3-H (4.76 ppm) and 4-H (4.99 ppm) in the precursor **15**, which is characteristic of epoxide protons.[1,4,16,17] Also the vicinal coupling constant $^3J_{H4,H5} = 3.2$ Hz in **17** is indicative of the L-*psico* configuration with *gauche* conformation of 4-H and 5-H, as compared with $^3J_{H4,H5} = 7.2$ Hz in the precursor **15** with *eclipsed* conformation and L-*sorbo* configuration (Table I). Accordingly, the ^{13}C NMR signals of C-3 and C-4 in **17** appear in the typical epoxide range at 52.8/53.0 ppm[1,4,16,17] in contrast to C-3 (77 ppm) and C-4 (86 ppm) in **15** (Table II).



SCHEME 5 (1): MsCl, pyridine; (2): HCl, MeOH; (3): Ph_3P, DIAD, AcSH, THF; (4): $NaHCO_3$, $MeOCH_2CH_2OH$.

In order to further explore the selectivity of the cyclization reactions, i.e., the formation of thietano (1,3-thioanhydro) versus thiolano (1,4-thioanhydro), or thiepano (1,6-thioanhydro) sugars we have prepared the anomeric thioacetates **22** and **24** as starting compounds (Scheme 5).

The β-anomer **22** was obtained from the known 1-*O*-acetyl-2,3-*O*-isopropylidene-α-L-sorbose **18**[18] in three steps. Mesylation to form **19** and deprotection under acidic conditions led to the two anomeric dimesylates **20** (12%) and **21** (19%). Their configuration could be assigned based on NOESY NMR spectra. The β-anomer **20** exhibits the expected interaction between 3-H and the glycosidic OCH_3 group whereas the α-anomer **21** shows an interaction between 3-H and the protons of the 1-CH_2 group. After separation, the β-anomer **20** was subjected to a thio-Mitsunobu reaction to yield **22** (35%). Reaction of 22 with sodium hydrogencarbonate in boiling 2-methoxyethanol led to the 1,4-thioanhydroglycoside **23** (71%) with β-L-*tagato*-configuration under intramolecular



SCHEME 6 (1): Ph_3P, DIAD, AcSH, THF; (2): MsCl, pyridine; (3): $NaHCO_3$, $MeOCH_2CH_2OH$.

nucleophilic replacement of the mesylate leaving group at C-4, as expected (Scheme 5). An attack of the intermediate 1-thiolate at the 6-position is of course not possible for stereochemical reasons. The structure and configuration of **23** is corroborated by its ^1H and ^{13}C NMR spectra.

The thio-Mitsunobu reaction of the α-anomer **21**, on the other hand, gave 61% of the 1-thioacetate **24**. This compound was nearly quantitatively transformed into the 3,4,5-trimesylate **25**, which exhibits two leaving groups in positions suitable for intramolecular S_N2 reactions. In this case, the cyclization of **25** with sodium hydrogencarbonate led to a mixture of both of the two possible products **26** (6%) and **27** (8%), which were separated by chromatography (Scheme 6).

The structures of **26** and **27** could be unequivocally assigned based on their NMR spectra. Due to the substitution of the mesylate group, the ^1H NMR signal of 3-H in **26** exhibits an up-field shift to $\delta = 3.53$ ppm as compared to $\delta = 5.17$ ppm in the starting compound **25**, whereas no significant difference is observed for the protons in the 6-position. In **27**, on the other hand, the mesylate group at C-6 is displaced. Accordingly, the signals of 6-H (2.35 ppm) and 6′-H (2.95 ppm) appear at higher field as compared with **25** [δ(6-H/6′-H) = 4.42 ppm] (Table I). Correspondingly, the C-3 signal of **26** is shifted to 45.5 ppm from 79.9 ppm in **25** and, in contrast, the C-6 signal of **27** is shifted to 23.8 ppm from 66.5 ppm in **25** (Table II).

As an overview and for comparison purposes, the relevant NMR data of the anhydro-thiosugars, which we have prepared, are compiled in Tables I and II.

CONCLUSION

Our study has shown that methyl α-L-sorbopyranoside **1** does not react in a thio-Mitsunobu reaction with thioacetic acid. This is probably due to steric hindrance which prevents an attack of the intermediate bulky phosphonium cation at the neopentyl position C-1.[19] The sorbopyranoside **1** can, however, be transformed into the 1,5-thioanhydrofructopyranosides **4** and **8** via its tetramesylate **2** or 1,3-*O*-benzylidene derivative **5**.

The 2,3-*O*-isopropylidene-sorbofuranosides **9** and **18**, on the other hand, undergo regioselective thio-Mitsunobu reactions in the 6-position. The resulting thioacetates lead to the 1,6-thioanhydro (*thiepano*) sugars **13**–**16** in two steps. The *thiolano* sugar methyl 1,4-anhydro-6-*O*-mesyl-1-thio-β-L-psicofuranoside **23** is formed from the 1-thioacetate **22** whereas the corresponding α-anomer **24** yields the 1,3-thioanhydro (*thietano*) and 1,6-thioanhydro (*thiepano*) sugars **26** and **27**.

Mesylate leaving groups in the thioanhydrosugars cannot be replaced by azido substituents in S_N2 reactions. Instead, the 3,4-epoxide **17** is formed from **15**.

EXPERIMENTAL

Corrected melting points were determined on an Electrothermal apparatus. Optical rotations were measured on a Perkin Elmer 341 polarimeter. Thin layer chromatography (TLC) was performed on Al foils coated with SiO_2 F_{254} (Merck, Darmstadt). The spots were detected by the extinction of the fluorescence or, after spraying with 20% H_2SO_4 in EtOH, by heating. Column chromatography (CC) was performed on Kieselgel 60 F, 0.063–0.200 mm (Merck, Darmstadt). Eluents [EtOAc, petroleum ether (PE)] were distilled prior to use. IR (KBr pellets or films) spectra were measured on an ATI Mattson Instruments Genesis Series FT-IR spectrometer. NMR spectra were measured on Bruker AMX 400 (^{1}H: 400 MHz; ^{13}C: 100.62 MHz) or DRX 500 (^{1}H: 500 MHz, if particularly stated) spectrometers. Chemical shifts δ (ppm) are related to $SiMe_4$ as internal standard in $CDCl_3$. Spectra measured in acetone-d_6 were calibrated to $\delta(^1H) = 2.09$ ppm of the CD_2H signal and $\delta(^{13}C) = 30.56$ ppm of the CD_3 signal and subsequently related to $SiMe_4$. In order to enhance the resolution, the ^{1}H NMR spectra were recalculated

from the FID by use of the program WinNMR 5.1 (Bruker). Assignments of the signals were achieved by performing ^{1}H-^{1}H-COSY-, ^{1}H-^{13}C-COSY-, NOESY-, DEPT-135-, or PENDANT experiments. Solvents were purified and dried by standard laboratory procedures,[20] THF was kept over KOH for several days and subsequently refluxed and distilled over metallic potassium. Thioacetic acid (Merck, Darmstadt) was purified by four times distillation at low temp. in vacuum. Removal of solvents was performed by vacuum distillation in a rotating evaporator.

