Organic & Biomolecular Chemistry

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/obc

Organic &

Biomolecular Chemistry

ROYAL SOCIETY OF CHEMISTRY

ARTICLE

Studies on the diastereoselective oxidation of 1-thio-β-D-glucopyranosides: Synthesis of the usually less favoured R_S sulfoxide as a single diastereoisomer

Cite this: DOI: 10.1039/x0xx00000x

Received ooth January 2012,
Accepted ooth January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

Juan Francisco Moya-López,[†] Eleonora Elhalem, [†] Rocío Recio, [‡] Eleuterio Álvarez, [†] Inmaculada Fernández,[*‡] and Noureddine Khiar*,[†]

Abstract: A detailed study on the diastereoselective oxidation of 1-thio-β-D-glucopyranosides is reported. It has been shown that the sense and the degree of stereochemical outcome of the oxidation is highly dependent on the substituent of the sulfur and on the protective group of the C2-OH. In the case of thioglycosides with a bulky aglycone, the mesylation of C2-OH has a dramatic effect on the stereochemical outcome of the oxidation, affording the usually less favoured R_S sulfoxide as a single diastereoisomer. The absolute configuration of the final sulfinyl glycosides was ascertained by NMR analysis and corroborated by X-ray crystallography.

Introduction

The last two decades have witnessed an exponential use of sulfoxides as chiral auxiliaries in asymmetric synthesis, establishing the chiral sulfinyl group as one of the privileged chiral controller in C-C and C-X bond formations.[1] Recent interesting applications of chiral sulfoxides include *inter alia* their utilization as chiral ligands or ligands precursors in metal catalyzed asymmetric reactions,[2] in coordination chemistry[3] and as Lewis base in organocatalysis.[4] Surprisingly, diastereopure sulfinylglycosides, where one of the substituent of the sulfinyl sulfur is a sugar moiety, have received much less interest. Indeed, the application of sulfinyl glycosides has been practically limited to their use as glycosyl donors for the synthesis of glycoconjugates. In this sense, Kahne's route using anomeric sulfoxides, introduced in the late 80's for the synthesis of glycosides is one of the most promising approaches for the ever seeked "general glycosylation reaction".[5] The sulfoxide method, which has been developed originally for the glycosylation of hindered alcohols,[6] has been recently used for the one pot sequential formation of various glycosidic bonds,[7] for the synthesis of carbohydrate libraries on solid support[8] and, finally, for the synthesis of β-mannosides.[9] The fact that the stereochemical outcome of the reaction is independent on the stereochemistry of the sulfinyl sulfur and the anomeric carbon, is probably responsible for the scarce interest in the asymmetric synthesis and in the determination of configuration of the sulfinyl glycosides. Nevertheless, we[10] and others[11] have reported that R_S and S_S sulfinyl glycosides are hydrolyzed with different kinetics by triflic acids, and react in a complete diastereoselective manner with glycosidases. Additionally, it has recently been shown that in some cases one diastereomeric sulfoxide is an active glycosylating agent while the other is not.[12] On the other hand, the use of thioglycosides as glycosidase resistant analogues of glycoside is well documented.[13] Therefore, the corresponding sulfinyl analogues are expected not only to alter the lipophilicity, but also to vary the geometrical disposition of the sugar moiety about the aglycone. Such analogues, which should markedly affect the biological activity, make sulfinyl glycosides interesting on their own, and the knowledge of their stereochemistry of sum interest. Moreover, sulfinylglycosides may also found applications in asymmetric synthesis either as cheap chiral auxiliary, or ligands for organic and metal-promoted enantioselective catalysis.[1,2] For this goal to be attained, diastereoselective approaches to the synthesis of diastereopure sulfinylglycosides in high diastreoselectivity and in a predictable manner are needed. This has been achieved in the special case of α-sulfinylglycosides, which are usually obtained as a single diastereoisomers with the *R* absolute configuration at the sulfinyl sulfur, through electrophilic oxidation of the parent α-thioglycosides with organic peracides.[14] The high diastereoselectivity has been rationalized by invoking the *exo*-anomeric effect, which imposes a conformation of the starting thioglycoside in which the *pro-S* lone pair is substantially hindered by the pyranose ring and by the axial H1 and H3

hydrogen atoms, whereas the *pro-R* lone pair of the thioglycoside is exposed to peracidic attack (Figure 1).[15]

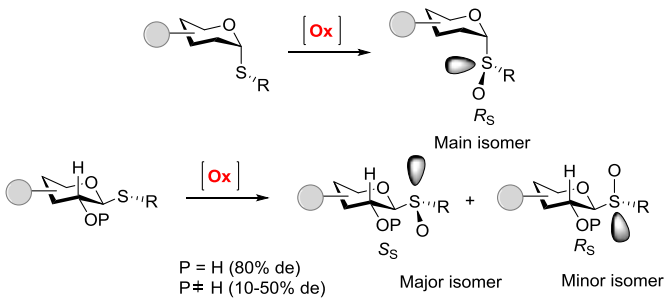


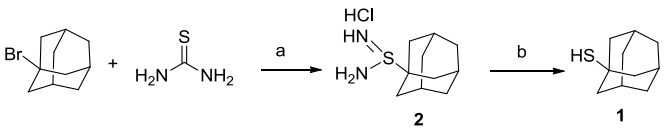
Figure 1: General trends in the diastereoselective oxidation of α- and β-thioglycosides

In the more interesting case of β-sulfinylglycosides the situation is far more complex and is still unsolved. The results obtained so far, indicate that the configuration and substitution of carbon 2 of the pyranose ring have crucial effect on the diastereoselectivity of the oxidation of β-thioglycosides. High diastetreoselectivity has been obtained in the case of β-mannothioglycoside (7:1)[16] and in case of β-thiogalactosides and β-thioglucoside (9:1) with a free OH at position 2.[17] While both oxidations afforded the *S*-diastereoisomer as the major isomer, the motives are different, being steric in the former due to the axial disposition at C2, and spatially directed in the later as a consequence of hydrogen bond between the peracid and free hydroxyl at C2. In all the other reported cases, the oxidation of β-thioglycosides is usually slightly diastereoselective, and with one exception the major isomer has the S_S absolute configuration at the sulfinyl sulfur. The accumulated results led to the belief that in the case of pyranosides with trans 1,2 diequatorial substituents, the sense (S_S), and the degree of diastereoselectivity (modest) are general features.[16] In a previous work we have shown that the last assumption is not correct, by reporting that the oxidation of 2-tetrachlorophtalimide-2-deoxy-1-thio-β-D-glucopyranosides is fully diastereoselective affording the usually favored S_S epimer in 100% diastereomeric excess regardless of the substituent at the sulfinyl sulfur.[18] In the present work, we show that the former assumption is similarly incorrect, and that the sense of the diastereoselective oxidation in favor of the S_S isomer is not general. Indeed, we have found that the stereochemical outcome of the oxidation of β-thioglycosides is the result of a synergetic performance of the *exo*-anomeric effect and the protective group of -OH, which can lead in some case to the usually less favored R_S isomer as a single diastereoisomer.

Results and discussion

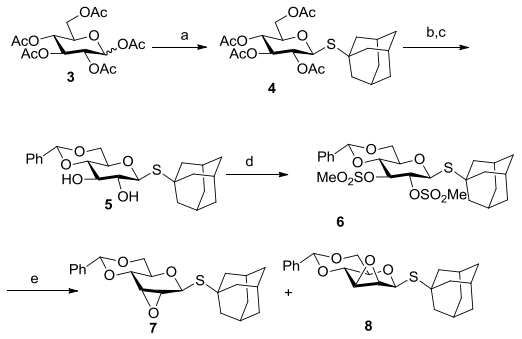
The present research was dictated by the rather surprising stereochemical outcome of the oxidation of fully protected β–thioglycosides with trans 1,2-diequatorial substituents. Indeed, in the stable *exo*-anomeric conformation of the starting thioglycosides, and based only on steric factors, it seems reasonable to think that the R_S diastereoisomer is the kinetically more favored isomer, figure 1. In this sense, the attack on the pro-*S* lone pair must skirt the bulky equatorial C2 substituent, while the attack of the pro-*R* lone pair requires that the oxidant past through a proton at C2 and lone pair ring oxygen, figure 1. Despite this situation, it is usually the *S*-isomer which is obtained as the main product. An analysis of the literature shows that the main diastereoselective oxidations of fully protected β–thioglycosides with trans 1,2-diequatorial substituents (gluco, galacto and xylopyranosides) reported to date have been performed on acylated starting materials.[19] In these cases, an incipient hydrogen bond between the oxidant and the acyl group cannot be ruled out and may be responsible for the observed selectivity. In order to get better insight in the stereochemical outcome of the oxidation, we decided to unravel to exact role played by the substituent at C-2. We choose as model, thioglycosides with different substituent at C2, and with a bulky adamantyl substituent at sulfur in order to lock the reactive conformation in solution in the *exo*-anomeric conformation.

The bulky adamantanethiol acceptor **1**, has been obtained in 80% yield by the treatment of 1-bromoadamantane with thiourea and hydrobromic acid in acetic acid, followed, by the hydrolysis of the adamantyl isotiouronium salt **2** (Scheme 1).[20]



Scheme 1: Synthesis of adamantanethiol **1**. a) HBr, AcOH, b) NaOH, EtOH / H_2O, 80%.

