JOC Article

# Highly Diastereoselective Oxidation of 2-Amino-2-deoxy-1-thio-β-D-glucopyranosides: Synthesis of Imino Sulfinylglycosides

Noureddine Khiar,*,† Inmaculada Fernández,‡ Cristina S. Araújo,†,‡ José-Antonio Rodríguez,† Belén Suárez,† and Eleuterio Álvarez†

*Instituto de Investigaciones Químicas, C.S.I.C.-Universidad de Sevilla, c/. Américo Vespucio, s/n., Isla de la Cartuja, 41092 Sevilla, Spain, and the Departamento de Química Orgánica y Farmacéutica, Facultad de Farmacia, Universidad de Sevilla, 41012 Sevilla, Spain*

*khiar@cica.es*

*Received October 3, 2002*

A synthetic route to imino thioglycosides and to imino sulfinylglycosides has been developed. A detailed study on the diastereoselective oxidation of 2-amino-2-deoxy-1-thio-β-D-glucopyranosides is reported. It has been shown that the stereochemical outcome of the oxidation is highly dependent on the protective group of the amine function. While the oxidation of iminothioglycosides is slightly diastereoselective (up to 30% de in favor of the $R_S$ sulfoxide), a single isomer is obtained in the case of tetrachlorophthalimido derivatives. The absolute configuration of the sulfinyl glycoside was ascertained by NMR analysis using our recent model on the basis of the exo-anomeric effect corroborated by X-ray crystallography.

## Introduction

As a part of our recent interest in the synthesis and utilization of chiral sulfoxides in catalytic asymmetric synthesis promoted by transition metals,[1] we became interested in the synthesis of bidentated S/N ligands derived from sugars such as **I** and **II** (Figure 1). These compounds are thought to chelate the transition metal through the nitrogen and the sulfur atoms in **I** and through the nitrogen and either the sulfur or the oxygen atoms in the case of **II**.[2] An inherent characteristic of thioether ligands such as **I** is that upon coordination to the metal the sulfur atom becomes stereogenic. While the close proximity of the stereogenic center to the coordination sphere of the transition metal may be beneficial,[3] the low inversion barrier of the sulfur metal bond may lead to an erosion of the enantioselectivity of the catalytic process.[4] Keeping this in mind, the synthesis of diastereomerically pure sulfinyl glycosides **II** was designed as a stereochemically well-defined S/N ligands. To undertake the investigation of **I** and **II** ligand capacities, two basic problems must be solved. The first one is a modular and general method for the synthesis of conveniently functionalyzed 2-amino-2-deoxy-β-thioglycosides, and the second problem is an easy method for the determination of the absolute configuration of the sulfinyl glycosides.

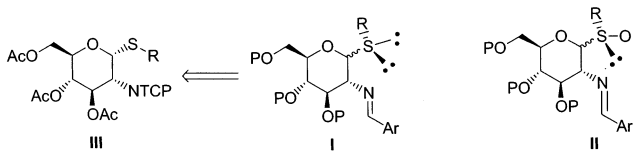



**FIGURE 1.**

In this paper, we report on a practical synthesis of tetrachlorophthalimide-protected phenyl and ethyl 2-amino-2-deoxy-1-thio-β-D-glucopyranosides **III** en route to compounds **I** and **II**. While the oxidation of iminothioglycosides **I** is slightly diastereoselective, the oxidation of **III** has resulted in an unusual highly diastereoselective process. Applying our empirical NMR rule for the determination of the absolute configuration of anomeric sulfoxides,[5] corroborated by X-ray analysis, we present a rationalization of the diastereoselectivity observed and extend it to other β-thioglycosides.[6] It is worth mentioning that the obtained sulfinyl glycosides, as well as the parent thioglycosides, are of interest for the synthesis of oligosaccharides containing β-linked hexosamines, components of many natural and biologically active carbohydrates.[7] Recently, Kahne's route using anomeric sulfoxides for the synthesis of glycosides has emerged as one

† Instituto de Investigaciones Químicas, C.S.I.C-Universidad de Sevilla.

‡ Facultad de Farmacia, Universidad de Sevilla.

(1) (a) Khiar, N.; Fernández, I.; Alcudia, F. *Tetrahedron Lett.* **1993**, *34*, 123. (b) Khiar, N.; Alcudia, F.; Espartero, J.-L.; Rodríguez, L.; Fernandez, I. *J. Am. Chem. Soc.* **2000**, *122*, 7598. (c) Khiar, N.; Araújo, C. S.; Alcudia, F.; Fernández, I. *J. Org. Chem.* **2002**, *67*, 345.

(2) For some use of S,N ligands in metal-catalyzed asymmetric synthesis see: (a) Allen J. V.; Bower, J. F.; Williams, J. M. J. *Tetrahedon*: *Asymmetry* **1994**, *5*, 1895. (b) Hiroi, K.; Watanabe, K.; Abe, I.; Koseki, M. *Tetrahedron Lett.***2001**, *42*, 7617. (c) Boog-Wick, K.; Pregosin, P. S.; Trabesinger, G. *Organometallics* **1998**, *17*, 3254.

(3) Evans, D. A.; Campos, K. R.; Tedrow, J. S.; Michael, F. E.; Gagné, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 7905.

(4) (a) Abel, E.; Bhargava, S. K.; Orrell, K. G. *Prog. Inorg. Chem.* **1984**, *32*, 1−118. (b) Abel, E.; Dormer, J.; Ellis, D.; Orrell, K. G.; Sik, V.; Hursthouse, M. B.; Mazid, M. A. *J. Chem. Soc., Dalton Trans.* **1992**, 1073−1080.

(5) Khiar, N. *Tetrahedron Lett.* **2000**, *41*, 9059.

(6) Crich, D.; Mataka, J.; Sun, S.; Lam, K.-C.; Rheingold, A. L.; Wink, D. J. *J. Am. Chem. Soc.* **2002**, *124*, 6028.

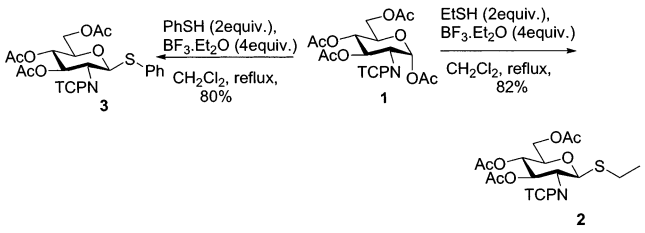
10.1021/jo026519q CCC: $25.00 
Published on Web 01/25/2003

of the most promising approaches for the ever seeked "general glycosidation reaction".[8] The sulfoxide method, which has been developed originally for the glycosidation of hindered alcohols, has been recently used inter alia for the one-pot sequential formation of various glycosidic bonds,[9] for the synthesis of carbohydrates, including carbohydrate libraries on solid support,[10] and finally, for the synthesis of $\beta$-mannosides.[11] While the stereochemical outcome of the reaction is independent of the stereochemistry of the sulfinyl sulfur and at the anomeric carbon, we[12] and others[13] 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.[14] Additionally, it has recently been shown that in some cases a diastereomeric sulfoxide is an active glycosylating agent while the other is not.[15] On the other hand, the use of thioglycosides as glycosidase-resistant analogues of glycoside is well documented.[16] 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 aglycon.[17] 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.

## Results and Discussion

The widely used method for the synthesis of thioglycosides is the Lewis-acid-catalyzed substitution of the anomeric acetate with the desired thiol.[18] A large number of catalysts have been used in this transformation, including zinc chloride, titanium tetrachloride, ferric chloride, boron trifluoride diethyl etherate, and zirconium chloride. Additionally, to obtain the desired 1,2-*trans*-iminothioglycoside in a diastereoselective manner, a glycosyl donor with an easily removable participating group at the 2-position is needed. Tetrachlorophthalimide-protected amino derivative **1**, introduced simultaneously by Fraser-Reid[19] and Schmidt,[20] which symbolizes the aforementioned requirement has been chosen as

**SCHEME 1**[a]




[a] One step synthesis of ethyl and phenyl thioglycosides **2** and **3**.

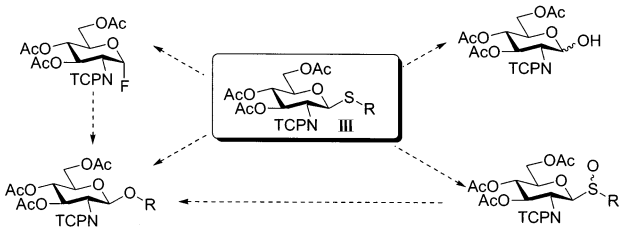



**FIGURE 2.** Possible transformations of thioglycoside type III.

starting material. Nevertheless, Olson et al. have recently reported on the inertness of the easily accessible axial acetate **1**[21] toward thioglycosidation, despite the use of different reagent systems, such as ethanethiol or trimethyl(ethylthio)silane in the presence of various Lewis acids.

As 1,2-*trans*-acetates are known to react faster than their 1,2-cis counterparts, a three-step process, isomerizing the α-acetate to the $\beta$-acetate, was developed, leading to the desired ethyl thioglycoside **2**, in 35% overall yield. We have actually found that the use of the standard conditions, ethanethiol (2 equiv) with boron trifluoride diethyl ether (4 equiv) at reflux, gives in 2 h cleanly the desired compound in nearly quantitative yield (Scheme 1).

Using the same conditions, phenyl thioglycoside **3** has also been obtained in excellent yield (Scheme 1). This finding makes this route very attractive for large-scale synthesis access to TCP-protected 2-amino-2-deoxythioglycosides, in good overall yields from glucosamine hydrochloride.

The usefulness of this synthon is illustrated in Figure 2, where all the possible transformations of **2** affording useful intermediates for the synthesis of oligosaccharides containing $\beta$-linked hexosamines are presented. Treatment with NBS and water in acetone can give the corresponding lactol[22,23] en route to the trichloroacetimidate derivative,[20] while the treatment with NBS and DAST will lead to the axial fluroride.[24]

(7) (a) Banoub, J.; Boullanger, P.; Lafont, D. *Chem. Rev.* **1992**, *92*, 1167. (b) Debenham, J.; Rodebaugh, R.; Fraser-Reid, B. *Liebigs Ann./Recueil* **1997**, 791.

(8) (a) Kahne, D.; Walker, S.; Cheng, Y.; Engen D. V. *J. Am. Chem. Soc.* **1989**, *111*, 6881. (b) Crich, D.; Sun, S. *J. Am. Chem. Soc.* **1997**, *119*, 11217. (c) Gildersleeve, J.; Pascal, R. A. Jr.; Kahne, D. *J. Am. Chem. Soc.* **1998**, *120*, 5961.

(9) Raghaven, S.; Kahne, D. *J. Am. Chem. Soc.* **1993**, *115*, 1580.

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

(11) Crich, D. Sun, S. *J. Org. Chem.* **1997**, *62*, 1198.

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

(13) Karthaus, O.; Shoda, S.; Kobayashi, S. *Tetrahedron*: *Asymmetry* **1994**, *5*, 2213.