Methyl 1,3,4,5-Tetra-O-mesyl-α-L-sorbopyranoside (2)

Methyl α-L-sorbopyranoside (1)[9] (1.00 g, 5.15 mmol) and methanesulfonyl chloride (4.85 mL, 62.27 mmol) were dissolved in dry pyridine (30 mL) under cooling with ice. After stirring at 20°C for 12 h, the pyridine was removed. The residue was dissolved in CH_2Cl_2 (50 mL). The solution was washed twice with H_2O (each 50 mL). The organic layer was dried over $MgSO_4$ and evaporated until dry. The residue was purified by CC (EtOAc) to give 2.50 g (96%) **2** as colorless crystals. Mp. 149–150°C. $[\alpha]_D^{20}$ –19.6 (1.04, $CHCl_3$). IR: ν 1176 (SO_2), 1360 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.11 (s, 3H, SO_2CH_3), 3.16 (s, 3H, SO_2CH_3), 3.21 (s, 3H, SO_2CH_3), 3.25 (s, 3H, SO_2CH_3), 3.40 (s, 3H, OCH_3), 3.65 (d, 1H, 6-H), 4.19 (dd, 1H, 6-H), 4.33 (d, 1H, 1-H), 4.44 (d, 1H, 1-H), 4.78 (ddd, 1H, 5-H), 4.87 (d, 1H, 3-H), 5.11 (vt, 1H, 4-H). $^2J_{H1,H1'} = 10.3$ Hz, $^3J_{H3,H4} = 9.5$ Hz, $^3J_{H4,H5} = 9.3$ Hz, $^3J_{H5,H6} = 1.4$ Hz, $^3J_{H5,H6'} = 6.2$ Hz, $^2J_{H6,H6'} = 11.1$ Hz. ^{13}C NMR ($CDCl_3$): δ 37.9 (SO_2CH_3), 38.7 (SO_2CH_3), 39.1 (SO_2CH_3), 39.3 (SO_2CH_3), 49.7 (OCH_3), 60.3 (C-6), 66.0 (C-1), 73.2 (C-5), 73.8 (C-3), 75.6 (C-4), 98.1 (C-2).

Methyl 5-S-Acetyl-1,3,4-tri-O-mesyl-5-thio-β-D-fructopyranoside (3)

AcSK (0.71 g, 6.22 mmol) and **2** (2.10 g, 4.15 mmol) were dissolved in dry DMF (16 mL) and stirred under N_2 at 20°C for 24 h. After addition of another portion of AcSK (0.57 g, 4.99 mmol) in DMF (12.5 mL), the solution was heated to reflux under N_2 for 6 h. The DMF was removed. The residue was extracted with EtOAc and the extract was evaporated until dry. The product was purified by CC (EtOAc/PE 3:1) to yield **3** (0.45 g, 22%) as a syrup. IR: ν 1176 (SO_2), 1360 (SO_2), 1734 (C=O) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.49 (s, 3H, CH_3CO), 3.11 (s, 3H, SO_2CH_3), 3.14 (s, 3H, SO_2CH_3), 3.20 (s, 3H, SO_2CH_3), 3.39 (s, 3H, OCH_3), 3.82 (dd, 1H, 6-H), 4.14 (dd, 1H, 6-H), 4.30 (d, 1H, 1-H), 4.39 (m, 1H, 5-H), 4.42 (d, 1H, 1-H), 4.80 (d, 1H, 3-H), 5.32 (dd, 1H, 4-H). $^2J_{H1,H1'} = 10.6$ Hz, $^3J_{H3,H4} = 10.3$

Hz, $^3J_{H4,H5} = 4.6$ Hz, $^3J_{H5,H6} = 1.6$ Hz, $^3J_{H5,H6'} = 2.3$ Hz, $^2J_{H6,H6'} = 12.5$ Hz. ^{13}C NMR ($CDCl_3$): δ 30.8 (CH_3CO), 37.9 (SO_2CH_3), 39.1 (SO_2CH_3), 39.2 (SO_2CH_3), 46.6 (C-5), 49.6 (OCH_3), 63.6 (C-6), 66.4 (C-1), 74.1 (C-4), 74.5 (C-3), 98.9 (C-2), 193.5 (C=O).

Methyl 1,5-Anhydro-3,4-di-O-mesyl-1-thio-β-D-fructopyranoside (4)

(a) The tetramesylate **2** (1.00 g, 1.97 mmol) and CH_3COSH (0.70 mL, 9.88 mmol) were dissolved in 2-methoxyethanol (90 mL). N_2 was bubbled through the solution and KOH (0.55 g, 9.80 mmol) was added. The mixture was heated to reflux (125°C) for 20 h, the solvent was removed and the residue was purified by CC (EtOAc/PE/EtOH 10:6:0.5) to yield **4** (40.4 mg, 6%) as crystals.

(b) The thioacetate **3** (0.45 g, 0.92 mmol) and $Na_2S \cdot 9H_2O$ (0.74 g, 3.07 mmol) were heated to 100°C in DMSO (6 mL) for 20 h. Ice-water (10 mL) was added, and the solution was extracted first with CH_2Cl_2 and then with PE. After drying with $MgSO_4$, the solvent was removed and the residue was purified by CC (EtOAc/PE 2:1) to give **4** (18.3 mg, 5%).

IR: ν 1171 (SO_2), 1180 (SO_2), 1350 (SO_2), 1360 (SO_2) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.71 (d, 1H, 1-H), 3.08 (m, 1H, 5-H), 3.14 (s, 3H, SO_2CH_3), 3.19 (s, 3H, SO_2CH_3), 3.42 (s, 3H, OCH_3), 3.48 (d, 1H, 1'-H), 4.47 (dd, 1H, 6-H), 4.50 (dd, 1H, 6-H), 4.93 (d, 1H, 3-H), 5.17 (vt, 1H, 4-H). $^2J_{H1,H1'} = 11.4$ Hz, $^3J_{H3,H4} = 3.6$ Hz, $^3J_{H4,H5} = 3.4$ Hz, $^3J_{H5,H6} = 1.6$ Hz, $^3J_{H5,H6'} = 3.0$ Hz, $^2J_{H6,H6'} = 10.2$ Hz. ^{13}C NMR ($CDCl_3$): δ 29.6 (C-1) 37.5 (C-5), 38.87 (SO_2CH_3), 38.91 (SO_2CH_3), 50.2 (OCH_3), 70.9 (C-6), 83.3 (C-3), 83.6 (C-4), 96.1 (C-2).

