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Stereoselective Synthesis of 2-Deoxy-2-iodo-glycosides from Furanoses. A New Route to 2-Deoxy-glycosides and 2-Deoxy-oligosaccharides of *ribo* and *xylo* Configuration

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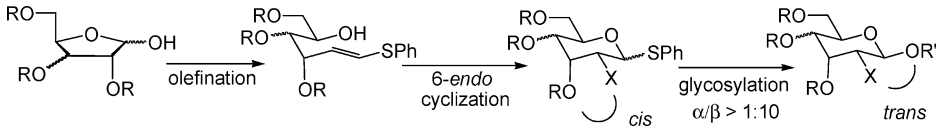

A general procedure for the stereoselective synthesis of 2-deoxy-2-iodo-hexo- and -hepto-pyranosyl glycosides from furanoses is reported. The proposed methodology provides a new route for accessing 2-deoxy-oligosaccharides. The procedure involves three reactions: Wittig−Horner olefination to give alkenyl sulfanyl derivatives, electrophilic iodine-induced cyclization to give phenyl 2-deoxy-2-iodo-1-thio-hexo-glycosides, and glycosylation. Protected furanoses **1**, **3**, and **6**−**11**, which include examples of the four possible isomeric configurations of furanoses, were reacted with diphenyl phenylsulfanylmethyl phosphine oxide to give the alkenyl sulfanyl derivatives **2**, **4**, and **12**−**16**. The iodine-induced cyclization of these compounds afforded the phenyl 2-deoxy-2-iodo-1-thio-glycosides **18**, **20**, and **22**−**27** with practically complete regio- and stereoselectivity. Products of 6-*endo* cyclization, in which the iodine at C-2 was in a *cis* relationship with the alkoxy at C-3, were almost exclusively produced. Better yields were obtained for compounds with a *ribo* or *xylo* configuration than for compounds with other configurations. Compounds **18**, **20**, and **22**−**27** were found to be efficient glycosyl donors in the glycosylation of cholesterol and glucopyranoside **29a**, affording the corresponding 2-deoxy-2-iodo-glycosides and 2-deoxy-2-iodo-oligosaccharides with good yields and stereoselectivities. The glycosydic bond in the major isomers was always *trans* to the iodine at C-2.

Introduction

The 2-deoxy- and 2,6-dideoxyglycoside structural motifs are present in many natural products with interesting biological properties, including the aureolic acid antibiotics (olivomycins, mithromycins, chromomycins), the anthracycline antibiotics (cyclamycin 0), the angucycline group of antibiotics (landomycin A), the enediynes (calicheamycin γ_1^I, esperamycins A_1 and C), cardiac glycosides (digitoxine), and antiparasital agents (avermectins). Removing deoxysugars from these clinically important molecules often severely decreases their efficiency and/or specificity. Deoxysugars also play an important role in lipopolysaccharides, glycoproteins, and glycolipids, where they act as ligands for cell−cell interactions or as targets for toxins, antibodies, and microorganisms.[1] These compounds contain monosaccharide units belonging to the D and L series with all possible configurations (Figure 1).

The stereocontrolled formation of the glycosidic linkage in 2-deoxy-oligosaccharides has proved to be one of the most challenging tasks in glycosylation reactions[2] because of the absence of a stereodirecting group at C-2. This problem can be overcome by using electron-donating groups (such as iodo, phenylsulfanyl, and phenylselenenyl) as stereodirecting groups at position 2 of the glycosyl donor in the glycosylation step. Once

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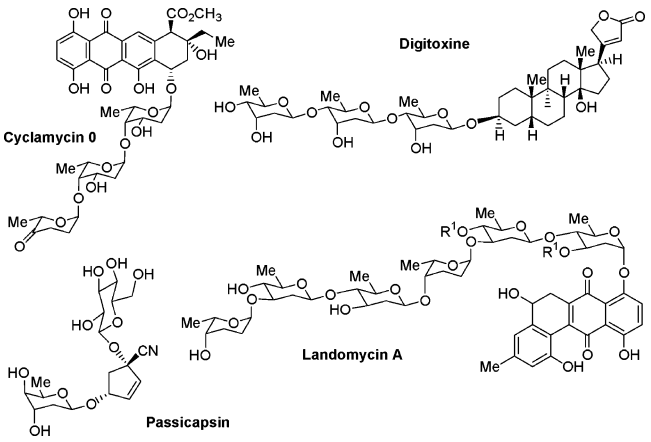
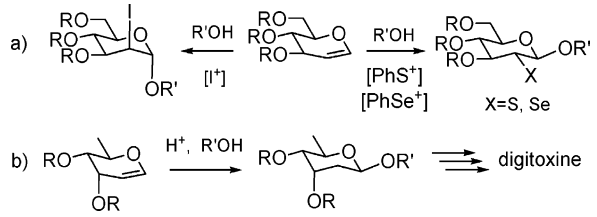


FIGURE 1. Examples of 2-deoxyoligosaccharide molecules containing configurationally different 2-deoxysugars.

SCHEME 1

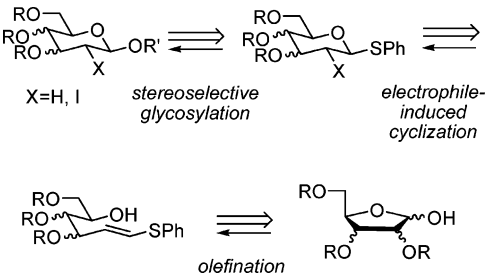


obtained, the 2-heteroatomic-substituted glycosides can be further reduced to provide the corresponding 2-deoxyglycosides.

Glycosylation can be performed from glycals by activation with iodine,[3] sulfanyl,[4] or selenenyl[5] electrophiles through a one-pot procedure to afford mainly *trans*-diaxial (I^+) or *trans*-diequatorial (S^+, Se^+) addition products (Scheme 1a). Glycosylation can also be performed in a two-step procedure by first isolating a 2-deoxy-2-X-glycosyl donor (X = I, SR, SeR) and then activating it in the presence of a glycosyl acceptor.[6] 2-Deoxyglycosides can also be directly synthesized by acid-catalyzed addition of an alcohol to a glycal, as exemplified in the synthesis of digitoxine, where the starting 6-deoxy-allal is prepared from a non-carbohydrate precursor (Scheme 1b).[7]

Most of these procedures have been applied to the synthesis of 2,6-dideoxy-D-*arabino*-hexo-pyranosides (D-olivose) and 2-deoxy-L-*fuco*-pyranosides. However, there are only a few reported examples of the synthesis of 2,6-dideoxy-D-*ribo*-hexo-glycosides (D-digitoxose),[7] and no examples of the synthesis of 2,6-dideoxy-D-*xylo*-hexo-glycosides (D-boivinose), probably because of the difficulty of obtaining the corresponding glycals.

SCHEME 2



2-Deoxy-phosphites,[8] -phosphoroimidates,[9] and -dithiophosphates[10] have also been used as glycosyl donors to provide mainly the α derivative.

Here we report a procedure for synthesizing phenyl 2-deoxy-2-iodo-1-thio-glycosides[11,12] and the use of these glycosides as glycosyl donors for the stereocontrolled synthesis of 2-deoxy-2-iodo-disaccharides. The key step in the proposed synthesis of 2-deoxy-2-iodo-1-thio-glycosides is a cyclization of alkenols induced by iodine-containing electrophiles. These alkenols can be prepared by an olefination reaction starting from protected furanoses (Scheme 2). This procedure is particularly efficient for the synthesis of 2-deoxy-β-hexo-glycosides of *ribo* or *xylo* configuration.[13]

Results and Discussion

The first step in the proposed synthesis of 2-deoxy-2-iodo-1-thio-glycosides was olefination of a series of properly protected furanoses to afford the corresponding enolthioethers. The hydroxyl groups in furanoses **1**, **3**, **6**, **8**, and **11** were protected as benzyl ethers, although acetonides (**7**, **9**, and **10**) and silyl ethers (**9**) were also used as protecting groups. The reaction conditions for olefination were optimized by starting from ribose derivative **1** and using different olefinating reagents, such as ylides,[14] phosphine oxides,[15] phosphonates,[14c] and silylcarbanions.[16] Aucagne et al. recently used a Wittig

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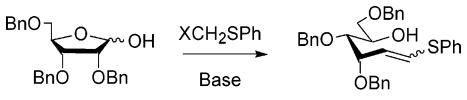
(16) (a) (review) van Staden, L. F.; Gravestock, D.; Ager, D. J. *Chem. Soc. Rev*. **2002**, *31*, 195. (b) Ager, D. J. *J. Chem. Soc., Perkins Trans. 1* **1986**, 183.

TABLE 1. Optimization of Olefination Conditions of Furanose 1 To Obtain Thioalkene 2[a]



1 2

entry	X	temp (°C)	yield (%) (*Z*/*E* ratio)[b]
1	PPh_3	0 → rt	
2	$(Et_2O)PO$	−78 → rt	18 (0:1)
3	Ph_2PO	−78 → rt	35 (1:4)
4	Ph_2PO	−78 → reflux	72 (1:4)
5	Me_3Si	−78 → rt	50 (3:2)

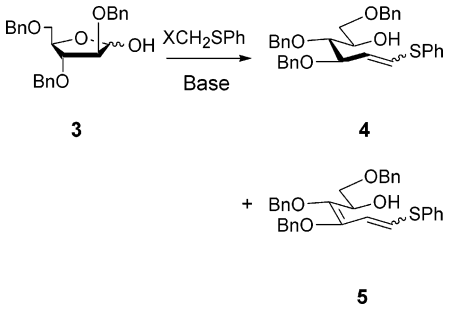
[a] Base = BuLi, solvent = THF. [b] Determined by integration of the olefinic proton signals in the ^{1}H NMR spectrum of the crude reaction mixture.

reaction to synthesize carbohydrate-derived vinyl sulfides in good yields with, in general, preferential formation of the *Z* isomer.[17] Reaction of **1** under Wittig conditions furnished a complex mixture (Table 1, entry 1). Wadsworth−Emmons olefination led to the formation of the desired alkene **2** in low yield regardless of the base used but with complete *E*-stereoselectivity (Table 1, entry 2). Peterson olefination with silyl carbanions afforded enolthioether **2** in 50% yield as a *Z*/*E* mixture, but small amounts of a secondary product, formed by epimerization at the allylic position, were isolated (Table 1, entry 5).[18] To prevent epimerization, cerium-modified Peterson olefination[19] was carried out, but only the starting material was recovered. The highest yields of alkene **2** (72%) were obtained when a phosphine oxide was used and *n*-BuLi was used as the base (Table 1, entries 3, 4). As expected for a semistabilized olefinating reagent, the stereoselectivity was low and an inseparable 1:4 *Z*/*E* mixture was obtained.

To determine the generality of the reaction and the influence of the stereochemistry at position 2, arabinose derivative **3** was also subjected to a range of olefination conditions. The behavior observed was similar to that found for furanose **1**. Wittig olefination afforded the alkene **4** in a 70% yield, together with a 10% of diene **5** as a result of a tandem olefination−elimination process (Table 2, entry 1).[17] As already observed for **1**, reaction of **3** with phosphonates afforded alkene **4** in modest yields with complete stereoselectivity (Table 2, entry 2). Peterson olefination of **3** yielded **4** in moderate yield (61%) as a Z/E mixture (Table 2, entry 5). The Wittig−Horner reaction with the corresponding phosphine oxide was the best choice; it afforded alkene **4** quantitatively as a 2:3 *Z*/*E* mixture (Table 2, entries 3 and 4).

The Wittig−Horner reaction with Li-bases is ideally described as a two-step procedure in which a β-hydroxyphosphine oxide intermediate is formed and then subsequently transformed to the alkene by reaction with KH or NaH.[20] With semistabilized reagents, however, the alkene can be obtained directly.[15c]

TABLE 2. Optimization of the Olefination Conditions of Furanose 3[a]

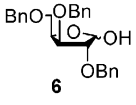
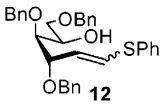
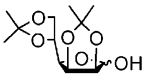
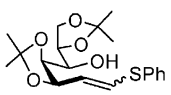
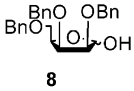
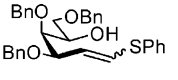
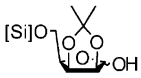
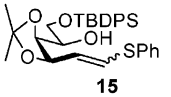
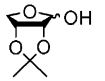
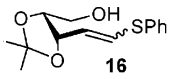
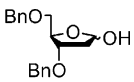
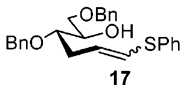


3 4 5

entry	X	temp (°C)	product	yield (%) (*Z*/*E* ratio)[b]
1	PPh_3	0 → rt	**4**	70 (1:4)
2	$(Et_2O)PO$[c]	−78 → rt	**4**	23 (0:1)
3	Ph_2PO	rt	**4**	85 (1:3)
4	Ph_2PO	−78 → rt	**4**	100 (2:3)
5	Me_3Si	−78 → rt	**4**	61 (3:2)

[a] Base = BuLi, solvent = THF. [b] Determined by integration of the olefinic proton signals in the ^{1}H NMR spectrum of the crude reaction mixture. [c] Base = LDA. [c] 10% of compound **5** was also obtained.