(14) It is interesting to note that the diastereoselective hydrolysis of $S_S$ sulfinyl glycosides reported in refs 12 and 13 can be well understood using Vasella's recent lateral protonation model for glycosidase enzymes; see: Heightman, T. D. Vasella, A. T. *Angew. Chem., Int. Ed.* **1999**, *38*, 750.

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

(16) Driguez, H. *Top. Curr. Chem.* **1997**, *187*, 85.

(17) Showalter, H. D. H.; Winters, R. T.; Sercel, A. D.; Michel, A. *Tetrahedron Lett.* **1991**, *32*, 2849.

(18) (a) Ferrier, R. J.; Furneaux, R. H. *Carbohydr. Res.* **1976**, *52*, 63. (b) Garegg, P. J. *Adv. Carbohydr. Chem. Biochem.* **1997**, *52*, 179 and references therein.

(19) Debenham, J. S.; Madsen, R.; Roberts, C.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1995**, *117*, 3302.

(20) Castro-Palomino, J. C.; Schmidt, R. R. *Tetrahedron Lett.* **1995**, *36*, 5343.

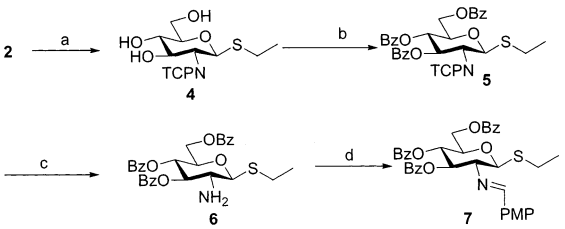
(21) Olsson, L.; Kelberlau, S.; Jia, Z. J.; Fraser-Reid, B. *Carbohydr. Res.* **1998**, *314*, 273.

(22) Groneberg, R. D.; Miyazaki, T.; Stylianides, N. A.; Shulze, T. J.; Stahl, W.; Schreiner, E. P.; Suzuki, T.; Iwabushi, Y.; Smith, A. L.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1993**, *115*, 7593.

(23) Motawia, M. S.; Marcussen J.; Moeller, B. L. *J. Carbohydr. Chem.* **1995**, *14*, 1279.

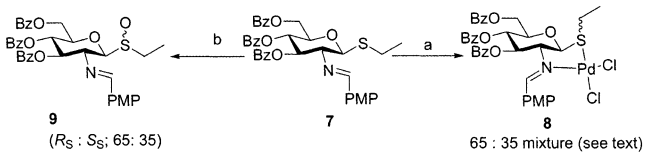
(24) Nicolaou, K. C.; Dolle, R. E.; Papahatjis, D. P. *J. Am Chem. Soc.* **1984**, *106*, 4189.

**SCHEME 2**[a]



[a] Key: (a) HCl, $H_2O$/acetone, 70 °C, quant; (b) BzCl, py, DMAP (66%); (c) $NH_2(CH_2)_2NH_2$, $CH_3CN$/EtOH/THF, 70 °C (43%); (d) *p*-$MeOC_6H_4CHO$, $CuSO_4$, $CH_2Cl_2$ (61%).

**SCHEME 3**[a]



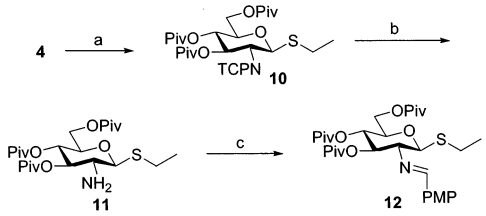
[a] Key: (a) $Pd(CH_3CN)_2Cl_2$, $CH_2Cl_2$ (80%); (b) *m*-CPBA, −78 °C, $CH_2Cl_2$ (80%).

To get the desired S/N ligands, it was necessary the deprotection of the amine group. Owing to the presence of acetates on the C-3, C-4, and C-5 positions, the aminolysis of the TCP group could not be made directly, because of the concomitant migration of the acetyl group to the amine function.

To resolve this problem the acetate groups were changed to benzoate esters. Acid hydrolysis of **2** leads to the triol **4**,[24] which upon treatment with 5 molar equiv of benzoyl chloride in pyridine afforded the tribenzoylated compound **5** in good yield. Treatment of the fully protected compound **5** with ethylenediamine at 60 °C, as described by Fraser-Reid, leads to the free amine **6** in modest yield (Scheme 2).[25] Imination of compound **6** with *p*-methoxybenzaldehyde using molecular sieves as dehydrating agent afforded the desired iminothioglycoside **7** in very low yield (<20%). Gratifyingly, using $CuSO_4$ as recently described by Ellman's group afforded the desired imine in acceptable yield.[26] Reacting the iminothioglycoside **7** with $PdCl_2(CH_3CN)_2$, in methylene chloride at room temperature, afforded the corresponding palladium(II) complexes **8** in excellent yield (Scheme 3). $^1H$ NMR analysis shows that the reaction product is a mixture of two diastereomeric compounds in a 65:35 ratio. This result indicates that the use of iminothioglycoside-type **7** in palladium-catalyzed asymmetric synthesis may be compromised by the formation of diastereomeric complexes having opposite configuration at the sulfur atom.

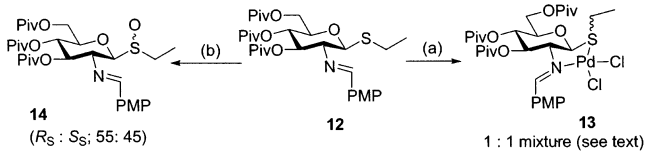
Diastereomerically pure imino sulfoxides embody a configurationally stable S/N ligand, able to give a single palladium complex. Unfortunately, oxidation of iminothioglycoside **7** with *m*-CPBA, in methylene chloride as usual, leads to the corresponding sulfoxides **9** in a 65:35 mixture. Surprisingly, the major isomer was shown unambiguously (vide infra) to have the *R* absolute configuration at the sulfinyl sulfur. It has recently been assumed that the oxidation of β-thioglycosides in the gluco, galacto and mano series always give the sulfoxides with *S* absolute configuration majoritarly.[6] Our actual results, as well as those recently reported by Ferrieres and Plusquellec,[27] indicate that the oxidation of β-thioglycosides depends not only on the configuration of C-2, but also on the nature of the protective group. To get better insight in the stereochemical outcome of the oxidation, iminothioglycosides with a bulky pivaloyl protective group were planned and synthesized as before.

**SCHEME 4**[a]



[a] Key: (a) PivCl, py, DMAP, reflux (56%); (b) $NH_2(CH_2)_2NH_2$, $CH_3CN$/EtOH/THF, 70 °C (41%); (c) *p*-$MeOC_6H_4CHO$, $CuSO_4$, $CH_2Cl_2$ (64%).

**SCHEME 5**[a]



[a] Key: (a) $Pd(CH_3CN)_2Cl_2$, $CH_2Cl_2$ (80%); (b) *m*-CPBA, −78 °C, $CH_2Cl_2$ (90%).

Pivaloylation of the triol **4**, using 6 equiv. of pivaloyl chloride in pyridine at 80 °C afforded **10,** aminolysis as before led to the amino thioglycoside **11** and imination with *p*-methoxybenzaldehyde using $CuSO_4$ as dehydrating agent afforded the desired imino thioglycoside **12** in acceptable yield (Scheme 4). Reacting the iminothioglycoside **12** with $PdCl_2(CH_3CN)_2$, as before, afforded the corresponding palladium(II) complexes **13** in good yield (Scheme 5). NMR analysis of the crude mixture showed the formation of a 1:1 diastereomeric mixture. On the other hand, the oxidation of **12** as usual, using *m*-CPBA at −78 °C, afforded a 55:45 mixture of anomeric sulfoxide **14**, paralleling again the Pd(II) complex formation (Scheme 5). Here again, the slightly major isomer was shown to have the $R_S$ absolute configuration at the sulfinyl sulfur.

**Determination of the Absolute Configuration of Sulfinyl Glycosides.** The stereochemical outcome of the diastereoselective oxidation of thioglycoside has received much interest recently. From our study on β-thioglycosides,[5,12] we have shown that the oxidation is highly dependent on the substituent at C-2 of the sugar. A high diastereoselection is observed in the case of sugars with a free C2-OH, while a slightly diastereoselective process results in the case of fully protected sugars. In the case of α-thioglycosides, Crich has recently shown that the oxidation is highly diastereoselective leading to $R_S$ sulfinyl glycosides mostly as single isomer.[28] The accumulated results have prompted the quick conclusion that in the

(25) Debenham, J. S.; Debenham, S. D.; Fraser-Reid, B. *Bioorg. Med. Chem.* **1996**, *4*, 1909.
(26) Liu, G., Cogan, D. A.; Owens, T. D.; Tang, T. P., Ellman, J. A. *J. Org. Chem.* **1999**, *64*, 1278.
(27) Misbahi, K.; Lardic, M.; Ferrière, V.; Noiret, N.; Kerbal, A.; Plusquellec, D. *Tetrahedron*: *Asymmetry* **2001**, *12*, 2389.
(28) Crich, D.; Mataka, J.; Sun, S.; Lam, K.-C.; Rheingold, A. L.; Wink, D. J. *Chem. Commun.* **1998**, 2763.

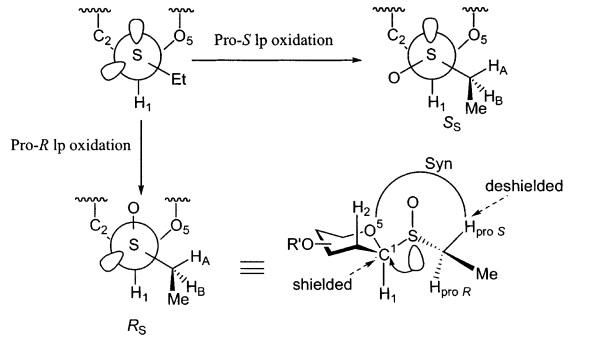
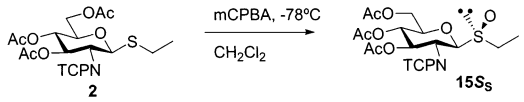



**FIGURE 3.** Newman projection of $\beta$-ethylthioglycosides, $\beta$-($R_S$)-sulfinyl glycosides, and $\beta$-($S_S$)-sulfinyl glycosides.

case of pyranosides with 1,2-trans-diequatorial substituents, the sense ($S_S$) and the degree of diastereoselectivity (modest) are a general feature.[6] To ascertain the diastereoselectivity observed during this work, it was necessary to determine the absolute configuration at the sulfinyl sulfur of the obtained sulfinyl glycosides. The widely used approach for the determination of the absolute configuration of chiral sulfoxides has been the utilization of NMR spectroscopy using chiral shift reagents such as 9-anthryl-1,1,1-trifluoroethanol,[29] α-methoxyphenylacetic acid,[30] and *R*-(−)-*N*-(3,5-dinitrobenzoyl)-α-phenylethylamine.[31] The success of using chiral shift reagents as tool for the elucidation of the stereochemistry of the sulfoxide depends on the stability of the complex formed by hydrogen bonds between their acidic OH groups and the basic sulfinic oxygen. Nevertheless, the instability of the complexes implies that the chemical shift differences between the diastereomeric complexes are usually very small or, in some cases, nonsystematic.