Methyl 1,3-O-Benzylidene-α-L-sorbopyranoside (5)

Compound **1**[9] (4.85 g, 25.0 mmol) was dissolved in dry DMF (20 mL). Benzaldehyde dimethylacetal (3.75 mL, 25.0 mmol) and camphorsulfonic acid (0.02 g, 0.2 mmol) were added and the reaction mixture was kept at 50°C under a slight vacuum (11 Torr) for 15 h. The solvent was removed. The resulting syrup was stirred with PE to yield a slightly syrupy solid. Recrystallization from 2-propanol gave pure **5** (3.81 g, 57%) as colorless crystals. M.p. 165–166°C, Lit.[10]: 183–184°C. $[\alpha]_D^{20}$ –63.1 (1.01, 2-propanol), Lit.[10]: –54.6. IR: ν 3496 (OH) cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6, assignment of OH by addition of D_2O): δ 3.21 (s, 3H, OCH_3), 3.29 (vt, 1H, 6-H), 3.33 (d, 1H, 5-OH), 3.40 (m, 1H, 5-H), 3.44 (d, 1H, 3-H), 3.52 (d, 1H, 1-H), 3.59 (dd, 1H, 6-H), 3.63 (m, 1H, 4-H),

4.26 (d, 1H, 1′-H), 5.13 (d, 1H, 4-OH), 5.62 (s, 1H, PhC*H*), 7.34–7.40 (m, 3H, H_{ar}), 7.45–7.47 (m, 2H, H_{ar}). $^{2}J_{H1,H1'} = 11.8$ Hz, $^{3}J_{H3,H4} = 9.9$ Hz, $^{3}J_{H4,H5} = 8.8$ Hz, $^{3}J_{H4,OH4} = 32.3$ Hz, $^{3}J_{H5,H6} = 10.8$ Hz, $^{3}J_{H5,H6'} = 6.0$ Hz, $^{3}J_{H5,OH5} = 9.6$ Hz, $^{2}J_{H6,H6'} = 10.9$ Hz. ^{13}C NMR (DMSO-d_6): δ 47.4 (OCH_3), 63.3 (C-6), 66.3 (C-1), 69.8 (C-5), 70.5 (C-4), 81.6 (C-3), 92.5 (C-2), 101.1 (Ph*C*H), 126.4 (2 C_{ar}), 127.9 (2 C_{ar}), 128.7 (1 C_{ar}), 137.9 (1 C_{ar}).

Methyl 1,3-O-Benzylidene-4,5-di-O-mesyl-α-L-sorbopyranoside (6)

The mesylate **6** was prepared by mesylation of 5 according to ref.[10] IR: ν 1176 (SO_2), 1360 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.95 (s, 3H, SO_2CH_3), 3.17 (s, 3H, SO_2CH_3), 3.38 (s, 3H, OCH_3), 3.62 (d, 1H, 1-H), 3.78 (vt, 1H, 6-H), 3.79 (d, 1H, 3-H), 4.08 (dd, 1H, 6-H), 4.39 (d, 1H, 1-H), 4.69 (ddd, 1H, 5-H), 5.16 (dd, 1H, 4-H), 5.61 (s, 1H, PhC*H*), 7.34–7.38 (m, 3H, H_{ar}), 7.46–7.49 (m, 2H, H_{ar}). $^{2}J_{H1,H1'} = 12.3$ Hz, $^{3}J_{H3,H4} = 10.0$ Hz, $^{3}J_{H4,H5} = 8.9$ Hz, $^{3}J_{H5,H6} = 6.6$ Hz, $^{3}J_{H5,H6'} = 10.4$ Hz, $^{2}J_{H6,H6'} = 10.8$ Hz. ^{13}C NMR ($CDCl_3$): δ 38.8 (SO_2CH_3), 38.9 (SO_2CH_3), 48.6 (OCH_3), 61.6 (C-6), 66.8 (C-1), 75.2 (C-5), 77.5 (C-4), 79.4 (C-3), 92.7 (C-2), 102.6 (Ph*C*H), 126.2 (2 C, C_{ar}), 128.5 (2 C, C_{ar}), 129.6 (C_{ar}-4′), 136.3 (C_{ar}-1′).

Methyl 3-O-Benzoyl-1-bromo-1-deoxy-4,5-di-O-mesyl-α-L-sorbopyranoside (7)

Compound **6** (1.50 g, 3.42 mmol) was dissolved in CCl_4 (33 mL) under N_2. NBS (0.77 g, 4.33 mmol) and $BaCO_3$ (2.85 g, 14.4 mmol) were added, and the reaction mixture was heated to reflux for 4 h. After cooling, the solution was filtered and the residue was washed with EtOAc. The combined solutions were evaporated and the product was purified by CC (EtOAc/PE 3:1) to yield **7** (1.42 g, 80%) as colorless crystals. Mp. 126–127°C. $[\alpha]_D^{20}$ –57.8 (1.00, $CHCl_3$). IR: ν 1178 (SO_2), 1363 (SO_2). ^{1}H NMR ($CDCl_3$): δ 2.81 (s, 3H, SO_2CH_3), 3.15 (s, 3H, SO_2CH_3), 3.35 (d, 1H, 1-H), 3.39 (s, 3H, OCH_3), 3.61 (d, 1H, 1-H), 3.70 (vt, 6-H), 4.20 (dd, 1H, 6-H), 4.79 (ddd, 1H, 5-H), 5.25 (vt, 1H, 4-H), 5.66 (d, 1H, 3-H), 7.44–7.50 (m, 2H, H_{ar}), 7.60–7.64 (m, 1H, H_{ar}), 8.11–8.13 (m, 2H, H_{ar}). $^{2}J_{H1,H1'} = 11.7$ Hz, $^{3}J_{H3,H4} = 10.1$ Hz, $^{3}J_{H4,H5} = 9.4$ Hz, $^{3}J_{H5,H6} = 10.6$ Hz, $^{3}J_{H5,H6'} = 6.2$ Hz, $^{2}J_{H6,H6'} = 11.0$ Hz. ^{13}C NMR ($CDCl_3$): δ 29.3 (C-1), 38.5 (SO_2CH_3), 38.9 (SO_2CH_3), 48.8 (OCH_3), 61.1 (C-6), 70.9 (C-3), 74.0 (C-5), 77.4 (C-4), 98.8 (C-2), 128.5 (1 C_{ar}), 128.8 (2 C_{ar}), 130.2 (2 C_{ar}), 133.9 (1 C_{ar}), 165.1 (C=O).