TABLE 3. Olefination of Furanoses 6−11[a]

entry	furanose	product	yield (%) (*Z*/*E* ratio)[b]
1	 **6**	 **12**	60 (1:4)
2	 **7**	 **13**	63 (1:10)
3	 **8**	 **14**	52 (1:17) 10[c] (7:1)
4[d]	 **9**	 **15**	21 (1:8) 10[c] (1:1)
5	 **10**	 **16**	35 (1:3) 33[c] (12:1
6	 **11**	 **17**	100 (1:1)

[a] Reaction conditions: ratio substrate/phosphine oxide/BuLi = 1:4:4.4, solvent = THF, temperature −78 °C to rt. [b] Determined by integration of the olefinic proton signals in the ^{1}H NMR spectrum of the crude reaction mixture. [c] Additional yield obtained by elimination of the isolated β-hydroxyphosphine intermediate. [d] [Si]: *tert*-butyldiphenylsilyl.

Once the optimal conditions had been established, furanoses **6**−**11** were olefinated. The yield of benzylated furanoses ranged from 60% (Table 3, entries 1 and 3) to 100% (entry 6). Isopropylidene-protected furanoses gave

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(18) Freeman, F.; Robarge, K. D. *Carbohydr. Res.* **1986**, *154*, 270.
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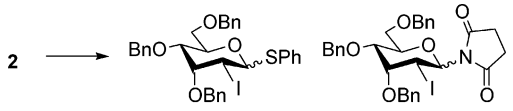
(20) Buss, A. D.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2307.

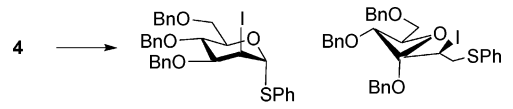
TABLE 4. Cyclization of Alkenyl Sulfide 2 Induced by Electrophilic Iodine Containing Reagents



entry	**2** (*Z*/*E* ratio)[a]	[I] (equiv)	base (equiv)	solvent	temp (°C)	*t* (h)	product	yield (%)	a/*β* ratio[b]
1	0:1	I_2 (3)	KH (1.3)	ether	−78 → rt	1	**18**	63	0:1
2	1:2	I_2 (3)	KH (1.3)	ether	−78 → rt	16	**18**	9	0:1
3	1:2	NIS (1.5)	$NaHCO_3$ (1.5)	CH_3CN	−30 → rt	15	**18**	77	1:9
4	2:3	NIS (1.5)		CH_2Cl_2	−78 → rt	12	mixture		
5[c]	1:2	NIS (1.5)		CH_2Cl_2	−30	0.75	**19**	64	1:41

[a] Determined by integration of the olefinic proton signals in the ^{1}H NMR spectrum of the crude reaction mixture. [b] Determined by integration of the anomeric proton signals in the ^{1}H NMR spectrum of the crude reaction mixture. [c] Molecular sieves were added to the reaction mixture.

TABLE 5. Cyclization of Alkenyl Sulfide 4 Induced by Electrophilic Iodine Containing Reagents



entry	**4** *Z*/*E* ratio[a]	[I] (equiv)	base (equiv)	solvent	temp (°C)	*t* (h)	product	yield (%)
1	0:1	I_2 (3)	KH (1.3)	ether	−78	1	**20**	61
2	1:3	I_2 (3)	KH (2.5)	ether	−78 → rt	1.5	**21**	31
3	3:2	I_2 (3)	$NaHCO_3$ (3)	CH_3CN	−30 → rt	16	**20**	18
4	1:3	NIS (3)	$NaHCO_3$ (3)	CH_3CN	−30	3	**20**	20
5	1:3	NIS (3)	$NaHCO_3$ (3)	CH_3CN	0	18	**20**	24
6	1:3	NIS (1.5)	$NaHCO_3$ (1.5)	CH_3CN	0	18	**20**[b]	36

[a] Determined by integration of the olefinic proton signals in the ^{1}H NMR spectrum of the crude reaction mixture. [b] Trace amounts of the succinimido glycoside were detected by TLC.

lower yields (21−63%), probably due to higher steric hindrance (Table 3, entries 2, 4, and 5). In contrast, olefination of the 2-deoxy-ribose derivative **11** yielded alkene **17** quantitatively. Starting from the lyxose and erythrose derivatives **8**, **9**, and **10**, the corresponding *β*-hydroxyphosphine oxide intermediate was recovered together with the alkene,[14b] so the former was subsequently treated with NaH. This increased the initial alkene yields (52%, 21%, and 35%, respectively) to 62%, 31%, and 68%, respectively (Table 3, entries 3, 4, and 5).

In all cases, the *Z*/*E* mixtures of alkenes proved to be inseparable; hence, the cyclization reactions were assayed directly on the mixture of diastereomers. Cyclization from the pure *E* alkenes was possible from the Wadsworth−Emmons alkene products.

Electrophile-induced cyclization was first studied for derivative **2**. The reaction of diastereoisomerically pure **2***E* with iodine as the electrophile and KH as the base afforded 2-deoxy-2-iodo-*β*-D-*allo*-thioglycoside **18** in 63% yield (Table 4, entry 1). In contrast, when the reaction was carried out starting from a 1:2 *Z*/*E* mixture under the same conditions, **18***β* was obtained with the dramatically decreased yield of 9% (Table 4, entry 2). Cyclization was also assayed using other electrophilic reagents such as *N*-iodosuccinimide (NIS) with $NaHCO_3$ as the base, and the best yields of thioglycoside **18** were obtained after 15 h (77%, α/*β* = 1:9) (Table 4, entry 3). Under these conditions, traces of the succinimido glycoside **19** were detected by ^{1}H NMR spectroscopy; this glycoside was presumably formed by activation of the anomeric phenylsulfanyl group in **18** and nucleophilic attack of the succinimido anion. To diminish the nucleophilicity of the succinimido group when NIS was used as the electrophilic reagent, the reaction was carried out in the absence of base. Under these conditions, either a complex mixture was obtained (Table 4, entry 4) or, when molecular sieves were added to the reaction mixture, **19** was exclusively recovered in 64% yield as a 1:41 α/*β* mixture (Table 4, entry 5).

The arabinose derivative **4** was then tested in the cyclization reaction. Reaction of diastereomerically pure **4***E* with iodine and KH in ether afforded 2-deoxy-2-iodo-α-*manno*-thioglycoside **20** exclusively in 61% yield (Table 5, entry 1). As for the ribose derivative **2**, cyclization of the *Z*/*E* mixture of **4** under the same conditions proved difficult. Forcing the reaction conditions (higher temperatures and KH concentration) did not yield the desired compound; rather it led to the formation of oxetane **21** in 31% yield as a result of isomerization of the double bond to an enol ether and subsequent cyclization (Table 5, entry 2). Although the mechanism by which **21** was formed was not studied in detail, deuteration experiments seemed to exclude base-promoted isomerization of the double bond. Isomerization may, however, have occurred through a radical mechanism. Using a weaker base such as $NaHCO_3$ in combination with iodine led to the formation of α-thioglycoside **20**, but only in 18% yield (Table 5, entry 3).

To increase the yield of the cyclization, the reaction was also studied using NIS as the electrophile under

various conditions. The best results (36% yield of **20**α) were obtained using 1.5 equiv of NIS and 1.5 equiv of $NaHCO_3$ at 0 °C in CH_3CN (Table 5, entry 6). The use of NIS as the electrophile always led to the formation of traces of the succinimido glycoside, similar to the behavior of **2** described above. The *Z* isomer of **4** did not cyclize under any of the conditions tested.

These preliminary cyclization assays revealed that the cyclization conditions are very sensitive to the configuration of the hexenyl sulfide. The optimal conditions for ribose derivative **2** are different from those for arabinose **4**, which proved to be very resistant to cyclization. The geometrical configuration of the alkene is also crucial for cyclization. The *E* isomer of the alkenes readily reacted to give the corresponding thioglycosides in moderate to good yield, whereas the *Z* isomers either required a higher temperature to cyclize or did not cyclize. This difference in reactivity between the *Z* and *E* alkenes makes it necessary to force the conditions to ensure full conversion when starting from inseparable *Z*/*E* mixtures of alkenes, which leads to partial decomposition of the thioglycoside products. This decomposition process is the cause of the low thioglycoside yields obtained from the cyclization reactions of the *arabino* derivative **4** and, to a lesser extent, the *ribo* derivative **2** (Table 4). In light of the results obtained, the cyclization conditions for compounds **12**−**17** had to be optimized. Table 6 summarizes the reaction conditions that gave the best result for each substrate. For the cyclization of **12**, the best conditions were to use iodonium dicollidine perchlorate (IDCP) as the electrophilic reagent in CH_3CN, which afforded 2-deoxy-2-iodo-guloside **22** (77%) as a 1:10 α/*β* mixture (Table 6, entry 1). As shown by the α/*β* ratio, the *Z* isomer undergoes cyclization, although it requires higher temperatures ($\Delta T \sim 10$ °C) than the *E* isomer. The same conditions were found to be the optimal for the cyclization of **13** into 2-deoxy-2-iodo-D-glycero-*talo*-pyranoside **23**.

From diastereomerically pure **13***E*, **23**α was exclusively obtained in 97% yield (Table 6, entry 2). In contrast, cyclization of a 1:6 *Z*/*E* mixture of **13** rendered **23**α but in a much lower yield (48%) (Table 6, entry 3). Forcing the reaction conditions (higher temperatures and longer reaction times) led to cyclization of both the *E* and *Z* isomers to give **23** in 60% yield (α/*β* ratio = 2:1) but also produced the corresponding 2-iodo-lactol (16%) as a consequence of the activation of the sulfanyl group in the product **23**.

Reaction of the *lyxo* derivative **14** with IDCP in CH_2Cl_2 afforded 2-iodo-α-*talo*-pyranoside **24** in 20% yield together with 2-iodo-*β*-*galacto*-pyranoside **25** in 15% yield.

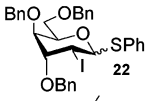
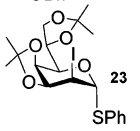
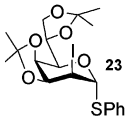
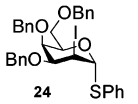
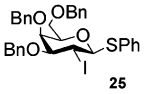
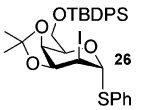
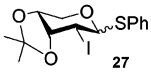
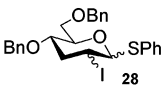
Slightly better results were obtained in the reaction of the isopropylidene-protected *lyxo* derivative **15** with NIS in acetonitrile, which gave the 2-iodo-*talo*-pyranoside **26** in 55% yield as a 42:1 α/*β* mixture.

The effect of the substitution of the hydroxyl-bearing carbon atom on the cyclization was also studied. Treatment of the erythrose derivative **16** with IDCP in propionitrile at −78 °C gave the 2-iodo-thioglycoside **27** in 33% yield, together with the corresponding 2-iodolactol in the same yield.

To gain insight into the stereochemical outcome, the cyclization was carried out starting from the alkenyl sulfide **17**, which lacks an allylic alkoxy group. The reaction of **17** with NIS afforded a mixture of four compounds that were separated into two fractions. On the basis of NMR spectroscopic analysis, these fractions were assigned to a 1:1 C-2 epimeric mixture of 2,3-dideoxy-2-iodo-thioglycosides with their corresponding α/*β* anomers (47% yield, Table 6, entry 7).

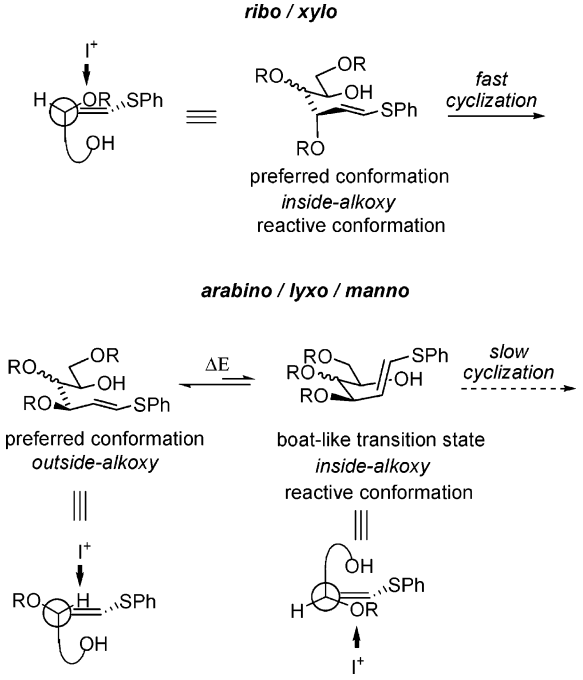
This series of experiments established that the hydroxy-hexenyl sulfides **2**, **4**, and **12**−**17** undergo a completely 6-*endo* regioselective electrophilic iodine reagent-induced cyclization. The normal 5-*exo* course observed in analogue hexenols is biased to the 6-*endo* mode by the presence of an electron-donating atom at the terminus of the double bond. Sulfur stabilizes a positive charge on the neighboring carbon atom, making the 6-*endo* cyclization possible.