After analyzing the physical data of a large number of sulfinyl glycosides, we have recently reported a simple method for the determination of the absolute configurations of sulfinyl glycosides.[5] This method is based on a simple analysis of $^1$H or $^{13}$C NMR data, thanks to a general characteristic conformational behavior of the two anomeric sulfoxides epimers. We have observed that in the case of ethyl (and most likely other alkyl) sulfoxides[6,32] the nonequivalence 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.This observation has been rationalized by the existence of a major conformation stabilized by the exo-anomeric effect[33] in the case of sulfoxides with the *R* absolute configuration at the sulfinyl sulfur. On the other hand, in most of the cases, the anomeric carbon in the $R_S$ sulfoxides is more shielded (around 3 ppm) than in the $S_S$ epimer,[34] supporting the existence of an hyperconjugative delocalization of the lone pair of the sulfinyl sulfur to σ* orbital of the C1-O5 (Figure 3).[35] In this regard, it is worth mentioning that Buist has recently determined the conformational behavior of the two ethyl sulfinyl glycosides epimers by semiempirical (AM1/MOPAC) calculation.[30b] While two low energy conformers were found for the $S_S$ sulfinyl glycoside, a single conformation was detected for the $R_S$ counterpart. Interestingly, the later conformation was that with the lone pair of the sulfinyl sulfur anti to O-5, and the ethyl substituent anti to C-2, that is the exo-anomeric conformation.

**SCHEME 6**



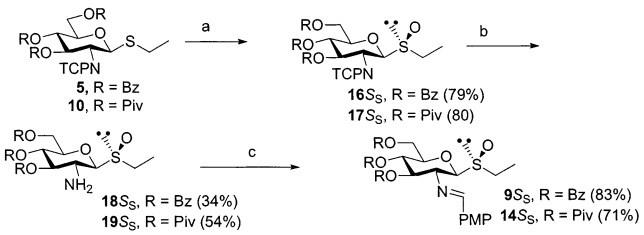

Accordingly, the chemical shift of the anomeric carbon of the major isomer of benzoylated sulfoxide **9** is 88.3 ppm and the nonequivalence of the diastereotopic protons $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$ is 108.6 Hz. Whereas the anomeric carbon of the minor is more deshielded (91.1 ppm), and the splitting of the diastereotopic protons $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$ is smaller (42.1 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. In the case of pivaloylated sulfoxides **14**, the same tendency is observed, both the shielding of the anomeric carbon (87.8 ppm vs 90.8 ppm) as well as the larger non equivalence ($\Delta\nu$) of the diastereotopic protons $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$ (115.6 vs 47.8 Hz) are indicative of an $R_S$ absolute configuration of the major isomer and an $S_S$ absolute configuration of the minor isomer. These assignments were corroborated by chemical correlation with a sulfinyl derivative whose absolute configuration was unambiguously determined by X-ray analysis (vide infra).

**Diastereoselective Synthesis of Amino and Imino Sulfinyl Glycosides.** To get a diastereomerically pure imino sulfoxide, as a stereochemically well-defined S/N ligand, either a totally diastereoselective process or a nonselective oxidation leading to sulfinyl glycosides epimers with a good separation factors was needed. We were delighted to find that the oxidation[36] of the TCP-protected derivative **2** with *m*-CPBA in methylene chloride at −78 °C gave the corresponding sulfoxide **15** in high yield as a single isomer (Scheme 6).

It is worth mentioning that this is the first example of totally diastereoselective oxidation of a fully protected $\beta$-thioglycoside with 1,2-trans-diequatorial dispositions. Opposing to the recent affirmation,[6] our results on the oxidation of imino thioglycosides and on the TCP protected derivatives, indicate that neither the sense nor the degree of the diastereoselection in the case of $\beta$-thiogly-

(29) Pirkle, W. H.; Sikkenga, D. L. *J. Chromatogr.* **1976**, *123*, 400.
(30) (a) Buist, P. H.; Marecak, D. M. *J. Am. Chem. Soc.* **1992**, *114*, 5073. (b) Buist, P. H.; Behrouzian, B.; MacIsaac, K. D.; Cassel, S.; Rollin, P.; Imberty, A.; Gautier, C.; Pérez, S.; Genix, P. *Tetrahedron: Asymmetry*, **1999**, *10*, 2881.
(31) Deshmukh, M.; Dunach, E.; Kagan, H. B. *Tetrahedron Lett.* **1984**, *25*, 3467.
(32) Aucagne, V.; Aversa, M. C.; Baratucci, A., Bonacorsi, P.; Gianneto, P.; Rollin, P.; Tatibouet, A. *J. Org. Chem.* **2002**, *67*, 6925.
(33) Lemieux, R. U.; Pavia, A. A.; Martin, J. C.; wartanabe, K. A. *Can. J. Chem.* **1969**, *47*, 4427. For reviews, see: (a) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon: New York, 1983. (b) Kirby, A. J.; *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer: New York, 1983. (c) Travoska, I.; Bleha, T. *Adv. Carbohydr. Chem. Biochem.* **1989**, *47*, 45. (c) Juaristi, E.; Cuevas, G. *The Anomeric Effect*; CRC Press: Boca Raton, 1995.
(34) We have observed that this rule is also operative for the α-thioglycosides.[5,6] In this case it is the oxidation of the *pro-S* lone pair which maintain the exo-anomeric conformation. As a consequence, in the reported cases, the anomeric carbons of the $S_S$ sulfoxides are more shielded (around 3 ppm) than in the $R_S$ epimer.
(35) For the effect of the orientation of the sulfinyl lone pair on the chemical shifts of the adjacent carbon, see: Carreño, M. C.; Garcia Ruano, J. L.; Martin, A. M.; Pedregal, C.; Rodriguez, J. H.; Rubio, A.; Sanchez, J.; Solladié, G. *J. Org. Chem.* **1990**, *55*, 2120 and references therein.
(36) Kakarla, R.; Dulina, R. G.; Hatzenbuhler, N. T.; Hui, Y. W.; Sofia, M. J. *J. Org. Chem.* **1996**, *61*, 8347 and references therein.

**SCHEME 7**[a]




[a] Key: (a) *m*-CPBA, $CH_2Cl_2$; (b) $NH_2(CH_2)_2NH_2$, $CH_3CN$/EtOH/THF, 70 °C; (c) *p*-$MeOC_6H_4CHO$, $CuSO_4$, $CH_2Cl_2$ (64%).

cosides are general. Owing to the absence of the other epimer at sulfur, we could not apply with confidence our NMR model for the determination of the stereochemistry of the sulfinyl sulfur of **15**, even though the non equivalence ($\Delta\nu$) of the diastereotopic protons $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$ (77 Hz) is indicative of an $S_S$ absolute configuration. Fortunately, compound **15** $S_s$ is crystalline, and we succeeded in preparing a single crystal suitable for X-ray crystallographic analysis (see the Supporting Information). The absolute configuration at the sulfinyl sulfur was *S*, confirming the previous assignment based on our empirical rule using the proton $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$.

Due to the diastereocontrol bias exerted by the TCP group, the access to diastereomerically pure imino sulfoxides is thus possible as long as the oxidation of thioglycosides is conducted at the TCP stage. Accordingly, oxidation of either **5** or **10** with *m*-CPBA in methylene chloride as usual leads to the corresponding sulfoxides **16$S_S$** and **17$S_S$** almost as a single isomer (see the Experimental Section) in good yields. Aminolysis with ethylenediamine as before leads to amino sulfoxides **18$S_S$** and **19$S_S$** in acceptable yields.

Imination with *p*-methoxybenzaldehyde using $CuSO_4$ afforded the desired imino sulfoxides **9**$S_S$ and **14**$S_S$ diastereomerically pure in good yields (Scheme 7). The obtained $S_S$ sulfoxide **9** has the anomeric carbon at 91.1 ppm with a small non equivalence ($\Delta\nu$) of the diastereotopic protons $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$ (42.1 Hz). In the same manner, sulfoxide **14$S_S$** has the anomeric carbon at 90.8 ppm with a small nonequivalence ($\Delta\nu$) of the diastereotopic protons $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$ (47.8 Hz) Contrasting these data with the $^1$H and $^{13}$CNMR spectra of the crude mixture of the oxidation of iminothioglycosides **7** and **12** (vide supra) permits the confirmation of our previous assignment based on our empirical model.

**Origin of the Diastereoselectivity.** The unusually high diastereoselective oxidation of **2**, **5**, and **10** makes necessary a detailed study of this transformation. To determine whether the high diastereoselection observed is a result of the protective group of the nitrogen atom, the substituent of the sulfur atom, or both, thioglycosides **20** and **21** were synthesized from the corresponding anomeric acetate as before and oxidized (Table 1). The oxidation has been carried out using *m*-CPBA in methylene chloride at −78 °C until completion, or stopped at 50% transformation of the thioglycoside (entries 3 and 5), to determine the extent of kinetic resolution. The diastereoselection was always determined by $^1$H NMR analysis of the crude.

As can be seen from Table 1, the diastereoselection is variable in all cases and depends on both substituent on the sulfur and the nitrogen. In the case of the TCP derivative **3**, the oxidation of the phenyl thioglycoside still gives the corresponding sulfoxide **22** in high diastereoselection (10/1 and 4/1, Table 1, entries 2 and 3). Surprisingly, in the case of phthalimide derivatives **20** and **21**, the diastereoselection is highly dependent on the substituent of the sulfinyl sulfur, giving rise to good diastereoselection in the case of the ethyl thioglycoside **20** (entry 4, Table 1) and modest diastereoselection in the case of the phenyl thioglycoside **21** (see Table 1, entries 5 and 6). The assignment of the stereochemistry at the sulfinyl sulfur was done on the basis of the result of the X-ray analysis, supported by our empirical rule. Accordingly, the anomeric carbons in the minor isomers of phenyl sulfinyl glycosides **22** ($\delta$ 84.7 ppm) and **24** ($\delta$ 86.4) are more shielded than the corresponding carbon in the major isomers **22** (88.7 ppm) and **24** (89.4 ppm), which is indicative of an $S_S$ absolute configuration in the major sulfoxides and $R_S$ absolute configurations in the minor sulfoxides. In the case of ethyl sulfinyl glycoside **23**, both the shielding of the anomeric carbon (83.4 ppm vs 85.0 ppm) as well as the larger non equivalence ($\Delta\nu$) of the diastereotopic protons $H_{pro\text{-}R}$ and $H_{pro\text{-}S}$ (158.4 vs 30.5 Hz) are indicative of an $R_S$ absolute configuration of the minor isomer and an $S_S$ absolute configuration of the major isomer.