Methyl 1,5-Anhydro-3-O-benzoyl-4-O-mesyl-1-thio-β-D-fructopyranoside (8)

The bromo compound 7 (0.64 g, 1.24 mmol) was dissolved in dry DMF (10 mL). N_2 was bubbled through the solution. Then AcSK (0.42 g, 3.68 mmol) was added and the solution was heated to reflux for 12 h. The reaction mixture was directly submitted to CC (EtOAc/PE) to yield 8 (120 mg, 26%) as crystals. M.p. 92–93°C (dec.). IR: ν 1176 (SO_2), 1361 (SO_2), 1728 (C=O) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 2.82 (d, 1H, H-1), 3.09 (s, 3H, SO_2CH_3), 3.11 (m, 1H, 5-H), 3.33 (s, 3H, OCH_3), 3.45 (d, 1H, 1-H), 4.52 (dd, 1H, 6-H), 4.56 (dd, 1H, 6-H), 5.26 (vt, 1H, 4-H), 5.53 (d, 1H, 3-H), 7.45–7.48 (m, 2H, H_{ar}), 7.58–7.61 (m, 1H, H_{ar}), 8.09–8.11 (m, 2H, H_{ar}). $^2J_{H1,H1'} = 11.3$ Hz, $^3J_{H3,H4} = 3.4$ Hz, $^3J_{H4,H5} = 3.4$ Hz, $^3J_{H5,H6} = 1.7$ Hz, $^3J_{H5,H6'} = 3.0$ Hz, $^2J_{H6,H6'} = 10.1$ Hz. ^{13}C NMR ($CDCl_3$): δ 29.7 (C-1), 37.3 (C-5), 38.8 (SO_2CH_3), 50.4 (OCH_3), 70.8 (C-6), 76.7 (C-3), 82.8 (C-4), 96.4 (C-2), 128.5 (2 C_{ar}), 129.2 (C_{ar}), 130.1 (2 C_{ar}), 133.5 (C_{ar}), 165.6 (C=O).

6-S-Acetyl-2,3-O-isopropylidene-6-thio-α-L-sorbofuranose (10) and 1,6-Di-S-acetyl-2,3-O-isopropylidene-1,6-dithio-α-L-sorbofuranose (11)

PPh_3 (6.39 g, 24.4 mmol) was dissolved in dry THF (50 mL) under N_2. After cooling to 0°C, diisopropyl azodicarboxylate (DIAD, 4.70 mL, 24.4 mmol) was dropped in and the solution (1) was stirred at 0°C for 30 min. AcSH (2.00 mL, 28.1 mmol) was dropped into a solution of 2,3-*O*-isopropylidene-α-L-sorbofuranose **9**[13,14] (4.27 g, 19.4 mmol) in dry THF (40 mL) under N_2 at 0°C. After 30 min stirring at 0°C, this solution (2) was dropped into solution (1). The reaction mixture was stirred at 20°C for 3 days. The solvent was removed and the residue was separated by CC (EtOAc/PE 3:2) to yield F1, $R_f = 0.76$ (0.71 g, contaminated with DIHD: 11% of 11), and F2, $R_f = 0.51$ (4.20 g, contaminated with DIHD: 62% of 10) as syrups.

10: IR: ν 1689 (C=O), 3464 (OH) cm^{-1}. ^1H NMR (acetone-d_6): δ 1.30 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 2.32 (s, 3H, $COCH_3$), 3.08 (dd, 1H, 6-H), 3.13 (dd, 1H, 6-H), 3.83–3.86 (m, 2H, 1-H, 1-H), 4.01 (dd, 1H, 4-H), 4.22 (m, 1H, 5-H), 4.34 (d, 1H, 4-OH), 4.43 (s, 1H, 3-H), 4.56 (dd, 1H, 1-OH). $^2J_{H1,H1'} = 10.3$ Hz, $^3J_{H1,OH} = 1.8$ Hz, $^3J_{H1',OH} = 5.8$ Hz, $^3J_{H4,H5} = 2.3$ Hz, $^3J_{H4,OH} = 8.1$ Hz, $^3J_{H5,H6} = 1.7$ Hz, $^3J_{H5,H6'} = 7.0$ Hz, $^2J_{H6,H6'} = 13.4$ Hz. ^{13}C NMR (acetone-d_6): δ 26.6 (CH_3), 27.6 (CH_3), 27.7 (C-6), 30.4 ($COCH_3$), 63.7 (C-1), 75.1 (C-4), 81.4 (C-5), 86.6 (C-3), 112.4 (C-2), 115.0 (CMe_2), 195.4 (C=O).

11: IR: ν 1709 (C=O), 1718 (C=O), 3315 (OH) cm^{-1}. ^1H NMR (acetone-d_6): δ 1.34 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 2.325 (s, 3H, $COCH_3$), 2.328

(s, 3H, $COCH_3$), 3.09–3.18 (m, 2H, 6-H, 6-H), 3.39 (d, 1H, 1-H), 3.43 (d, 1H, 1-H), 4.11 (ddd, 1H, 4-H), 4.22 (vtd, 1H, 5-H), 4.29 (bs, 1H, 3-H), 4.50 (dd, 1H, 4-OH). $^2J_{H1,H1'} = 13.9$ Hz, $^3J_{H3,H4} = 0.5$ Hz, $^3J_{H4,H5} = 2.1$ Hz, $^3J_{H4,OH} = 4.6$ Hz, $^3J_{H5,H6} = 7.1$ Hz, $^3J_{H5,H6'} = 7.1$ Hz, $^2J_{H6,H6'} = 13.4$ Hz. ^{13}C NMR (acetone-d_6): δ 26.8 (CH_3), 27.6 (CH_3), 27.7 (C-1), 30.8 ($COCH_3$), 30.9 ($COCH_3$), 35.2 (C-6), 75.3 (C-4), 81.6 (C-5), 87.6 (C-3), 112.3 (C-2), 114.3 (CMe_2), 194.6 (C=O), 195.6 (C=O).

