On the Use of 3,5-Di-*O*-benzylidene and 3,5-Di-*O*-(di-*tert*-butylsilylene)-2-*O*-benzylarabinothiofuranosides and their Sulfoxides as Glycosyl Donors for the Synthesis of β-Arabinofuranosides: Importance of the Activation Method

David Crich[a,*], **Christian Marcus Pedersen**[a,b], **Albert A. Bowers**[a], and **Donald J. Wink**[a]

a*Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607-7061*

b*Department of Chemistry, University of Aarhus, Langelandsgade 140, DK-8000 Aarhus C, Denmark*

Abstract

A 2-*O*-benzyl-3,5-di-*O*-benzylidene-α-ᴅ-thioarabinofuranoside was obtained by reaction of the corresponding diol with α,α-dibromotoluene under basic conditions. On activation with 1-benzenesulfinyl piperidine, or diphenyl sulfoxide, and trifluoromethanesulfonic anhydride in dichloromethane at −56 °C, reaction with glycosyl acceptors affords anomeric mixtures with little or no selectivity. The analogous 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-α-ᴅ-thioarabinofuranoside also showed no significant selectivity under the 1-benzenesulfinyl piperidine or diphenyl sulfoxide conditions. With *N*-iodosuccinimide and silver trifluoromethanesulfonate the silylene acetal showed moderate to high β-selectivity, independent of the configuration of the starting thioglycoside. High β-selectivity was also obtained with a 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-α-arabinofuranosyl sulfoxide donor on activation with trifluoromethanesulfonic anhydride. The high β-selectivities obtained by the *N*-iodosuccinimide/silver trifluoromethanesulfonate and sulfoxide methods are consistent with a common intermediate, most likely to be the oxacarbenium ion. The poor selectivity observed on activation of the thioglycosides with the 1-benzenesulfinyl piperidine, or diphenyl sulfoxide, and trifluoromethanesulfonic anhydride methods appears to be the result of the formation of a complex mixture of glycosyl donors, as determined by low temperature NMR work.

Introduction

Arabinose is a very common component of natural oligosaccharides, and together with galactose it is one of the most common sugars found in the furanose form in naturally occurring polysaccharides.[1] Arabinose is found in both enantiomeric modifications in nature with the ʟ-version being very common in plants where it occurs mostly in the α-furanoside form. β-ʟ-arabinofuranosides are less common but are still key building blocks in glycoproteins as, for example, at the reducing end of the potato lectin saccharide.[2] The ᴅ-arabinofuranosides are less common in nature, being found primarily in the *Actinomycetes*, including *Mycobacterium tuberculosis* and *Mycobacterium leprae*, where both the α- and β-anomers are components of the bacterial cell wall.[3]

Dcrich@uic.edu.

In contrast to the α-ᴅ-arabinofuranosides, which are readily obtained through neighboring group participation, the synthesis of β-ᴅ-arabinofuranosides with a high degree of stereocontrol is problematic.[4] In early work on the methanolysis of α-ᴅ-arabinofuranosyl chlorides carrying non-participating O2 protecting groups, Fletcher and Glaudemans obtained primarily the β-anomer and proposed a mechanism involving an ion pair.[5] Working with trimethylsilyl 2,3,5-tri-*O*-benzyl-ᴅ-arabinofuranoside as donor Mukaiyama and coworkers described β-selective couplings to trimethylsilyl protected acceptors in the presence of an oxotitanium catalyst.[6] However, Lowary et al. reported that the selectivity of NIS/AgOTf-mediated couplings of arabinofuranosyl thioglycosides is strongly dependent on temperature, with the β-arabinofuranosides being obtained in good yields but with varying degrees of stereocontrol at − 78 °C.[7] Singh et al. employed arabinofuranosyl propane-1,3-diyl phosphates as glycosyl donors and obtained good β-selectivity with simple acceptors, but not with more typical glycosyl acceptors when the α-anomeric products were formed preferentially.[8] Most recently, Kim and coworkers reported a series of highly β-selective arabinofuranosylation reactions using a tri-*O*-benzyl protected arabinofuranosyl (2-carboxy)benzyl glycoside in conjunction with triflic anhydride as donor, and have employed their methodology in a synthesis of an octaarabinofuranoside.[9]

Indirect approaches to the problem have also been developed with notable success by the Prandi and Lowary groups. Prandi adapted Ogawa's variant on the intermolecular aglycon delivery method[10] in syntheses of the tetrasaccharidic cap of the lipoarabinomannan of *Mycobacterium tuberculosis*,[11] and of a mycobacterial cell wall pentaarabinofuranoside,[12] while Lowary developed a method based on the use of a highly β-selective 2,3-anhydro-β-ᴅ-lyxofuranosyl thioglycoside donor, with subsequent, regioselective epoxide opening to give the β-ᴅ-arabinofuranosides.[13]