To ascertain the high diastereoselectivity obtained, it is necessary to determine the stable conformation at equilibrium of the starting thioglycoside. While the conformational studies of thiosaccharides are scarce, it has been recently shown, by means of NMR (NOE) and molecular mechanics calculations, that stable conformations at equilibrium of thiocellobiose are those of the exo-anomeric effect.[37] On the other hand, we and others[5,12] have recently invoked the exo-anomeric conformation of thioglycosides in order to explain their reactivity toward electrophiles. The crystal structure of compound **15**$S_S$ remains that of exo-anomeric conformation of the starting thioglycoside **2** (see the Supporting Information)**.** Additionally, a careful analysis of a large number of the reported crystalline structure of sulfinyl glycosides in the literature shows that they all crystallize in the exo-anomeric conformation.[5,12,30b,38] Based on these assumptions, we propose that the conformation of the starting thioglycoside is that of the exo-anomeric effect, Figure 4. In this conformation, the *pro-S* lone pair (lp) of the sulfur atom is in a syn relationship with the bulky TCP group, while the *pro-R* lp is at the 1,3-diaxial disposition with regard to the H-2 and the O-5 lp. On the other hand, the mechanism of oxidation of thioether has been studied from both kinetic[39] and theoretical aspects.[40] From the above studies, the following conclusions, which are of

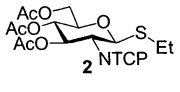
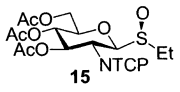
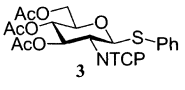
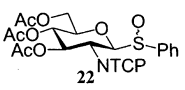
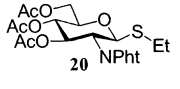
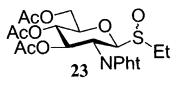
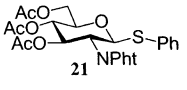
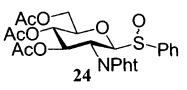
(37) Montero, E.; Vallmitjana, M.; Pérez-Pons, J. A.; Querol, E.; Jiménez-Barbero, J.; Cañada, F. J. *FEBS Lett.* **1998**, *421*, 243.

(38) It is worth noting that the crystalline sulfoxides reported in refs 17 and 30 have an $R_S$ absolute configuration at the sulfinyl sulfur and both adopt the conformation with the exo anomeric effect, in spite an unfavorable gauche relationship between the C1−O5 and the S−O dipoles.

(39) (a) Davis, F. A.; Billmers, J. M.; Gosciniak, D. J.; Towson, J. C.; Bach, R. D. *J. Org. Chem.* **1986**, *51*, 4240. (b) Overberger, C. G.; Cummins, R. W. *J. Am. Chem. Soc.* **1953**, *75*, 4250. (c) Curci, R.; DiPrete, R. A.; Edwards, J. O.; Modena, G. *J. Org. Chem.* **1970**, *35*, 740. (d) Behrman, E. J. Edwards, J. O. *Prog. Phys. Org. Chem.* **1967**, *4*, 93.

(40) Bach, R. D.; Coddens, B. A.; McDouall, J. J. W.; Schlegel, H. B.; Davis, F. A. *J. Org. Chem.* **1990**, *55*, 3325.

**TABLE 1**[a]

| Entry | Thioglycoside | Sulfinyl glycoside | Ratio (SM/$S_S$ /$R_S$/Sulfone )[d] | Spectroscopical data Isomer | $\Delta\nu(\delta_A - \delta_B)$[c] | C-1 (δ ppm)[b] |
|---|---|---|---|---|---|---|
| 1 |  **2** |  **15** | 4.5/92/0/3.5[e] | **15**$S_S$ | 77.0 Hz | 83.9 |
| 2 |  **3** |  **22** | 0/82/8/10 | **22**$R_S$ | - | 84.7 |
| 3 | **3** | **22** | 50/40/10/0 | **22**$S_S$ | - | 88.7 |
| 4 |  **20** |  **23** | 0/80/20/0 | **23**$R_S$ | 158.4 Hz | 83.4 |
| | | | | **23**$S_S$ | 30.5 Hz | 85.0 |
| 5 |  **21** |  **24** | 50/34/16/0 | **24**$R_S$ | - | 86.4 |
| 6 | **21** | **24** | 0/60/40/0 | **24**$S_S$ | - | 89.4 |

[a] All reactions were carried out at −78 °C, in dry $CH_2Cl_2$, using 1.05 equiv of *m*-CPBA. [b] Chemical shift of the anomeric carbon. [c] Nonequivalence of the diastereomeric methylenic protons of EtSO. [d] Determined by $^1$HNMR of the crude. [e] No trace of the $R_S$ isomer was detected by $^1$H NMR or by $^{13}$C NMR analysis of the crude.

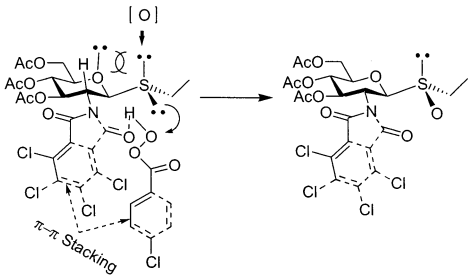



**FIGURE 4.** Plausible mechanism of the highly diastereoselctive oxidation of thioglycoside **2**.

interest to our discussion, can be drawn: (a) the peracids are electrophilic toward sulfides; (b) the oxidations are second-order reactions (first order for each component); thus, the transition state contains both peracid and thioether; (c) by ab initio calculation a model has been proposed where the peracid approaches the sulfur atom along the 3p orbital. Taken together, the model in Figure 4 for the transition state of oxidation of thioglycosides can be drawn.

Both steric and stereoelectronic factors can be evoked to explain the high diastereoselectivity observed. The known characteristic of the amide to adopt a syn conformation forces the phthalimide group to be quasi-parallel to the axis of the 3p orbital of the *pro-S* lp. In this conformation, the Pht and the TCP group leave a free space around the *pro-S* lp facilitating the approach to the peracid, while the attack of the *pro-R* lp of the thioglycoside is hindered by the O-5 lp, and H-2. From a stereoelectronic point of view, the parallel positioning of the tetrachlorophthalimide group can stabilize the transition state leading to the *S* diastereoisomer by a $\pi-\pi$ stacking, between the highly electron-deficient benzene ring of the TCP group and the aromatic ring of the peracid with higher electrondensity. Additionally, a hydrogen bond between the peracid and the amidic oxygen can no be ruled out, to explain the selectivity.[41] The modest selectivity observed in the oxidation of the *N*-phthalimide phenylthioglycoside **21,** can be explained taking into account that the above charge-transfer complex between the benzene ring of the Pht group and the ring of mCPBA is less favored. Additionally, one can propose that in this case, the starting thioglycoside exist in two different conformations, one stabilized by the exo-anomeric effect leading to the *S* diastereoisomer, and another stabilized by a $\pi-\pi$ stacking leading to the *R* diastereoisomer.

## Conclusions

We have reported on an effective synthetic route to β-D-2-desoxy-2-imino thioglycosides and to diastereomerically pure β-D-2-desoxy-2-iminosulfinyl glycosides. Tetrachlorophthalimide-protected 2-amino-2-desoxy-β-D-thioglycosides, for which a single high-yielding step has been developed, were shown to be excellent intermediates for these new S/N ligands. The tetrachlorophthalimide group performs different functions in our synthetic design: a participating group allowing a stereospecific construction of a β-thioglycosidic linkage, an orthogonal temporary amine protective group, and finally, an excellent diastereocontrol bias allowing the stereoselective synthesis of a single sulfoxide diastereoisomer. Following our previous studies on the oxidation of thioglycosides, in the present work we demonstrate that the oxidation of β-thioglycosides depends on the nature of the protective group of the amine function. While a single isomer is always obtained in the case of tetrachlorophthalimide-protected compounds, a mixture of isomers is obtained in the case of the phthalimide counterpart, and most importantly, a slightly diastereoselective process in favor of the nonde-

(41) In this regard, it is interesting to note that in the crystal structure of **15**$S_S$ a water molecule appears hydrogen bonded to one of the carbonyl oxygens of the tetrachlophthalimide moiety.

tected *R* isomer is observed in the case of imino thioglycoside. The diastereoselectivity of β-D-thioglycosides is a fine balance of steric and stereoelectronic effects. In the exo-anomeric stabilized conformations of the starting thioglycosides of the gluco and galacto series, the approximation of the peracids to the pro-*S* lp is favored by hydrogen bonding and $\pi-\pi$ stacking as in the case of acyl protected compounds. In the absence of these stabilizing factors, as in the case of ether and imine protected compounds, the approximation to the pro-*R* lp is favored. The configuration at the sulfinyl sulfur of all the sulfoxides reported in this study has been determined by our empirical rule using anomeric carbon as well as vicinal proton to the sulfur chemical shifts as NMR probe. In all the cases the assignment was corroborated either by X-ray analysis or by chemical correlation. These new S/N ligands are actually being used in palladium catalyzed asymmetric transformations and the results will be reported in due courses.

## Experimental Section

**General Methods.** All reactions were run under an atmosphere of dry argon using oven-dried glassware and freshly distilled and dried solvents. THF and diethyl ether were distilled from sodium benzophenone ketyl. Dichloromethane was distilled from calcium hydride. TLC was performed on silica gel with detection by charring with phosphomolybdic acid/EtOH. For flash chromatography, silica gel (230−400 mesh) was used. Columns were eluted with positive air pressure. Chromatographic eluents are given as volume-to-volume ratios (v/v). $^1$H NMR and $^{13}$C NMR spectra were recorded at 500 and 125 MHz, respectively. 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. The organic extracts were dried over anhydrous sodium sulfate and concentrated in a vacuum.

**1-Ethylsulfenyl-3,4,6-tri-*O*-acetyl-1,2-dideoxy-2-*N*-tetrachlorophthalimido-β-D-glucopyranoside (2).** To a mixture of **1** (7.28 g, 11.8 mmol) and ethanethiol (2.2 mL, 29.5 mmol) in methylene chloride (40 mL) was added $BF_3{\cdot}Et_2O$ (6 mL, 65.2 mmol) at room temperature and then heated to reflux. After 2 h, a TLC analysis of a diluted aliquot showed the total consumption of **1**. The mixture was diluted with methylene chloride and washed successively with saturated aqueous sodium bicarbonate ($NaHCO_3$) and brine. The organic layer was dried ($Na_2SO_4$) and concentrated. The crude mixture was purified over silica gel (EtOAc/Hex 3:7) affording **2** (6.0 g, 82%) as a white solid: mp 147−151 °C; $[\alpha]_D = +56.7$ (*c* 0.9, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) δ 5.72 (dd, 1H, *J* = 10.1, 9.1 Hz), 5.41 (d, 1H, *J* = 10.6 Hz), 5.16 (dd, 1H, *J* = 10.2, 9.1 Hz), 4.34 (t, 1H, *J* = 10.4 Hz), 4.27 (dd, 1H, *J* = 12.4, 5.0 Hz), 4.14 (dd, 1H, *J* = 12.4, 2.3 Hz), 3.82 (dd, 1H, *J* = 10.2, 4.9, 2.3 Hz), 2.71−2.60 (m, 2H), 2.08 (s, 3H), 2.01 (s, 3H), 1.88 (s, 3H), 1.20 (t, 3H, *J* = 7.4 Hz); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 170.7, 170.5, 169.4, 163.2, 162.4, 140.8, 140.6, 130.1, 127.1, 126.8, 80.8, 76.0, 71.6, 68.6, 62.2, 54.4, 24.5, 20.8, 20.6, 20.5, 14.9. Anal. Calcd for $C_{22}H_{21}Cl_4NO_9S$: C, 42.81; H, 3.43; N, 2.27. Found: C, 42.95; H, 3.16; N, 2.38.