6-S-Acetyl-2,3-O-isopropylidene-1,4-di-O-mesyl-6-thio-α-L-sorbofuranose (12)

Compound **10** (5.81 g = 16.8 mmol of 10) was mesylated with methanesulfonyl chloride (9.80 mL, 126 mmol) in pyridine (65 mL) as described for **2**. Purification by CC (EtOAc) gave **12** as a syrup (7.56 g, contaminated with 14% DIHD: 90% of **12**). IR: ν 1176 (SO_2), 1360 (SO_2), 1697 (C=O) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.39 (d, 3H, CH_3), 1.52 (s, 3H, CH_3), 2.37 (s, 3H, $COCH_3$), 3.08 (s, 3H, SO_2CH_3), 3.158 (dd, 1H, 6-H), 3.159 (s, 3H, SO_2CH_3), 3.23 (dd, 1H, 6-H), 4.33 (d, 1H, 1-H), 4.37 (d, 1H, 1-H), 4.48 (vtd, 1H, 5-H), 4.82 (s, 1H, 3-H), 5.05 (d, 1H, 4-H). $^2J_{H1,H1'} = 11.4$ Hz, $^3J_{H4,H5} = 2.8$ Hz, $^3J_{H5,H6} = 7.2$ Hz, $^3J_{H5,H6'} = 6.9$ Hz, $^2J_{H6,H6'} = 13.8$ Hz. ^{13}C NMR ($CDCl_3$): δ 26.3 (CH_3), 26.4 (C-6), 27.2 (CH_3), 30.5 ($COCH_3$), 37.7 (SO_2CH_3), 38.7 (SO_2CH_3), 67.5 (C-1), 79.2 (C-5), 80.7 (C-4), 83.5 (C-3), 111.5 (C-2), 113.8 (C-Me_2), 194.4 (C=O).

1,6-Anhydro-2,3-O-isopropylidene-4-O-mesyl-1-thio-α-L-sorbofuranose (13)

Irrespective of its contamination, **12** (2.56 g, 5.05 mmol **12**) and $NaHCO_3$ (1.00 g, 11.9 mmol) were refluxed under N_2 in 2-methoxyethanol/H_2O (19:1) for 14 h. The solvents were removed and the residue chromatographed (EtOAc/PE 1:1) to yield **13** (0.40 g, contaminated with DIHD, 18% **13**) as a syrup. IR: ν 1180 (SO_2), 1360 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 3H, CH_3), 1.57 (s, 3H, CH_3), 2.36 (dd, 3H, 6-H), 2.42 (d, 1H, 1-H), 3.03 (dd, 1H, 6-H), 3.15 (s, 3H, SO_2CH_3), 3.31 (d, 1H, 1′-H), 5.05 (d, 1H, 3-H), 5.07–5.10 (m, 1H, 5-H), 5.15 (dd, 1H, 4-H). $^2J_{H1,H1'} = 12.5$ Hz, $^3J_{H3,H4} = 1.8$ Hz, $^3J_{H4,H5} = 6.9$ Hz, $^3J_{H5,H6} = 0.7$ Hz, $^3J_{H5,H6'} = 3.2$ Hz, $^2J_{H6,H6'} = 13.8$ Hz. ^{13}C NMR ($CDCl_3$): δ 24.1 (C-6), 27.6 (CH_3), 28.3 (CH_3), 30.6 (C-1), 38.1 (SO_2CH_3), 81.0 (C-5), 82.2 (C-4), 86.4 (C-3), 110.4 (C-2), 117.7 (CMe_2).

1,6-Anhydro-4-O-mesyl-1-thio-α-L-sorbofuranose (14)

Without further purification, **13** (0.30 g = 0.68 mmol **13**) was refluxed in aqueous HOAc (10 mL, 20%) for 4 h. $NaHCO_3$ (1.85 g) was added for

neutralization. The solution was saturated with NaCl and extracted with CH_2Cl_2. After drying, the organic phase was evaporated and the residue was chromatographed (EtOAc/PE 3:1) to yield pure **14** as a syrup (31 mg, 18%). ^{1}H NMR (acetone-d_6): δ 2.28 (dd, 1H, 6-H), 2.36 (d, 1H, 1-H), 2.87 (dd, 1H, 6-H), 3.02 (m, 3H, 1′-H, 2-OH, 3-OH), 3.25 (s, 3H, SO_2CH_3), 4.65 (d, 1H, 3-H), 4.69–4.72 (m, 1H, 5-H), 4.94 (dd, 1H, 4-H). $^2J_{H1,H1'} = 12.5$ Hz, $^3J_{H3,H4} = 3.1$ Hz, $^3J_{H4,H5} = 7.3$ Hz, $^3J_{H5,H6} = 1.0$ Hz, $^3J_{H5,H6'} = 3.2$ Hz, $^2J_{H6,H6'} = 13.7$ Hz. ^{13}C NMR (acetone-d_6): δ 23.9 (C-6), 33.4 (C-1), 38.0 (SO_2CH_3), 75.76 (C-3 or C-5), 75.82 (C-5 or C-3), 87.1 (C-4), 99.7 (C-2).

Methyl 1,6-Anhydro-4-O-mesyl-1-thio-α-L-sorbofuranoside (15) and Methyl 1,6-Anhydro-1-thio-α-L-sorbofuranoside (16)

Acetyl chloride (3.40 mL) was dissolved in MeOH (23 mL) to form a solution of HCl in MeOH. Purified **13** (0.42 g, 1.42 mmol) was added and the mixture was stirred at 20°C for 4 d. After neutralization with NEt_3, the solvents were removed and the residue was extracted with EtOAc. The solvent was removed from the extract. Chromatography (EtOAc/PE 3:1) gave **15** (0.233 g, 61%) as a syrup.

15: IR: ν 1178 (SO_2), 1354 (SO_2), 3454 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.25 (d, 1H, 1-H), 2.35 (dd, 1H, 6-H), 2.79 (bs, 1H, OH), 2.94 (dd, 1H, 6-H), 3.19 (s, 3H, SO_2CH_3), 3.35 (d, 1H, 1′-H), 3.54 (s, 3H, OCH_3), 4.76 (d, 1H, 3-H), 4.84 (m, 1H, 5-H), 4.99 (dd, 1H, 4-H). $^2J_{H1,H1'} = 12.3$ Hz, $^3J_{H3,H4} = 3.2$ Hz, $^3J_{H4,H5} = 7.2$ Hz, $^3J_{H5,H6} = 1.0$ Hz, $^3J_{H5,H6'} = 3.1$ Hz, $^2J_{H6,H6'} = 13.8$ Hz. ^{13}C NMR ($CDCl_3$): δ 23.8 (C-6), 30.4 (C-1), 38.0 (SO_2CH_3), 51.9 (OCH_3), 76.6 (C-3 or C-5), 76.9 (C-3 or C-5), 86.0 (C-4), 102.4 (C-2).