In the pyranosides the equivalent problem to the β-arabinofuranosides is that of the β-mannopyranosides, which we have solved by the use of 4,6-*O*-benzylidene protected mannosyl donors,[14] or their surrogates such as the 4,6-*O*-polystyryl boronate esters.[15] This method, which has been applied successfully to the preparation of numerous oligosaccharides containing β-ᴅ-mannosides, [16] β-ᴅ-rhamnosides,[17] and β-ᴅ-glycero-ᴅ-mannoheptopyranosides,[18] relies on the preactivation of glycosyl sulfoxides with trifluoromethanesulfonic anhydride, or of thioglycosides with either of 1-benzenesulfinyl piperidine (BSP),[19] benzenesulfenyl triflate,[20] or diphenyl sulfoxide (DPSO),[21] in the presence of triflic anhydride and a hindered non-nucleophilic base such as tri-*tert*-butylpyrimidine (TTBP).[22,23] These reactions allow the rapid clean formation of an observable intermediate α-mannosyl triflate,[24] which acts as a reservoir for a β-selective transient contact oxacarbenium ion/triflate ion pair (Scheme 1).[25] In this chemistry the 4,6-*O*-benzylidene acetal plays the crucial role raising the energy barrier to formation of the oxacarbenium ion, by enforcing the more electron-withdrawing *tg* conformer of the C5-C6 bond,[26,27] and so of limiting the concentration of the α-selective solvent separated ion pair.

The generally excellent results in the mannose series prompted the investigation which we describe here into the applicability of a 3,5-di-*O*-benzylidene protecting group, or its equivalent, as a stereocontrolling element in the arabinofuranose series. During the late stages of this work, and in the course of the review process, comparable investigations into the effect of 3,5-*O*-(di-*tert*-butylsilylene) and 3,5-*O*-(tetraisopropyldisilylene) acetals on the stereochemical outcome of arabinofuranosylation reactions were reported by Boons,[28] and Ito,[29] and their respective coworkers.

Results

Donor Synthesis

The literature on the existence and use of 3,5-di-*O*-acetal type protecting groups in the furanosides is very sparse,[30] with few descriptions of the direct introduction of a cyclic acetal onto the 3,5-position of a pre-exisitng furanose ring.[31] In the arabinofuranose series the few known 3,5-*O*-alkylidene acetals were obtained by indirect methods, involving fusion of the furanose ring onto the existing acetal, and their relative instability was noted in at least one case. Thus, a pair of 3,5-di-*O*-benzylidene protected arabinofuranose derivatives, unstable in chloroform, was obtained in a DAST-mediated contraction of a 4,6-*O*-benzylidene protected pyranoside.[32] 3,5-Di-*O*-benzylidene protected tetrahydrofurans were also accessed from the solvolysis of a 1,3;4,6-di-*O*-benzylidene protected mannitol derivative,[33] by radical ring closure reactions on existing benzylidene acetal frameworks,[34] and by fusion of a furanose ring onto an existing benzylidene acetal through a nucleophilic ring closure.[35]

The synthesis of the 3,5-di-*O*-benzylidene protected donor **6** began with the preparation of the triol **3**, which was obtained from ᴅ-arabinose. Among the various literature protocols for the synthesis of the methyl arabinofuranoside investigated,[36] the one of Lowary and coworkers was optimal.[37] The methyl arabinofuranoside so-obtained was esterified under standard conditions and then transformed into the glycosyl acetate **2** with sulphuric acid in acidic acetic anhydride. The corresponding *p*-cresyl thioglycoside was obtained by Lewis acid hydrolysis in presence of thiocresol,[38] and subsequent saponification afforded the desired triol **3** (Scheme 2).

As the obvious next step in the synthesis of the donor, direct introduction of the benzylidene protecting group was attempted by the standard acetalization method, albeit to no avail. For example, reaction with benzaldehyde dimethyl acetal with acid catalysis under a variety of conditions gave complex mixtures of products.[39] Similarly, with α,α-dibromotoluene under basic conditions complex mixtures of products were obtained. We speculated that in both cases the problem arose from migration of the benzylidene group around the furan ring giving multiple products, and resolved to protect O2 before attempted introduction of the acetal (Scheme 3). Thus, **3** was converted to the tetraisopropyldisiloxane derivative **4** under standard conditions.[40] Benzylation of **4** with sodium hydride and benzyl bromide, which was more effective in THF than in DMF as described in the literature,[41] was followed by desilylation with TBAF to give the diol **5** in 69 % for 2 steps ready for the introduction of the benzylidene acetal. However, attempted acid catalysed benzylidenation of this diol under a variety of conditions failed and only starting material could be recovered from the reaction mixtures. Fortunately, exposure to α,α-dibromotoluene, DMAP and triethylamine[42] in pyridine at reflux afforded the desired compound **6** in 40% yield as a very acid labile white crystalline product, in the form of a single diastereomer with the phenyl group equatorial as established crystallographically. Given the evident instability of **6**, the method of formation, and the modest yield we consider it possible that its diastereomer, with the axial phenyl group, is simply too unstable for us to isolate.

Thioglycoside **6** crystallizes with an approximate E_4 conformation of the furanoside, with C4 below the plane occupied by the other ring atoms, that places the 2-*O*-benzyl group in a pseudoequatorial position and maximizes the anomeric stabilization.[43] With a O4-C4-C5-O5 torsion angle of 174°, little deviation is seen from the *tg* conformation about the C4-C5 bond which, by analogy with the pyranosides,[27] is expected to maximize the electron withdrawing/ disarming effect of the C5-O5 bond.