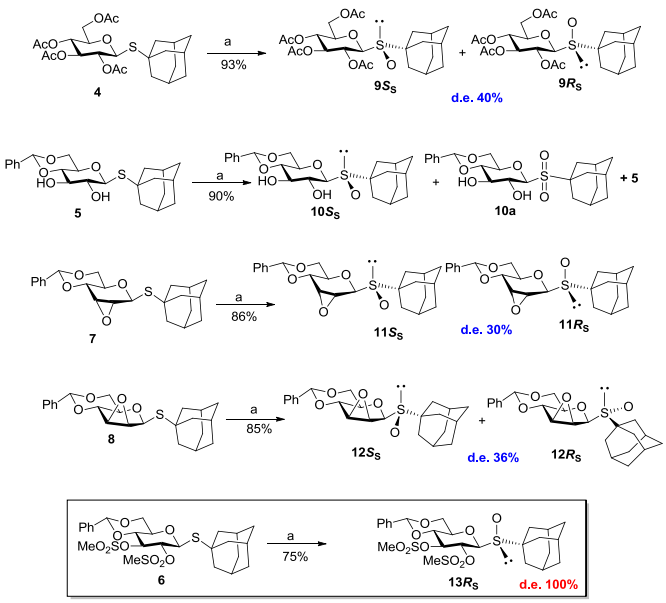
The synthesis of the desired thioglycosides has been performed using our recently developed approach to the synthesis of 2,3-anhydro-β-thioglycoside *in route* to mixed S/P ligand with a phosphine moiety at C2.[21] The first step is a thioglycosylation using the sterically hindered adamatanethiol **1** as glycosyl acceptor, glucose pentaacetate **3** as glycosyl donor, and BF_3Et_2O as activator (Scheme 2). We have recently found that in the case of sterically hindered *tert*-butanethiol the thioglycosilation takes place under thermodynamic control, being the α-thioglycoside the more stable isomer.[22] Similarly, and in order to obtain the kinetic isomer, the reaction was conducted at 0ºC affording the desired product **4** in 70% yield as a white solid.



Scheme 2: Synthesis of bulky β-(D)-adamantyl thioglucopyranosides **4-8**. (a) **1**, CH_2Cl_2, BF_3Et_2O, 0ºC, 70%; (b) MeONa, MeOH, quant.; (c) $PhCH(OMe)_2$, *p*-TsOH, DMF, 50ºC, 90%; (d) MsCl, pyridine, 0ºC-rt, 90%; (e) MeONa, CH_2Cl_2/MeOH, 75%.

A Zemplen deacetylation followed by acid catalyzed benzylidene acetal formation in DMF afforded diol **5** in 90% yield. The double protection of 3,4-diol **5** afforded the dimesylate **6** which, upon treatment with sodium methoxide, afforded the two possible altro- and manno-epoxides **7** and **8** in a 3 : 2 ratio.

The oxidation of compounds **4-8** has been carried out using *m*-CPBA in methylene chloride at -78ºC and was generally stopped immediately after disappearance of the starting thioglycoside (Scheme 3), and the diastereoselection was always determined by ^{1}H NMR analysis of the crude.



Scheme 3: Diastereoselective oxidation of bulky β-(D)-adamantyl thioglucopyranosides **4-8**. a) *m*-CPBA, CH_2Cl_2, -78 ºC.

With no surprise the oxidation of the fully acetylated thioglycoside **4** afforded the corresponding sulfinyl glycosides **9*S*$_S$** and **9*R*$_S$** with modest diastereoselectivity (40%), probably in favor of the S_S as reported. The oxidation of diol **5** in the same conditions afforded a mixture of the corresponding sulfoxide **10*S*$_S$** the sulfone **10a** and the starting material in 9.5 : 1.0 : 1.1 ratio. This result can be rationalized by a high diastereoselection, in favor of the **10*S*$_S$**, due to the hydrogen bond pre-coordination of the *m*-CPBA to the free hydroxyl at position 2 favoring the pro-*S* lone pair attack of the oxidant, together with a kinetic resolution responsible for the overoxidation of the minor isomer to the corresponding sulfone. The oxidation of the altro-epoxide **7** led to a 2:1 mixture of the corresponding sulfoxides **11*S*$_S$** and **11*R*$_S$**. In the case of the manno-epoxide **8**, where the approximation of the oxidant to the pro-*R* lone pair is hampered by the steric hindrance of the epoxide, high diastereoselection in favor of the S_S isomer was expected. Nevertheless, addition of *m*-CPBA to the thioglycoside **8**, leads to the formation of the two epimeric sulfoxides **12*S*$_S$** /**12*R*$_S$** in a modest 36% de. The determination of the absolute configuration of the sulfinyl sulfur of the minor isomer could be confidentially assigned as R_S by the X-ray analysis (see supporting information)[23] which allowed us to conclude that the oxidation of **8** actually favor the formation of the S_S diastereoisomer.

Surprisingly, the oxidation of the dimesylate protected derivative **6** with *m*-CPBA in methylene chloride at -78ºC gave the corresponding sulfoxide **13** in high yield, as a single isomer (Scheme 3) as shown by the analysis of the crude reaction mixture by ^{1}H and ^{13}C NMR (see supporting informations). It is worth to mention that this is the first example of a totally diastereoselective oxidation of a fully protected β–thioglycoside with S/O-*trans* diequatorial dispositions (gluco, galacto and xylo for instance). This result together with our results on the oxidation of imino thioglycosides and on the TCP protected derivatives; indicate that neither the sense nor the degrees of the diastereoselection in the case of β–thioglycosides are general. Owing to the absence of the other epimer at sulfur, we could not apply with confidence our proposed NMR model for the determination of the stereochemistry of the sulfinyl sulfur of **13**. Fortunately, compound **13** is crystalline and we succeeded to prepare a single crystal suitable for X-ray crystallographic analysis (Figure 2).

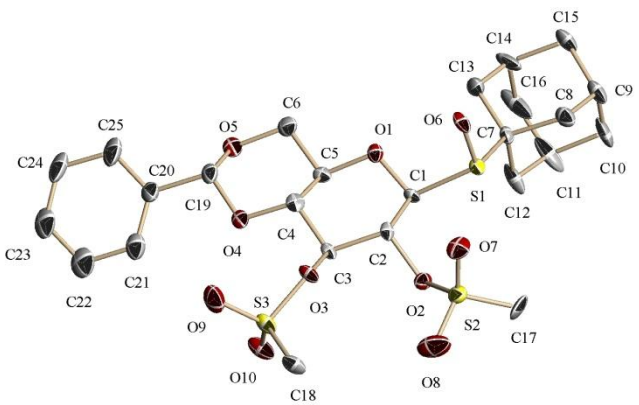


Figure 2: ORTEP drawing of R_S sulfinylglucopyranoside **13*R*$_S$**. Thermal ellipsoids are shown at the 50% probability level. The hydrogen atoms are omitted for clarity.

As it can be seen from figure 2, to the surprise of having a single diastereoisomer add the surprise of the absolute configuration at sulfur which is the unexpected R_S, normally obtained as minor isomer. The molecule adopts the *exo*-anomeric conformation, positioning the bulky adamantly group *anti* to the C1-C2 bond with a dihedral angle with C7-S1-C1-C2 of 172.33º. It is interesting to note that the sulfinyl oxygen and the endocyclic O5 are in *syn* relationship with a dihedral angle O1-C1-S1-O6 of 42.6º, indicative of an unfavorable dipole-dipole interaction. This result, and those reported by Gindley group[24] is pointing out that the dipole-dipole interaction is not essential[16] in determining the stable conformation of sulfinyl glycosides.[25]

On the other hand, it is worth indicating the spatial proximity of the sulfinyl oxygen and the H-2 proton ($d_{O6\text{-}H2}$ = 2.775Aº), which explains the deshielding of this proton in **13** (5.12 ppm), compared to **6** (4.62 ppm), and point out that the *exo*-anomeric conformation is maintained in solution. Additionally, the C1-S1 distance (1.838 Aº) is shorter than that of S_S β-sulfinyl glycosides described to date in the literature, which indicates an important contribution of the n–σ* of the pro-*S* lone pair of the sulfinyl sulfur. Finally, the conformation of the mesyl group is worth of mention, as it places the methyl group in front of the sulfoxide lone pair (Figure 2).

In order to get better insight in this unusual diastereoselective oxidation, we decided to conduct a detailed study on the importance of the mesyl protective group on the stereochemical outcome of the process. Starting from glucose pentaacetate, we synthetize in 4 steps three additional dimesylated sufinyl thioglycosides, **14-16** with substituents at the sulfinyl sulfur with varied steric and electronic nature (Figure 3).

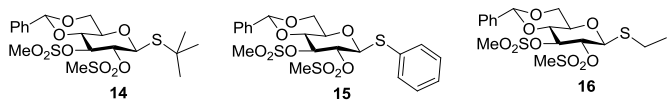
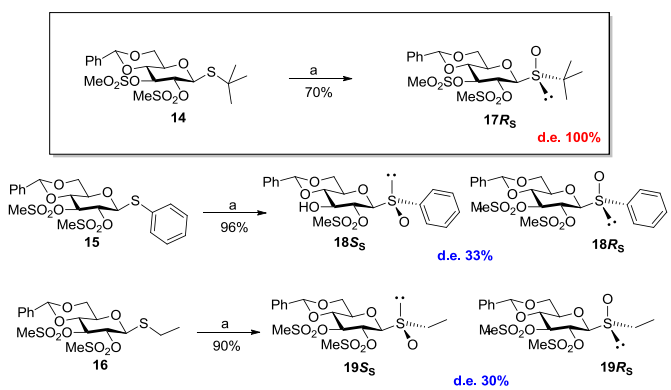


Figure 3: Structure of 2,3-dimesylated β–D-thioglucopyranosides **14-16**.

Subsequently, the oxidation of **14-16** has been carried out as before using *m*-CPBA in methylene chloride at -78ºC until completion, and the diastereoselection of the process determined by ^{1}H NMR analysis of the crude.