**1-Phenylsulfenyl-3,4,6-tri-*O*-acetyl-1,2-dideoxy-2-*N*-tetrachlorophthalimido-β-D-glucopyranoside (3).** Obtained using the same procedure as for **2**, using **1** (0.59 g, 0.96 mmol), thiophenol (0.25 mL, 2.4 mmol), and $BF_3{\cdot}Et_2O$ (0.48 mL, 3.84 mmol). The crude mixture was purified over silica gel (EtOAc/Hex 2:8) affording **3** (0.4 g, 82%) as a white solid: $^1$H NMR ($CDCl_3$, 500 MHz) δ 7.40−7.38 (m, 2H), 7.29−7.25 (m, 3H), 5.70 (t, 1H, *J* = 9.6 Hz), 5.65 (d, 1H, *J* = 10.5 Hz), 5.13 (t, 1H, *J* = 9.5 Hz), 4.32 (t, 1H, *J* = 10.3 Hz), 4.26 (dd, 1H, *J* = 12.3, 5.2 Hz), 4.18 (dd, 1H, *J* = 12.2, 2.1 Hz), 3.85 (ddd, 1H, *J* = 10.1, 5.1, 2.2 Hz), 2.08 (s, 3H), 2.01 (s, 3H), 1.86 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 170.6, 170.5, 169.4, 163.2, 162.2, 140.8, 140.6, 133.3, 130.5, 130.1, 129.0, 128.6, 127.1, 126.8, 82.4, 76.0, 71.7, 68.4, 62.1, 54.4, 20.7, 20.6, 20.4.

**1-Ethylsulfenyl-1,2-dideoxy-2-*N*-tetrachlorophthalimido-β-D-glucopyranoside (4).** To a mixture of **2** (10 g, 16.7 mmol) in acetone (220 mL) was added a solution of concentrated HCl (20 mL) in $H_2O$ (71 mL). The reaction was heated at 70 °C for 1 h, 40 mL of $H_2O$ was added, and stirring was continued overnight. After evaporation of acetone, the aqueous layer was extracted with AcOEt (4 × 125 mL). The organic layer was washed successively with saturated $NaHCO_3$ (150 mL) and brine (150 mL), dried ($Na_2SO_4$), and evaporated, giving pure **4** in quantitative yield (7.5 g), which was used in the next transformations without further purification: mp 103−105 °C; $^1$H NMR ($CDCl_3$, 500 MHz) δ 5.25 (d, 1H, *J* = 10.4 Hz), 4.26 (t, 1H, *J* = 9.5 Hz), 4.04 (t, 1H, *J* = 10.4 Hz), 3.88 (s, 2H), 3.66 (t, 1H, *J* = 9.2 Hz), 3.49 (d, 1H, *J* = 9.6 Hz), 2.66−2.60 (m, 2H), 1.16 (t, 3H, *J* = 7.4 Hz); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 163.6, 163.2, 140.2, 130.1, 129.6, 127.4, 127.3, 81.1, 79.6, 72.0, 70.8, 61.7, 56.3, 24.6, 14.9; HRMS calcd for $C_{16}H_{15}NO_6SCl_4Na$ $(M + Na)^+$ 511.9271, found 511.9264 (1.4 ppm).

**1-Ethylsulfenyl-3,4,6-tri-*O*-benzoyl-1,2-dideoxy-2-*N*-tetrachlorophthalimido-β-D-glucopyranoside (5).** To a solution of **4** (2 g, 4.05 mmol) in dry pyridine (13 mL) were added benzoyl chloride (2.37 mL, 20.41 mmol) and a catalytic amount of DMAP (100 mg), and the reaction was stirred for 3 h at room temperature. After evaporation of pyridine, the residue was diluted with $CH_2Cl_2$ (250 mL) and washed with 10% HCl (2 × 100 mL). The aqueous layer was extracted with $CH_2Cl_2$ (4 × 100 mL), and the organic layer was successively washed with saturated $NaHCO_3$ and brine, dried ($Na_2SO_4$), and evaporated. The crude mixture was purified by flash column chromatography (AcOEt/Hex, 1:4) giving **5** (2.17 g, 66.17%) as a white solid: mp 145−147 °C; $[\alpha]_D = +76.1$ (*c* 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) δ 8.03−8.01 (m, 2H), 7.90−7.88 (m, 2H), 7.79−7.77 (m, 2H), 7.56−7.17 (m, 9H), 6.25(dd, 1H, *J* = 9.4, 9.9 Hz), 5.72 (t, 1H, *J* = 9.5 Hz), 5.65 (d, 1H, *J* = 10.5 Hz), 4.66−4.61 (m, 2H), 4.52 (dd, 1H, *J* = 5.5, 12.2 Hz), 4.28−4.24 (m, 1H), 2.78−2.67 (m, 2H), 1.24 (t, 3H, *J* = 7.4 Hz); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 166.0, 165.2, 163.4, 162.4, 140.7, 140.5, 133.6, 133.5, 133.1, 130.1, 129.9, 129.8, 129.7, 129.6, 128.7, 128.6, 128.4, 127.2, 126.9, 81.1, 76.3, 72.0, 69.9, 63.3, 54.7, 24.6, 15.0; HRMS calcd for $C_{37}H_{27}NO_9SCl_4Na$ $(M + Na)^+$ 824.0058, found: 824.0061 (0.3 ppm). Anal. Calcd for $C_{37}H_{27}Cl_4NO_9S$: C, 55.31; H, 3.39; N, 1.74. Found: C, 54.95; H, 3.26; N, 1.99.

**1-Ethylsulfenyl-1,2-dideoxy-2-amino-3,4,6-tri-*O*-benzoyl-β-D-glucopyranoside (6).** To a solution of **5** (693 mg, 1.29 mmol) in 14 mL of a mixture of $CH_3CN$/EtOH/THF (2:1:1) was added ethylenediamine (0.26 mL, 3.88 mmol), and the mixture was heated to 70 °C for 3 h. After evaporation of the solvents, the crude was purified by flash column chromatography (EtOAc/Hex, 2:7), giving **6** (199 mg, 43%) as a yellow solid: mp 51−53 °C; $[\alpha]_D = -54.6$ (*c* 0.9, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) δ 7.98 (d, 2H, *J* = 7.2 Hz), 7.94 (d, 2H, *J* = 7.2 Hz), 7.87 (d, 2H, *J* = 7.2 Hz), 7.53−7.26 (m, 9H), 5.54 (t, 1H, *J* = 9.5 Hz), 5.49 (t, 1H, *J* = 9.5 Hz), 4.58 (m, 2H), 4.46 (dd, 1H, *J* = 5.8, 12.1 Hz), 4.09−4.05 (m, 1H), 3.20 (t, 1H, *J* = 9.5 Hz), 2.81−2.61 (m, 2H), 1.61(bs, 2H), 1.31 (t, 3H, *J* = 7.4 Hz); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 166.3, 166.1, 165.5, 133.4, 133.3, 133.1, 129.8, 129.7, 129.1, 128.9, 128.4, 87.8, 77.1, 76.1, 69.9, 63.7, 55.9, 24.8, 15.3; HRMS calcd for $C_{29}H_{30}NO_7S$ $(M + H)^+$ 536.1742, found 536.1734 (1.7 ppm).

**1-Ethylsulfenyl-1,2-dideoxy-2-*p*-methoxybenzylideneamino-3,4,6-tri-*O*-benzoyl-β-D-glucopyranoside (7).** To a mixture of **6** (85 mg, 0.159 mmol) and $CuSO_4$ (71 mg) in $CH_2Cl_2$ (3 mL) was added *p*-anisaldehyde (39 μL, 0.036 mmol). After 12 h, the mixture was filtered over Celite, the solvent was evaporated, and the residue was purified by flash column chromatography ($Et_2O$/Hex 1:1), using silica gel pretreated with 1% $NEt_3$, affording **7** (63 mg, 61%) as a white solid: mp 66−68 °C; $[\alpha]_D = +45.0$ (*c* 0.3, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500

MHz) $\delta$ 8.13 (s, 1H), 7.99 (d, 2H, $J$ = 7.6 Hz), 7.90 (d, 2H, $J$ = 7.6 Hz), 7.77 (d, 2H, $J$ = 7.6 Hz), 7.54 (d, 2H, $J$ = 8.7 Hz), 7.53−7.25 (m, 9H), 6.81 (d, 2H, $J$ = 8.7 Hz), 5.88 (t, 1H, $J$ = 9.4 Hz), 5.62 (t, 1H, $J$ = 9.8 Hz), 5.07 (d, 1H, $J$ = 9.8 Hz), 4.61 (dd, 1H, $J$ = 3.0, 12.0 Hz), 4.52 (dd, 1H, $J$ = 6.0, 12.0 Hz), 4.23−4.19 (m, 1H), 3.75 (s, 3H), 3.59 (t, 1H, $J$ = 9.5 Hz), 2.80−2.27 (m, 2H), 1.27 (t, 1H, $J$ = 7.3 Hz); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 166.1, 165.6, 165.3, 163.8, 162.0, 133.3, 133.0, 130.2, 129.8, 129.7, 129.5, 129.3, 129.0, 128.4, 128.3, 128.2, 113.9, 84.8, 76.2, 74.8, 74.5, 70.0, 63.9, 55.3, 24.9, 15.0; HRMS calcd for $C_{37}H_{36}NO_8S$ $(M + H)^+$ 654.2161, found 654.2129 (4.9 ppm).