A more robust 3,5-*O*-di-*tert*-butylsilylene acetal **7** was obtained by reaction of triol **3** with di-(*tert*-butyl) silyl bis(trifluoromethanesulfonate), with the optimum results obtained in pyridine

as solvent. That the correct 3,5-*O*-silylene acetal had been obtained was confirmed by acetylation, when the anticipated significant downfield shift of the H2 resonance in the ^{1}H-NMR spectrum was observed, and by correlations of subsequent products with literature data as described below. Benzylation of **7** with sodium hydride and benzyl bromide afforded the glycosyl donor **8**, with THF again proving to be a better solvent than DMF for this reaction (Scheme 4).

Glycosylation Reactions

Glycosylation of **6** with cyclohexanol in dichloromethane between −55 and −45 °C, following activation with BSP and trifluoromethanesulfonic anhydride, gave an approximately 1:1 mixture of the two anomeric glycosides **9** (Table 1). Difficulties in the separation of the α-anomer from aromatic byproducts prompted the in situ cleavage of the benzylidene acetal and the isolation of the products in the form of the 3,5-diols **10**. The stereochemical assignment of **10** was based on the chemical shift of the anomeric carbon, which is known to resonate up field relative to its α-counterpart.[44] Furthermore, the β-anomer showed a significantly larger (3–5 Hz) $^3J_{H1\text{-}H2}$ coupling constant than the α-anomer which was consistent with subsequent products, as discussed below. Coupling of **6** to cyclohexanol was also attempted with activation by DPSO and trifluoromethanesulfonic anhydride, when a slight increase in selectivity in favour of the α-anomer was observed (Table 1). Finally, coupling to the primary glucose-based acceptor **11** under the BSP conditions afforded an approximately 1:1 mixture of anomeric saccharides **12** (Table 1). Again, it was necessary to remove the benzylidene acetal in order to obtain pure samples of the anomeric products **13**, whose ^{1}H and ^{13}C-NMR spectra exhibited similar trends to those noted above for the cyclohexyl glycosides. Additional confirmation of the stereochemistry was provided by comparison of the spectral data of the known α-diol **13** with that found in the literature.[13c]

10   **13**

Glycosylation reactions with the silylene protected donor **8**, under both the BSP and DPSO conditions gave results (Table 2) that were directly analogous to those obtained with the benzylidene acetal **6** (Table 1). On the basis of variable temperature NMR experiments described below a modified protocol was devised which involved warming the donor/DPSO/ triflic anhydride mixture to −25 °C for 30 min before recooling to −70 °C and addition of the acceptor. This did afford improved β-selectivity (Table 2) but at the expense of lower overall yields. Difficulties in the purification of **21** prompted its hydrolysis to the diols **22** (Table 2). Overall, with comparable selectivities, the silylene acetal **8** presents the clear advantage over its benzylidene counterpart **6** of more facile preparation and improved stability.

22   **23**

At this stage in our investigation we became aware of the work of Boons and co-workers in the enantiomeric series in which activation of the *S*-phenyl thioglycoside **24** with *N*-iodosuccinimide and silver triflate in dichloromethane at −30 °C afforded β-selective couplings to a range of acceptors, albeit none of those employed in our initial study. Accordingly, we

synthesized donors **24**[28] and **25** by the same method as employed for the synthesis of **8**. Additionally, adapting a successful method for the synthesis β-thiomannopyranosides,[45] donor **24** was converted, via its sulfoxide **26**, to the β-thioarabinofuranoside **27** in 70% yield as a separable 6:1 β:α mixture. A series of coupling reactions were then conducted as reported in Table 3.

Assignment of Configuration[46]

With a view to establishing a rapid means of assignment of anomeric configuration in the 3,5-*O*-di-*tert*-butylsilylene protected arabinofuranosides key parameters have been collected in Table 4. It is evident from this Table that neither the anomeric chemical shift in the ^{1}H-NMR spectra, nor the anomeric $^1J_{CH}$ coupling constants[47] are suitable determinants in this series. There is, however, a reliable trend in the $^3J_{H1,H2}$ coupling constants, with the β-isomer being consistently larger by 2–3 Hz, and in the anomeric chemical shifts in the ^{13}C-NMR spectra in CDCl$_3$ where the β-isomer is typically more upfield by approximately 7 ppm. The H4 chemical shift also appears to be a reliable indicator of anomeric configuration. The trends in the $^3J_{H1,H2}$ coupling constants and in the anomeric ^{13}C chemical shifts were used to assign stereochemistry in the couplings described in this paper, with verification by correlation with the literature following hydrolysis of **14α** and **17α** to the diols **23α** and **13α**, respectively,[7,13c] as described above. Yet further support is provided by the consistent Hudson's rule-like trend in the specific rotations of the two anomeric series.[48]

Low Temperature NMR studies of Glycosylation Intermediates

In an attempt to understand the different stereoselectivities obtained with donors **8** and **26** under the BSP/trifluoromethanesulfonic anhydride conditions, and with the sulfoxide/trifluoromethanesulfonic anhydride combination, low temperature experiments on the activation of **8** with BSP/trifluoromethanesulfonic anhydride, and of **27** with trifluoromethanesulfonic anhydride were conducted (see Supporting Information). In the 4,6-di-*O*-benzylidene protected mannopyranose series[14] this type of experiment demonstrated the very rapid formation of an intermediate α-mannopyranosyl triflate and was instrumental in subsequent mechanistic work in that series.[24b]