Scheme 4: Diastereoselective oxidation of 2,3-dimesylated β–(D)-thioglucopyranosides **14-16**. a) *m*-CPBA, CH_2Cl_2, -78 ºC

Similar to the result obtained in the oxidation of thioglycoside **6** with an adamantyl substituent; the oxidation of thioglycoside **14** with a bulky *tert*-butyl group afforded sulfoxide **17** as a single diastereoisomer (Scheme 4). Taking into account the structural similarity of both thioglycosides, it is legitimate to think that the final sulfoxide has an R_S absolute configuration at the sulfinyl sulfur. In this sense, it is worth pointing out that as in the case of crystallographically determined R_S sulfinylglucoside **13**, there is a large difference in the chemical shift of the H-2 proton between the oxidized sulfoxide **17** (5.18 ppm) and the starting thioglycoside **14** (4.68 ppm). In the case of thioglycoside **15** with a phenyl ring at the sulfur the reaction was slightly diatereoselective affording the two possible diastereoisomer **18*R*$_S$** and **18*S*$_S$** in a 2 : 1 ratio (d.e. 33%). Similarly, the oxidation of thioglycoside **16** with a small ethyl substituent at the sulfinyl sulfur, was also slightly selective affording both distaereoisomers **19*R*$_S$** and **19*S*$_S$** in a 2 : 1 ratio (d.e. 33%). For the determination of the sense of the diastereoselectivity, we need to determine the absolute configuration of the formed diasteroisomers. To do so, we apply our proposed empirical methods based on NMR data for making direct configurational assignments. In the special case of ethyl sulfoxides, the non-equivalence of the diastereotopic protons $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$, vicinal to the sulfoxide group, is larger in the case of R_S sulfoxides than in the case of S_S sulfoxides.[26] Additionally, the chemical shift of anomeric carbon in the sulfoxides with the R_S absolute configuration is more shielded (< 2 ppm) when compared to those with the S_S absolute configurations. This observation has been rationalized by the existence of a major conformation stabilized by the exo-anomeric effect[27] in the case of sulfoxides with the *R* absolute configuration at the sulfinyl sulfur. In this sense, an analysis of the crystal structure of the reported sulfoxides shows that with the exception of compound **12*R*$_S$,** all the sulfoxides with the R_S absolute configuration reported to date crystalize in the *exo*-anomeric conformation.

In the case of ethyl sulfoxides **19**, the chemical shift of the anomeric carbon of the major isomer is 87.2 ppm, and the non-equivalence of the diastereotopic protons $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$ is 189 Hz. Whereas the anomeric carbon of the minor isomer is more deshielded (90.4 ppm), and the splitting of the diastereotopic protons $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$ is smaller (68.0 Hz). These data indicate that the major isomer has an R_S absolute configuration at the sulfinyl sulfur, while the minor isomer has an S_S one. Additionally, we get adequate crystals of the major sulfoxide **19** and we could determine its structure by X-ray crystallography (Figure 4).

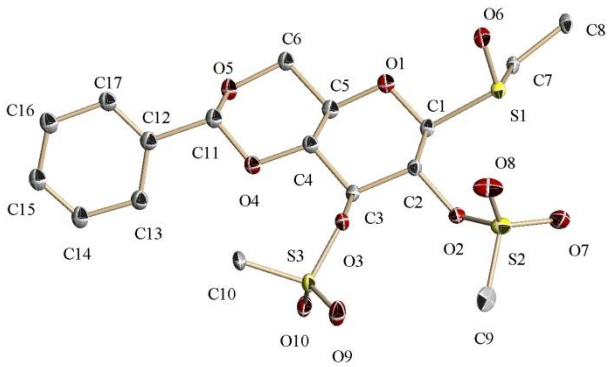


Figure 4: ORTEP drawing of R_S sulfinylglucoside **19*R*$_S$**. Thermal ellipsoids are shown at the 50% probability level. The hydrogen atoms are omitted for clarity.

As can be seen from figure 4, the major sulfoxide **19** has the R_S absolute configuration at the sulfinyl sulfur, confirming once again our direct assignment by NMR analysis. The molecule adopt also the *exo*-anomeric conformation, positioning the ethyl group in anti to the C1-C2 bond with a dihedral angle with C7-S1-C1-C2 of 165.56º. It is interesting to note that the sulfinyl oxygen and the endocyclic O1 are in *syn* relationship with a dihedral angle O1-C1-S1-O6 of 42.6º, indicative of an unfavorable dipole-dipole interaction. Taking into account that the sulfinyl oxygen is also in a *syn* disposition with carbon 2 (dihedral angle O1-S1-C1-C2 = -85.29º), it can be concluded that the sulfur lone pair is an *anti* disposition with the endocyclic oxygen, well disposed to establish n–σ* interaction with the C-O1 bond. In this sense it is important to remark that in this case also the C_1-S_1 bond is shorter (d_{C1-S1} = 1.844 Aº) than those reported for S_S sulfoxides (d_{C1-S1} = 1.886 Aº), indicative of an important contribution of the n–σ* of the pro-*S* lone pair of the sulfinyl sulfur and explaining the shielding of the anomeric carbon in R_S sulfinylglycosides. On the other hand, the *exo*-anomeric conformation seems to be mayor also in solution as indicated by the chemical shift of H-2 of the mayor isomer **19*R*$_S$** (5.18 ppm) compared with the minor **19*S*$_S$** (4.83 ppm) and the starting thioglycoside **15** (4.89 ppm). Interestingly, the methyl of the mesyl group is directed toward the C-3 of the pyranose ring instead of the lone pair of the sulfur atom as in the case of **13*R*$_S$**.

Possible origin of the diastereoselectivity:
From the reported data, it is clear that neither the *exo*-anomeric effect alone, nor the mesyl substituent are responsible for the observed stereochemical outcome of the process, and that indeed the high diastereoselectivity observed is the result of a synergetic effect of both. In this sense, if we consider the rotamers around the glycosidic bound in thioglycosides (Figure 5), there are three staggered conformation: the *exo*-anomeric conformations (A) and (B) and the non *exo*-conformation (C), being the conformation (A) the most stable one.

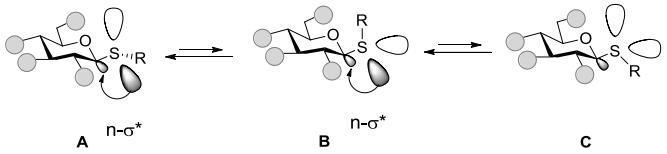


Figure 5: Staggered rotamers around the glycosidic bond in thioglycosides

In agreement with Vazquez's conclusions,[28] NMR (NOE) studies conducted on compounds **6** and **16**, showed that while thioglycoside **6** with the adamantyl group is rigid and mainly exists in the *exo*-anomeric conformation (A), thioglycoside **16** with an ethyl group, is more flexible, and the *exo*-conformation (B) (Figure 5), is also involved in the conformational equilibrium.[29] Based on these data, we can conclude that the diastereoselective oxidation of β–thioglycosides is the result of a fine balance between steric and stereoelectonic effect where the *exo*-anomeric effect plays a prominent role. In the case of thioglycosides with a bulky aglycone the *exo*-anomeric effect lock the reactive conformation in the exo-anomeric conformation (A), and paves the way for a high diastereselectivity by allowing the mesyl group to shield the approximation of the peracid to pro-(S) lone pair of the sulfur (Figure 6).[30]

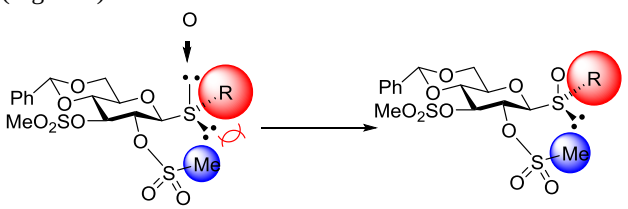


Figure 6. Plausible origin of the high diastereoselctive oxidation of bulky thioglycosides.

CONCLUSIONS

Following on our previous studies on the oxidation of thioglycosides, in the present work we have reported the first totally diastereoselective process in the oxidation of β–thioglucosides. The results reported here demonstrate that neither the sense (usually the major isomer has an *S* absolute configuration at sulfur) nor the magnitude (low diastereselectivity) of the oxidation of β–thioglycosides are general features. In this sense, the mesylation of the C2-OH, allows the formation of the sulfinyl glycoside with R_S absolute configuration at sulfur as the major isomer. Significantly, it was found that in the case of thioglycosides with a bulky aglycone, the mesylation of C2-OH has a dramatic effect on the stereochemical outcome of the oxidation, affording the usually less favoured R_S sulfoxide as a single diastereoisomer. The absolute configuration of the obtained sulfinyl glycosides was ascertained by NMR analysis and corroborated by X-ray

crystallography. The results reported here shed some light on the diastereoselctive oxidation of β–D-thioglycosides, and will help in the design of diastereopure sulfinyl glycosides and their application in asymmetric synthesis either as a chiral auxiliaries or chiral ligands.

Experimental

General Methods.

All reactions were run under an atmosphere of dry argon using oven-dried glassware and freshly distilled dried solvents. THF and diethyl ether were distilled from sodium benzophenone ketyl. Dichloromethane and toluene were distilled from calcium hydride. TLC was performed on Silica Gel GF254 (Merck) with detection by charring with phosphomolybdic acid/EtOH. For flash chromatography, silica Gel (Merck 230-400 mesh) was used. Columns were eluted with positive air pressure. Chromatographic eluents are given as volume to volume ratios (v/v). NMR spectra were recorded with a Bruker Avance DPX300 (1H, 300 MHz) and Bruker Avance DRX500 (1H, 500 MHz) spectrometers. Chemical shifts are reported in ppm, and coupling constants are reported in Hz. Routine spectra were referenced to the residual proton or carbon signals of the solvent. High-resolution mass spectra were recorded on a Kratos MS-80RFA 241-MC apparatus. The organic extracts were dried over anhydrous sodium sulfate and concentrated in vacuum.