TABLE 6. Cyclization of Alkenyl Sulfides 12−17 Induced by Electrophilic Iodine-Containing Reagents

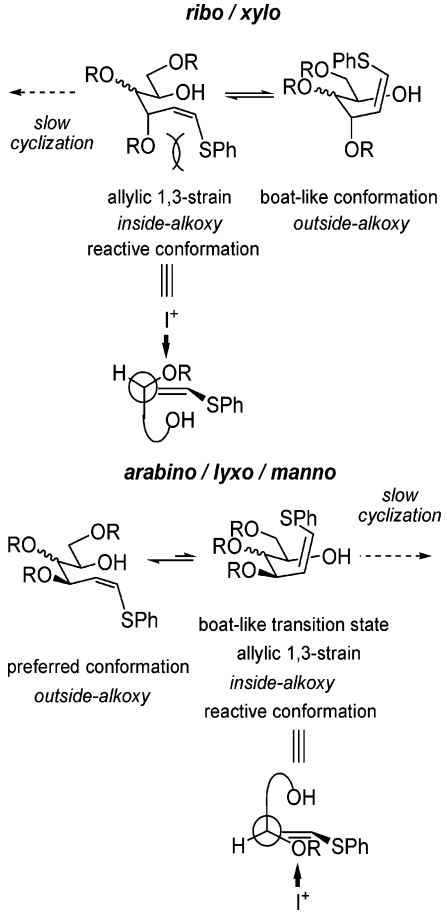
entry	starting material (*Z*/*E* ratio)[a]	cyclization conditions	cyclization product	yield (%)	α/β ratio[b]
1	**12** (1:10)	IDCP (2.2) CH_3CN -30ºC, 3h	 **22**	77	1:10
2	**13** (0:1)	IDCP (2.2) CH_3CN -45--30ºC, 2h	 **23**	97	1:0
3	**13** (1:6)	IDCP (2.2) CH_3CN -45ºC-rt, 1.5h	 **23**	48[c]	1:0
4	**14**[d] (1:7)	IDCP (2.2) CH_2Cl_2 -78ºC, 2.5h	 **24**	20	1:0
			 **25**	15	0:1
5	**15** (1:8)	NIS (1.5) CH_3CN -30ºC, 15h	 **26**	55	42:1
6	**16** (2:3)	IDCP (2.2) CH_3CH_2CN -78ºC, 23h	 **27**	33[e]	1.1:1
7	**17** (1:1)	NIS (1.5) CH_3CN -30ºC, 0.5 h	 **28**	47[f]	-

[a] Determined by integration of the olefinic protons signals in the ^1H NMR spectrum of the crude reaction mixture. [b] Determined by integration of the anomeric protons signals in the ^1H NMR spectrum of the crude reaction mixture. [c] 60% of **23** (2:1 α/*β* ratio) and the corresponding 2-iodo-lactol (16%) were obtained when the reaction mixture was stirred at room temperature for a prolonged time. [d] Conversion: 69%. [e] 33% of the corresponding 2-iodo-lactol was also obained. [f] A 1:1 C-2 epimeric mixture was obtained, which decomposed on standing.

SCHEME 3. Proposed Models for the Electrophile-Induced Cyclization Reactions of *E*-Hydroxy-alkenyl Sulfides 2, 4, and 12−17



SCHEME 4. Proposed Models for the Electrophile-Induced Cyclization of *Z*-Hydroxy-alkenylsulfides 2, 4, and 12−17



Furthermore, the cyclization reaction is highly stereoselective and very predictable in terms of the stereochemical outcome. The relative stereochemistry of C-1 and C-2 in thioglycosides depends on the configuration of the starting alkene. Thus, the reaction of the *E*-alkenyl sulfide yields a cyclization product in which the iodine atom and phenylsulfanyl group are in a *trans* arrangement. In all cases where the *Z* alkene underwent cyclization, 2-iodo-thioglycosides were obtained with the substituents at C-1 and C-2 in a *cis* disposition.

Another important issue associated with stereoselectivity is the formation of cyclized products in which the iodo group at C-2 is always *cis* with respect to the alkoxy group at C-3. This is a key point in the global process because the iodine configuration determines the configuration of the anomeric center in the glycosylated products. The stereoselectivity observed for the alkenes considered here is consistent with that reported for alkenols with an allylic alkoxy group[21] and is determined by a stereoelectronic effect known as the "inside-alkoxy effect".[22] This effect favors cyclization from the most reactive conformation, in which the allylic alkoxy group is placed inside the plane that configures the framework of the double bond. In this conformation, the σ^* C−O orbital is perpendicular to the π-system of the double bond, which minimizes the electron-withdrawing effect, causing the double bond to be more electron-rich and hence more reactive toward electrophiles.

The stereodirecting role of the allylic group is evident in the cyclization of **17**, which lacks an allylic OR group. Since there is no stereoelectronically preferred conformation in the cyclization of **17**, the cyclization reaction yields a C-2 epimeric mixture of 2-iodo-thioglycosides.

The inside-alkoxy effect may well explain why the *Z* thioether is less reactive than the corresponding *E* isomer (Schemes 3 and 4). Specifically, the inside-alkoxy conformation of the *Z* alkenes is sterically crowded and, therefore, the activation energy that must be overcome to form the transition state in the cyclization will be higher than for the corresponding *E* alkenes. For some compounds, such as the arabinose derivative, the activation energy is sufficiently high that cyclization is precluded. Although such compounds could also undergo cyclization via the outside-alkoxy conformation, this conformation is insufficiently reactive to promote cyclization.

An exception to the inside-alkoxy effect rule is the *lyxo* derivative **14**, which undergoes cyclization to give a mixture of the expected pyranoside **24** together with **25**, where the latter product is formed by cyclization of the *E* isomer of **14** through a transition state in which the alkoxy group is located in an outside position. The formation of outside-alkoxy products has previously been described in relation to electrophile-induced cyclizations of *Z*-enolethers to give cyclohexyl pyranosides.[23] These previous results, however, can be accounted for in terms

(21) (a) Landais, Y.; Panchenault, D. *Synlett* **1995**, 1191. (b) Bravo, F.; Castillón, S. *Eur. J. Org. Chem.* **2001**, 507.

(22) (a) Stork, G.; Kahn, M. *Tetrahedron Lett.* **1983**, *24*, 3951. (b) Houk, K. N.; Moses, S. R.; Wu, Y.-D.; Rondan, N. G.; Jäger, V.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880. (c) Halter, J.; Strassner, T.; Houk, K. N. *J. Am. Chem. Soc.* **1997**, *119*, 8031.

(23) (a) Suzuki, K.; Mukaiyama, T. *Chem. Lett.* **1982**, 683−686. (b) Suzuki, K.; Mukaiyama, T. *Chem. Lett.* **1982**, 1525.

of the high steric hindrance of the inside-alkoxy conformation in the *Z* alkenes and the presence of an electron-rich double bond, which will be reactive toward cyclization even in the outside-alkoxy conformation. In contrast, cyclization of **14***E* is not subject to 1,3-allylic strain and therefore the inside-alkoxy conformation should be the lowest-energy conformation. In fact, aside from **14**, none of the other alkenes studied, including the isopropylidene *lyxo* derivative **15**, gave outside-alkoxy products. At present we do not have an explanation for the formation of **25**.

The inside-alkoxy effect can also explain why the reactivities of the *ribo* and *xylo* derivatives differed from those of the *arabino* and *lyxo* derivatives (Scheme 3). For the *ribo* and *xylo* derivatives **2** and **12**, the most stable conformer is the one that leads to the preferred transition state for cyclization, that is, the conformation in which the large alkyl group is *anti* to the incoming electrophile and the allylic alkoxy group occupies the inside position. As a result, the cyclization readily proceeds. For the *arabino* and *lyxo* derivatives **4** and **14**, by contrast, the preferred conformation (outside-alkoxy) is not the one that favors cyclization, and hence a conformational change must occur for cyclization to proceed. For these molecules, the preferred transition state has a boatlike conformation, which is higher in energy than the transition states of the *ribo* and *xylo* derivatives. Consequently, the cyclization is slower for the *arabino* and *lyxo* derivatives than for the *ribo* and *xylo* derivatives.

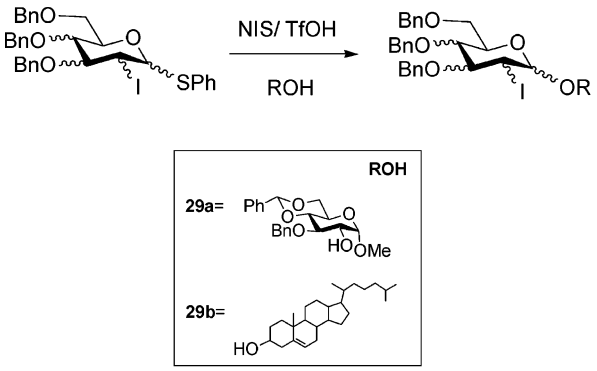
The higher reactivity of **13** compared to **4** can be explained by the presence of the isopropylidene group, which restricts the conformational freedom and accordingly favors cyclization. The cyclization yield of thioalkenes with *arabino* and *lyxo* configurations is low because the initially produced thioglycoside is further activated under the cyclization conditions because the electrophilic reagent used for the cyclization, NIS, can also activate the thioglycoside.

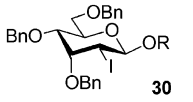
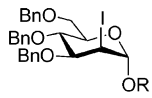
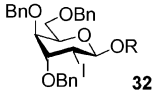
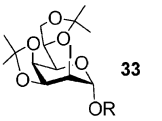
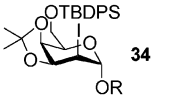
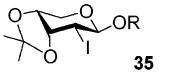
Cyclization of the *erythro* derivative **16** to produce **27** should be easy, as for the *ribo* and *xylo* derivatives **2** and **12**. The low yield (33%) of **27** is a consequence of its high reactivity toward the activation of an anomeric phenylsulfanyl group in the presence of IDCP even at −78 °C. This reactivity is general to all 6-deoxy-glycosides.[24] Under these conditions, the initially formed 2-iodo-thioglycoside **27** was partially consumed to produce the corresponding 2-iodo-lactol in 33% yield. In this context, the α/*β* ratio of **27** may not reflect the diastereoselectivity of the cyclization, because the two thioglycoside anomers may be activated at different rates.

The 2-deoxy-2-iodo-thioglycosides **18**, **20**, **22**, **23**, **24**, **26**, and **27** were found to be quite stable and can be stored in the refrigerator for several months without significant decomposition. The only labile 2-deoxy-2-iodo-thioglycosides were **25** and **28**, which decomposed on standing.

The glycosyl donors **18**, **20**, **22**, **23**, **26**, and **27** were tested for stereoselective glycosylation of methyl 4,6-*O*-benzylidene-3-*O*-benzyl-α-D-glucoside (**29a**) and cholesterol (**29b**) under typical conditions for thioglycosides[25] (Table 7). Starting from 1,2-*trans*-diequatorial substituted glycosyl donors **18** and **22**, glycosides **30** and **32** were obtained in yields of 61% to 81% with α/*β* ratios between 1:6 and 1:16 (Table 7, entries 1 and 3). Treatment of **20** with NIS/TfOH in the presence of **29a** afforded 2-deoxy-2-iodo-mannoside **31a** as a 45:1 α/*β* mixture in 71% yield. Glycosylation of **29b** afforded **31b** with slightly lower stereoselectivity (α/*β* ratio = 37:1) in 71% yield (Table 7, entry 2). Similar behavior was observed in the glycosylation of **29a** and **29b** with **23** to afford **33a** and **33b** in 69% and 57% yield, respectively, although the glycosylation of **29b** proceeded with lower α-selectivity (8:1), probably due to the higher temperature required to promote glycosylation (Table 7, entry 4).

TABLE 7. Stereoselective Glycosylation of 29a and 29b from 2-Deoxy-2-iodo-thioglycosides 18, 20, 22, 23, 26, and 27



entry	starting material	glycosylation product	glycosylation conditions[a]	yield (%)	α/β ratio[b]
1	**18**	 **30**	**30a** -40°C 2.5h **30b** -40°C 2.5h	74% 81%	1:6 1:9
2	**20**	 **31**	**31a** -40°C 2h **31b** -40°C 2h	71% 71%	45:1 37:1
3	**22**	 **32**	**32a** -40°C 3h **32b** -40°C 3h	61% 66%	1:16 1:8
4	**23**	 **33**	**33a** -60°C 1h **33b** -20°C 20h	69% 57%	40:1 8:1
5	**26**	 **34**	**34a** -78°C 1.5h **34b** -78°C 1.5h	59% 36%	20:1 10:1
6	**27**	 **35**	**35a** -78°C 0.5h **35b** 0°C 12h	44% 46%	1:3 1:25

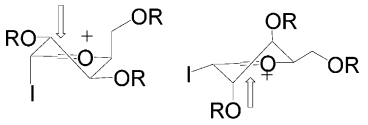
[a] 1 mmol glycosyl donor, 2 mmol glycosyl acceptor, dry CH_2Cl_2, NIS (2.2 mmol), 20 mol % TfOH. [b] Determined by integration of the anomeric proton signals in the ^1H NMR spectrum of the crude reaction mixture.

(24) See ref 6e and references therein.

(25) Veeneman, G. H.; van Leeuwen, S. H.; van Boom, J. H. *Tetrahedron Lett.* **1990**, *31*, 1331.

When compared with **18** and **22**, the 1,2-*trans*-diaxial substituted glycosyl donors **20**, **23** and **26** provided improved stereoselectivities, especially in the glycosylation of **29a**. These results are in agreement with those reported by Roush and Narayan for the glycosylation of 2-deoxy-2-iodo-*manno*- and 2-deoxy-2-*talo*-pyranosyl acetates.[6g]

To address the stereoselectivity of glycosylation of the *gulo* derivative **22**, both the conformational preferences and relative reactivities of the intermediate pyranosyl oxocarbenium ions **a** and **b** implicated in this reaction must be taken into account.[26,6a]



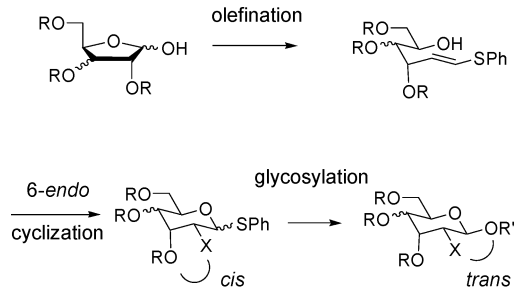
According to the work of Ayala et al.,[26a] the diaxial oxocarbenium **b** is likely to be more stable than **a**, suggesting that the attack of the alcohol would preferentially give the α-derivative. However, for the nucleophile to attack the lower energy diaxial conformer **b**, it must overcome steric interactions with the pseudoaxial C-3 benzyloxy substituent, which will attenuate the reactivity of **b**. By contrast, the incoming nucleophile does not need to overcome this steric interaction with the C-3 substituent when approaching the diequatorial conformer **a**. Hence, although **a** is predicted to be higher in energy than **b**, it is potentially more reactive. Consistent with this, glycosylation of **22** affords the *β*-anomers **32a** and **32b**, indicating that the nucleophile attacks the diequatorial oxocarbenium ion conformer. This type of stereochemical control is consistent with Curtin−Hammett kinetics.