With the 3,5-di-*O*-silylene acetal protected thioglycoside **8**, activation at −55 °C with the BSP/Tf$_2$O combination in CD$_2$Cl$_2$ was surprisingly complex and provided several apparent anomeric resonances. On gradual warming to approximately 0 °C, these signals collapsed in favour of one major doublet δ 6.1 ($J = 2.5$ Hz), which is tentatively identified as an α-anomeric triflate **30**. On further warming to approximately 10 °C decomposition set in, with the formation of a single major product, that was isolated and identified as the intramolecular Friedel Crafts product **31** (Supporting Information).[49] Directly analogous results were observed with the benzylidene acetal protected thioglycoside **6** on activation with BSP and triflic anhydride at −55 °C in CD$_2$Cl$_2$ (Supporting Information) with the exception that the apparent anomeric triflate (δ 6.2, d, $J = 2.3$ Hz) underwent decomposition at approximately −30 °C.[50] In a further series of VT-NMR experiments a mixture of the silylene protected donor **8**, BSP and triflic anhydride was warmed to −25 °C to enable formation of the presumed intermediate triflate **30**, then recooled to −70 °C at which point only the one species was observed. Addition of methanol at −55 °C then resulted in the formation of a 1:3 α:β anomeric mixture of the methyl glycosides **14** as determined from the crude reaction mixture (Table 2)

Activation of sulfoxide **26** with trifluoromethanesulfonic anhydride at −70 °C also gave a relatively complex mixture, but on warming to −50 °C the spectrum was enormously simplified and displayed predominantly one product whose spectrum was consistent with that assigned to the enantiomeric glycosyl triflate **30** arising from activation of thioglycoside **8** with BSP and triflic anhydride. Quenching of this intermediate with methanol at −40 °C provided the methyl glycoside with excellent β-selectivity (Supporting Information).

Discussion

It is apparent from the results presented in Table 3 that the stereoselectivity of the NIS/AgOTf-mediated glycosylations reported originally by Boons and coworkers[28] is independent of the nature of the thioglycoside (SPh or SCr), and of the anomeric stereochemistry (α-SPh, or β-SPh). A common intermediate is therefore indicated and, in line with the arguments of Boons, this is most likely the glycosyl oxacarbenium ion. The sulfoxide donor **26** cleanly provides the triflate *ent*-**30** which, in line with our work in the mannosyl series (Scheme 1), is likely to act as a reservoir for the same oxacarbenium ion, thereby accounting for the commonality of the results from the NIS-mediated couplings and those from the sulfoxide method.

The poor diastereoselectivity obtained with donor **8** (and **6**), when activated by the BSP method (Tables 1 and 2), is the result of incomplete conversion of the thioglycoside to the glycosyl triflate under the reaction conditions, as is clear from a comparison of the results of the low temperature NMR experiments (Supporting Information). The exact nature of the various species formed on activation of **8** (and **6**) on treatment with BSP and triflic anhydride is not clear at the present time. It appears that they may be intermediates on the way to the formation of the glycosyl triflate, as this latter species dominates at higher temperatures, but it is also possible that they are metastable species formed by interaction of the glycosyl oxacarbenium ion and byproducts from the activation process. The relatively high temperatures required for the activation of the sulfoxide **26**, as compared to those noted earlier in the mannopyranosyl series, and the clean activations of mannopyranosyl thioglycosides by the BSP/Tf$_2$O combination previously, suggest that it is slow activation of the thioglycosides by the BSP/Tf$_2$O that is the problem.

Furanose sugars are generally thermodynamically less stable than the isomeric pyranoses for most configurations as is clear from the relative populations of the five and six membered rings under equilibrating conditions.[51] Furanosides are also generally more reactive, and display different kinetic parameters, than the corresponding pyranosides as is well-known from studies on the acid catalyzed hydrolysis of simple glycosides.[52] Accordingly, and taking into further account the greater ease with which sp^2-hybridized atoms are accommodated into five-membered rather than six-membered rings,[53] we had anticipated that the furanosyl donors **6**, **8**, and **24–27** would be more reactive than the 4,6-di-*O*-benzylidene mannopyranosides studied previously in our group. We were therefore surprised by the slow activation of **6**, **8**, and **26** revealed by the variable temperature NMR experiments. Nevertheless, the situation is not without precedent and resembles both the slow activation of the 2,3-anhydrofuranosyl donors **32** and **33** observed by Lowary and coworkers,[54] and the comparably slow activation of certain mannosyl thioglycosides bearing electron-deficient 4,6-di-*O*-alkylidene groups such as in **34**.[17]

The parallel between the slow activation observed for **32** and **33** by Lowary and coworkers and that observed here for **6** and **8** is striking. It is unlikely that the epoxide in **32** and **33** is unusually strongly electron-withdrawing, just as it is improbable that the acetals in the donors studied here are more electron-withdrawing than the 4,6-di-**O**-benzylidene acetal in simple thiomannopyranoside donors, therefore we do not consider an electronic effect to be at the root of the poor reactivity. Rather, we suggest that the fusion of the epoxide in **32** and **33**, and the presence of the cyclic acetals in **6**, **8**, and **24**–**27** serves both to limit the rapid, facile pseudorotational motion common to simple furanosides and, perhaps more importantly, remove some of the torsional interactions present in unrestricted furanosides, thereby minimizing any advantage to be gained from oxacarbenium ion formation with its two sp^2-hybridized centers.