1-Adamantanethiol, (1). To a suspension of 1-bromoadamantane (10.7g, 0.05 mol), and thiourea (7.6g, 0.10 mol), in glacial acetic acid (50 mL) was added 25 mL of 48% hydrobromic acid, and the mixture was refluxed (115ºC) under argon atmosphere. After 4 h, the solution was allowed to cool to room temperature overnight. The obtained 1-adamantyl isothiuronium salt 2 was filtered and hydrolyzed by stirring in a solution of 10 g of NaOH (10g, 0.25 mole), in water (200 mL) and ethanol (75 mL) during 48 h. The resulting solution was acidified using 1 mM HCl, and extracted successively with chloroform methylene chloride and hexanes. The organic extracts were dried over anhydrous Na_2SO_4, filtred and evaporated under argon, affording 1-adamantanethiol 1 (6.8g, 80%) as a white solid. m.p. 100-102 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.03 (s, 3H), 1.94 (s, 6H), 1.67 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 47.5, 43.1, 35.8, 30.1

Adamantyl 2,3,4,6-tetra-*O*-acetyl-1-thio-*β*-D-glucopyranoside, (4). To a 1M solution of β–D-glucose pentaacetate **3** (10g, 25 mmol**)** in anhydrous methylene chloride (25 mL) was added 1-adamantanethiol **1** (5.0 g, 29 mmol) in methylene chloride (10 mL), followed by boron trifluoride etherate (14 mL, 100 mmol) at 0ºC. The reaction was followed by TLC and stopped once the starting material consumed (usually 0.5 to 1h) by addition of saturated aqueous sodium bicarbonate ($NaHCO_3$). The aqueous layer was extracted three times with methylene chloride, and the combined organic layers washed with brine and dried over anhydrous sodium sulfate. After concentration under vacuum, the crude mixture was purified by column chromatography (EtOAc : Hexanes, 2:3), affording 4 as a white solid (8 g, 64%). m.p. 136.5-138.7 ºC. $[\alpha]_D$ = +2.2 (c. 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.27 (t, 1H, *J* = 9.3 Hz), 5.05 (t, 1H, *J* = 9.7 Hz), 4.96 (t, 1H, *J* = 9.7 Hz), 4.72 (d, 1H, *J* = 10.2 Hz), 4.21 (dd, 1H, *J* = 12.2 and *J* = 6.2 Hz), 4.13 (dd, 1H, *J* = 12.2 and *J* = 2.3 Hz), 3.77-3.74 (m, 1H), 2.07 (s, 6H), 2.06 (s, 3H), 2.05 (s, 3H), 2.02-1.69 (m, 15 H).^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.6, 170.2, 169.4, 169.3, 80.0, 75.4, 74.0, 70.1, 68.6, 62.6, 46.4, 43.9, 36.1, 29.7, 20.8, 20.6, 20.6, 20.6. HRMS Calcd. for $C_{24}H_{34}O_9NaS$: 521.1821 [M + Na]. Found: 521.1828 (+1.3 ppm.).

Adamantyl 4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside (5). To a 0.1M suspension of **4** (2.9 g, 5.80 mmol) in dry methanol was added a catalytic amount of freshly prepared 1M MeONa solution in MeOH (0.1 equiv.). The solution was stirred at room temperature until total consumption of the starting material (1 h), then neutralized with acidic resin (Amberlyst IR 120), filtered and evaporated affording adamantyl 1-thioglucopyranoside as a white solid, which was used in the next step without further purification.

To a solution of the obtained crude in DMF (50 mL) was added benzaldehyde dimethyl acetal (2.1 mL, 13.90 mmol), followed by catalytic amount of *p*-toluenesulfonic acid. The mixture was stirred at 50 ºC for 4 hrs, and then the DMF was evaporated under vacuum. The crude mixture obtained was purified by column chromatography (EtOAc : Hexanes, 1:1) affording 5 (2g, 82% for the two steps) as a white solid. m.p.: 97-99 ºC. $[\alpha]_D$ = 26.9 (c. 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ : 7.47-7.46 (m, 2H), 7.34-7.33 (m, 3H), 5.50 (s, 1H), 4.60 (d, 1H, *J* = 10.0 Hz), 4.29 (dd, 1H, *J* = 10.6 and *J* = 4.9 Hz), 3.82 (t, 1H, *J* = 8.7 Hz), 3.74 (t, 1H, *J* = 9.3 Hz), 3.56-3.47 (m, 2H), 3.38 (t, 1H, *J* = 9.1 Hz), 2.97 (brs, 1H), 2.67(brs, 1H), 2.06-1.66 (m, 15H). ^{13}C NMR (125MHz, CDCl3) δ: 137.0, 129.2, 128.23 126.3 , 102.0, 82.6, 80.3, 74.4, 73.2, 70.3, 68.7, 46.8, 44.1, 36.0, 29.7. HRMS Calcd. for $C_{23}H_{30}O_5NaS$: 441.1712 [M + Na]. Found: 441.1699 (-2,9 ppm.).

Adamantyl 4,6-*O*-benzylidene-2,3-di-*O*-methanesulfonyl-1-thio-*β*-D-glucopyranoside (6). To a solution of **5** (2 g, 4.78 mmol) in pyridine (15 mL) was added at 0ºC methanesulfonyl chloride (2.07 g, 18.07 mmol). After stirring at room temperature for 24 hrs, the reaction was stopped by addition of water, extracted with methylene chloride, and the organic layer dried under Na_2SO_4. After evaporation of the solvent, the crude solid was recrystallized with acetone/methanol, affording **6** (2.2 g, 80%) as a yellowish solid. m.p.: 85-87 ºC. $[\alpha]_D$ = -8.4 (c. 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.45-7.43 (m, 2H), 7.35-7.33 (m, 3H), 5.53 (s, 1H), 4.91 (t, 1H, *J* = 9.2 Hz), 4.77 (d, 1H, *J* = 10.3 Hz), 4.62 (t, 1H, *J* = 9.3 Hz), 4.34 (dd, 1H, *J* = 10.6 and *J* = 5.1 Hz), 3.78-3.71 (m, 2H, H-4), 3.58-3.53 (m, 1H), 3.23 (s, 3H), 3.01 (s, 3H), 2.06-1.66 (m, 15H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 136.2, 129.5, 128.5 126.1, 101.8, 81.0, 80.7, 78.3, 77.6, 70.1, 68.4, 47.4, 43.9, 40.5, 39.4, 36.0, 29.8. HRMS Calcd. for $C_{25}H_{34}O_9NaS_3$: 597.1263 [M + Na]. Found: 597.1246 (-2.8 ppm.).

Adamantyl 4,6-*O*-benzylidene-2,3-anhydro-1-thio-*β*-D-allo- and manopyranosides, 7 and 8. To a solution of **6** (200 mg, 0.35 mmol) in a 2 : 1 mixture CH_2Cl_2 : MeOH (3 mL) was added MeONa (200 mg, 3.70 mmol) at room temperature. After stirring overnight, the reaction was stopped by addition of water (3 mL), and the aqueous phase extracted with CH_2Cl_2, and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (EtOAc : Hexanes, 1 : 8) affording the desired epoxides (90 mg, 64%) **7** and **8** in a 2 : 1 ratio.

Adamantyl 2,3-anhydro-4,6-*O*-benzylidene-1-thio-*β*-D-allopyranoside (7). White solid. m.p.: 136-138. $[\alpha]_D^{20}$: -14.0 (c. 1.0, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.50-7.48 (m, 2H), 7.36-7.34 (m, 3H), 5.55 (s, 1H), 5.33 (s, 1H), 4.20 (dd, 1H, *J* = 10.1, *J* = 4.7 Hz), 4.08 (d, 1H, *J* = 8.9 Hz), 3.85-3.80 (m, 1H), 4.70 (t, 1H, *J* = 10.4 Hz), 3.54-3.49 (m, 2H), 2.06-1.66 (m, 15H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 137.0, 129.2, 128.3 126.3, 102.6, 77.3, 75.4, 68.9, 64.9, 64.2, 57.4, 47.1, 44.0, 36.1, 29.7. HRMS Calcd. for: $C_{23}H_{28}O_4NaS$: 423.1606 $[M + Na]^+$. Found: 423.1607 (+0.2 ppm.).

Adamantyl 2,3-anhydro-4,6-*O*-benzylidene-1-thio-*β*-D-manopyranoside (8). White solid. m.p. : 170-173ºC. $[\alpha]_D^{20}$: -3,3 (c 1.0, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.48-7.47 (m, 2H), 7.37-7.35 (m, 3H), 5.53 (s, 1H), 5.25 (s, 1H), 4.25 (dd, 1H, *J* = 10.4, *J* = 4.5 Hz, H-6), 3.78-3.7 (m, 2H), 4.49 (d, 1H, *J* = 3.5 Hz), 3.36-3.31 (m, 1H), 3.27 (d, 1H, *J* = 3.5 Hz), 2.06-1.66 (m, 15H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 137.0, 129.2, 128.3 126.1, 102.6, 76.3, 74.6, 70.4, 69.3, 55.5, 53.3, 46.0, 44.0, 36.1, 29.7. HRMS Calcd. for: $C_{23}H_{28}O_4NaS$: 423.1606 $[M + Na]^+$. Found: 423.1598 (-1.90 ppm.).

General procedure for the diastereoselective oxidation of thioglycosides.