**Palladium Complex: 7·PdCl$_2$ (8).** A solution of **7** (22.5 mg, 0.034 mmol) in dry deoxygenated $CH_2Cl_2$ (5 mL) in a Schlenk flask was treated with $PdCl_2(CH_3CN)_2$ (8.58 mg, 0.033 mmol) under argon atmosphere. After 1 h, the solvent was removed by vacuum and the residue obtained washed three times with dry deoxygenated diethyl ether, affording **8** as yellow orange solid in 80% yield, as a 2.5:1 epimer mixture. **Major isomer:** $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 8.39−8.38 (m, 3H), 8.05−7.19 (m, 15H), 6.70 (d, 2H, $J$ = 8.7 Hz), 6.53 (t, 1H, $J$ = 9.4 Hz), 5.84 (t, 1H, $J$ = 9.5 Hz), 5.32 (t, 1H, $J$ = 9.5 Hz), 5.12 (d, 1H, $J$ = 10.2 Hz), 4.62−4.60 (m, 1H), 4.56 (d, 1H, $J$ = 12.5 Hz), 4.41 (dd, 1H, $J$ = 3.8, 12.5 Hz), 3.72 (s, 3H), 3.21−3.04 (m, 2H), 1.61 (t, 3H, $J$ = 7.5 Hz). **Minor isomer:** $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 8.54 (d, 2H, $J$ = 8.2 Hz), 8.33 (s, 1H), 8.05−7.19 (m, 15H), 6.88 (d, 2H, $J$ = 8.8 Hz), 6.27 (t, 1H, $J$ = 9.5 Hz), 5.80 (t, 1H, $J$ = 9.5 Hz), 5.43(t, 1H, $J$ = 9.5 Hz), 4.84−4.78 (m, 2H), 4.39−3.82 (m, 2H), 3.80 (s, 3H), 3.40−3.38 (m, 2H), 1.61 (t, 3H, $J$ = 7.5 Hz); $^{13}$C NMR ($CDCl_3$, 50 MHz) spectroscopic data for the mixture of both isomers, $\delta$ 169.8, 166.6, 166.0, 164.9, 164.7, 135.2, 134.9, 134.4, 133.8, 133.6, 133.2, 130.2, 129.8, 129.7, 128.8, 128.4, 127.5, 123.6, 114.0, 113.8, 87.5, 86.4, 83.0, 76.4, 74.9, 71.2, 70.7, 69.1, 68.8, 62.3, 61.6, 55.6, 33.9, 30.3, 14.9.

**1-(*R*)- and 1-(*S*)-Ethylsulfinyl-1,2-dideoxy-2-*p*-methoxybenzylideneamino-3,4,6-tri-*O*-benzoyl-$\beta$-D-glucopyranoside (9).** To a solution of **7** (22.5 mg, 0.036 mmol) in $CH_2Cl_2$ (4 mL) at −78 °C was added a solution of *m*-CPBA (0.036 mmol) in $CH_2Cl_2$ (3 mL) via cannula. After 1 h, the reaction was stopped by addition of saturated sodium bisulfite and diluted with $CH_2Cl_2$ (40 mL). The organic layer was washed with $NaHCO_3$, and the aqueous layer was further extracted with $CH_2Cl_2$ (4 × 50 mL). The organic layer was washed with brine, dried ($Na_2SO_4$), and evaporated. The crude mixture was purified by flash column chromatography (EtOAc/Hex, 9:1) affording **9** (80% yield) as a 65:35 mixture of both epimers at sulfur. Diastereoisomer **9*R*$_S$** was obtained as the major diastereomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 8.35 (s, 1H), 7.98 (d, 2H, $J$ = 7.5 Hz), 7.91 (d, 2H, $J$ = 7.6 Hz), 7.80 (d, 2H, $J$ = 7.4 Hz), 7.57−7.26 (m, 11H), 6.82 (d, 2H, $J$ = 8.6 Hz), 5.99 (t, 1H, $J$ = 9.6 Hz), 5.64 (t, 1H, $J$ = 9.8 Hz), 4.66 (dd, 1H, $J$ = 3.0, 12.2 Hz), 4.60 (dd, 1H, $J$ = 6.7, 12.1 Hz), 4.56 (d, 1H, $J$ = 9.9 Hz), 4.32−4.27 (m, 1H), 4.23 (t, 1H, $J$ = 9.7 Hz), 3.79 (s, 3H), 3.17−3.13 (m 1H), 2.94−2.89 (m 1H), 1.25 (t, 1H, $J$ = 7.5 Hz); $^{13}$C NMR ($CDCl_3$, 125 MHz, taken from a mixture of both epimers at sulfur) $\delta$ 166.4, 165.4, 162.3, 133.4, 133.1, 130.4, 129.9, 129.8, 129.5, 128.4, 128.2, 113.9, 88.3, 77.4, 74.4, 69.7, 68.2, 63.7, 55.3, 41.2, 7.2.

The minor diastereomer **9*S*$_S$** has the same physical data as that obtained optically pure from the imination of **18*S*$_S$** (vide infra).

**1-Ethylsulfenyl-3,4,6-tri-*O*-pivaloyl-1,2-dideoxy-2-*N*-tetrachlorophthalimido-$\beta$-D-glucopyranoside (10).** To a solution of **4** (2 g, 4.05 mmol) in dry pyridine (13 mL) were added pivaloyl chloride (3 mL, 24.4 mL) and a catalytic amount of DMAP (100 mg), and the reaction was refluxed for 60 h. After evaporation of pyridine, the residue was diluted with $CH_2Cl_2$ (250 mL) and washed with 10% HCl (2 × 100 mL). The aqueous layer was extracted with $CH_2Cl_2$ (4 × 100 mL), and the organic layer was successively washed with saturated $NaHCO_3$ and brine, dried ($Na_2SO_4$), and evaporated. The crude mixture was purified by flash column chromatography (AcOEt/Hex, 1:9) giving **10** (1.78 g, 56%) as a yellow solid: mp 87−90 °C; $[\alpha]_D$ = +36.7 (*c* 0.9, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 5.74 (t, 1H, $J$ = 9.6 Hz), 5.48 (d, 1H, $J$ = 10.6 Hz), 5.20 (t, 1H, $J$ = 9.7 Hz), 4.36 (t, 1H, $J$ = 10.4 Hz), 4.25 (dd, 1H, $J$ = 12.3, 1.3 Hz), 4.09 (dd, 1H, $J$ = 12.3, 5.8 Hz), 3.88−3.84 (m, 1H), 2.73−2.68 (m, 1H), 2.67−2.62 (m, 1H), 1.25−1.22 (m, 12H), 1.17 (s, 9H), 0.94 (s, 9H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 178.0, 177.9, 176.4, 163.2, 162.4, 140.7, 140.4, 130.1, 129.9, 127.1, 126.8, 80.5, 76.6, 71.2, 67.9, 62.2, 54.6, 38.9, 38.8, 38.7, 27.1, 27.0, 24.3, 15.0; HRMS calcd for $C_{31}H_{39}Cl_4NO_9SNa$ $(M + Na)^+$ 764.0997, found 764.1002 (0.7 ppm). Anal. Calcd for $C_{31}H_{39}Cl_4NO_9S$: C, 50.08; H, 5.29; N, 1.88. Found: C, 50.10; H, 5.19; N, 1.94.

**1-Ethylsulfenyl-3,4,6-tri-O-pivaloyl-1,2-dideoxy-2-amino-$\beta$-D-glucopyranoside (11).** To a solution of **10** (538 mg, 0.73 mmol) in 8 mL of a mixture of $CH_3CN$/EtOH/THF (2:1:1) was added ethylenediamine (0.2 mL, 3.27 mmol), and the mixture was heated to 70 °C for 8 h. After evaporation of the solvents, the crude was purified by flash column chromatography (EtOAc/Hex, 2:7), giving **11** (142 mg, 41%) as a yellow solid: mp 106−109 °C; $[\alpha]_D$ = −8.6 (*c* 0.4, MeOH); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 5.05−4.99 (m, 2H), 4.33 (d, 1H, $J$ = 9.9 Hz), 4.20 (d, 1H, $J$ = 12.0 Hz), 4.02 (dd, 1H, $J$ = 6.1, 12.2 Hz), 3.71−3.69 (m, 1H), 2.92 (t, 1H, $J$ = 9.5 Hz), 2.72 (AB fragment of an $ABX_3$ system, 2H, $\Delta\upsilon$ = 31 Hz, $J$ = 7.3, 12.8 Hz), 1.40 (broad s, 2H), 1.30 (t, 3H, $J$ = 7.3 Hz), 1.20, 1.17 and 1.15 (3s, 27H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 178.0, 177.8, 176.7, 87.3, 76.4, 76.1, 68.1, 62.6, 55.8, 38.9, 38.8, 38.7, 27.2, 27.1, 24.4, 15.2; HRMS calcd for $C_{23}H_{41}NO_7S$ $(M)^+$ 475.2603, found 475.2615 (2.4 ppm). Anal. Calcd for $C_{23}H_{41}NO_7S$: C, 58.08; H, 8.69; N, 2.94. Found: C, 58.26; H, 8.28; N, 2.89.

**1-Ethylsulfenyl-1,2-dideoxy-2-*p*-methoxybenzylideneamino-3,4,6-tri-*O*-pivaloyl-$\beta$-D-glucopyranoside (12).** To a mixture of **11** (70 mg, 0.147 mmol) and $CuSO_4$ (70 mg) in $CH_2Cl_2$ (5 mL) was added *p*-anisaldehyde (36 $\mu$L, 0.036 mmol). After 12 h, the solvent was evaporated and the mixture was purified by flash column chromatography ($Et_2O$/Hex, 3:7), using silica gel pretreated with 1% $NEt_3$, affording **12** (56 mg, 64%) as a white solid: mp 101−102 °C; $[\alpha]_D$ = +36.2 (*c* 0.6, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 8.1 (s, 1H), 7.62 (d, 2H, $J$ = 8.2 Hz), 6.88 (d, 2H, $J$ = 8.6 Hz), 5.44 (t, 1H, $J$ = 9.4 Hz), 5.11 (t, 1H, $J$ = 9.8 Hz), 4.88 (d, 1H, $J$ = 9.8 Hz), 4.26 (dd, 1H, $J$ = 1.4, 12.1 Hz), 4.08 (dd, 1H, $J$ = 6.3, 12.1 Hz), 3.87−3.83 (m, 1H), 3.82 (s, 3H), 3.35 (t, 1H, $J$ = 9.8 Hz), 2.69 (AB fragment of an $ABX_3$ system, 2H, $\Delta\upsilon$ = **31 Hz**, $J$ = 7.3, 12.8 Hz), 1.26 (t, 3H, $J$ = 7.4 Hz), 1.22, 1.15 and 0.96 (3s, 27H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 178.1, 176.9, 176.5, 163.6, 162.1, 130.3, 128.3, 114.0, 84.2, 76.5, 74.8, 73.8, 68.1, 62.7, 55.4, 38.9, 38.8, 38.6, 27.3, 27.2, 27.1, 24.6, 15.0; HRMS calcd for $C_{31}H_{47}NO_8S$ $(M)^+$ 593.3022, found 593.3005 (2.8 ppm). Anal. Calcd for $C_{31}H_{47}NO_8S$: C, 62.71; H, 7.98; N, 2.36. Found: C, 62.54; H, 8.02; N, 2.11.