When unpurified **13** (containing its hydrolysis product *1,6-anhydro-2,3-*O*-isopropylidene-1-thio-α-L-sorbofuranose*) was used as starting material, a 4% yield of **16** was isolated after CC (EtOAc/PE 3:1) in addition to **15**.

16: ^{1}H NMR ($CDCl_3$): δ 2.25 (ddd, 1H, 1-H), 2.34 (ddd, 1H, 6-H), 2.58 (s, 2H, 3-OH, 4-OH), 2.91 (dd, 1H, 6-H), 3.36 (d, 1H, 1-H), 3.52 (s, 3H, OCH_3), 4.28 (d, 1H, 3-H), 4.41 (dd, 1H, 4-H), 4.70 (dvt, 1H, 5-H). $^2J_{H1,H1'} = 12.3$ Hz, $^4J_{H1,H6} = 0.4$ Hz, $^5J_{H1,H5} = 0.8$ Hz, $^3J_{H3,H4} = 2.3$ Hz, $^3J_{H4,H5} = 7.4$ Hz, $^3J_{H5,H6} = 2.2$ Hz, $^3J_{H5,H6'} = 2.8$ Hz, $^2J_{H6,H6'} = 13.6$ Hz. ^{13}C NMR ($CDCl_3$): δ 24.2 (C-6), 30.0 (C-1), 51.8 (OCH_3), 78.0 (C-5), 80.8 (C-3 or C-4), 81.0 (C-3 or C-4), 100.7 (C-2).

Methyl 1,6:3,4-Dianhydro-1-thio-α-L-psicofuranoside (17)

The mesylate **15** (0.144 g, 0.53 mmol) and LiN_3 (0.080 g, 1.63 mmol) were refluxed in DMF (10 mL) for 18 h. The solvent was removed

and the residue was purified by CC (EtOAc/PE 3:1) to yield **17** as a syrup (0.085 g, 92%). ^{1}H NMR ($CDCl_3$): δ 2.30 (dd, 1H, 6-H), 2.48 (d, 1H, 1-H), 3.05 (d, 1H, 1-H), 3.15 (dd, 1H, 6-H), 3.54 (s, 3H, OCH_3), 3.63 (d, 1H, 3-H or 4-H), 3.71 (d, 1H, 3-H or 4-H), 4.51 (ddd, 1H, 5-H). $^2J_{H1,H1'} = 12.9$ Hz, $^3J_{H3,H4} = 3.2$ Hz, $^3J_{H4,H5} = 3.2$ Hz, $^3J_{H5,H6} = 1.8$ Hz, $^3J_{H5,H6'} = 3.2$ Hz, $^2J_{H6,H6'} = 13.4$ Hz. ^{13}C NMR ($CDCl_3$): δ 25.7 (C-6), 30.1 (C-1), 52.5 (CH_3), 52.8 (C-3 or C-4), 53.0 (C-3 or C-4), 74.3 (C-5), 101.6 (C-2).

1-O-Acetyl-2,3-O-isopropylidene-α-L-sorbofuranose (18)[18]

Reaction of **9**[12–14] with Ac_2O gave *1-O-acetyl-2,3:4,6-di-O-isopropylidene-α-L-sorbofuranose*[18] (purified by CC with EtOAc instead of distillation,[18] 99% yield). The di-*O*-isopropylidene derivative (5.70 g, 18.85 mmol) was dissolved in 60% aqueous HOAc (67 mL) and heated to 80–85°C for 1 h. The solvent was removed. After repeated codistillation with toluene and CC (EtOAc), **18** ($R_f = 0.47$, 4.51 g, 91%) was obtained as a syrup. $[\alpha]_D^{20}$ –51.0 (1.0, acetone). IR: ν 1747 (C=O), 3423 (OH) cm^{-1}. ^{1}H NMR (acetone-d_6): δ 1.30 (s. 3H, CH_3), 1.40 (s, 3H, CH_3), 2.02 (s, 3H, $COCH_3$), 3.71 (dd, 1H, 6-H), 3.78 (dd, 1H, 6-H), 4.02 (d, 1H, 1-H), 4.19 (d, 1H, 4-H), 4.23 (dvt, 2H, 5-H, OH), 4.35–4.38 (m, 2H, 1-H, 3-H), 4.58 (d, 1H, OH). $^2J_{H1,H1'} = 11.8$ Hz, $^3J_{H4,H5} = 2.8$ Hz, $^3J_{H5,H6} = 5.6$ Hz, $^3J_{H5,H6'} = 5.5$ Hz, $^2J_{H6,H6'} = 11.6$ Hz, $^3J_{H,OH} = 2.8$ Hz. ^{13}C NMR (acetone-d_6): δ 20.7 ($COCH_3$), 26.6 (CH_3), 27.7 (CH_3), 60.7 (C-6), 63.9 (C-1), 75.8 (C-4), 82.4 (C-5), 86.4 (C-3), 112.3 (C-2), 113.4 (CMe_2), 170.4 (C=O).

1-O-Acetyl-2,3-O-isopropylidene-4,6-di-O-mesyl-α-L-sorbofuranose(19)

Compound **18**[18] (4.39 g, 16.7 mmol) was mesylated as described for **2**. CC (EtOAc) gave **19** (6.64 g, 95%) as a colorless syrup. IR: ν 1174 (SO_2), 1361 (SO_2), 1745 (C=O) cm^{-1}. ^{1}H NMR (acetone-d_6): δ 1.38 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 2.07 (s, 3H, $COCH_3$), 3.17 (s, 3H, SO_2CH_3), 3.30 (s, 3H, SO_2CH_3), 4.23 (s, 1H, 1-H), 4.37 (d, 1H, 1-H), 4.40 (dd, 1H, 6-H), 4.50 (dd, 1H, 6-H), 4.71 (ddd, 1H, 5-H), 4.83 (s, 1H, 3-H), 5.18 (dd, 1H, 4-H). $^2J_{H1,H1'} = 12.0$ Hz, $^3J_{H3,H4} = 0.5$ Hz, $^3J_{H4,H5} = 3.0$ Hz, $^3J_{H5,H6} = 7.4$ Hz, $^3J_{H5,H6'} = 4.4$ Hz, $^2J_{H6,H6'} = 10.9$ Hz. ^{13}C NMR (acetone-d_6): δ 20.7 ($COCH_3$), 26.6 (CH_3), 27.4 (CH_3), 37.3 (SO_2CH_3), 38.2 (SO_2CH_3), 63.5 (C-1), 67.7 (C-6), 78.3 (C-5), 82.4 (C-4), 86.8 (C-3), 113.7 (C-2), 113.8 (CMe_2), 170.5 (C=O).