The good to excellent β-selectivity observed with donors **24**, **25**, and **27** (Table 3) under the NIS/AgOTf conditions applied originally by Boons and co-workers, as well as with the sulfoxide **26** on activation with trifluoromethanesulfonic anhydride (Table 3) is suggestive of a common intermediate in these glycosylation reactions, and that intermediate is likely the glycosyl oxacarbenium ion **35**. As discussed by Boons it seems likely that this oxacarbenium ion resides in the E_3 conformer **36**, and undergoes attack on the β-face, *syn* to the C2-O2 bond and *anti*-to the C2-H2 bond in such a manner as to minimize torsional interactions with the incoming nucleophile.

It is of some interest that this model contradicts Woerpel's inside attack model for nucleophilic attack on five-membered cyclic oxacarbenium ions,[55] as applied to the conformationally constrained oxabicyclo[4.3.0]nonanyl system **37**, on which attack by carbon nucleophiles is unselective.[56] This has been explained by the ring flip caused by inside attack imposing a destabilizing twist on the six-membered ring that is sufficient to counteract any advantages gained from the minimization of torsional strain around the five-membered ring. On the other hand, outside attack gives rise to more torsional strain in the five-membered ring but maintains the six-membered ring in the ideal chair conformation. The overall result is diminished selectivity in the reaction of carbon nucleophiles with the oxabicyclo[4.3.0]nonane system **37**. Evidently, the Woerpel model for nucleophilic attack on oxabicyclic cations such as **37** does not apply to the related cation **35** for which "inside attack" (**36**) is preferred. Interestingly, the standard Woerpel model for inside attack on monocyclic five-membered oxacarbenium ions predicts poor selectivity for the simple tri-*O*-benzylarabinofuranosyl cation such as might be derived from the glycosyl triflate **38**. This prediction, which holds for carbon nucleophiles, contrasts with the observations of Kim and coworkers who obtain good β-selectivity with alcohol nucleophiles on activation of donor **39** with trifluoromethanesulfonic anhydride in chemistry that is thought to pass through the triflate **38** and the associated oxacarbenium ion.[9] Evidently, the situation with *O*-nucleophiles is more complex than with carbon nucleophiles and other factors need to be taken into consideration, perhaps including hydrogen bonding of the incoming alcohol to the donor.

37 **38** **39**

Conclusion

In conclusion a somewhat acid sensitive 3,5-di-*O*-benzylidene protected arabinofuranosyl system may be prepared provided that O2 is protected before attempted introduction of the acetal. The corresponding 3,5-di-*O*-di-*tert*-butylsilylene system is both easier to prepare and considerably more stable. Both systems were activated only slowly by the 1-benzenesulfinyl piperidine/trifluoromethanesulfonic anhydride combination and both gave poor selectivity in the glycosylation reactions, apparently because of the formation of the generation of several glycosylating species under these conditions. On the other hand the activation of the 3,5-di-*O*-di-*tert*-butylsilylene protected thioglycosides with *N*-iodosuccinimide and silver triflate, or of the corresponding sulfoxides with trifluoromethanesulfonic anhydride affords reactions that are moderately to highly selective for the formation of the β-arabinofuranosides. This chemistry, which does not depend on the anomeric configuration of the thioglycoside, is best explained by the intermediacy of an oxacarbenium ion intermediate.

Experimental Section

p-Cresyl 1-thio-α-ᴅ-arabinofuranoside (3)[13c,55]

A suspension of ᴅ-arabinose **1** (5.0 g, 33.3 mmol) in MeOH (100 mL) was treated with a solution of acetyl chloride (2.5 mL) in methanol (30 mL) and stirred at rt for approximately 2.5 h, after which the white crystalline starting material was observed to have fully dissolved, and TLC (CH$_2$Cl$_2$/MeOH 4:1) showed full conversion of **1** (R$_f$ = 0.1) to 2 new spots (R$_f$ = 0.5 and 0.6). The reaction mixture was quenched with pyridine, evaporated, then co-evaporated with CH$_2$Cl$_2$ to give a crude product which was dissolved in pyridine (40 mL), cooled to 0 °C and treated with acetic anhydride (20 mL, 0.21 mol). The reaction mixture was allowed to stir overnight. Then solvent was evaporated, the reaction diluted with CH$_2$Cl$_2$ (300 mL) and finally washed thoroughly with water, 1M HCl (aq), NaHCO$_3$ (sat), and brine. The organic phase was dried (Na$_2$SO$_4$) and concentrated in vacuo to give a crude product, which was submitted to the next step without further purification. This mixture was dissolved in acetic anhydride (80 mL) and cooled to 0 °C when acetic acid (20 mL) and then H$_2$SO$_4$ (5 mL) were added drop wise. After 1.5 h at rt TLC (hexanes - EtOAc 4:1) indicated completion. The reaction mixture was poured slowly over a mixture of ice, aqueous NaHCO$_3$, and CH$_2$Cl$_2$. The organic layer was separated and washed thoroughly with additional NaHCO$_3$ (sat) and brine, dried (Na$_2$SO$_4$), and concentrated in vacuo to give a crude product (15.45 g). The crude product was dissolved in dry CH$_2$Cl$_2$ (150 mL) and cooled to 0 °C when BF$_3$·OEt$_2$ (11.5 mL, 92 mmol) was added slowly by syringe. After 15 min. *p*-thiocresol (4.18 g, 33.7 mmol) was added and the reaction mixture was stirred at rt overnight before it was neutralized with Et$_3$N and diluted to 300 mL with CH$_2$Cl$_2$, washed with water, brine, dried (Na$_2$SO$_4$) and concentrated in vacuo. TLC indicated the presence of a minor amount of another isomer in addition to the major product. This was not separated at this time, but instead a short column was performed, washing first with hexanes followed by elution of the mixture with in pure ethyl acetate. The triacetate was dissolved in MeOH (150 mL), treated with sodium methoxide (25 % in MeOH, 1 mL) and the solution was stirred overnight before it was neutralized with IR-120 resin, evaporated and purified by flash chromatography on silica gel (CH$_2$Cl$_2$ - MeOH 10:1) to give 4.06 g (71 %) of the title triol. R$_f$ = 0.3 (EtOAc); [α]$_\text{D}$ +235.6 (*c*, 1.0, CHCl$_3$); lit.[55] [α]$_\text{D}$ +236.2 (*c* 2.6, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.35 (d, 2 H, *J* = 8.5 Hz), 7.05 (d, 2 H, *J* = 8.5 Hz), 5.31 (d, 1 H, *J* = 3.5 Hz), 4.24 (m, 4 H), 4.11 (m, 2 H), 4.04 (m, 1 H), 3.78 (dd, 1 H, *J* = 2.5,