Glycosylation of **29a** with the glycosyl donor **27** afforded **35a** in 44% yield with moderate (1:3) *β*-selectivity. As observed previously for 6-deoxy-glycosides,[24] thioglycoside **27** was very reactive toward glycosylation and required very low temperatures (−78 °C). Because glycosylation of cholesterol was difficult to monitor by TLC, higher temperatures and a longer reaction time were used to ensure maximum conversion to glycoside **35b**, which was obtained in 46% yield with selectivity α/β = 1:25 (Table 7, entry 6).

Conclusion

We have presented a general procedure for the stereoselective synthesis of 2-deoxy-2-iodo-hexo-pyranosyl glycosides from furanoses. The proposed methodology provides a new avenue for accessing 2-deoxy-oligosaccharides. The procedure involves three reactions: Wittig−Horner olefination to give alkenyl sulfanyl derivatives; electrophilic iodine-induced cyclization to give phenyl 2-deoxy-2-iodo-1-thio-pyranosides, a new type of glycosyl donor; and glycosylation. The olefination reaction affords the alkenyl sulfanyl derivatives in good to excellent yields, except in cases where the conformational freedom is constrained by protecting groups such as isopropylidene groups. The cyclization reaction proceeds with complete regio- and stereoselectivity. The reaction proceeds exclusively as 6-*endo* cyclization to give phenyl 1-thio-pyranoside derivatives. The stereochemistry of the iodine at C-2 is always *cis* to the neighboring alkoxy group, except for **25**. This is a key point in the overall process because the iodine controls the stereoselectivity of the glycosylation reaction. The yield of the cyclization depends on the configuration of the starting material; it is very good for substrates with a *ribo* or *xylo* configuration but more modest for those with an *arabino* or *lyxo* configuration. The glycosylation reaction carried out with cholesterol, which can be looked upon as a model of the aglycones present in natural products, and with monosaccharide **29a** proceeded with good yields and good to excellent stereoselectivities. The glycosidic bond created in the major isomers was always *trans* to the iodine at C-2.

SCHEME 5



	olefination (%)	cyclization (%)	glycosylation (%)	(α:β)	
ribose **2**	72	77	74	1:6	**30a**
			81	1:9	**30b**
xylose **6**	60	77	61	1:16	**32a**
			66	1:8	**32b**

Although phenyl 2-deoxy-2-iodo-1-thio-glycosyl donors of all configurations can be accessed using the proposed procedure, it is particularly effective at providing 2-deoxy-2-iodo-D-*gulo*- and -D-*allo*-glycosides (Scheme 5). These glycosides are precursors of 2-deoxy-glycosides of *ribo* and *xylo* configuration, which are difficult to obtain by the classical methodology starting from glycals.[3e,27]

Experimental Section

General Remarks. Optical rotations were measured at room temperature in 10 cm cells. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded using a 300 and 400 MHz apparatus, with $CDCl_3$ as solvent, Me_4Si as an internal reference, and H_3PO_4 (^{31}P) as external standard, unless specified otherwise. Elemental analyses were performed in the Servei de Recursos Científics (URV). Flash column chromatography was performed using silica gel 60 A CC (230−400 mesh). Radial chromatography was performed on 1, 2, or 4 mm plates of Kieselgel 60 PF_{254} silica gel, depending on the amount of product. Medium-pressure liquid chromatography (MPLC) was performed using silica gel 60 A CC (6−35 μm). Solvents were purified using standard procedures.

(26) (a) Ayala, L.; Lucero, C. G.; Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. *J. Am. Chem. Soc.* **2003**, *125*, 15521. (b) Bravo, F.; Viso, A.; Alcázar, E.; Molas, P.; Bo, C.; Castillón, S. *J. Org. Chem.* **2003**, *68*, 686.

(27) Wittman, M. D.; Halcomb, R. L.; Danishefsky, S. J. *J. Org. Chem.* **1990**, *55*, 1979.

Wittig−Horner Olefination of Furanoses 1, 3, and 6−11. To a solution of diphenyl phenylsulfanylmethyl phosphine oxide (4 mmol) in THF (26 mL) at −78 °C was added BuLi (4.4 mmol). The mixture was left to stir at low temperature for 30 min. A solution of the corresponding furanose (1 mmol) in THF (2 mL) was then added dropwise. The mixture was allowed to warm to room temperature overnight. A saturated solution of NH_4Cl was then added and the olefination product was extracted with ether. The combination of ethereal layers was dried with $MgSO_4$ and concentrated. The reaction crude was purified by chromatographic techniques.

Elimination from the β-Hydroxy-phosphine Oxide Intermedeate To Afford the Alkene. A mixture of the β-hydroxyphosphine oxide intermediate and diphenyl (phenylthiomethyl)phosphine oxide, recovered from the Wittig−Horner reaction, was solved in THF (30 mL) and then the same amount in weight of NaH 60% was added. The reaction mixture was stirred at room temperature for 5 h and then quenched by adding saturated aqueous NH_4Cl. The mixture was extracted with Et_2O, dried over $MgSO_4$, and concentrated under reduced pressure. The crude was purified by chromatographic techniques to afford the alkene.

(*Z*/*E*)-3,4,6-Tri-*O*-benzyl-1,2-dideoxy-1-phenylsulfanyl-D-*ribo*-hex-1-enitol (2). As described in the general procedure, **1** (5.5 g, 13 mmol) was olefinated by reaction with diphenyl (phenylthiomethyl)phosphine oxide (16.9 g, 52.2 mmol) and BuLi (35.9 mL of 1.6 M hexane solution, 57.4 mmol) for 48 h under refluxing conditions. Column chromatography (hexane to EtOac/hexane 1:3) afforded **2** (4.96 g, 72%) as an inseparable 1:4 *Z*/*E* mixture as a yellowish syrup. Data obtained from the mixture. R_f (EtOAc/hexane 1:3): 0.27. Anal. Calcd for $C_{33}H_{34}O_4S$: 75.25 C, 6.51 H, 6.09 S. Found: 75.27 C, 6.50 H, 6.12 S. **2*E***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35−7.22 (m, 20H), 6.50 (d, *J* = 16, 1H), 5.91 (dd, *J* = 16, 8, 1H), 4.77 (d, *J* = 11.2, 1H), 4.67 (d, *J* = 11.6, 1H), 4.56 (d, *J* = 11.2, 1H), 4.51 (d, *J* = 12, 1H), 4.48 (d, *J* = 12, 1H), 4.40 (d, *J* = 11.6, 1H), 4.23 (dd, *J* = 8.8, 4.4, 1H), 4.84−3.82 (m, 1H), 3.64−3.58 (m, 2H), 3.70 (dd, *J* = 7.6, 4, 1H), 2.72 (d, *J* = 4.4, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.6−134.8, 130.2−126.9, 129.0, 128.7, 81.5, 81.0, 74.4, 73.6, 71.1, 71.0, 70.7. **2*Z***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35−7.22 (m, 20H), 6.58 (d, *J* = 9.6, 1H), 5.95 (dd, *J* = 9.6, 9.6, 1H), 4.84−4.45 (m, 6H), 3.87−3.85 (m, 1H), 3.77 (dd, *J* = 8.4, 4, 1H), 3.68−3.65 (m, 1H), 3.64−3.58 (m, 2H), 2.78 (d, *J* = 4.8, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.6−134.8, 130.2−126.9, 81.2, 77.4, 74.3, 73.5, 71.2, 71.0, 70.7.

(*Z*/*E*)-3,4,6-Tri-*O*-benzyl-1,2-dideoxy-1-phenylsulfanyl-D-*arabino*-hex-1-enitol (4). According to the general procedure above, the title compound was synthesized starting from 2,3,5-tri-*O*-benzyl-β-D-arabino-furanoside (**3**) (2 g, 4.76 mmol), diphenyl (phenylthiomethyl)phosphine oxide (6.17 g, 19 mmol) and BuLi (13 mL of 1.6 M hexane solution, 20.9 mmol). Column chromatography (EtOac/hexane 1:3) afforded **4** (2.50 g, 100%) as an inseparable 1:3 *Z*/*E* mixture as a yellowish syrup. R_f (EtOAc/hexane 1:3): 0.16. Data obtained from the mixture. Anal. Calcd for $C_{33}H_{34}O_4S$: 75.25 C, 6.51 H, 6.09 S. Found: 74.97 C, 6.49 H, 6.07 S. **4*E***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40−7.15 (m, 20H), 6.46 (d, *J* = 15.2, 1H), 5.87 (dd, *J* = 15.2, 7.6, 1H), 4.65 (d, *J* = 12.0, 1H), 4.57 (d, *J* = 11.4, 1H), 4.52 (d, *J* = 11.4, 1H), 4.49 (s, 2H), 4.38 (d, *J* = 12.0, 1H), 4.16 (dd, *J* = 8.0, 3.6, 1H), 4.00 (m, 1H), 3.58 (m, 3H), 2.76 (d, *J* = 5.2, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 140.8, 137.7, 137.5, 134.0, 130.2−126.0, 80.4, 79.1, 74.1, 73.2, 70.7, 70.1, 69.9. **2*Z***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35−7.25 (m, 20H), 6.52 (d, *J* = 9.6, 1H), 5.96 (dd, *J* = 9.6, 9.6, 1H), 4.71 (m, 1H), 4.68 (d, *J* = 11.6, 1H), 4.67 (d, *J* = 11.6, 1H), 4.57 (d, *J* = 11.2, 1H), 4.52 (d, *J* = 11.6, 1H), 4.48 (d, *J* = 11.6, 1H), 4.42 (d, *J* = 11.6, 1H), 3.88 (m, 1H), 3.69 (dd, *J* = 7.2, 4 Hz, 1H), 3.61 (m, 2H), 2.92 (d, *J* = 5.2, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.3−135.7, 129.6−127.1, 80.4, 75.9, 74.29, 73.6, 71.4, 71.3, 70.8.

(*Z*/*E*)-3,4,6-Tri-*O*-benzyl-1,2-dideoxy-1-phenylsulfanyl-D-*xylo*-hex-1-enitol (12). The title compound was prepared following the general procedure above starting from **6** (1 g, 2.38 mmol) solved in THF (12 mL), diphenyl (phenylthiomethyl)phosphine oxide (3.1 g, 9.54 mmol) in 10 mL of THF, and *n*-BuLi (6.6 mL of 1.6 M hexane solution, 10.5 mmol) for 14 h. The reaction was monitored by TLC (EtOAc/hexane 1:3). The crude was purified by column chromatography (EtOAc/hexane 1:3) to afford **12** (60%) as an inseparable 1:4 *Z*:*E* mixture as a yellowish syrup. **12*E*** (obtained pure under Wadsworth−Emmons conditions): $[\alpha]^{20}_D$ +6.48 (*c* 0.8 $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.27−7.15 (m, 20H), 6.42 (d, *J* = 15.6, 1H), 5.68 (dd, *J* = 15.6, 8.2, 1H), 4.75 (d, *J* = 11.0, 1H), 4.57 (d, *J* = 11.7, 1H), 4.46 (d, *J* = 11.0, 1H), 4.34 (d, *J* = 11.0, 3H); 4.10 (dd, *J* = 8.2, 7.5, 1H), 3.83 (m, *J* = 6.0, 6.0, 2.6, 1H), 3.51 (dd, *J* = 7.2, 2.6, 1H), 3.35 (m, *J* = 6.0, 6.0, 5.7, 2H), 2.43 (s, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.2−127.2, 128.8, 128.0, 81.4, 80.2, 75.1, 73.3, 71.0, 70.8, 70.0. 0.37. Anal. Calcd for $C_{33}H_{34}O_4S$: 75.25 C, 6.51 H, 6.09 S. Found: 75.15 C, 6.53 H, 6.10 S. **12*Z*** (spectroscopic data extracted from the mixture): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38−7.24 (m, 20H), 6.55 (d, *J* = 9.2, 1H), 5.82 (dd, *J* = 9.6, 9.2, 1H), 4.88 (d, *J* = 11.2, 1H), 4.69 (d, *J* = 12.0, 1H), 4.67 (dd, *J* = 9.0, 3.0, 1H), 4.57 (d, *J* = 11.2, 1H), 4.45 (d, *J* = 12.0, 3H), 3.96 (m, *J* = 6.8, 6.0, 2.8, 2.8, 1H), 3.72 (dd, *J* = 6.0, 3.0, 1H), 3.43 (m, *J* = 6.0, 2.8, 2.8, 2H), 2.53 (d, *J* = 6.8, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.4−127.1, 128.7, 128.0, 80.0, 77.3, 75.1, 73.4, 71.3, 71.1, 70.2.