To a solution of the parent thioglycoside (1mmol), in CH_2Cl_2 (20 mL), was added a solution of 70% of *m*-CPBA (1.05mmol) in CH_2Cl_2 (2 ml) at -78ºC. The reaction is instantaneous, and stopped after 15 min by addition of saturated sodium sulfite and diluted with CH_2Cl_2. The organic layer was washed with $NaHCO_3$, the aqueous layer was further extracted with CH_2Cl_2 (4 x 50ml), the organic layer was washed with brine, dried (Na_2SO_4), and evaporated. After analyzing the diastereomeric excess by ^{1}HNMR, the crude mixture was purified by flash column chromatography affording pure diasteromeric sulfinyl glycosides.

(R_S) and (S_S) Adamantyl 2,3,4,6-tetra-*O*-acetyl-1-thio-*β*-D-glucopyranoside S-oxides (9R_S and 9S_S). Starting from compound **4** (316 mg, 0.63 mmol) and following the general procedure for the oxidation of the thioglycosides, the obtained sulfinylglycosides were purified by column chromatography (EtOAc : Hexanes, 1 : 1) affording **9S_S** and **9R_S** (93%) in a 70 : 30 ratio.

(S_S) Adamantyl 2,3,4,6-tetra-*O*-acetyl-1-thio-*β*-D-glucopyranoside S-oxide (9S_S): white solid m.p.: 172 ºC. $[\alpha]_D$ = - 55.1 (c. 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.44 (t, 1H, *J* = 9.5 Hz), 5.32 (t, 1H, *J* = 9.4 Hz), 5.06 (t, 1H, *J* = 9.8 Hz), 4.39 (d, 1H, *J* = 10.1 Hz), 4.22 (d, 1H, *J* = 12.0 Hz), 4.15 (dd, 1H, *J* = 12.3 and *J* = 6.7 Hz), 3.83 (t, 1H, *J* = 8.2 Hz), 2.17 (s, 3H), 2.76-2.00 (m, 15H), 1.94 (d, 3H, *J* = 11.8 H), 1.76 (m, 6H); ^{13}C NMR (CDCl3, 100 MHz) δ 170.5, 170.4, 169.2, 168.7, 84.3, 76.7, 73.8, 68.0, 67.2, 62.7, 58.3, 36.3, 36.2, 28.8, 20.6, 20.6, 20.5, 20,5. MS (ESI): $[M + Na]^+$ *m/z* 537.3.

(R_S) Adamantyl 2,3,4,6-tetra-*O*-acetyl-1-thio-*β*-D-glucopyranoside S-oxide (9R_S): white solid. m.p.: 94-97 ºC. $[\alpha]_D$ = + 24.1 (c. 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.56 (t, 1H, *J* = 9.3 Hz), 5.27 (t, 1H, *J* = 9.1 Hz), 5.08 (t, 1H, *J* = 9.7 Hz), 4.46 (d, 1H, *J* = 9.6 Hz), 4.16 (d, 2H, *J* = 3.8 Hz), 3.76 (dt, 1H, *J* = 9.6 and *J* = 3.9 Hz), 2.18 (s, 3H), 2.06 (s, 3H), 2.04 (s, 3H), 2.02 (s, 6H), 1.93 (s, 6H), 1.76 (m, 6H); ^{13}C NMR (CDCl3, 100 MHz) δ 170.4, 170.3, 169.3, 169.3, 84.5, 76.3, 73.8, 68.6, 67.7, 62.0, 58.0, 36.2, 35.2, 28.8, 20.7, 20.6, 20.6, 20,5. MS (ESI): $[M + Na]^+$ *m/z* 537.3.

(S_S) Adamantyl 4,6-*O*-benzylidene-1thio-*β*-D-glucopyranoside S-oxide (10S_S). Starting from compound **5** (100mg, 0.25 mmol) and following the general procedure the oxidation of thioglycosides, afforded a crude mixture whose ^{1}HNMR analysis shows the presence of the sulfone **10a**, starting thioglycoside **5** and **10S_S** in 1.1:1.0:9.5 ratio. The crude mixture was purified by flash column chromatography (EtOAc/Hex, 1:1) affording diastereomerically pure **10S_S** (73%) as a white solid. m.p.: 123 ºC. $[\alpha]_D$ = - 6.7 (c 0.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.50 (m, 2H), 7.40-7.37 (m, 3H), 5.58 (s, 1H), 4.48 (d, 1H, *J* = 9.6 Hz), 4.30 (dd, 1H, *J* = 10.4 and *J* = 4.8 Hz), 4.22 (dd, 1H, *J* = 9.5 and *J* = 8.5 Hz), 3.97 (dd, 1H, *J* = 9.2 and *J* = 8.5 Hz), 3.77 (t, 1H, *J* = 10.2 Hz), 3.68 (t, 1H, *J* = 9.3 Hz), 3.6 (dt, 1H, *J* = 9.6 and *J* = 8.5 Hz), 2.25 (brs, 3H), 1.98-1.76 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz,) δ: 136.7, 129.3, 128.3, 126.3, 102.0, 82.9, 79.5, 74.0, 72.4, 70.7, 68.2, 57.0, 36.2, 34.9, 28.5. MS (ESI): $[M + Na]^+$ *m/z* 457.3.

Adamantyl 4,6-*O*-benzylidene-1thio-*β*-D-glucopyranoside S-dioxide (10a). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.46 (m, 2H), 7.38-7.35 (m, 3H), 5.56 (s, 1H), 4.67 (d, 1H, *J* = 9.4 Hz), 4.31 (dd, 1H, *J* = 10.4 and *J* = 5.0 Hz), 4.23 (t, 1H, *J* = 8.9 Hz), 3.93 (t, 1H, *J* = 8.9 Hz), 3.84 (t, 1H, *J* = 10.3 Hz), 3.67 (t, 1H, *J* = 9.4 Hz), 3.59 (dt, 1H, *J* = 9.4 and *J* = 4.6 Hz), 2.21 (brs, 3H), 2.15-2.05 (m, 6H), 1.81-1.70 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz,) δ: 136.6, 129.4, 128.3, 126.3, 102.0, 86.0, 78.6, 74.2, 70.4, 69.2, 68.1, 63.4, 35.7, 34.9, 28.2. MS (ESI): $[M + Na]^+$ *m/z* 473.3.

(R_S) and (S_S) Adamantyl 2,3-anhydro-4,6-*O*-benzylidene-1-thio-*β*-D-allopyranoside S-oxide (11R_S and 11S_S)

Starting from compound **7** (100mg, 0.25 mmol) and following the general procedure the oxidation of thioglycosides, the obtained sulfinylglycosides were purified by column chromatography (EtOAc : Hexanes, 2 : 1) affording **11*R*** and **11*S*** (90 mg, 86%) in a 1 : 2 ratio.

Major isomer. $[\alpha]_D^{20}$: -54,1 (c 1.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.47-7.45 (m, 2H), 7.37-7.32 (m, 3H), 5.56 (s, 1H), 5.08 (s, 1H), 4.34 (d, 1H, *J* = 8.8 Hz), 4.18 (dd, 1H, *J* = 10.0, *J* = 4.6 Hz), 4.06-4.01 (m, 1H), 3.80 (t, 1H, *J* = 10.3 Hz), 3.70-3.64(m, 2H), 2.01-1.68 (m, 15H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 136.9, 129.2, 128.3, 126.2 , 102.5, 81.2 , 76.5, 68.5, 64.5, 58.3, 54.4 , 51.3, 36.1, 36.1, 28.8. HRMS Calcd. for:

$C_{23}H_{28}O_4NaS$: 439.1555 [M + Na]$^+$. Found: 439.1540 (-3.5 ppm.).

Menor isomer. [α]$_D^{20}$: +23.1 (c 1.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.49-7.47 (m, 2H), 7.37-7.33 (m, 3H), 5.56 (s, 1H), 4.96 (s, 1H), 4.20 (dd, 1H, *J* = 9.8 Hz, *J* = 5.1 Hz), 4.13 (d, 1H, *J* = 9.2 Hz), 3.98-3.90 (m, 2H), 3.68-3.62(m, 2H), 2.18-1.71 (m, 15H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 136.8, 129.31, 128.3, 126.20, 102.7, 81.3, 77.0, 68.5, 64.6, 57.4, 52.8, 51.6, 36.2, 35.3, 28.7. HRMS Calcd. for: $C_{23}H_{28}O_4NaS$: 439.1555 [M + Na]$^+$. Found: 439.1541 (-3.2 ppm.).

(*R*$_S$) and (*S*$_S$) Adamantyl 2,3-anhydro-4,6-*O*-benzylidene-1-thio-*β*-D-manopyranoside S-oxides (12*R*$_S$ and 12*S*$_S$)

Starting from compound **7** (149mg, 0.37 mmol) and following the general procedure the oxidation of thioglycosides, the obtained sulfinylglycosides were purified by column chromatography (EtOAc : Hexanes, 2 : 1) affording **12*S*$_S$** and **12*R*$_S$** (85%) in a 68 : 32 ratio.

(*S*$_S$)-Adamantyl 2,3-anhydro-4,6-*O*-benzylidene-1-thio-*β*-D-manopyranoside S-oxide (12*S*$_S$). White solid. m.p. : 169-171ºC. [α]$_D$ = + 76.2 (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.46 (m, 2H), 7.42-7.37 (m, 3H), 5.58 (s, 1H), 4.93 (s, 1H), 4.27 (dd, 1H, *J* = 10.5 and *J* = 4.6 Hz), 3.80-3.66 (m, 4H), 3.37 (dt, 1H, *J* = 9.7 Hz and *J* = 4.6 Hz), 2.19 (s, 3H), 2.02-1.91 (m, 6H), 1.85-1.70 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.6, 129.4, 128.4, 126.1, 102.6, 84.7, 74.7, 70.4, 68.9, 56.7, 55.3, 49.4, 36.3, 35.2, 28.8. MS (ESI): [M + Na] $^+$ *m/z* 439.3.