**Palladium Complex: 12·Pd(Cl)$_2$ (13).** A solution of **12** (54 mg, 0.091 mmol) in dry deoxygenated $CH_2Cl_2$ (5 mL) in a Schlenk flask was treated with $PdCl_2(CH_3CN)_2$ (23 mg, 0.091 mmol) under argon atmosphere. After 1 h, the solvent was removed by vacuum and the residue obtained washed three times with dry deoxygenated diethyl ether, affording **13** as yellow orange solid in 80% yield and as a 1:0.8 epimers mixture. Spectroscopical data were taken from the mixture of both diastereoisomers: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ major isomer 8.60 (d, 2H, $J$ = 8.3 Hz), 7.96 (s, 1H), 7.04 (d, 2H, $J$ = 8.3 Hz), 5.74 (t, 1H, $J$ = 9.3 Hz), 5.29−5.23 (m, 1H), 4.89 (t, 1H, $J$ = 9.3 Hz), 4.43 (d, 1H, $J$ = 10.4 Hz), 4.26−4.08 (m, 2H), 3.90−3.89 (m, 4H), 3.08−3.02 (m, 2H), 1.58 (t, 3H, $J$ = 7.2 Hz), 1.23, 1.16, 1.14 (3s, 27H); minor isomer 8.60 (d, 2H, $J$ = 8.3 Hz), 7.89 (s, 1H), 7.02 (d, 2H, $J$ = 8.3 Hz), 5.69 (t, 1H, $J$ = 9.3 Hz), 5.31−5.23 (m, 2H), 4.49 (d, 1H, $J$ = 9.9 Hz), 4.26−4.08 (m, 2H), 3.90−3.89 (m, 4H), 3.52−3.47 (m, 2H), 1.74 (t, 3H, $J$ = 7.2 Hz), 1.23, 1.16, 1.14 (3s, 27H); $^{13}$C NMR ($CDCl_3$, 50 MHz) both isomers $\delta$ 177.9, 177.6, 176.5, 176.1, 168.8, 168.5,

165.3, 134.8, 123.3, 114.1, 114.0, 87.6, 78.1, 77.8, 75.3, 69.3, 69.0, 67.1, 66.8, 61.2, 60.9, 55.8, 39.0, 38.8, 26.8, 26.7, 26.6, 14.7.

**1-(*R*)- and 1-(*S*)-Ethylsulfinyl-1,2-dideoxy-2-*p*-methoxybenzylideneamino-3,4,6-tri-*O*-pivaloyl-β-D-glucopyranoside (14).** To a solution of **12** (24.7 mg, 0.042 mmol) in $CH_2Cl_2$ (4 mL) at −78 °C was added a solution of *m*-CPBA (0.042 mmol) in $CH_2Cl_2$ (3 mL) via cannula. After 1 h, the reaction was stopped by addition of saturated sodium bisulfite and diluted with $CH_2Cl_2$ (40 mL). The organic layer was washed with $NaHCO_3$, and the aqueous layer was further extracted with $CH_2Cl_2$ (4 × 50 mL). The organic layer was washed with brine, dried ($Na_2SO_4$), and evaporated. The crude mixture of **14** was shown by NMR to be a 55:45 mixture of both epimers at sulfur. Diastereoisomer **14*R*$_S$** was the major diastereomer (see text): $^1$H NMR ($CDCl_3$, 500 MHz) δ 8.34 (s, 1H), 7.63 (d, 2H, *J* = 8.6 Hz), 6.89 (d, 1H, *J* = 8.6 Hz), 5.54 (t, 1H, *J* = 9.5 Hz), 5.14 (t, 1H, *J* = 9.7 Hz), 4.39−4.34 (m, 2H), 4.09−4.07 (m, 1H), 4.00−3.93 (m, 2H), 3.83 (s, 3H), 3.14−3.07 (m, 1H), 2.92−2.98 (m, 1H), 1.28−1.23 (m, 12H), 1.14 (s, 3H), 0.97 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 177.9, 176.7, 176.5, 165.6, 162.3, 130.3, 128.1, 114.1, **87.9**, 77.7, 68.9, 67.2, 61.8, 40.9, 31.6, 29.7, 27.1, 22.6, 14.1.

The minor diastereomer **14*S*$_S$** has the same physical data than that obtained optically pure from the imination of **19*S*$_S$** (vide infra).

**1-(*S*)-Ethylsulfinyl-3,4,6-tri-*O*-acetyl-1,2-dideoxy-2-*N*-tetrachlorophthalimido-β-D-glucopyranoside (15*S*$_S$).** To a solution of **2** (1.29 g, 2 mmol) in $CH_2Cl_2$ (40 mL) at −78 °C was added a solution of *m*-CPBA (2.1 mmol) in $CH_2Cl_2$ (4 mL) via cannula. After 1 h, the reaction was stopped by addition of saturated sodium bisulfite and diluted with $CH_2Cl_2$ (250 mL). The organic layer was washed with $NaHCO_3$, and the aqueous layer was further extracted with $CH_2Cl_2$ (4 × 50 mL). The organic layer was washed with brine, dried ($Na_2SO_4$), and evaporated. The crude mixture can be purified by flash column chromatography (EtOAc/Hex, 1:4) or recrystallized from EtOAc/Hex, affording pure **15*S*$_S$** (89%) as a white solid: mp 149−152 °C; $[\alpha]_D$ = +104.7 (*c* 0.9, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) δ: 5.88 (t, 1H, *J* = 9.5 Hz), 5.17 (t, 1H, *J* = 9.6 Hz), 5.02 (d, 1H, *J* = 10.5 Hz), 4.80 (t, 1H, *J* = 10.5 Hz), 4.26 (dd, 1H, *J* = 12.5, 4.9 Hz), 4.17 (dd, 1H, *J* = 2.0, 12.5 Hz), 3.92 (m, 1H), 2.94 (m, 1H), 2.78 (m, 1H), 2.09 (s, 3H), 1.92 (s, 3H), 1.3 (t, 3H, *J* = 7.5 Hz); $^{13}$C NMR ($CDCl_3$, 50 MHz) δ 170.4, 170.3, 169.3, 140.6, 130.2, 127.1, 83.9, 70.8, 68.1, 67.8, 61.5, 52.9, 43.7, 20.7, 20.6, 20.5, 5.8; HRMS calcd for $C_{22}H_{21}Cl_4NO_{10}SNa$ (M + Na)$^+$ 653.9538, found 653.9544 (0.9 ppm). Anal. Calcd for $C_{22}H_{21}Cl_4NO_{10}S$: C, 41.72; H, 3.34; N, 2.21. Found: C, 41.80; H, 2.96; N, 2.28.

**1-(*S*)-Ethylsulfinyl-3,4,6-tri-*O*-benzoyl-1,2-dideoxy-2-*N*-tetrachlorophthalimido-β-D-glucopyranoside (16*S*$_S$).** To a solution of **7** (1.1 g, 1.36 mmol), in $CH_2Cl_2$ (10 mL), was added a solution of 70% of *m*-CPBA (354 mg, 1.43 mmol) in $CH_2Cl_2$ (6 mL) at −78 °C. The reaction was 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 × 50 mL), and the organic layer was washed with brine, dried ($Na_2SO_4$), and evaporated. Depending on the run, the $^1$HNMR spectra of the crude shows only the desired product **16*S*$_S$**, or together with small amount (<10%) of the sulfone and another compound. The crude mixture was purified by flash column chromatography (EtOAc/Hex, 1:2), affording **16*S*$_S$** (880 mg, 79%) as a white solid: mp 93−94 °C; $[\alpha]_D$ = +51.6 (*c* 0.3, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) δ 8.02 (d, 2H, *J* = 7.1 Hz), 7.90 (d, 2H, *J* = 7.1 Hz), 7.80 (d, 2H, *J* = 7.1 Hz), 7.60−7.26 (m, 9H), 6.41 (t, 1H, *J* = 9.7 Hz), 5.71(t, 1H, *J* = 9.7 Hz), 5.20 (d, 1H, *J* = 10.4 Hz), 5.09 (t, 1H, *J* = 10.4 Hz), 4.62 (dd, 1H, *J* = 2.6, 12.4 Hz), 4.50 (dd, 1H, *J* = 5.7, 12.4 Hz), 4.34−4.30 (m, 1H), 2.89 (AB fragment of an $ABX_3$ system, 2H, Δν = 73 Hz, *J* = 7.3, 7.5, 13.5 Hz), 1.30 (t, 3H, *J* = 7.5 Hz); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 171.2, 171.1, 165.9, 165.8, 165.1, 140.5, 133.7, 133.4, 130.2, 129.9, 129.7, 129.3, 128.7, 128.5, 128.4, 128.2, 127.1, 84.0, 77.3, 71.1, 69.3, 62.6, 53.3, 43.8, 5.7; HRMS calcd for $C_{37}H_{27}NO_{10}SCl_4Na$ (M + Na)$^+$ 840.0007, found 840.0050 (5.1 ppm).

**1-(*S*)-Ethylsulfinyl-3,4,6-tri-*O*-pivaloyl-1,2-dideoxy-2-*N*-tetrachlorophthalimido-β-D-glucopyranoside (17*S*$_S$).** To a solution of **10** (1.22 g, 1.65 mmol), in dry $CH_2Cl_2$ (10 mL), was added a solution of 70% of *m*-CPBA (426 mg, 1.73 mmol) in $CH_2Cl_2$ (6 mL) at −78 °C. The reaction was 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 × 50 mL), and the organic layer was washed with brine, dried ($Na_2SO_4$), and evaporated. The $^1$HNMR spectra of the crude shows mainly the desired product **17*S*$_S$** (>90%) with a small amount of other compound which could not be isolated (<10%). The crude mixture was purified by flash column chromatography (EtOAc/Hex, 1:4), affording **17*S*$_S$** (984 mg, 79%) as a white solid: mp 169−172 °C; $[\alpha]_D$ = +77.8 (*c* 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) δ 5.89 (t, 1H, *J* = 9.7 Hz), 5.21(t, 1H, *J* = 9.7 Hz), 5.09 (d, 1H, *J* = 10.5 Hz), 4.80 (t, 1H, *J* = 10.3 Hz), 4.26 (dd, 1H, *J* = 1.1, 12.3 Hz), 4.06 (dd, 1H, *J* = 5.9, 12.5 Hz), 3.95−3.93 (m, 1H), 2.85 (AB fragment of an $ABX_3$ system, 2H, Δν= 86 Hz, *J* = 7.3, 7.6, 13.4 Hz), 1.30 (t, 3H, *J* = 7.5 Hz), 1.25, 1.15 and 1.00 (3s, 27H); $^{13}$C NMR ($CDCl_3$, 50 MHz) δ 178.0, 177.9, 176.4, 163.2, 162.4, 140.8, 140.5, 130.1, 129.9, 127.1, 126.8, 86.0, 80.5, 76.6, 71.3, 67.9, 62.2, 54.6, 38.9, 38.8, 38.7, 27.1, 27.0, 24.3, 17.6, 15.0; HRMS calcd for $C_{31}H_{39}NO_{10}SCl_4Na$ (M + Na)$^+$ 780.0946, found 780.0992 (5.9 ppm). Anal. Calcd for $C_{31}H_{39}Cl_4NO_{10}S$: C,49.02; H, 5.18; N, 1.84. Found: C, 50.13; H, 5.40; N, 2.30.