(*Z*/*E*)-3,4:6,7-Di-*O*-isopropylidene-1,2-dideoxy-1-phenylsulfanyl-D-*manno*-hep-1-enitol (13). Compound **7** (500 mg, 1.92 mmol) was olefinated according to the general procedure by reaction with diphenyl (phenylthiomethyl)phosphine oxide (2.49 g, 7.68 mmol) and *n*-BuLi (4.9 mL, 7.87 mmol). The reaction was left to stir at room temperature for 21 h (TLC control (EtOAc/hexane 1:3)). The crude was purified by column chromatography (hexane to EtOAc/hexane 1:3) to afford **13** (447 mg, 63%) as a partially separable 1:4 *Z*:*E* mixture as a colorless syrup. R_f (EtOAc/hexane 1:3): 0.28. **13*E*** (obtained pure under Wadsworth−Emmons conditions): $[\alpha]^{20}_D$ +23.10 (*c* 1.15 CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40−7.25 (m, 5H), 6.56 (d, *J* = 15.2, 1H), 6.03 (dd, *J* = 15.2, 8.4, 1H), 4.78 (dd, *J* = 8.4, 7.6, 1H), 4.36 (dd, *J* = 7.6, 1.6, 1H), 4.09 (m, 1H), 4.01 (m, 2H), 3.45 (ddd, *J* = 8.5, 8.4, 1.6, 1H) 2.21 (d, *J* = 8.4 Hz, 1H), 1.51 (s, 3H), 1.40 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 134.4, 130.6, 129.3, 127.4, 130.4, 126.6, 109.5, 108.7, 78.6, 76.9, 76.2, 70.7, 67.2, 26.9, 26.8, 25.4, 24.6. Anal. Calcd for $C_{19}H_{26}O_5S$: 62.27 C, 7.15 H, 8.75 S. Found: 62.06 C, 7.13 H, 8.73 S. **13*Z*** (spectroscopic data extracted from the mixture): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.20 (m, 5H); 6.49 (d, *J* = 9.6, 1H); 6.08 (dd, *J* = 9.6, 7.6, 1H), 5.25 (dd, *J* = 8.0, 5.7, 1H), 4.51 (d, *J* = 8.0, 1H), 4.05 (m, 3H), 3.44 (m, 1H), 2.17 (d, *J* = 8.8, 1H), 1.55 (s, 3H), 1.44 (s, 3H), 1.43 (s, 3H), 1.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 135.1, 130.7, 129.7, 129.4, 128.3, 128.2, 109.6, 109.0, 76.6, 76.3, 74.8, 70.6, 67.0, 27.1, 26.8, 25.5, 24.5.

(*Z*/*E*)-3,4,6-Tri-*O*-benzyl-1,2-dideoxy-1-phenylsulfanyl-D-*lyxo*-hex-1-enitol (14). As described in the general procedure, the title compound was synthesized by reaction of **8** (386 mg, 0.92 mmol), diphenyl (phenylthiomethyl)phosphine oxide (1.19 g, 3.67 mmol), and *n*-BuLi (2.5 mL of 1.6M hexane solution, 4 mmol). Radial chromatography (from hexane to EtOAc/hexane 1:1) furnished **14** (252 mg, 52%) as an inseparable 1:17 *Z*/*E* mixture as a yellowish syrup and a low R_f mixture of diphenyl (phenylthiomethyl)phosphine oxide and the corresponding β-hydroxyphosphine oxide intermediate. The mixture of phosphine oxides was submitted to elimination conditions described above to afford an additional fraction of **14** (47 mg, 10%) as a 7:1 *Z*/*E* mixture. Data obtained from the mixture. R_f (EtOAc/hexane 1:3): 0.22. Anal. Calcd for $C_{33}H_{34}O_4S$: 75.25 C, 6.51 H, 6.09 S. Found: 75.23 C, 6.52 H, 6.06 S. **14*E***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33−7.20 (m, 20H), 6.46 (d, *J* = 15.2, 1H), 5.78 (dd, *J* = 15.2, 8, 1H), 4.63 (d, *J* = 11.2, 1H),

4.62 (d, J = 11.2, 1H), 4.49 (d, J = 12.0, 1H), 4.45 (d, J = 11.2, 1H), 4.44 (d, J = 12.0, 1H), 4.38 (d, J = 11.2, 1H), 4.13 (dd, J = 7.0, 7.0, 1H), 4.06 (m, 1H), 3.57 (dd, J = 7.0, 3.0, 1H), 3.50 (m, 2H), 2.71 (bs, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.1−134.4, 130.3−127.2, 128.8, 128.5, 80.1, 79.8, 74.3, 73.4, 71.4, 70.8, 69.7. **14*Z***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36−7.23 (m, 20H), 6.56 (d, J = 9.2, 1H), 5.89 (dd, J = 9.2, 9.2, 1H), 4.76 (d, J = 12.0, 1H), 4.67 (m, 1H), 4.67 (d, J = 11.6, 1H), 4.51 (d, J = 11.6, 1H), 4.50 (d, J = 12.0, 1H), 4.46 (d, J = 12.0, 1H), 4.45 (d, J = 12.0, 1H), 4.05 (m, 1H), 3.71 (dd, J = 5, 3.4, 1H), 3.54 (m, 2H), 2.98 (bs, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.3−135.7, 129.6−127.0, 79.7, 76.4, 74.0, 73.5, 71.2, 71.1, 70.3.

(*Z*/*E*)-6-*O*-(*tert*-Butyldiphenylsilyl)-3,4-*O*-isopropylidene-1,2-dideoxy-1-phenylsulfanyl-D-*lyxo*-hex-1-enitol (15). According to the general olefination procedure, compound **9** (723.9 mg, 1.69 mmol), diphenyl (phenylthiomethyl)phosphine oxide (2.19 g, 6.76 mmol), and *n*-BuLi (4.6 mL of 1.6 M hexane solution, 7.43 mmol) were left to react for 14 h. The reaction was monitored by TLC (EtOAc/hexane 1:3). Column chromatography (from hexane to EtOAc/hexane 1:3) afforded **15** (192 mg, 21%) as an inseparable 1:8 *Z*/*E* mixture as a yellowish syrup and a low R_f mixture of diphenyl (phenylthiomethyl)-phosphine oxide and the corresponding β-hydroxyphosphine oxide intermediate that was submitted to the elimination conditions described above to afford an additional fraction of **15** (80 mg, 10%) as a 1:1 *Z*/*E* mixture. **15*E*** (obtained pure under Wadsworth−Emmons conditions): R_f (EtOAc/hexane 1:3): 0.48. $[\alpha]^{20}_D$ +40.5 (*c* 1.00, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.72−6.32 (m, 15H), 6.34 (d, J = 15.2, 1H), 5.86 (dd, J = 15.2, 8.8, 1H), 4.55 (dd, J = 8.0, 6.4, 1H), 4.29 (dd, J = 6.4, 3.6, 1H), 3.72−3.64 (m, 3H), 2.43 (d, J = 6.0, 1H), 1.48 (s, 3H), 1.37 (s, 3H), 1.07 (s, 9H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 135.7−127.4, 130.0, 126.6, 108.8, 78.4, 77.4, 72.6, 70.1, 27.0, 26.7, 25.1, 19.4. Anal. Calcd for $C_{33}H_{34}O_4SSi$: 69.62 C, 7.16 H, 6.00 S. Found: 69.66 C, 7.14 H, 6.04 S. **15*Z*** (spectroscopic data extracted from the mixture): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.39 (d, J = 9.6, 1H), 5.99 (dd, J = 9.6, 8.0, 1H), 5.15 (app. t, J = 8.0, 1H), 4.40 (dd, J = 6.0, 3.0, 1H), 3.73−364 (m, 3H), 2,62 (bs, 1H), 1.52 (s, 3H), 1.42 (s, 3H), 1.1 (s, 9H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 135.7−126.6, 114.2, 77.0, 74.5, 70.2, 65.2, 26.7, 27.2, 26.3, 19.1.

(*Z*/*E*)-3,4-*O*-Isopropylidene-1-phenylsulfanyl-D-*erythro*-pent-1-enitol (16). The title compound was obtained from 2,3-*O*-isopropylidene-D-erythrose **10** (915.4 mg, 5.7 mmol), diphenyl (phenylthiomethyl)phosphine oxide (7.4 g, 22.9 mmol), and *n*-BuLi (15.7 mL of 1.6 M hexane solution, 25.1 mmol). The reaction mixture was left to react for 16 h, monitored by TLC (EtOAc/hexane 1:1). Column chromatography (from hexane to EtOAc/hexane 1:1) rendered **16** (520 mg, 35%) as an inseparable 1:3 *Z*/*E* mixture as a yellowish syrup and a low R_f mixture of diphenyl (phenylthiomethyl)phosphine oxide and the corresponding β-hydroxyphosphine oxide intermediate that was submitted to the elimination conditions described above to afford an additional fraction of **16** (500 mg, 33%) as a 12:1 *Z*/*E* mixture. Data obtained from the mixture: R_f (EtOAc/hexane 1:1): 0.38. Anal. Calcd for $C_{14}H_{18}O_3S$: 63.13 C, 6.81 H, 12.04 S. Found: 63.12 C, 6.81 H, 12.05 S. **16*E***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.21 (m, 5H), 6.52 (d, J = 15.0, 1H), 5.71 (dd, J = 15.0, 8.0, 1H), 4.69 (t, J = 6.4, 1H), 4.25 (m, 1H), 3.55 (m, 2H), 1.48 (s, 3H), 1.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 134.9, 130.5−126.8, 128.9, 125.5, 108.9, 78.5, 77.6, 61.9, 27.8, 25.2. **16*Z***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41−7.22 (m, 5H), 6.45 (d, J = 9.2, 1H), 5.86 (t, J = 9.2, 1H), 5.15 (dd, J = 7.6, 7.6, 1H), 4.35 (m, 1H), 3.60 (m, 2H), 1.53 (s, 3H), 1.42 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 135.0, 132.2−124.5, 128.4, 126.9, 109.1, 78.3, 74.3, 62.1, 27.8, 25.2.

(*Z*/*E*)-4,6-Di-*O*-benzyl-1,2,3-trideoxy-1-phenylsulfanyl-D-*ribo*-hex-1-enitol (17). As described in the general procedure, the title compound was synthesized by reaction of **11** (100 mg, 0.31 mmol), diphenyl (phenylthiomethyl)phosphine oxide (400 mg, 31.24 mmol), and *n*-BuLi (0.81 mL of 1.6 M hexane solution, 1.30 mmol) for 4 h. The reaction was monitored by TLC (EtOAc/hexane 1:3). Column chromatography (EtOAc/hexane 1:3) furnished **17** (134 mg, 100%) as an inseparable 1:1 *Z*/*E* mixture as a colorless syrup. Data obtained from the mixture: R_f (EtOAc/hexane 1:4): 0.28. Anal. Calcd for $C_{26}H_{28}O_4S$: 74.25 C, 6.71 H, 7.62 S. Found: 74.26 C, 6.74 H, 7.65 S. **17*E***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36−7.25 (m, 15H), 6.24 (d, J = 15, 1H), 6.00 (ddd, J = 15.0, 7.5, 7.5, 1H), 4.67−4.49 (m, 4H), 3.87−3.84 (m, 1H), 3.70−3.53 (m, 3H), 2.66−2.64 (m, 1H), 2.54−2.43 (m, 1H), 2.44 (d, J = 5.2, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.4−124.5, 128.6, 125.4, 79.0, 73.6, 72.3, 71.5, 71.2, 34.1. **17*Z***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36−7.25 (m, 15H), 6.31 (d, J = 11.0, 1H), 5.94 (ddd, J = 11.0, 7.2, 7.2, 1H), 4.67−4.49 (m, 4H), 3.89−3.86 (m, 1H), 3.70−3.53 (m, 3H), 2.66−2.64 (m, 1H), 2.54−2.43 (m, 1H), 2.49 (d, J = 4.8, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.3−124.2, 128.5, 125.4, 78.8, 73.6, 72.5, 71.7, 71.1, 30.0.

Procedure for Electrophile-Induced Cyclization. Method A. To a 0.5 M solution of alkene (0.16 mmol) in CH_3CN was added $NaHCO_3$ (0.24 mmol). The mixture was cooled to −30 °C and left to stir at this temperature for 5 min. NIS (0.24 mmol) was then added and the reaction mixture stirred for several hours. The reaction temperature was left to increase depending on the reactivity of the substrate (−30 °C to room temperature). The mixture was diluted with dichloromethane and washed with a saturated solution of $Na_2S_3O_3$. The combined aqueous layer was extracted with dichloromethane. The combination of organic layers was dried with $MgSO_4$ and concentrated. The residue was purified by chromatographic techniques.

Method B. IDCP (0.35 mmol) was added to a 0.5 M solution of alkene (0.16 mmol) at −30 °C in CH_3CN. The reaction temperature was left to increase depending on the reactivity of the substrate (−30 °C to room temperature). The mixture was diluted with dichloromethane and washed with a saturated solution of $Na_2S_3O_3$. The combined aqueous layer was extracted with dichloromethane. The combination of organic layers was dried with $MgSO_4$ and concentrated. The residue was purified by chromatographic techniques.

Phenyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-1-thio-α/β-D-*allo*-pyranoside (18). The title compound was obtained following cyclization method A from **2** (202 mg, 0.38 mmol), dry $NaHCO_3$ (48.3 mg, 0.55 mmol), NIS (141 mg, 0.57 mmol) in dry CH_3CN (900 μL) from −30 °C to room temperature for 15 h. TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) afforded **18** (194 mg, 77%) as an inseparable 1:9 α/β anomeric mixture as a yellowish syrup. **18**β (obtained pure from pure **2E**): R_f (EtOAc/hexane 1:3): 0.39. $[\alpha]^{20}_D$ +16.8 (*c* 0.89 CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.62−7.22 (m, 20H), 5.12 (d, J = 10.8, 1H), 4.92 (d, J = 10.4, 1H), 4.76 (d, J = 10.4, 1H), 4.63 (d, J = 11.2, 1H), 4.60 (d, J = 12, 1H), 4.53 (d, J = 11.2, 1H), 4.51 (d, J = 12.0, 1H), 4.20−4.16 (m, 2H), 4.02 (dd, J = 10.8, 2.4, 1H), 3.78−3.62 (m, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.6−137.8, 133.4−127.7, 84.6, 79.0, 76.4, 76.1, 75.9, 73.6, 72.4, 69.5, 32.0. Anal. Calcd for $C_{33}H_{33}IO_4S$: 60.74 C, 5.10 H, 4.91 S. Found: 60.96 C, 5.13 H, 4.97 S. **18**α (data obtained from the spectrum of mixture): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.62−7.20 (m, 20H), 5.41 (d, J = 5.6, 1H), 4.99 (d, J = 11.6, 1H), 4.87 (d, J = 11.6, 1H), 4.65−4.58 (m, 2H), 4.52 (d, J = 10.4, 2H), 4.42 (d, J = 11.2, 1H), 4.40 (d, J = 12.0, 1H), 4.09 (m, 1H), 3.86−3.80 (m, 2H), 3.70 (m, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.6−127.5, 90.2, 78.4, 76.6, 75.8, 73.6, 72.2, 69.0, 67.8, 27.0.

***N*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-α/β-D-*allo*-pyranosyl)succinimide (19).** As described in cyclization method A, compound **2** (216 mg, 0.41 mmol), NIS (150.7 mg, 0.62 mmol), and 4Å MS (293 mg) in dry CH_2Cl_2 (900μL) were left to react from −78 °C to room temperature for 19.5 h. TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) rendered compound **19** (169 mg, 64%) as an inseparable 1:41 α/β anomeric mixture as a yellow foam. Data obtained from the mixture: R_f (EtOAc/hexane 1:3): 0.07. Anal.

Calcd for $C_{31}H_{32}INO_6$: 58.04 C, 5.03 H, 2.18% N. Found 58.09 C, 5.02 H, 2.20% N. **19*β***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38−7.24 (m, 15H), 5.81 (d, J = 11.2, 1H), 5.63 (dd, J = 11.2, 11.2, 1H), 4.68 (d, J = 3, 2H), 4.50 (s, 2H), 4.47 (s, 2H), 4.27 (m, 1H), 3.94 (dd, J = 11.2, 3.0, 1H), 3.67 (m, 1H), 3.64 (dd, J = 10.8, 5.6, 1H), 3.59 (dd, J = 10.8, 4.8, 1H), 2.70 (s, 4H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 175.9, 138.1−137.4, 128.7−127.8, 80.1, 80.0, 75.8, 73.8, 73.1, 72.3, 72.2, 69.9, 28.6, 28.0.

Phenyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-1-thio-α-D-*manno*-pyranoside (20). As described in cyclization method A, the title compound was synthesized starting from **4** (*Z*/*E* ratio 1:3) (116.3 mg, 0.22 mmol), dry $NaHCO_3$ (27.8 mg, 0.33 mmol), and NIS (81.1 mg, 0.33 mmol) in dry CH_3CN (300 μL) at −30 °C for 3 h. TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) furnished 20 (52 mg, 36%) as a yellowish syrup. R_f (EtOAc/hexane 1:3): 0.51. $[\alpha]^{20}_D$ +68 (*c* 0.02 CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.46−7.19 (m, 20H), 5.78 (s, 1H), 4.89 (d, J = 10.8, 1H), 4.87 (d, J = 3.6, 1H), 4.72 (d, J = 11.6, 1H), 4.71 (d, J = 11.6, 1H), 4.55 (d, J = 11.6, 1H), 4.52 (d, J = 10.8, 1H), 4.48 (d, J = 11.6, 1H), 4.42 (m, 1H), 3.99 (dd, J = 8.8, 8.4, 1H), 3.86 (dd, J = 10.8, 4.8, 1H), 3.73 (dd, J = 10.8, 2, 1H), 3.10 (dd, J = 8.4, 3.6, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.5−134.1, 132.2−127.7, 89.8, 77.8, 76.5, 75.6, 73.6, 71.3, 69.0, 35.0. Anal. Calcd for $C_{33}H_{33}IO_4S$: 60.74 C, 5.10 H, 4.91 S. Found: 60.70 C, 5.10 H, 4.94 S.

2,3-Bis-benzyloxy-4-benzyloxymethyl-2-(1-iodo-2-phenylsulfanyl-ethyl)-oxetane (21). A suspension of KH 30% (70.2 mg, 0.52 mmol) in dry ether (1.8 mL) was added dropwise to a solution of **4** (*Z*/*E* ratio 1:2) (103 mg, 0.19 mmol) in dry ether (2.9 mol) at 0 °C, and the resulting mixture was allowed to stir for 30 min until complete formation of the alcoholate. The mixture was cooled to −78 °C and a solution of iodine (187 mg, 0.74 mmol) in dry Et_2O (1.5 mL) was then added. The reaction mixture was allowed to stir from −78 °C to room temperature for 1.5 h. TLC (EtOAc/hexane 1:3). A solution of $Na_2S_3O_3$ was then added and the reaction product was extracted with ether. The combination of the etheral layers was concentrated and the residue purified by radial chromatography (from hexane to EtOAc/hexane 1:3) to afford **21** (39 mg, 31%) as a yellowish syrup. R_f (EtOAc/hexane 1:3): 0.38. $[\alpha]^{20}_D$ −2.34 (*c* 1.57, CH_2Cl_2,). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41−7.12 (m, 20H), 5.26 (d, J = 12.0, 1H), 5.12 (d, J = 12.0, 1H), 5.00 (d, J = 11.6, 1H), 4.60 (d, J = 11.6, 1H), 4.42−4.40 (m, 1H), 4.38 (s, 2H), 4.36−4.31 (m, 2H), 3.62 (dd, J = 15.0, 2.6, 1H), 3.45 (dd, J = 11.4, 2.6 Hz, 1H), 3.34 (dd, J = 11.4, 3.8 Hz, 1H), 3.22 (dd, J = 15.0, 10.2, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.8−135.4, 129.5−126.4, 108.3, 81.4, 81.1, 73.5, 69.5, 67.1, 37.6, 37.2. Anal. Calcd for $C_{33}H_{33}IO_4S$: 60.74 C, 5.10 H, 4.91 S. Found: 60.75 C, 5.11 H, 4.90 S.

Phenyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-1-thio-α/*β*-D-*gulo*-pyranoside (22). As described in cyclization method B, compound **22** (611 mg, 77%, α/*β* ratio 1:12, inseparable mixture) was obtained as a yellowish syrup starting from compound **12** (*Z*:*E* ratio 1:10) (640 mg, 1.2 mmol) and IDCP (1.25 g, 2.67 mmol) in dry CH_3CN (17 mL), at −30 °C for 3 h. The reaction was monitored by TLC (EtOAc/hexane 1:3). The reaction mixture was purified by radial chromatography (from hexane to EtOAc/hexane 1:3). Data obtained from the mixture. R_f (EtOAc/hexane 1:4): 0.47. Anal. Calcd for $C_{33}H_{33}IO_4S$: 60.74 C, 5.10 H, 4.91 S. Found: 60.68 C, 5.11 H, 5.00 S. **22*β***:^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.61−7.18 (m, 20H), 5.13 (d, J = 11.2, 1H), 4.69−4.36 (m, 6H), 4.44 (dd, J = 11.2, 2.8, 1H), 4.23 (td, J = 1.2, 6.4, 6.4, 1H), 3.81 (dd, J = 3.4, 2.8, 1H), 3.57 (m, J = 9.6, 9.6, 6.4, 2H), 3.37 (dd, J = 3.4, 1.2, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.0−127.6, 85.0, 78.1, 74.9, 74.0, 73.6, 73.3, 72.6, 68.9, 31.3. **22**α: R_f (EtOAc/hexane 1:4): 0.47. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54−7.20 (m, 20H), 5.41 (d, J = 5.2, 1H), 5.06 (dd, J = 5.2, 2.8, 1H), 4.89 (s, 1H), 4.80−4.36 (m, 6H), 3.73 (d, J = 2.8, 1H), 3.63−3.54 (m, 2H), 3.48 (bs, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.2−127.1, 89.7, 77.4, 75.0, 73.5, 73.3, 73.1, 69.2, 66.3, 28.0.

Phenyl 2-Deoxy-2-iodo-3,4:6,7-di-*O*-isopropylidene-1-thio-D-*glycero*-α/*β*-D-*talo*-heptopyranoside (23). (A) From 13*E*. According to method B, cyclization was carried out starting from compound **13***E* (350 mg, 0.95 mmol) and IDCP (981 mg, 2.09 mmol) in dry CH_3CN from −45 to −30 °C for 2 h. Control by TLC (EtOAc/hexane 1:4). The mixture was purified by radial chromatography (from hexane to EtOAc/hexane 1:3) to afford **23**α (453 mg, 97%) as a white foam. **(B) From 13*Z*/*E*.** Compound **13** (*Z*:*E* ratio 1:6) (360 mg, 0.98 mmol, 1eq) was treated with IDCP (1.01 g, 2.16 mmol) in dry CH_3CN (20 mL) from −45 °C to room temperature for 1.5 h to afford **23**α product (233 mg, 48%) as a white foam. **(C) From 13*Z*/*E* and Long Reaction Times.** Compound **13** (*Z*:*E* ratio 1:6) (360 mg, 0.98 mmol) was treated with IDCP (1.01 g, 2.16 mmol) in dry CH_3CN (20 mL) from −30 °C to room temperature for 3.5 h to furnsih **23**α (60 mg, 41%) as a white foam, **23*β*** (28 mg, 19%) as a yellowish syrup, and the corresponding 2-iodopyranose (19 mg, 19%) as a pale yellow syrup. **23**α: R_f (EtOAc/hexane 1:4): 0.14. $[\alpha]^{20}_D$ +109.9 (*c* 1.25, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52−7.50 (m, 2H), 7.34−7.25 (m, 3H), 5.59 (d, J = 9.6, 1H), 4.68 (dd, J = 7.9, 2.4, 1H), 4.40 (dd, J = 7.9, 1.6, 1H), 4.18 (m, 1H), 4.04 (dd, J = 9.6, 2.4, 1H), 3.98 (dd, J = 8.4, 6.2, 1H), 3.90 (dd, J = 8.4, 4.4, 1H), 3.61 (dd, J = 8.4, 1.6, 1H), 1.50 (s, 3H), 1.42 (s, 3H), 1.40 (s, 3H), 1.34 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 133.4, 132.1, 129.1, 127.7, 109.6, 109.5, 90.1, 76.5, 73.9, 73.0, 69.8, 66.9, 27.1, 26.2, 25.3, 25.2, 21.2. Anal. Calcd for $C_{19}H_{25}IO_5S$: 46.35 C, 5.12 H, 6.51 S. Found: 46.25 C, 5.09 H, 6.54 S. **23*β***: R_f (EtOAc/hexane 1:4): 0.13. (spectroscopic data obtained from the mixture) ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52−7.24 (m, 5H) 5.09 (d, J = 4.4, 1H), 4.83 (dd, J = 4.5, 5.2, 1H), 4.51 (dd, J = 8.0, 3.6, 1H), 4.39 (dd, J = 8.0, 2.4, 1H), 4.34 (dd, J = 6.6, 5.2, 1H), 4.09 (m, 2H), 3.72 (dd, J = 6.6, 2.4, 1H), 1.41 (s, 3H), 1.40 (s, 3H), 1.39 (s, 3H), 1.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 137.1, 131.3, 129.2, 127.5, 110.5, 109.5, 88.2, 74.1, 74.5, 74.3, 73.1, 66.9, 27.5, 26.1, 25.5, 24.7, 21.8.

Phenyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-1-thio-α-D-*talo*-pyranoside (24) and Phenyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-1-thio-*β*-D-*galacto*-pyranoside (25). Compound **14** (*Z*/*E* ratio 1:7) (89 mg, 0.35 mmol) was treated with IDCP (174.2 mg, 0.37 mmol) in dry CH_2Cl_2 (390 μL) at −78 °C for 2.5 h. The reaction was monitored by TLC (EtOAc/hexane 1:3). After the standard workup described in method B, radial chromatography (from hexane to EtOAc/hexane 1:3) afforded **24** (22 mg, 20%) and **25** (16 mg, 15%) as a yellowish syrups. **24**: R_f (EtOAc/hexane 1:3): 0.48. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.48−7.21 (m, 20H), 5.91 (s, 1H), 5.07 (d, J = 12.0, 1H), 4.76 (d, J = 11.2, 1H), 4.69 (m, 1H), 4.61−4.38 (m, 5H), 3.98 (m, 1H), 3.73−3.71 (m, 2H), 3.38 (m, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.1, 132.3−127.6, 90.3, 74.6, 73.8, 73.7, 73.6, 72.3, 71.0, 69.3, 25.0. Anal. Calcd for $C_{33}H_{33}IO_4S$: 60.74 C, 5.10 H, 4.91 S. Found: 60.70 C, 5.10 H, 4.91 S. **25**: decomposes on standing. R_f (EtOAc/hexane 1:3): 0.43. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.59−7.17 (m, 20H), 4.87 (d, J = 10.8, 1H), 4.83 (d, J = 11.6, 1H), 4.71 (d, J = 11.2, 1H), 4.64 (d, J = 11.2, 1H), 4.49 (d, J = 11.6, 1H), 4.48 (d, J = 11.2, 1H), 4.42 (d, J = 11.2, 1H), 4.29 (app. t, J = 10.8, 1H), 3.83 (m, 1H), 3.71−3.67 (m, 1H) 3.65−3.60 (3H, m, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.6−137.3, 133.2−127.7, 89.2, 85.4, 77.9, 74.6, 73.8, 73.1, 72.9, 68.6, 33.1.