Methyl 4,6-Di-O-mesyl-β-L-sorbofuranoside(20) and Methyl 4,6-Di-O-mesyl-α-L-sorbofuranoside (21)

Compound **19** (4.18 g, 11.5 mmol) was dissolved in methanolic HCl (96 mL), prepared from acetyl chloride (14.4 mL). The solution was stirred at 20°C for 42 h, then neutralized with NEt_3 (21 mL), and the solvent was removed. The residue was extracted with EtOAc, the solvent was removed from the extract, and the residue was repeatedly chromatographed (EtOAc) to yield **20** (0.420 g, 10%, $R_f = 0.39$) and 21 (0.674 g, 17%, $R_f = 0.31$) as syrups.

20: $[\alpha]_D^{20}$+15.4 (1.0, acetone). IR: ν 1174 (SO_2), 1350 (SO_2), 3427 (OH) cm^{-1}. ^1H NMR (acetone-d_6): δ 3.17 (s, 3H, SO_2CH_3), 3.22 (s, 3H, SO_2CH_3), 3.32 (s, 3H, OCH_3), 3.70 (d, 1H, 1-H), 3.81 (d, 1H, 1-H), 4.36 (dd, 1H, 6-H), 4.43 (dd, 1H, 6-H), 4.45 (d, 1H, 3-H), 4.70–4.74 (m, 1H, 5-H), 5.16 (dd, 1H, 4-H). $^2J_{H1,H1'} = 12.0$ Hz, $^3J_{H3,H4} = 3.2$ Hz, $^3J_{H4,H5} = 6.3$ Hz, $^3J_{H5,H6} = 7.2$ Hz, $^3J_{H5,H6'} = 4.1$ Hz, $^2J_{H6,H6'} = 10.8$ Hz. ^{13}C NMR (acetone-d_6): δ 37.9 (SO_2CH_3), 38.2 (SO_2CH_3), 49.2 (OCH_3), 59.8 (C-1), 69.5 (C-6), 77.5 (C-5), 79.0 (C-3), 84.4 (C-4), 109.8 (C-2).

21: $[\alpha]_D^{20}$+74.8 (1.02, acetone). IR: ν 1174 (SO_2), 1352 (SO_2), 3408 (OH) cm^{-1}. ^1H NMR (acetone-d_6): δ 3.16 (s, 3H, SO_2CH_3), 3.26 (s, 3H, SO_2CH_3), 3.36 (s, 3H, OCH_3), 3.66 (d, 1H, 1-H), 3.73 (d, 1H, 1-H), 3.94 (m, 1H, OH), 4.22 (d, 1H, OH), 4.32 (dd, 1H, 6-H), 4.43 (dd, 1H, 6-H), 4.46 (dd, 1H, 3-H), 4.57 (vtd, 1H, 5-H), 5.17 (dd, 1H, 4-H). $^2J_{H1,H1'} = 12.1$ Hz, $^3J_{H3,H4} = 6.3$ Hz, $^3J_{H3,OH3} = 7.7$ Hz, $^3J_{H4,H5} = 6.9$ Hz, $^3J_{H5,H6} = 6.2$ Hz, $^3J_{H5,H6'} = 3.5$ Hz, $^2J_{H6,H6'} = 11.3$ Hz. ^{13}C NMR (acetone-d_6): δ 36.6 (SO_2CH_3), 38.4 (SO_2CH_3), 49.7 (OCH_3), 60.5 (C-1), 68.9 (C-6), 74.3 (C-5), 76.7 (C-3), 85.3 (C-4), 104.8 (C-2).

Methyl 1-S-Acetyl-4,6-di-O-mesyl-1-thio-β-L-sorbofuranoside (22)

Thio-Mitsunobu reaction of 20 (0.29 g, 0.84 mmol) with AcSH (0.15 mL, 2.11 mmol), DIAD (0.40 mL, 2.03 mmol), and PPh_3 (0.54 g (2.06 mmol) in THF as described for 10, and CC (EtOAc) gave **22** as a syrup, which was slightly contaminated with DIHD (0.117 g, 35% of pure **22** according to its ^1H NMR spectrum). IR: ν 1178 (SO_2), 1369 (SO_2), 1724 (C=O), 3352 (OH) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.37 (s, 3H, $COCH_3$), 3.09 (s, 6H, 2 SO_2CH_3), 3.28 (s, 3H, OCH_3), 3.39 (s, 2H, 1-H, 1-H), 4.28 (d, 1H, 3-H), 4.35–4.46 (m, 2H, 6-H, 6-H), 4.77 (vt, 1H, 5-H), 5.09 (dd, 1H, 4-H). $^3J_{H3,H4} = 1.4$ Hz, $^3J_{H4,H5} = 5.9$ Hz, $^3J_{H5,H6} = 5.9$ Hz, $^3J_{H5,H6'} = 5.9$ Hz. ^{13}C NMR ($CDCl_3$): δ 28.2 (C-1), 30.2 ($COCH_3$), 38.2 (SO_2CH_3), 38.4 (SO_2CH_3), 49.0 (OCH_3), 66.9 (C-6), 77.5 (C-5), 78.4 (C-3), 82.3 (C-4), 109.8 (C-2), 194.4 (C=O).

Methyl 1,4-Anhydro-6-O-mesyl-1-thio-β-L-psicofuranoside(23)

The thioacetate **22** (0.117 g, 0.29 mmol) and $NaHCO_3$ (0.200 g, 2.38 mmol) were refluxed in 2-methoxyethanol/H_2O (19:1, 200 mL) for 22 h as described for **13**. CC (EtOAc) gave **23** as a syrup, which was slightly contaminated with DIHD (55 mg, 70% of pure **23**). IR: ν 1176 (SO_2), 1354 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.02 (s, 2H, 1H, 1-H), 3.06 (s, 3H, SO_2CH_3), 3.26 (d, 1H, 4-H), 3.39 (s, 3H, OCH_3), 4.22 (d, 1H, 6-H), 4.23 (d, 1H, 6-H), 4.44 (m, 1H, 3-H), 4.61 (vt, 1H, 5-H). $^3J_{H3,H4} = 2.5$ Hz, $^3J_{H5,H6} = 5.7$ Hz, $^3J_{H5,H6'} = 5.0$ Hz. ^{13}C NMR ($CDCl_3$): δ 33.0 (C-1), 37.7 (SO_2CH_3), 48.1 (C-4), 58.9 (OCH_3), 69.1 (C-6), 70.3 (C-3), 82.6 (C-5), 111.8 (C-2).