(*R*$_S$) Adamantyl 2,3-anhydro-4,6-*O*-benzylidene-1-thio-*β*-D-manopyranoside S-oxide (12*R*$_S$). [α]$_D$ = + 29.4 (c 0.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.46 (m, 2H), 7.42-7.36 (m, 3H), 5.59 (s, 1H), 4.84 (s, 1H), 4.36 (dd, 1H, *J* = 10.6 and *J* = 4.7 Hz), 3.90-3.83 (m, 2H), 3.61 (d, 1H, *J* = 3.8 Hz) 3.46 (d, 1H, *J* = 3.8 Hz), 3.42 (dt, 1H, *J* = 10.0 Hz y *J* = 5.0 Hz), 2.20 (s, 3H), 2.07-1.96 (m, 6H), 1.84-1.72 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.7, 129.3, 128.4, 126.1, 102.4, 83.9, 74.4, 70.3, 69.1, 57.9, 54.5, 49.5, 36.2, 35.9, 28.8. MS (ESI): [M + Na] $^+$ *m/z* 439.3.

For crystallographic data see supporting information.

(*R*$_S$) Adamantyl 4,6-*O*-benzylidene-2,3-di-*O*-methanesulfonyl-1thio-*β*-D-glucopyranoside S-oxide (13*R*$_S$)

Starting from compound **6** (500mg, 0.87 mmol) and following the general procedure of the oxidation of thioglycosides, afforded the corresponding sulfoxide as a single isomer. After column chromatography compound **13*R*$_S$** (380 mg, 75%) was obtained as a white solid. m.p. : 123.0-128.5 ºC. [α]$_D^{20}$: -64.6 (c 1.0, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.45-7.42 (m, 2H), 7.35-7.33 (m, 3H), 5.52 (s, 1H), 5.16 (t, 1H, *J* = 9.5 Hz), 4.99 (t, 1H, *J* = 9.5 Hz), 4.44 (d, 1H, *J* = 9.7 Hz), 4.32 (dd, 1H, *J* = 10.8 Hz, *J* = 5.0 Hz), 3.89-3.81 (m, 2H), 3.69-3.64 (m, 1H), 3.22 (s, 3H), 3.00 (s, 3H), 2.16-1.69 (m, 15H).^{13}C-NMR (100 MHz, $CDCl_3$) δ: 136.0, 129.4, 128.4, 126.0 , 101.7, 84.6 , 80.3, 77.3, 74.1, 70.6, 67.9, 58.7 , 39.9, 39.2, 36.2, 36.0, 28.7. HRMS Calcd. for: $C_{23}H_{28}O_4NaS$: $C_{25}H_{34}O_{10}NaS_3$ 613.1212 [M + Na]$^+$. Found: 613.1240 (+4.6 ppm.).

For crystallographic data see supporting information.

***tert*-Butyl 4,6-*O*-benzylidene-2,3-di-*O*-methanesulfonyl-1-thio-*β*-D-glucopyranoside (14)**

To a solution of *tert*-Butyl 4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside[21] (3.1g, 9.10 mmoles) in pyridine (20 mL) was added at 0ºC methanesulfonyl chloride (3.13g, 27.4 mmol). After stirring at room temperature for 24 hrs, the reaction was stopped by addition of water, extracted with methylene chloride, and the organic layer dried under Na_2SO_4. After evaporation of the solvent, the crude solid was recrystallized with acetone/methanol, affording **14** (3.5g, 7.10 mmol, 77%) as a white solid. m.p.: 101-104 ºC. [α]$_D$ = +27.2 (c. 10.6, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.46 (m, 2H), 7.37 (m, 3H), 5.55 (s, 1H), 4.93 (t, 1H, *J* = 8.8 Hz), 4.72 (d, 1H, *J* = 9.9 Hz), 4.64 (t, 1H, *J* = 8.7 Hz), 4.37-4.34 (m, 1H), 3.80-3.74 (m, 2H, H-6´), 3.59-3.55 (m, 1H), 3.23 (s, 3H), 3.02 (s, 1H), 1.39 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 136.2, 129.5, 128.5, 126.1, 101.8, 83.3, 80.6, 78.3, 77.6, 70.2, 68.4, 45.2, 40.4, 39.3, 31.4.

Phenyl 4,6-*O*-benzylidene-2,3-di-*O*-methanesulfonyl-1-thio-*β*-D-glucopyranoside (15)

To a solution of phenyl 4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside,[31] (223 mg, 0.62 mmol) in pyridine (5 mL) was added dropwise methanesulfonyl chloride (180 μl, 2.36 mmol) at 0 °C. After 2 h, the reaction was stopped by addition of water and the solution was extracted three times with CH_2Cl_2. The organic layer was washed with brine, dried (Na_2SO_4) and coevaporated with toluene. The crude mixture was purified by flash column chromatography (EtOAc/Hex, 3:7) affording **15** (250 mg, 78% yield) as a white solid: m.p.: 95-97 ºC. [α]$_D$ = - 47.5 (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.57 (m, 2H), 7.47-7.42 (m, 2H), 7.39-7.33 (m, 6H), 5.55 (s, 1H), 4.91 (t, 1H, *J* = 9.0 Hz), 4.81-4.71 (m, 2H), 4.42 (dd, 1H, *J* = 10.6 and *J* = 5.0 Hz), 3.80 (t, 1H, *J* = 10.4 Hz), 3.74 (t, 1H, *J* = 9.7 Hz), 3.55 (dt, 1H, *J* = 9.5 and 5.2 Hz), 3.30 (s, 3H), 3.00 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.0, 133.5, 131.3, 129.6, 129.2, 128.9, 128.5, 126.0, 101.9, 87.5, 80.6, 78.2, 70.2, 68.2, 40.3, 39.3. HRMS Calcd. For $C_{19}H_{28}O_{10}NaS_3$: 535.0742 [M + Na]$^+$. Found: 535.0748 (+1.1 ppm.).

Ethyl 4,6-*O*-benzylidene-2,3-di-*O*-methanesulfonyl-1-thio-*β*-D-glucopyranoside (16).

To a solution of ethyl 4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside,[32] (1.84 g, 5.90 mmol) in pyridine (7 mL) was added at 0ºC methanesulfonyl chloride (2.57 g, 22.40 mmol). After stirring at room temperature for 2 hrs, the reaction was stopped by addition of water, extracted with methylene chloride, and the organic layer dried under Na_2SO_4. After evaporation of the solvent, the crude mixture was purified by flash column chromatography (EtOAc/Hex, 4:6) affording **16** (2.2 g, 79%) as a white solid. [α]$_D$ = -33.8 (c. 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.46-7.42 (m, 2H), 7.36-7.34 (m, 3H), 5.54 (s, 1H), 4.89 (t, 1H, *J* = 9.7 Hz), 4.70 (t, 1H, *J* = 8.9 Hz), 4.60 (d, 1H, *J* = 9.7 Hz), 4.40 (dd, 1H, *J* = 10.5 Hz, *J* = 4.7 Hz), 3.80-3.72 (m, 2H), 3.59-3.51 (m, 1H), 3.24 (s, 3H), 3.01 (s, 3H), 2.77(c, 2H, *J* = 7.1 Hz), 1.30 (t, 3H, *J* = 7.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 136.2, 129.5, 128.5 126.1,

101.8, 84.3, 80.5, 78.4, 77.4 , 70.4, 68.3, 40.2, 39.3, 24.6, 14.7. HRMS Calcd. for $C_{15}H_{24}O_9NaS_3$: 491.0480 $[M + Na]^+$. Found: 491.0486 (+1.2 ppm).

(R_S)-*tert*-Butyl 4,6-*O*-benzylidene-2,3-di-*O*-methanesulfonyl-1-thio-*β*-D-glucopyranoside (17R_S).

Starting from compound **15** (100mg, 0.20 mmol) and following the general procedure of the oxidation of thioglycosides, afforded the corresponding sulfoxide as a single isomer. After column chromatography compound **17R_S** (44.8 mg, 70%) was obtained as a white solid. m.p. : 123.0-128.5 ºC. $[\alpha]_D^{20}$: -5.4 (c 1.0, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.45-7.43 (m, 2H), 7.37-7.35 (m, 3H), 5.54 (s, 1H), 5.18 (t, 1H, *J* = 9 Hz), 5.00 (t, 1H, *J* = 9Hz), 4.39-4.34 (m, 2H), 3.91 (t, 1H, *J* = 10.5 Hz), 3.85 (t, 1H, *J* = 9.5 Hz), 3.68-3.65 (m, 1H), 3.26 (s, 3H), 3.02 (s, 3H), 1.35 (s, 9H).^{13}C-NMR (125 MHz, $CDCl_3$) δ: 135.9, 129.5, 128.4, 126.0, 101.9, 85.8, 80.3, 77.3, 74.1, 70.8, 67.8, 56.5, 39.9, 39.2, 24.2. HRMS Calcd. For $C_{19}H_{28}O_{10}NaS_3$: 535.0742 $[M + Na]^+$. Found: 535.0748 (+1.1 ppm).

(R_S) and (S_S) Phenyl 4,6-*O*-benzylidene-2,3-di-*O*-methanesulfonyl-1-thio-*β*-D-glucopyranoside S-oxides (18R_S and 18S_S).

Starting from compound **15** (170mg, 0.33 mmol) and following the general procedure the oxidation of the thioglycosides, the obtained sulfinylglycosides were purified by column chromatography (EtOAc : Hexanes, 2 : 3) affording **18R_S** and **18$_S$** (96% yield) in a 65:35 ratio.