12.5 Hz), 3.69 (dd, 1 H, J = 2.5, 12.5 Hz), 2.28 (s, 3 H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 137.9, 132.5, 129.9, 129.8, 91.8, 82.7, 81.8, 76.5, 60.9, 21.1.

p-Cresyl 2-*O*-benzyl-1-thio-α-ᴅ-arabinofuranoside (5)[40,41]

The triol **3** (1.46 g, 5.7 mmol) was dissolved in pyridine (10 mL), cooled to 0 °C and treated with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane. The reaction mixture was allowed to reach rt and then stirred for 2 h before it was diluted with diethyl ether, washed with water, HCl (1 M, 5 x), NaHCO$_3$ (sat), brine, dried (Na$_2$SO$_4$), and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (hexanes-CH$_2$Cl$_2$ 1:1 - then CH$_2$Cl$_2$) to give the 3,5-di-*O*-tetraisopropyldisiloxane adduct (2.30 g, 81 %) as a colorless syrup. This compound (2.30 g, 4.6 mmol), together with benzyl bromide (1.10 mL, 9.2 mmol), was dissolved in THF (80 mL), cooled to 0 °C and treated portion wise with NaH (60 % dispersion in oil, 370 mg, 9.2 mmol). After 8 h. at rt an additional 1 equivalent (185 mg, 4.7 mmol) of NaH was added and the reaction mixture was left overnight before it was filtered through silica gel and concentrated in vacuo to give an oily product which was dissolved in THF (15 mL) and treated with TBAF (1 M in THF, 9.5 mL). The crude reaction mixture was concentrated and purified by column chromatography on silica gel (CH$_2$Cl$_2$ then CH$_2$Cl$_2$-EtOAc 1:1) to give **5** (1.08g, 69 % for 2 steps) as a colorless syrup. R$_f$ = 0.25 (CH$_2$Cl$_2$ - EtOAc 2:1); ^{1}H NMR[40] (300 MHz, CDCl$_3$) δ 7.39-7.29 (m, 6 H), 7.12 (d, 2 H, J = 7.92), 5.46 (d, 1 H, J = 3.3 Hz), 4.67 (d, 1 H, J = 11.7 Hz), 4.60 (d, 1 H, J = 11.7 Hz), 4.22 (m, 1 H), 4.09 (dd, 1 H, J = 3.8, 7.0 Hz), 4.00 (t, 1 H, J = 3.8 Hz), 3.80 (dt, 1 H, J = 4.4, 12.2 Hz), 3.71 (dd, 1 H, J = 3.8, 12.0 Hz), 3.19 (bd, 1 H, J = 6.1, OH), 2.57 (m, 1 H, OH), 2.33 (s, 3 H); ^{13}C NMR[40] (75 MHz, CDCl$_3$) δ 138.0, 137.4, 132.5, 130.3, 130.0, 128.7, 128.2, 90.2, 89.7, 82.6, 75.9, 72.6, 61.4, 21.3.

p-Cresyl 2-*O*-benzyl-3,5-di-*O*-benzylidene-1-thio-α-ᴅ-arabinofuranoside (6)