Methyl 1-S-Acetyl-4,6-di-O-mesyl-1-thio-α-L-sorbofuranoside (24)

Thio-Mitsunobu reaction of **21** (0.584 g, 1.667 mmol) with AcSH (0.30 mL, 4.22 mmol), DIAD (0.75 mL, 3.81 mmol) and PPh_3 (1.00 g, 3.81 mmol) in THF as described for **22**, and CC (EtOAc) gave **24** as a syrup, which was slightly contaminated with DIHD (0.418 g, 61% of pure **24** according to its NMR spectrum). IR: ν 1178 (SO_2), 1360 (SO_2), 1729 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.39 (s, 3H, $COCH_3$), 3.08 (s, 3H, SO_2CH_3), 3.17 (s, 3H, SO_2CH_3), 3.27 (d, 1H, 1-H), 3.31 (d, 1H, 1-H), 3.37 (s, 3H, OCH_3), 4.20 (d, 1H, 3-H), 4.33 (dd, 1H, 6-H), 4.39 (dd, 1H, 6-H), 4.45 (m, 1 H, 5-H), 5.16 (vt, 1 H, 4-H). $^2J_{H1,H1'} = 14.6$ Hz, $^3J_{H3,H4} = 6.3$ Hz, $^3J_{H4,H5} = 6.9$ Hz, $^3J_{H5,H6} = 4.9$ Hz, $^3J_{H5,H6'} = 3.8$ Hz, $^2J_{H6,H6'} = 11.0$ Hz. ^{13}C NMR ($CDCl_3$): δ 29.7 (C-1), 30.4 ($COCH_3$), 37.5 (SO_2CH_3), 38.5 (SO_2CH_3), 49.4 (OCH_3), 67.0 (C-6), 73.5 (C-5), 77.6 (C-3), 83.6 (C-4), 103.2 (C-2), 195.1 (C=O).

Methyl 1-S-Acetyl-2,4,6-tri-O-mesyl-1-thio-α-L-sorbofuranoside (25)

Mesylation of **24** (0.418 g, 1.022 mmol, 2 h) as described for **2**, and CC (EtOAc) gave **25** as a syrup, which was slightly contaminated with DIHD (0.492 g, 99% of pure **25** according to its NMR spectrum). IR: ν 1178 (SO_2), 1361 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.40 (s, 3H, $COCH_3$), 3.10 (s, 3H, SO_2CH_3), 3.19 (s, 3H, SO_2CH_3), 3.20 (s, 3H, SO_2CH_3), 3.32 (d, 1H, 1-H), 3.39 (s, 3H, OCH_3), 3.52 (d, 1H, 1′-H), 4.42 (m, 2H, 6-H, 6′-H), 4.51 (dvt, 1H, 5-H), 5.17 (d, 1H, 3-H), 5.43 (vt, 4-H). $^2J_{H1,H1'} = 14.7$ Hz, $^3J_{H3,H4} = 6.5$ Hz, $^3J_{H4,H5} = 7.0$ Hz, $^3J_{H5,H6} = 4.9$ Hz, $^3J_{H5,H6'} = 3.8$ Hz. ^{13}C NMR ($CDCl_3$): δ 29.3 (C-1), 30.4 ($COCH_3$), 37.7 (SO_2CH_3), 38.5

(SO_2CH_3), 38.9 (SO_2CH_3), 49.5 (OCH_3), 66.5 (C-6), 73.7 (C-5), 79.90 (C-3), 79.94 (C-4), 103.3 (C-2), 194.1 (C=O).

Methyl 1,3-Anhydro-4,6-di-O-mesyl-1-thio-α-L-tagatofuranoside(26) and Methyl 1,6-Anhydro-3,4-di-O-mesyl-1-thio-α-L-sorbofuranoside (27)

Irrespective of the contamination, the thioacetate **25** (1.98 g, 1.011 mmol of pure **25**) and $NaHCO_3$ (0.35 g, 4.17 mmol) were refluxed in 2-methoxyethanol/H_2O (19:1, 200 mL) for 18 h as described for **13**. CC (EtOAc/PE 3:1) gave 26 (0.019 g, 6%) and **27** (0.029 g, 8%) as pure syrups.

26: IR: ν 1178 (SO_2), 1358 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.10 (d, 1H, 1-H), 3.13 (s, 3H, SO_2CH_3), 3.14 (d, 1H, 1-H), 3.15 (s, 3H, SO_2CH_3), 3.52 (s, 3H, OCH_3), 3.53 (d, 1H, 3-H), 4.23 (dd, 1H, 6-H), 4.32 (dd, 1H, 6-H), 4.69 (dd, 1H, 5-H), 5.25 (d, 1H, 4-H). $^2J_{H1,H1'} = 12.8$ Hz, $^3J_{H3,H4} = 2.5$ Hz, $^3J_{H4,H5} = 6.6$ Hz, $^3J_{H5,H6} = 4.6$ Hz, $^3J_{H5,H6'} = 4.2$ Hz, $^2J_{H6,H6'} = 11.6$ Hz. ^{13}C NMR ($CDCl_3$): δ 34.1 (C-1), 37.9 (SO_2CH_3), 39.1 (SO_2CH_3), 45.5 (C-3), 53.5 (OCH_3), 68.2 (C-6), 74.8 (C-4), 84.0 (C-5), 110.2 (C-2).

27: IR: ν 1176 (SO_2), 1354 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.25 (d, 1H, 1-H), 2.35 (dd, 1H, 6-H), 2.95 (dd, 1H, 6-H), 3.07 (s, 3H, SO_2CH_3), 3.19 (s, 3H, SO_2CH_3), 3.36 (d, 1H, 1-H), 3.54 (s, 3H, OCH_3), 4.77 (d, 1H, 3-H), 4.84 (m, 1H, 5-H), 5.00 (dd, 1H, 4-H). $^2J_{H1,H1'} = 12.4$ Hz, $^3J_{H3,H4} = 3.1$ Hz, $^3J_{H4,H5} = 7.2$ Hz, $^3J_{H5,H6} = 1.0$ Hz, $^3J_{H5,H6'} = 3.1$ Hz, $^2J_{H6,H6'} = 13.8$ Hz. ^{13}C NMR ($CDCl_3$): δ 23.8 (C-6), 30.4 (C-1), 37.7 (SO_2CH_3), 38.0 (SO_2CH_3), 51.9 (OCH_3), 76.6 (C-3), 76.9 (C-5), 86.1 (C-4), 100.4 (C-2).

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