**1-(*S*)-Ethylsulfinyl-1,2-dideoxy-2-amino-3,4,6-tri-*O*-benzoyl-β-D-glucopyranoside (18*S*$_S$).** To a solution of **16*S*$_S$** (752 mg, 0.919 mmol) in 15 mL of a mixture of solvents $CH_3CN$/EtOH/THF (2:1:1) was added ethylendiamine (0.28 mL, 4.137 mmol). After 3 h at reflux, the mixture was evaporated to dryness and purified by flash column chromatography ($Et_2O$/Hex, 1:1) affording **18*S*$_S$** (177 mg, 34%) as a slightly yellow solid: mp 79−81 °C; $[\alpha]_D$ = −26.0 (*c* 0.8, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) δ 7.98 (d, 2H, *J* = 7.2 Hz), 7.93 (d, 2H, *J* = 7.2 Hz), 7.87 (d, 2H, *J* = 7.2 Hz), 7.55−7.26 (m, 9H), 5.59−5.52 (m, 2H), 4.56 (dd, 1H, *J* = 2.8, 12.3 Hz), 4.44 (dd, 1H, *J* = 5.6, 12.3 Hz), 4.28 (d, 1H, *J* = 9.7 Hz), 4.15−4.11 (m, 1H), 3.76(t, 1H, *J* = 9.3 Hz), 2.98 (c, 2H, *J* = 7.5 Hz), 1.92 (bs, 2H), 1.34 (t, 3H, *J* = 7.5 Hz); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 166.3, 166.0, 165.4, 133.5, 133.3, 129.8, 129.7, 128.9, 128.7, 128.4, 91.6, 76.8, 69.0, 63.0, 54.0.9, 43.9, 6.2; HRMS calcd for $C_{29}H_{29}NO_8SNa$ (M + Na)$^+$ 574.1511, found 574.1506 (0.5 ppm).

**1-(*S*)-Ethylsulfinyl-1,2-dideoxy-2-*p*-methoxybenzylideneamino-3,4,6-tri-*O*-benzoyl-β-D-glucopyranoside (9*S*$_S$) Obtained from 18*S*$_S$.** To a mixture of **18*S*$_S$** (145 mg, 0.256 mmol) and $CuSO_4$ (140 mg) in dry $CH_2Cl_2$ (9 mL) was added *p*-anisaldehyde (62 μL, 0.51 mmol). After the mixture was stirred for 24 h, the solvent was evaporated and the mixture was purified by flash column chromatography (EtOAc/Hex, 1:1), using silica gel pretreated with 1% $NEt_3$, affording **9*S*$_S$** in 83% yield as a white solid: mp 76−78 °C; $[\alpha]_D$ = +24.8 (*c* 0.8, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) δ: 8.24 (s, 1H), 8.01 (d, 2H, *J* = 7.4 Hz), 7.89 (d, 2H, *J* = 7.4 Hz), 7.79 (d, 2H, *J* = 7.4 Hz), 7.55−7.26 (m, 11H), 6.80 (d, 2H, *J* = 8.6 Hz), 5.89 (t, 1H, *J* = 9.3 Hz), 5.68 (t, 1H, *J* = 9.7 Hz), 4.87 (d, 1H, *J* = 9.3 Hz), 4.66 (dd, 1H, *J* = 2.7, 12.2 Hz), 4.52 (dd, 1H, *J* = 5.1, 12.2 Hz), 4.30−4.25 (m, 2H), 3.78 (s, 3H), 2.97−2.93 (m 1H), 2.86−2.82 (m 1H), 1.26 (m, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 166.1, 165.7, 165.3, 162.3, 133.4, 133.1, 130.2, 129.8, 129.7, 129.6, 129.5, 129.1, 128.9, 128.4, 128.3, 128.1, 114.0, 91.1, 77.0, 74.3, 69.1, 68.3, 63.2, 55.3, 42.7, 7.3; HRMS calcd for $C_{37}H_{35}NO_9SNa$ (M + Na)$^+$ 692.1930, found 692.1893 (5.4 ppm).

**1-(*S*)-Ethylsulfinyl-3,4,6-tri-*O*-pivaloyl-1,2-dideoxy-2-amino-β-D-glucopyranoside (19*S*$_S$).** To a solution of **17*S*$_S$** (834 mg, 1.11 mmol) in 16 mL of a mixture of solvents $CH_3CN$/EtOH/THF (2:1:1) was added ethylendiamine (0.33 mL).

After 3 h at reflux, the mixture was evaporated to dryness and purified by flash column chromatography (EtOAc/Hex, 3:2) affording **19*S*$_S$** (294 mg, 54%) as a slightly yellow solid: mp 118−120 °C; $[\alpha]_D = -22.3$ (*c* 0.1, MeOH); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 5.08−5.01 (m, 2H), 4.20 (d, 1H, $J = 12.1$ Hz), 4.06 (d, 1H, $J = 9.7$ Hz), 3.98 (dd, 1H, $J = 5.5, 12.4$ Hz), 3.77−3.74 (m, 1H), 3.47 (t, 1H, $J = 9.4$ Hz), 2.97−2.91 (m, 2H), 1.70 (broad s, 2H), 1.35 (t, 3H, $J = 7.5$ Hz), 1.18, 1.17 and 1.13 (3s, 27H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 177.8, 176.6, 91.4, 76.8, 75.7, 67.2, 61.8, 54.8, 43.7, 38.9, 38.8, 38.7, 27.2, 27.1, 27.0, 6.1; HRMS calcd for $C_{23}H_{42}NO_8S$ $(M + H)^+$ 492.2631, found 492.2635 (0.8 ppm).

**1-(*S*)-Ethylsulfinyl-1,2-dideoxy-2-*p*-methoxybenzylideneamino-3,4,6-tri-*O*-pivaloyl-$\beta$-D-glucopyranoside (14*S*$_S$) Obtained by Imination of 19*S*$_S$.** To a mixture of **19*S*$_S$** (294 mg, 0.6 mmol) and $CuSO_4$ (250 mg) in dry $CH_2Cl_2$ (16 mL) was added *p*-anisaldehyde (146 $\mu$L, 1.2 mmol). After being stirred 12 h, the solvent was evaporated and the mixture was purified by flash column chromatography (EtOAc/Hex, 2:1), using silica gel pretreated with 1% $NEt_3$, affording **14*S*$_S$** in 71% yield as a white solid: mp 164−166 °C; $[\alpha]_D = -17$ (*c* 0.7, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 8.24 (s, 1H), 7.61 (d, 2H, $J = 8.6$ Hz), 6.89 (d, 1H, $J = 8.6$ Hz), 5.46 (t, 1H, $J = 9.4$ Hz), 5.19 (t, 1H, $J = 9.8$ Hz), 4.68 (d, 1H, $J = 9.5$ Hz), 4.27 (d, 1H, $J = 12.3$ Hz), 4.15 (dd, 1H, $J = 4.7, 12.4$ Hz), 3.98 (t, 1H, $J = 9.4$ Hz), 3.94−3.92 (m, 1H), 3.83 (s, 3H), 2.92−2.84 (m, 1H), 2.80−2.73 (m, 1H), 1.26−1.23 (m, 12H), 1.14 (s, 3H), 0.98 (s, 3H); $^{13}$C NMR ($CDCl_3$, 50 MHz) $\delta$ 178.0, 176.8, 176.7, 166.3, 162.4, 130.4, 128.1, 114.1, **90.8**, 73.3, 68.4, 67.8, 62.6, 55.4, 42.2, 38.9, 38.8, 27.1, 17.0, 7.5; HRMS calcd for $C_{31}H_{48}NO_9S$ $(M + H)^+$ 610.3049, found 610.3051 (0.2 ppm).

**1-(*S*)-Phenylsulfinyl-3,4,6-tri-*O*-acetyl-1,2-dideoxy-2-*N*-tetrachlorophthalimido-$\beta$-D-glucopyranoside (22*S*$_S$).** Oxidation of **3** using the same procedure as that used for the synthesis of **15*S*$_S$** afforded **22** in quantitative yield as a 10:1 mixture. **Major diastereomer (22*S*$_S$):** $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.48−7.47 (m, 2H), 7.27−7.25 (m, 2H), 7.17−7.14 (m, 1H), 5.70 (t, 1H, $J = 9.6$ Hz), 5.27 (d, 1H, $J = 10.2$ Hz), 5.16 (dd, 1H, $J = 9.4, 10.1$ Hz), 4.93 (t, 1H, $J = 10.1$ Hz), 4.24 (dd, 1H, $J = 5.0, 12.5$ Hz), 4.15 (dd, 1H, $J = 2.0, 12.4$ Hz), 3.86−3.83 (m, 1H), 2.07 (s, 3H), 2.00 (s, 3H), 1.88 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 170.6, 170.5, 169.2, 163.0, 162.0, 140.4, 140.0, 131.9, 128.9, 126.8, 125.0, 124.4, **88.7**, 76.6, 71.6, 67.8, 61.7, 48.8, 20.7, 20.5, 20.4.

**1-Phenylsulfinyl-3,4,6-tri-*O*-acetyl-1,2-dideoxy-2-*N*-phthalimido-$\beta$-D-glucopyranoside (24).** Oxidation of the known **21** using the same procedure used to oxidize **2**, afforded **24** in quantitative yield as 3:1 mixture. **Major diastereomer (24*S*$_S$):** $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.82−7.26 (m, 4H), 5.92 (t, 1H, $J = 9.3$ Hz), 5.21−5.11 (m, 2H), 4.74 (t, 1H, $J = 10.4$ Hz), 4.36−4.13 (m, 2H), 3.97−3.94 (m, 1H), 2.95−2.70 (m, 2H), 2.07 (s, 3H), 2.01 (s, 3H), 1.86 (s, 3H), 1.28 (t, 3H, $J = 7.5$ Hz); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$:170.4, 169.9, 169.3, 134.5, 134.3, 131.4, 123.8, **85.1**, 70.8, 68.4, 61.6, 51.9, 43.0, 29.6, 20.6, 20.5, 20.4, 6.0. **Minor diastereomer (24*R*$_S$):** $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.80−7.70 (m, 4H), 5.81 (t, 1H, $J = 9.3$ Hz), 5.21−5.10 (m, 2H), 4.88 (t, 1H, $J = 10.4$ Hz), 4.36−4.13 (m, 2H), 3.97−3.94 (m, 1H), 3.12−3.05 (m, 1H), 2.82−2.70 (m, 1H), 2.07 (s, 3H), 2.01 (s, 3H), 1.86 (s, 3H), 1.28 (t, 3H, $J = 7.5$ Hz); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 170.3, 169.2, 134.5, 134.3, 131.4, 123.8, **83.8**, 71.5, 68.4, 62.0, 49.3, 41.2, 29.6, 20.7, 20.5, 20.4, 7.2.

**Acknowledgment.** We thank the Dirección General de Investigación Científica y Técnica for financial support (Grant No. PB PPQ 2000-1341 and BQU2001-2425) and Ms. Inmaculada Romero Luque for experimental help. We are grateful to the Bruker-CSIC Excellence Centre of the Instituto de Ciencia de Materiales de Aragón for the acquisition and preliminary treatment of the X-ray diffraction data of **15*S***.

**Supporting Information Available:** X-ray structural data of sulfinyl glycoside **15*S*** and NMR spectra of compounds **3**, **8**, **9*R*/*S***, **13**, **14*R*/*S***, **17*S*$_S$**, **9*S*$_S$**, **14*S*$_S$**, **9*S*$_S$**, **14*S*$_S$**, **22**, and **24**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO026519Q