Diol **5** (225 mg, 0.65 mmol) and DMAP (16 mg, 0.13 mmol) were heated to reflux in pyridine (5 mL), and treated with α,α-dibromotoluene (0.44 mL, 3.3 mmol) and Et$_3$N (180 µL, 1.3 mmol). After 1 h further α,α-dibromotoluene (0.18 mL, 1.3 mmol) was added to the reaction mixture, which was then maintained at reflux 1 h before it was cooled to rt and diluted with EtOAc. The purple-red solution was filtered through silica gel and concentrated to give a yellow crude product, which was purified by flash chromatography on silica gel (hexane/CH$_2$Cl$_2$ 4:1 then 2:1) to give **6** (111 mg, 40%) as white crystals, which were recrystallized from *tert*-butyl methyl ether. Mp 120 °C; R$_f$ = 0.2 (hexanes/CH$_2$Cl$_2$); [α]$_D$ +177 (*c*, 1.0, CH$_2$Cl$_2$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.50-7.49 (m, 2 H), 7.42-7.30 (m, 2 H), 7.13 (d, 1 H, J = 8.0 Hz), 5.55 (s, 1H), 5.45 (d, 1 H, J = 5.0 Hz), 4.77 (d, 1 H, J = 11.8 Hz), 4.74 (d, 1 H, J = 11.7 Hz), 4.55 (m, 1 H), 4.22 (dd, 1 H, J = 5.0, 7.7 Hz), 3.98-3.91 (m, 2 H) 3.84 (pseudo t, 1 H, J = 8.0 Hz), 2.34 (s, 3H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 137.9, 137.4, 136.8, 132.0, 129.9, 129.3. 128.5, 128.4, 127.9, 126.3, 102.3, 90.8, 84.9, 72.8, 70.8, 69.4, 21.2; HRMS calc. for [C$_{26}$H$_{26}$O$_4$S]$^+$: 434.1552, found: 434.1547.

p-Cresyl 3,5-di-*O*-(di-*tert*-butylsilylene)-1-thio-α-ᴅ-arabinofuranoside (7)

Triol **3** (1.63 g, 6.4 mmol) and DMAP (39 mg, 0.32 mmol) were dissolved in pyridine (25 mL), cooled to 0 °C and treated with di-*tert*-butylsilyl bis(trifluoromethanesulfonate) (2.1 mL, 6.4 mmol). The reaction mixture was allowed to reach rt, and was then stirred for 12 h before it was quenched with MeOH (2 mL). The crude reaction mixture was concentrated in vacuo to give a colorless oil, which was purified by flash chromatography on silica gel (hexanes-EtOAc 10:1) to give **7** (2.26 g, 89 %) as a white solid. Mp 150 °C; R$_f$ = 0.3 (CH$_2$Cl$_2$); [α]$_D$ +196 (*c*, 1.0, CH$_2$Cl$_2$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.41 (d, 2 H, J = 8.1 Hz), 7.12 (d, 2 H, J = 8.0 Hz), 5.24 (d, 1 H, J = 5.9 Hz), 4.32 (dd, 1 H, J = 4.7, 8.7 Hz), 4.13 (m, 1 H), 4.00 (dd, 1 H, J = 7.4, 9.2 Hz), 3.93 (dd, 1 H, J = 8.9, 10.3 Hz), 3.88 (m, 1 H), 2.74 (d, 1 H, J = 4.0 Hz) 2.32

(s, 3 H), 1.06 (s, 9 H), 0.97 (s, 9 H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 138.0, 132.3, 130.2, 129.8, 91.4, 81.1, 80.8, 73.7, 67.4, 27.4, 27.1, 22.7, 21.1, 20.1; HRMS calc. for [C$_{20}$H$_{32}$O$_4$SSi]$^+$: 396.1791, found: 396.1791.

p-Cresyl 2-O-acetyl-3,5-di-O-(di-tert-butylsilylene)-1-thio-α-ᴅ-arabinofuranoside (7-O-Ac)

Microscale acetylation of **7** with pyridine an acetic anhydride gave **7-O-Ac** quantitatively as a white crystalline solid. Mp 72.1 °C; R$_f$ = 0.8 (CH$_2$Cl$_2$); [α]$_ᴅ$ +145.5 (*c*, 1.0, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.42 (d, 2 H, *J* = 8.1 Hz), 7.12 (d, 2 H, *J* = 8.1 Hz), 5.26 (dd, 1 H, *J* = 4.9, 6.9 Hz), 5.22 (d, 1 H, *J* = 4.8 Hz), 4.34 (m, 1 H), 4.11 (dd, 1 H, *J* = 7.2, 9.1 Hz), 4.00-3.92 (m, 3 H), 2.32 (s, 3 H), 2.15 (s, 3 H), 1.04 (s, 9 H), 0.97 (s, 9 H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 169.9, 138.0, 132.7, 129.8, 129.7, 89.5, 80.6, 79.5, 73.5, 67.2, 27.4, 27.0, 22.6, 21.1, 21.0, 20.1; HRMS calc. for [C$_{22}$H$_{34}$O$_5$SSiNa]$^+$: 461.1794, found: 461.1772.

p-Cresyl 2-O-benzyl-3,5-di-O-(di-tert-butylsilylene)-1-thio-α-ᴅ-arabinofuranoside (8)