Major isomer (More polar). White solid. m.p.: 115-117 ºC. $[\alpha]_D$ = -111.7 (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.65 (m, 2H), 7.57-7.52 (m, 3H), 7.43-7.39 (m, 2H), 7.37-7.33 (m, 3H), 5.52 (s, 1H), 5.24 (dd, 1H, *J* = 9.5 and *J* = 8.9 Hz), 5.01 (dd, 1H, *J* = 9.7 and *J* = 8.9 Hz), 4.18 (d, 1H, *J* = 9.6 Hz), 4.11 (dd, 1H, *J* = 10.7 and *J* = 5.1 Hz), 3.83 (t, 1H, *J* = 9.6 Hz), 3.79 (t, 1H, *J* = 10.3 Hz), 3.43 (dt, 1H, *J* = 9.7 and 5.0 Hz), 3.35 (s, 3H), 3.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.6, 135.9, 131.8, 129.6, 129.1, 128.5, 126.0, 125.3, 101.9, 91.7, 80.3, 77.5, 74.0, 70.7, 67.6, 39.9, 39.2. MS (ESI): $[M + Na]^+$ *m/z* 555.2.

Minor isomer (less polar). White solid: m.p.: 126-128 ºC. $[\alpha]_D$ = -34.9 (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.82 (m, 2H), 7.60-7.53 (m, 3H), 7.42-7.38 (m, 2H), 7.37-7.33 (m, 3H), 5.44 (s, 1H), 4.94 (dd, 1H, *J* = 9.7 and *J* = 8.4 Hz), 4.74 (dd, 1H, *J* = 9.7 and *J* = 8.4 Hz), 4.59 (d, 1H, *J* = 9.8 Hz), 4.38-4.34 (m, 1H), 3.61-3.51 (m, 2H), 3.46 (t, 1H, *J* = 9.4 Hz), 3.33 (s, 3H), 3.00 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.7, 135.8, 132.4, 129.6, 128.9, 128.5, 126.9, 126.0, 101.8, 92.5, 80.0, 77.6, 74.1, 70.3, 67.7, 39.9, 39.2. MS (ESI): $[M + Na]^+$ *m/z* 555.2.

1-Ethylsulfinyl 4,6-*O*-benzylidene-2,3-di-*O*-methanesulfonyl-*β*-D-glucopyranoside (19R_S and 19S_S).

Starting from compound **16** (400mg, 0.85 mmol) and following the general procedure the oxidation of the thioglycosides, the obtained sulfinylglycosides were purified by column chromatography (EtOAc : Hexanes, 4 : 1) affording **18R_S** and **18$_S$** (300 mg, 72%) in a 2 : 1 ratio.

(R_S)-Ethyl 4,6-*O*-benzylidene-2,3-di-*O*-methanesulfonyl-1-thio-*β*-D-glucopyranoside S-oxide (19R_S). Major isomer. White solid. m.p.: 168.0-173.0 ºC. $[\alpha]_D^{20}$: -67.7 (c 1.0, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.47-7.44 (m, 2H), 7.37-7.35 (m, 3H), 5.55 (s, 1H), 5.18 (t, 1H, *J* = 9.2 Hz), 5.04 (t, 1H, *J* = 8.9 Hz), 4.40 (dd, 1H, *J* = 11.1 Hz, *J* = 4.7 Hz), 4.20 (d, 1H, *J* = 9.2 Hz), 3.90 (t, 1H, *J* = 9.8 Hz), 3.85 (t, 1H, *J* = 9.6 Hz), 3.70-3.66 (m, 1H), 3.27 (s, 3H), 3.20-3.13 (m,1H), 3.03 (s, 3H), 2.83-2.76 (m, 1H),1.36 (t, 3H, *J* = 7.7 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 136.1, 129.4, 128.3, 126.0, 101.5, 87.2 , 80.0, 77.3, 73.3, 70.5, 67.7, 41.3 , 39.6, 39.2 , 7.3. HRMS Calcd. for: $C_{17}H_{24}O_{10}NaS_3$: 507.0429 $[M + Na]^+$. Found: 507.0446 (+3.3 ppm).

For crystallographic data see supporting information.

(S_S)-Ethyl 4,6-*O*-benzylidene-2,3-di-*O*-methanesulfonyl-1-thio-*β*-D-glucopyranoside S-oxide (19S_S). Minor isomer. White solid. m.p.: 168.0-173.0 ºC. $[\alpha]_D^{20}$: -75.8 (c 1.0, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.47-7.40 (m, 2H), 7.37-7.32 (m, 3H), 5.53 (s, 1H), 4.96 (t, 1H, *J* = 9.7 Hz), 4.83 (t, 1H, *J* = 9.2 Hz), 4.49 (d, 1H, *J* = 9.6 Hz), 4.45 (dd, 1H, *J* = 10.7 Hz, *J* = 5.1 Hz), 3.76-3.72 (m, 2H), 3.65-3.62 (m, 1H), 3.22 (s, 3H), 3.02 (s, 3H), 2.98-2.95 (m,1H), 2.86-2.79 (m, 1H),1.38 (t, 3H, *J* = 7.7 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 135.9, 129.5, 128.4, 126.0 , 101.8, 90.4 , 79.6, 78.0 , 74.2 , 71.1 , 67.8 , 40.7, 39.8, 39.3, 6.9 . HRMS Calcd. for: $C_{17}H_{24}O_{10}NaS_3$: 507.0429 $[M + Na]^+$. Found: 507.0446 (+3.3 ppm).

X-Ray structural analysis of compounds 12R_S, 13R_S and 19R_S.

Crystals of suitable size for X-ray diffraction analysis, were coated with dry perfluoropolyether and mounted on glass fibers and fixed in a cold nitrogen stream (T = 100 K) to the goniometer head. Data collections were performed on a Bruker-Nonius X8Apex-II CCD diffractometer, using monochromatic radiation λ(Mo Kα) = 0.71073 Å, by means of ω and φ scans with a width of 0.50 degree. The data were reduced (SAINT)[33] and corrected for absorption effects by the multi-scan method (SADABS).[34] The structures were solved by direct methods (SIR-2002)[35] and refined against all F^2 data by full-matrix least-squares techniques (SHELXTL-6.12)[36] minimizing $w[F_o^2-F_c^2]^2$. All the non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were included in calculated positions and allowed to ride on the attached atoms with the isotropic temperature factors (*U*iso values) fixed at 1.2 times (1.5 times for methyl groups) those *U*eq values of the corresponding attached atoms.

Crystal data for 12RS: $C_{23}H_{28}O_5S$, *M* = 416.51, monoclinic, *a* = 20.294(3) Å, *b* = 6.4701(8) Å, *c* = 15.4757(17) Å, *α* = 90.00°, *β* = 96.306(4)°, *γ* = 90.00°, *V* = 2019.7(4) Å^3, *T* = 213(2) K, space group C_2, *Z* = 4, *μ* = 0.193 mm^{-1}, 10600 reflections measured, 3042 independent reflections (R_{int} = 0.0391). The final R_1 values were 0.0598 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.1608 ($I > 2\sigma(I)$). The final R_1 values were 0.0768 (all data). The final $wR(F^2)$ values were 0.1720 (all data). The goodness of fit on F^2 was 1.170. *Flack parameter* = -0.05(15).

Crystal data for 13RS: $C_{29}H_{42}O_{12}S_3$, *M* = 678.81, monoclinic, *a* = 10.4931(8) Å, *b* = 11.5171(10) Å, *c* = 28.284(2) Å, *α* = 90.00°, *β* = 91.379(4)°, *γ* = 90.00°, *V* = 3417.1(5) Å^3, *T* =

173(2) K, space group $P2_1$, Z = 4, μ = 0.275 mm^{-1}, 39325 reflections measured, 9661 independent reflections (R_{int} = 0.0800). The final R_1 values were 0.0605 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.1574 ($I > 2\sigma(I)$). The final R_1 values were 0.0843 (all data). The final $wR(F^2)$ values were 0.1826 (all data). The goodness of fit on F^2 was 0.994. *Flack parameter* = 0.06(3). **Crystal data for 19RS**: $C_{17}H_{24}O_{10}S_3$, M = 484.54, monoclinic, a = 5.2270(6) Å, b = 25.122(3) Å, c = 16.5667(18) Å, α = 90.00°, β = 99.08°, γ = 90.00°, V = 2148.2(4) Å^3, T = 173(2) K, space group $P2_1$, Z = 4, μ = 0.397 mm^{-1}, 17443 reflections measured, 5111 independent reflections (R_{int} = 0.0427). The final R_1 values were 0.0674 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.1116 ($I > 2\sigma(I)$). The final R_1 values were 0.0896 (all data). The final $wR(F^2)$ values were 0.1632 (all data). The goodness of fit on F^2 was 1.029. *Flack parameter* = -0.01(3).

Acknowledgements

This work was supported by the Ministerio de Economía y Competitividad (grants No. CTQ2010-21755-CO2-01, CTQ2010-21755-CO2-01, CTQ2013-49066-C2-1-R, CTQ2013-49066-C2-2-R), the Junta de Andalucía (grant No. P11-FQM-8046). We gratefully thank CITIUS for NMR facilities.

Notes and references

[a] *Instituto de Investigaciones Químicas, C.S.I.C-Universidad de Sevilla, c/. Américo Vespucio, 49., Isla de la Cartuja, 41092 Sevilla, Spain*.
[b] *Departamento de Química Orgánica y Farmacéutica, Facultad de Farmacia, Universidad de Sevilla, 41012 Sevilla, Spain.*

†Electronic Supplementary Information (ESI) available: Copies of ^{1}H, and ^{13}C spectra of compounds **4-13**, **17-19**, and X-ray CIF files for compounds **12*R*$_S$**, **13*R*$_S$** and **19*R*$_S$**. CCDC 1025652–1025654. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b000000x/

1 (a) I. Fernández, N. Khiar, *Chem. Rev*., 2003, **103**, 3651. (b) C. H. Senanayake, D. Krishnamurthy, Z. H. Lu, Z. X. Han, I. Gallou, *Aldrichchim. Acta*, 2005, **38**, 93 (c) W. Elzbieta, W. Jacek, *Chem. Rev.*, 2009, **110**, 4303. (d) M. C. Carreño, G. Hernández-Torres, M. Ribagorda, A. Urbano, *Chem. Commun.*, 2009, 6129.