Phenyl 6-*O*-*tert*-Butyldiphenylsilyl-2-deoxy-2-iodo-3,4-*O*-isopropylidene-1-thio-α/*β*-D-*talo*-pyranoside (26). Compound **15** (*Z*/*E* ratio 1:8) (103.8 mg, 0.19 mmol) was treated with dry $NaHCO_3$ (24.5 mg, 0.29 mmol) and NIS (71.3 mg, 0.29 mmol) in dry CH_3CN (500 μL) at −30 °C for 15 h. The reaction was monitored by TLC (EtOAc/hexane 1:3). After the standard workup described in method A, radial chromatography (from hexane to EtOAc/hexane 1:3) rendered **26** (71 mg, 55%) as an inseparable 42:1 α/*β* mixture as a yellowish syrup. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.53. Anal. Calcd for $C_{31}H_{37}IO_4SSi$: 56.36 C, 5.64 H, 4.85 S. Found: 56.34 C, 5.61 H, 4.87 S. **26**α: ^{1}H NMR ($CDCl_3$, 400 MHz) δ

7.71−7.21 (m, 15H), 5.52 (d, J = 9.6, 1H), 4.65 (dd, J = 7.6, 2.4, 1H), 4.31 (dd, J = 7.6, 1.2, 1H), 4.05 (dd, J = 9.6, 2.4, 1H), 3.89 (m, 1H), 3.82−3.72 (m, 2H), 1.42 (s, 3H), 1.35 (s, 3H), 1.04 (s, 9H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 135.9−133.4, 129.9−127.8, 109.7, 89.9, 77.0, 74.4, 70.0, 62.5, 27.0, 26.3, 25.5, 22.4, 19.4.

Phenyl 2-Deoxy-2-iodo-3,4-*O*-isopropylidene-1-thio-α/*β*-D-*erythro*-pyranoside (27). Compound **17** (*Z*/*E* ratio 2:3) (35 mg, 0.13 mmol) was treated with IDCP (135.1 mg, 0.29 mmol) in dry CH_3CH_2CN (300 μL) at −78 °C for 23 h. The reaction was monitored by TLC (EtOAc/hexane 1:1). After the standard workup described in method B, radial chromatography (from hexane to EtOAc/hexane 1:1) afforded **27** (17 mg, 33%) as an inseparable 1.1:1 α/β mixture as a yellowish syrup. Data extracted from the mixture. R_f (EtOAc/hexane 1:1): 0.56. Anal. Calcd for $C_{14}H_{17}IO_3S$: 42.87 C, 4.37 H, 8.17 S. Found: 42.85 C, 4.38 H, 8.20 S. **27α**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58−7.25 (m, 5H), 5.33 (d, J = 10.4, 1H), 4.59 (m, 1H), 4.32 (m, 1H), 4.27 (m, 1H), 4.08 (dd, J = 10.4, 2.8, 1H), 3.89 (dd, J = 9.6, 4, 1H), 1.54 (s, 3H), 1.49 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 132.8, 129.4−128.2, 109.5, 88.3, 76.5, 71.7, 64.0, 28.4, 27.2, 22.9. **27*β***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58−7.25 (m, 5H), 5.09 (d, J = 7.6, 1H), 4.59 (m, 1H), 4.27 (m, 1H), 4.15 (dd, J = 7.6, 6.8, 1H), 3.92 (dd, J = 12.4, 4.0, 1H), 3.58 (dd, J = 12.4, 4.0, 1H), 1.38 (s, 3H), 1.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 133.2, 129.4−128.2, 110.8, 88.5, 80.3, 72.8, 64.1, 29.7, 26.4, 25.7.

General Procedure of Glycosylation. A solution of the glycosyl donor (1 mmol) and the glycosyl acceptor (2 mmol) in CH_2Cl_2 (4 mL) was stirred with 4Å molecular sieves for 2 h. The mixture was then cooled to −78 °C, and NIS (3 mmol) and TfOH (0.2 mmol) were added. The mixture was allowed to warm to −40 °C and stirred until the reaction had finished. The reaction mixture was then diluted with CH_2Cl_2 and washed with a solution of $Na_2S_3O_3$. The ethereal layer was dried with Na_2SO_4 and concentrated. The residue was then purified by radial chromatography.

Methyl (3′,4′,6′-Tri-*O*-benzyl-2′-deoxy-2′-iodo-α/*β*-D-*allo*-pyranosyl)-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-*gluco*-pyranoside (30a). According to the general glycosylation conditions, **18** (α/β ratio 1:9) (80.9 mg, 0.12 mmol), NIS (66.8 mg, 0.27 mmol), **29a** (92.3 mg, 0.25 mmol), 4Å MS (120 mg), and TfOH (1 drop) in dry CH_2Cl_2 (3 mL) were allowed to react at −78 °C for 1 h and then at −40 °C for 2.5 h. The reaction progress was monitored by TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) afforded **30a** (84 mg, 74%) as an inseparable 1:6 α/β mixture as a white solid. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.23. Anal. Calcd for $C_{48}H_{51}IO_{10}$: 63.02 C, 5.62 H. Found: 62.96 C, 5.64 H. **30a*β***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52−7.05 (m, 25H), 5.54 (s, 1H), 5.08 (d, J = 9.2, 1H), 5.07 (d, J = 10.8, 1H), 4.93 (d, J = 3.2, 1H), 4.89 (d, J = 10.4, 1H), 4.79 (d, J = 10.8, 1H), 4.78 (d, J = 10.4, 1H), 4.65−4.47 (m, 4H), 4.27 (dd, J = 9.5, 4.4, 1H), 4.17−4.10 (m, 3H), 4.00 (app. t, J = 9.2, 1H), 3.90−3.78 (m, 1H), 4.75−3.67 (m, 5H), 3.59 (app. t, J = 9.2, 1H), 3.38 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 139.0−137.7, 129.2−126.3, 102.1, 101.6, 100.6, 82.8, 80.3, 78.8, 77.7, 76.8, 76.0, 75.6, 73.8, 73.2, 72.6, 69.8, 69.5, 62.4, 55.6, 30.9.

Cholesteryl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-α/*β*-D-*allo*-pyranoside (30b). Following the general glycosylation procedure, **18** (α/β ratio 1:9) (100 mg, 0.15 mmol), NIS (82.6 mg, 0.34 mmol), cholesterol (118.5 mg, 0.31 mmol), 4Å MS (150 mg), and TfOH (1 drop) in dry CH_2Cl_2 (3.5 mL) were allowed to react at −78 °C for 1 h and then at −40 °C 2.5 h. The reaction was monitored by TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) provided **30b** (115 mg, 81%) as an inseparable 1:9 α/β mixture as a yellow foam. Data obtained from the mixture: R_f (EtOAc/hexane 1:3): 0.53. Anal. Calcd for $C_{54}H_{73}IO_5$: 69.81 C, 7.92 H. Found: 69.68 C, 7.89 H. **30b*β***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52−7.22 (m, 15H), 5.35 (d, J = 4.8, 1H), 4.88 (d, J = 10.4, 1H), 4.87 (d, J = 9.0, 1H), 4.77 (d, J = 10.4, 1H), 4.64−4.49 (m, 4H), 4.17−4.09 (m, 2H), 4.02 (dd, J = 9.0, 2.8, 1H), 3.73−3.64 (m, 3H), 4.48 (m, 1H), 2.40−0.67 (m, 43H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 140.8, 138.5−137.7, 128.6−126.8, 122.0, 99.3, 79.9, 78.6, 76.9, 75.8, 73.5, 73.1, 72.4, 69.5, 56.9−12.0, 33.3.

Methyl (3′,4′,6′-Tri-*O*-benzyl-2′-deoxy-2′-iodo-α/*β*-D-*manno*-pyranosyl)-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-*gluco*-pyranoside (31a). As described in the general glycosylation procedure, **20** (37.3 mg, 0.06 mmol), NIS (30.8 mg, 0.13 mmol), **29a** (42.6 mg, 0.11 mmol), 4Å MS (60 mg), TfOH (1 drop) in dry CH_2Cl_2 (1.4 mL) were allowed to react at −78 °C for 1 h and then at −40 °C for 2 h. The reaction progress was monitored by TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) afforded **31a** (37 mg, 71%) as an inseparable 45:1 α/β mixture as a white crystalline solid. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.24. Anal. Calcd for $C_{48}H_{51}IO_{10}$: 63.02 C, 5.62 H. Found: 63.16 C, 5.65 H. **31aα**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.49−6.99 (m, 25H), 5.53 (s, 1H), 5.38 (s, 1H), 4.88 (d, J = 10.4, 1H), 4.89 (d, J = 3.2, 1H), 4.72 (d, J = 10.8, 1H), 4.69 (d, J = 11.6, 1H), 4.68−4.62 (m, 3H), 4.50 (d, J = 11.6, 1H), 4.48 (d, J = 10.8, 1H), 4.35 (d, J = 12.0, 1H), 4.29 (dd, J = 9.6, 4.0, 1H), 4.20 (dd, J = 9.6, 2.8, 1H), 3.97 (dd, J = 9.0, 9.0, 1H), 3.89−3.85 (m, 2H), 4.79 (dd, J = 10.0, 4.4, 1H), 3.74−3.53 (m, 3H), 3.58−3.53 (m, 1H), 3.44 (s, 1H), 3.38 (dd, J = 8.4, 4, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.8−137.5, 128.9−126.1, 101.4, 98.3, 97.1, 82.2, 77.1, 76.8, 75.9, 75.4, 74.0, 73.1, 72.1, 71.0, 69.1, 68.6, 62.4, 55.4, 33.5.

Cholesteryl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-α/*β*-D-*manno*-pyranoside (31b). According to the general glycosylation procedure, **20** (22.1 mg, 0.034 mmol) was treated with NIS (18.3 mg, 0.075 mmol), cholesterol (26.2 mg, 0.068 mmol), 4Å MS (34 mg), and TfOH (1drop) in dry CH_2Cl_2 (800 μL). The reaction mixture was stirred at −78 °C for 1 h and then at −40 °C 2 h. TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) provided **31b** (23 mg, 72%) as an inseparable 37:1 α/β mixture as a yellowish foam. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.63. Anal. Calcd for $C_{54}H_{73}IO_5$: 69.81 C, 7.92 H. Found: 69.79 C, 7.92 H. **31bα**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.50−7.15 (m, 15H), 5.38 (s, 1H), 5.28 (d, J = 5.2, 1H), 4.85 (d, J = 10.8, 1H), 4.71 (dd, J = 11.6, 1H), 4.58−4.46 (m, 4H), 3.96−3.88 (m, 2H), 4.81 (dd, J = 10.8, 4.4, 1H), 3.71 (dd, J = 10.8, 1.6, 1H), 4.48 (m, 1H), 3.36 (dd, J = 8.0, 4.0, 1H), 3.35−0.67 (m, 43H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 140.5, 138.5−138.0, 129.2−127.2, 122.2, 99.6, 77.5, 77.2, 76.1, 75.5, 73.4, 72.2, 71.0, 69.0, 56.2−12.0, 34.6.

Methyl (3′,4′,6′-Tri-*O*-benzyl-2′-deoxy-2′-iodo-α/*β*-D-*gulo*-pyranosyl)-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-*gluco*-pyranoside (32a). According to the general glycosylation procedure, the title compound was prepared starting from **22** (α:β ratio 10:1 or 1:5) (55 mg, 0.08 mmol), NIS (42 mg, 0.18 mmol), **29a** (63 mg, 0.17 mmol), 4Å MS (80 mg), and TfOH (1 drop) in dry CH_2Cl_2 (2.1 mL, 0.04 M). The reaction mixture was stirred at −78 °C for 1 h and then at −40 °C for 3 h. TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) furnished **32a** (49 mg, 62%) as an inseparable 1:12 α/β mixture as a transparent syrup. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.31. Anal. Calcd for $C_{48}H_{51}IO_{10}$: 63.02 C, 5.62 H. Found: 63.17 C, 5.60 H. **32a*β***: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.49−7.16 (m, 20H), 5.54 (s, 1H), 5.08 (d, J = 9.2, 1H), 5.07 (d, J = 10.8, 1H), 4.86 (d, J = 3.8, 1H), 4.80 (d, J = 10.8, 1H), 4.65 (d, J = 11.2, 1H), 4.44 (m, 6H), 4.28 (dd, J = 10.0, 4.8, 1H), 4.16 (td, J = 6.6, 1.2, 1H), 4.03 (dd, J = 9.6, 9.2, 1H), 3.85 (ddd, J = 10.0, 9.6, 4.8, 1H), 3.80 (dd, J = 3.6, 3.0, 1H), 3.75 (dd, J = 9.6, 3.8, 1H), 3.72 (app. t, J = 10.0, 1H), 3.59 (dd, J = 9.6, 9.2, 1H), 3.53 (d, J = 6.6, 2H), 3.39 (s, 3H), 3.36 (dd, J = 3.6, 1.2, 1H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.9−126.2, 101.5, 101.4, 100.4, 82.8, 79.2, 79.1, 77.8, 75.3, 74.2, 73.9, 73.5, 73.0, 72.8, 69.4, 69.0, 62.3, 55.5, 30.8.