2 I. Fernández, N. Khiar, in *Organosulfur Chemistry in Asymmetric Synthesis*, ed. T. Toru and C. Bolm, Wiley-VCH-Verlag, Weinheim, 2008, pp. 265.

3 (a) D. R. Evans, M. S. Huang, W. M. Seganish, J. C. Fettinger, T. L. Williams, *Inrog. Chem. Commun.*, 2003, **6**, 462. (b) N. Khiar, C. S. Araújo, F. Alcudia, I. Fernández, *J. Org. Chem.*, 2002, **67**, 345. (c) C. Pettinari, M. Pellei, G. Cavicchio, M. Crucianelli, W. Panzeri, M. Colapietro, A. Caseta, *Organometallics*, 1999, **18**, 555.

4 (a) S. Kobayashi, C. Ogawa, H. Konishi, M. Sugiura, M. *J. Am. Chem. Soc*., 2003, **125**, 6610. (b) A. Massa, A. V. Malkov, P. Kocovky, A. Scettri, *Tetrahedron Lett.*, 2003, **44**, 7179. (c) G. Rowlands, W. K. Barnes, *Chem Commun*., 2003, 2712. (d) I. Fernández, V. Valdivia, B. Gori, F. Alcudia, E. Álvarez, N. Khiar, *Org. Lett*., 2005, **7**, 1307. (e) I. Fernández, V. Valdivia, M. Pernía Leal, N. Khiar, N. *Org. Lett*., 2007, **9**, 2215. (f) I. Fernández, A. Alcudia, B. Gori, V. Valdivia, V. M. García, N. Khiar, *Org. Biomol. Chem*., 2010, **8**, 4388.

5 L. Yan, D. Kahne, *J. Am. Chem. Soc.*, 1996, **118**, 9239.

6 (a) D. Kahne, S. Walker, Y. Cheng, D. V. Engen, *J. Am. Chem. Soc.*, 1989, **111**, 6881. (b) D. Crich, S. Sun, S. *J. Am. Chem. Soc.*, 1997, **119**, 11217. (c) J. Gildersleeve, R. A. Jr. Pascal, D. Kahne, *J. Am. Chem. Soc.*, 1998, **120**, 5961. (d) J. G. Taylor, X. C. Li, M. Oberthur, W. J. Zhu, D. Kahne, *J. Am. Chem. Soc.*, 2006, **128**, 1584.

7 S. Raghaven, D. Kahne, *J. Am. Chem. Soc*., 1993, **115**, 1580.

8 R. Liang, L. Yan, J. Loebach, M. Ge, Y. Uozumi, K. Sekanina, N. Horan, J. Gildersleeve, C. Thompson, A. Smith, K. Biswas, W. C. Still, D. Kahne, D. *Science*, 1996, **274**, 1520.

9 D. Crich, S. Sun, *J. Org. Chem*., 1997, **62**, 1198.

10 N. Khiar, I. Alonso, N. Rodriguez, A. Fernandez-Mayoralas, J. Jimenez-Barbero, O. Nieto, F. Cano, C. Foces-Foces, M. Martin-Lomas, M. *Tetrahedron Lett*. 1997, **38**, 8267.

11 O. Karthaus, S. Shoda, S. Kobayashi, S. *Tetrahedron Asymmetry*, 1994, **5**, 2213.

12 V. Ferrières, J. Joutel, R. Boulch, M. Roussel, L. Toupet, D. Plusquellec, *Tetrahedron Lett.*, 2000, **41**, 5515.

13 H. Driguez, *Top. Curr. Chem.* 1997, **187**, 85.

14 (a) D. Crich, S. Sun, *Tetrahedron*, 1998, **54**, 8321. (b) D. Crich, S. Sun, J. Brunkova, J. *J. Org. Chem.* 1996, **61**, 605.

15 D. Crich, J. Mataka, S. Sun, K.-C. Lam, A. L. Rheingold, D. J. Wink, *Chem. Commun*., 1998, 2763.

16 D. Crich, J. Mataka, L. N. Zakharov, A. L. Rheingold, D.. J. Wink, *J. Am. Chem. Soc.*, 2002, **124**, 6028.

17 N. Khiar, N. *Tetrahedron Lett.* 2000, **41**, 9059.

18 N. Khiar, I. Fernández, C. S. Araújo, J. A. Rodríguez, B. Suárez , E. Alvarez. *J. Org. Chem*. 2003, **68**, 1433.

19 (a) P. H. Buist, B. Behrouzian, K. D. MacIsaac, S. Cassel, P. Rollin, A. Imberty, C. Gautier, S. Pérez, P. Genix, P. *Tetrahedron: Asymmetry*, 1999, **10**, 2881. (b) D. Crich, Z. Dai, *Tetrahedron*, 1999, **55**, 1569. (c) C. A. Sanhueza, A. C. Arias, R. L. Dorta, J. T. Vázquez, *Tetrahedron: Asymmetry*, 2010, **21**, 1830. (d) C. A. Sanhueza, C. R. L. Dorta, J. T. Vázquez, *Tetrahedron: Asymmetry*, 2013, **24**, 582.

20 (a) K. K. Khullar, J. Bauer, J. *J. Org. Chem.*, 1971, **36**, 3038. (b) B. Mair, M. Shamaiengar, N. C. Krouskop, F. D. Rossini, *Anal. Chem*., 1959, **31**, 2082. (c) A. A. Dameron, L. F. Charles, P. S. Weiss, *J. Am. Chem. Soc.*, 2005, **127**, 8697.

21 N. Khiar, R. Navas, E. Alvarez, I. Fernández, *ARKIVOC*, 2008, **8**, 211.

22 N. Khiar, B. Suárez, V. Valdivia, I. Fernández, *Synlett.*, 2005, 2963.

23 Interestingly, The sulfinyl epoxide **12*R*$_S$** crystallize under the non *exo*-anomeric conformation, contrary to the crystal structures of R_S sulfinyl glycosides reported to date.

24 H. Liang, M. MacKay, T. B. Gindley, K. N. Robertson, K. T. S. Cameron, *Can. J. Chem.*, 2010, **88**, 1154.

25 In reference 16, the adoption in an S_S sulfinyl β–xyloside glycoside of a partially eclipsed glycosidic bond with *syn* conformation of the aglycon and the C1-C2 bond, has been interpreted in term of relieving the unfavorable dipolar interaction. We believe that the conformation of this particular xylopyranoside is dictated mainly by the π–π interaction between the two phenyl rings on sulfur and in the 2-position, see ref. 18 and 24.

26 R. U. Lemieux, A. A. Pavia, J. C. Martin, K. A. Wartanabe, *Can. J. Chem.*, 1969, **47**, 4427. For reviews see: (a) Deslongchamps, *Stereoelectronic Effects in Organic Chemistry*, Pergamon, New York. 1983. (b) A. J. Kirby, *The Anomeric Effect and Related stereoelectronic Effects at Oxygen*, Springer, New York, 1983. (c) I. Travoska, T. Bleha, *Adv. Carbohydr. Chem. Biochem.*, 1989, **47**, 45. (c) E. Juaristi, G. Cuevas, *The Anomeric Effect*, CRC Press, Boca Raton, 1995.

27 Crich *et al.*[16] commented in footnote that they have found exceptions to this rule in particular cases (no data were given).

28 C. A. Sanhueza, R. L. Dorta, J. T. Vázquez, *J. Org. Chem.* 2011, **76**, 7769.

29 Both compounds adopt a $^4C_1$ conformation as shown by the NOE contacts detected between H-1, H-3 and H-5, and between H-2 and H-4. However, while in compound **16** NOE contacts were observed between the ethyl group and protons H-1 and H-2 of the sugar, in the case of compound **6** only NOE contact between the protons of the adamantyl group and proton H-1 of the sugar were detected.

30 In accord with this hypothesis are the the different positions occupied by the methyl of the mesyl group in the sulfinyl glycosides **13*R*$_S$** (Figure 2) and **19*R*$_S$** (Figure 4)

31 (a) Nicolaou, K. C.; Wissinger, N.; Pastor, J.; DeRoose, F. *J. Am Chem. Soc.* 1997, **119**. 449. (b) Blom, P.; Ruttens, B.; Van Hoof, S.; Hubrecht, I.; Van Der Eycken, J.; Sas, B.; Van Hemel, J.; Vandenkerckhove, J. *J. Org. Chem.* 2005 , **70**, 10109.

32 (a) A. M. P. van Steijn, J. P. Kamerling, J. F. G. Vliegenthart, *Carbohydr. Res.*1992, **225**, 229. (b) J. J. Gridley, A. J. Hacking, H. M. I. Osborn, D. G. Spackman, *Tetrahedron*, 1998, **54**, 14925. (c) S. –F. Lu, Q. Q. O'Yang, Z. –W. Guo, B. Yu, Y. –Z. Hui, *J. Org. Chem.*, 1997, **62**, 8400.

33 Bruker (2007). APEX2. Bruker AXS Inc., Madison, Wisconsin, USA.

34 Bruker (2001). SADABS. Bruker AXS Inc., Madison, Wisconsin, USA.

35 Burla, M. C., Camalli, M., Carrozzini, B., Cascarano, G. L., Giacovazzo, C., Poliori, G.,Spagna, R. SIR2002: the program; (2003). *Appl.Cryst.* 36, 1103.

36 Sheldrick, G. M. (2008). *Acta Cryst*. A, 64, 112-122.