Cholesteryl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-α/*β*-D-*gulo*-pyranoside (32b). Following the general glycosylation procedure, **22** (α:*β* ratio2:7) (120 mg, 0.18 mmol), NIS (91 mg, 0.40 mmol), cholesterol (142 mg, 0.37 mmol), 4Å molecular sieves (160 mg), and TfOH (1 drop) in dry CH_2Cl_2 (6.1 mL) were allowed to react at −78 °C for 1 h and then at −40 °C for 3 h. TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) afforded **32b** (113 mg, 66%) as an inseparable 1:8 α:*β* mixture as a pale yellow solid. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.62. Anal. Calcd for $C_{54}H_{73}IO_5$: 69.81 C, 7.92 H. Found: 69.87 C, 7.89 H. **32b*β***: ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 7.36−7.18 (m, 15H), 5.34 (bs, 1H), 4.82 (d, *J* = 9.2, 1H), 4.65 (d, *J* = 11.6, 1H), 4.43 (m, 6H), 4.16 (t, *J* = 6.4, 1H), 3.79 (dd, *J* = 3.6, 3.2, 1H), 3.56 (d, *J* = 6.4, 2H), 3.49 (m, 1H), 3.34 (d, *J* = 3.2, 1H), 2.39−0.67 (m, 44H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) *δ* 140.9−127.8, 121.9, 98.9, 79.7, 76.0, 74.1, 73.8, 73.5, 72.9, 72.8, 69.1, 57.0−12.1, 33.5.

Methyl (2′-Deoxy-2′-iodo-3′,4′:6′,7′-di-*O*-isopropylidene-D-*glycero*-α/*β*-D-*talo*-heptopyranosyl)-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-gluco-pyranoside (33a). As described in the glycosylation procedure, the title compound was prepared starting from **23α** (200 mg, 0.40 mmol), NIS (201 mg, 0.89 mmol), **29a** (302 mg, 0.81 mmol), 4Å MS (200 mg), and TfOH (7 *μ*L, 0.08 mmol) in dry CH_2Cl_2 (13 mL). The reaction mixture was stirred at −78 °C for 1 h and then at −60 °C for 1 h. TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) of the crude provided **33a** (210 mg, 69%) as an inseparable 40:1 α:*β* mixture as a white solid. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.30. Anal. Calcd for $C_{34}H_{43}IO_{11}$: 54.12 C, 5.74 H. Found: 53.89 C, 5.75 H. **33aα**: ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 7.44−7.23 (m, 10H), 5.54 (s, 1H), 5.22 (d, *J* = 7.2, 1H), 4.89 (d, *J* = 4.0, 1H), 4.88 (d, *J* = 12.2, 1H), 4.80 (d, *J* = 12.2, 1H), 4.66 (dd, *J* = 7.8, 2.4, 1H), 4.41 (dd, *J* = 7.8, 2.0, 1H), 4.28 (dd, *J* = 10.4, 4.6, 1H), 4.22 (dd, *J* = 8.8, 3.6, 1H), 4.19 (ddd, *J* = 8.4, 3.6, 2.8, 1H), 4.02 (s, 1H), 3.99 (dd, *J* = 8.8, 2.8, 1H), 3.96 (dd, *J* = 7.2, 2.4 Hz, 1H), 3.87 (dd, *J* = 9.6, 4.0, 1H), 3.83 (dd, *J* = 9.8, 4.6, 1H), 3.73 (dd, *J* = 10.4, 9.8, 1H), 3.61 (d, *J* = 9.6, 1H), 3.57 (dd, *J* = 8.4, 2.0, 1H), 3.47 (s, 3H), 1.51 (s, 3H), 1.41 (s, 3H), 1.33 (s, 3H), 1.31 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) *δ* 139.1, 137.5, 129.1, 128.4, 128.3, 128.2, 127.5, 126.3, 109.7, 109.6, 101.5, 100.2, 97.6, 82.3, 76.8, 76.4, 76.0, 74.9, 74.0, 73.4, 70.1, 69.3, 67.0, 62.6, 55.7, 27.3, 26.2, 25.2, 23.1.

Cholesteryl 2′-deoxy-2′-iodo-3′,4′:6′,7′-di-*O*-isopropylidene-D-glycero-α/*β*-D-*talo*-heptopyranoside (33b). According to the general glycosylation procedure, **23α** (200 mg, 0.40 mmol) was treated with NIS (201 mg, 0.89 mmol), cholesterol (299 mg, 0.81 mmol), 4Å molecular sieves (200 mg), and TfOH (7 *μ*L, 0.08 mmol) in dry CH_2Cl_2 (13 mL) at −78 °C for 1 h and then at −20 °C for 20 h. TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:4) provided **33b** (177 mg, 57%) as an inseparable 8:1 α:*β* mixture as a pale yellow solid. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.43. Anal. Calcd for $C_{40}H_{65}IO_6$: 62.49 C, 8.52 H. Found: 62.26 C, 8.53 H. **33bα**: ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 5.34 (bs, 1H), 5.20 (d, *J* = 8.0, 1H), 4.64 (dd, *J* = 7.8, 2.8, 1H), 4.37 (dd, *J* = 7.8, 1.8, 1H), 4.22 (m, 1H), 4.09 (dd, *J* = 8.4, 6.0, 1H), 3.99 (dd, *J* = 8.0, 2.8, 1H), 3.94 (dd, *J* = 8.4, 4.4, 1H), 3.58 (dd, *J* = 8.0, 1.8, 1H), 3.47 (m, 1H), 2.30−0.68 (m, 44H), 1.51 (s, 3H), 1.42 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) *δ* 140.9, 122.0, 109.7, 109.6, 100.4, 77.7, 76.6, 74.1, 73.6, 69.7, 67.3, 56.9−12.1, 27.3, 26.2, 25.2, 24.1, 21.3.

Methyl (6′-*O*-*tert*-Butyldiphenylsilyl-2′-deoxy-2′-iodo-3′,4′-*O*-isopropylidene-α/*β*-D-*talo*-pyranosyl)-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-*gluco*-pyranoside (34a). Following the general glycosylation procedure, compound **26** (α/*β* ratio 49:1) (58 mg, 0.09 mmol), NIS (47.3 mg, 0.19 mmol), **29a** (65.4 mg, 0.18 mmol), 4Å MS (88 mg), and TfOH (1 drop) in dry CH_2Cl_2 (2 mL) were allowed to react at −78 °C for 1.5 h. The reaction was monitored by TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) afforded **34a** (48 mg, 59%) as an inseparable 20:1 α/*β* mixture as a white crystalline solid. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.38. Anal. Calcd for $C_{46}H_{55}IO_{10}Si$: 59.86 C, 6.01 H. Found: 59.83 C, 5.98 H. **34aα**: ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 7.68−7.17 (m, 20H), 5.50 (s, 1H), 5.23 (d, *J* = 7.6, 1H), 4.89 (d, *J* = 3.6, 1H), 4.77 (s, 2H), 4.64 (dd, *J* = 8, 2.8, 1H), 4.41 (dd, *J* = 8, 2.0, 1H), 4.26 (dd, *J* = 9.6, 4.8, 1H), 4.11 (dd, *J* = 7.6, 2.8, 1H), 3.99−3.68 (m, 7H), 3.54 (dd, *J* = 9.6, 9.6, 1H), 3.47 (s, 3H), 1.40 (s, 3H), 1.36 (s, 3H), 1.03 (s, 9H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) *δ* 139.2−137.6, 136.0−126.3, 109.3, 101.5, 101.1, 98.1, 82.1, 77.2, 77.0, 76.5, 75.0, 73.7, 69.4, 69.3, 61.6, 61.9, 55.6, 27.1, 26.2, 25.2, 24.5, 19.5.

Cholesteryl 6-*O*-*tert*-Butyldiphenylsilyl-2-deoxy-2-iodo-3,4-*O*-isopropylidene-α/*β*-D-*talo*-pyranoside (34b). As described in the general glycosylation procedure, compound **26** (α/*β* ratio 42:1) (70 mg, 0.11 mmol), NIS (57.1 mg, 0.23 mmol), cholesterol (82 mg, 0.21 mmol), 4Å MS (106 mg), and TfOH (1 drop) in dry CH_2Cl_2 (2.5 mL) were allowed to react at −78 °C for 1.5 h. The reaction was monitored by TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) produced **34b** (35.4 mg, 36%) as a 10:1 α/*β* mixture as a yellowish syrup. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.55. Anal. Calcd for $C_{52}H_{77}IO_5Si$: 66.64 C, 8.28 H. Found: 66.61 C, 8.30 H. **34bα**: ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* in ppm: 7.71−7.26 (10H, m, Ar), 5.23 (d, *J* = 7.2, 1H), 5.18 (d, *J* = 4.0, 1H), 4.64−4.60 (m, 1H), 4.29−4.21 (m, 1H), 4.02−3.98 (m, 1H), 3.92 (m, 1H), 3.88−3.72 (m, 2H), 3.50 (m, 1H), 2.27−0.67 (m, 58H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) *δ* 148.4, 145.6, 140.7, 135.9−127.8, 122.0, 109.5, 100.2, 77.1, 75.1, 74.4, 68.8, 61.6, 56.9−12.1, 27.1, 26.3, 25.8, 24.8, 19.6.

Methyl (3′,4′-*O*-Isopropylidene-2′-deoxy-2′-iodo-α/*β*-D-*erythro*-pyranosyl)-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-*gluco*-pyranoside (35a). According to the general glycosylation conditions, compound **27** (α/*β* ratio 14:1) (80.1 mg, 0.20 mmol), NIS (110.1 mg, 0.45 mmol), **29a** (152.1 mg, 0.41 mmol), 4Å MS (20 mg) and and TfOH (1 drop) in dry CH_2Cl_2 (4.7 mL) were allowed to react at −78 °C for 30 min. The reaction was monitored by TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) afforded **35a** (59.4 mg, 44%) as an inseparable 1:3 α/*β* mixture as a white solid. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.17. Anal. Calcd for $C_{29}H_{35}IO_9$: 53.22 C, 5.39 H. Found: 53.40 C, 5.41 H. **35aα**: ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 7.48−7.22 (m, 10H), 5.56 (s, 1H), 5.30 (d, *J* = 7.6, 1H), 5.06 (d, *J* = 10.8, 1H), 4.88−4.78 (m, 2H), 4.58 (dd, *J* = 7.2, 3, 1H), 4.33−4.26 (m, 2H), 4.13 (m, 1H), 4.09−3.55 (m, 7H), 3.42 (s, 3H), 1.53 (s, 3H), 1.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) *δ* 138.9−137.5, 129.1−126.2, 109.3, 103.9, 101.4, 100.5, 82.3, 79.3, 77.8, 76.3, 75.5, 73.4, 69.2, 62.2, 61.5, 55.5, 26.7, 25.2, 21.9. **35a*β***: ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 7.48−7.22 (m, 10H), 5.56 (s, 1H), 4.95 (d, *J* = 4.0, 1H), 4.88−4.78 (m, 3H), 4.45 (dd, *J* = 9.6, 6.0, 1H), 4.33−4.26 (m, 1H), 4.13 (m, 1H), 4.09−3.55 (m, 8H), 3.50 (s, 3H), 1.53 (s, 3H), 1.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) *δ* 138.9−137.5, 129.1−126.2, 110.6, 103.4, 101.4, 98.5, 82.3, 80.6, 79.3, 77.3, 75.54, 73.1, 69.2, 62.7, 62.6, 55.7, 32.8, 28.1, 25.9.

Cholesteryl 3,4-*O*-Isopropylidene-2-deoxy-2-iodo-α/*β*-D-*erythro*-pyranoside (35b). Following the general glycosylation procedure, compound **27** (α/*β* ratio 14:1) (53.2 mg, 0.14 mmol) was treated with NIS (73.1 mg, 0.30 mmol), cholesterol (104.9 mg, 0.27 mmol), 4Å MS (14 mg), and TfOH (1drop) in dry CH_2Cl_2 (3.3 mL) at −78 °C. The reaction temperature was left to increase to 0 °C for 17 h. The reaction was monitored by TLC (EtOAc/hexane 1:3). Radial chromatography (from hexane to EtOAc/hexane 1:3) furnished **35b** (42.1 mg, 46%) as an inseparable 1:25 α/*β* mixture as a yellow foam. Data extracted from the mixture. R_f (EtOAc/hexane 1:3): 0.5. Anal. Calcd for $C_{35}H_{57}IO_4$: 62.86 C, 8.59 H. Found: 62.80 C, 8.56 H. ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 5.35 (d, *J* = 4.0, 1H), 4.63 (d, *J* = 8.8, 1H), 4.50 (dd, *J* = 9.2, 5.6, 1H), 4.25 (dd, *J* = 13.2, 2.8, 1H), 4.08 (m, 1H), 3.87−3.82 (m, 2H), 4.54−3.46 (m, 1H),

2.37−0.67 (m, 43H), 1.53 (s, 3H), 1.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 140.8, 122.1, 101.2, 81.4, 79.4, 73.4, 63.0, 56.9−12.1, 33.6, 28.4, 26.1.

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Supporting Information Available: NMR spectra of compounds **2**, **12**, **13**, **15**, **18**, **22**, **23**, **25**, **30a**, **30b**, **32a**, and **32b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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