Compound **7** (1.17 g, 2.9 mmol) was dissolved in THF (30 mL) and treated with benzyl bromide (0.70 mL, 5.9 mmol) followed by portion wise addition of NaH (360 mg, 9 mmol) at 0 °C. After 6 h TLC showed full conversion of **7** and the reaction mixture was filtered through silica gel, concentrated in vacuo and purified by flash chromatography (hexane/CH$_2$Cl$_2$) to give **8** (1.19, 83%) as a white crystalline solid. Mp 80 °C; R$_f$ = 0.8 (CH$_2$Cl$_2$); [α]$_ᴅ$ +154 (*c*, 1.0, CH$_2$Cl$_2$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.45-7.30 (m, 7 H), 7.10 (d, 2 H, *J* = 8.0 Hz), 5.35 (d, 1 H, *J* = 5.3 Hz), 4.84 (d, 1 H, *J* = 12.0 Hz), 4.76 (d, 1 H, *J* = 12.0 Hz), 4.34 (dd, 1 H, *J* = 4.7, 8.7 Hz), 4.15 (dd, 1 H, *J* = 7.0, 9.2 Hz), 4.00-3.87 (m, 3 H), 2.32 (s, 3 H), 1.08 (s, 9 H), 0.99 (s, 9 H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 137.8, 137.6, 132.2, 130.5, 129.7, 128.4, 128.0, 127.9, 90.3, 86.7, 81.3, 73.7, 72.2, 67.3, 27.5, 27.1, 22.6, 21.1, 20.1; HRMS calc. for [C$_{27}$H$_{38}$O$_4$SSi]$^+$: 486.2260, found: 486.2257.

Activation of Thioglycoside 6 with 1-Benzenesulfinyl Piperidine and Trifluoromethanesulfonic Anhydride (Method A). Cyclohexyl 2-O-benzyl-β-ᴅ-arabinofuranoside (10β) and Cyclohexyl 2-O-benzyl-α-ᴅ-arabinofuranoside (10α)

Thioglycoside **6** (45 mg, 0.10 mmol), BSP (31 mg, 0.15 mmol), TTBP (159 mg, 0.54 mmol) and crushed activated 4 Å molecular sieves (100 mg) were dried in vacuo and dissolved in CH$_2$Cl$_2$ (4 mL) under argon, then stirred at rt for 1 h prior to cooling to −55 °C. After 15 min. Tf$_2$O (21 μL, 0.13 mmol) and, after an additional 15 min, cyclohexanol (55 μL, 0.52 mmol) was added. The reaction mixture was allowed to warm to −45 °C with stirring and then quenched with several drops of Et$_3$N, filtered and concentrated in vacuo. The crude mixture was purified by flash chromatography on silica gel (Hexanes-CH$_2$Cl$_2$ 1:1) to give cyclohexyl 2-O-benzyl-3,5-di-O-benzylidene-α-ᴅ-arabinofuranoside (**9α**) (17 mg) and cyclohexyl 2-O-benzyl-3,5-di-O-benzylidene-α-ᴅ-arabinofuranoside (**9β**) (18 mg) (82 % combined yield) as colorless syrups. **9α**: ^{1}H NMR(500 MHz, CDCl$_3$) δ 7.52-7.26 (m, 9 H), 5.53 (s, 1 H), 5.24 (d, 1 H, *J* = 2.9 Hz), 4.70 (d, 1 H, *J* = 11.7 Hz), 4.64 (d, 1 H, *J* = 11.7 Hz), 5.50 (dd, 1 H, *J* = 4.1, 9.1 Hz), 4.19 (dd, 1 H, *J* = 2.8, 8.0 Hz), 3.95 (ddd, 1 H, *J* = 4.3, 9.4, 10.0 Hz), 3.89 (dd, 1 H, *J* = 9.3, 10.0 Hz), 3.76 (dd, 1 H, *J* = 8.1, 9.3 Hz), 3.58 (m, 1 H), 1.88 (m, 2H), 1.73 (m, 2 H), 1.53 (m, 1H), 1.40-1.10 (m, 5 H). **9β**: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.50 (m, 2 H), 7.40-7.29 (m, 7 H), 5.57 (s, 1 H), 5.24 (d, 1 H, *J* = 5.3 Hz), 4.71 (d, 1 H, *J* = 11.5 Hz), 4.66 (d, 1 H, *J* = 11.5 Hz), 4.47 (dd, 1 H, *J* = 4.4, 9.5 Hz), 4.15 (dd, 1 H, *J* = 5.3, 9.5 Hz), 4.06 (t, 1 H, *J* = 9.4 Hz), 3.92 (t, 1 H, *J* = 9.9 Hz), 3.57 (m, 1 H), 1.96 (m, 2 H), 1.77 (m, 2 H), 1.56-1.19 (m, 6 H) ^{13}C NMR (125 Hz, CDCl$_3$) δ 137.8, 137.1, 129.1, 128.4, 128.3, 128.0, 127.8, 126.3, 102.3, 98.8, 82.8, 78.6, 78.0, 72.0, 71.7, 68.5, 33.8, 32.2, 29.7, 25.6, 24.3. Further characterization was not attempted and both compounds were treated with trifluoroacetic acid (1 drop) in CH$_2$Cl$_2$ (1 mL) at room temperature for 1 min. Concentration and purification by flash chromatography on silica gel gave cyclohexyl 2-O-benzyl-α-ᴅ-arabinofuranoside (**10α**) (6 mg)

and cyclohexyl 2-*O*-benzyl-β-ᴅ-arabinofuranoside (**10β**) (10 mg). **10α**: Colorless syrup. $R_f =$ 0.3 (Hexanes-ethyl acetate 1:1); $[\alpha]_D$ +70.1 (*c*, 1.3, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.37-7.29 (m, 5 H), 5.25 (s, 1 H), 4.65 (d, 1 H, *J* = 11.6 Hz), 4.57 (d, 1 H, *J* = 11.6 Hz), 4.17 (dd, 1 H, *J* = 3.1, 7.1 Hz), 4.13 (bs, 1 H), 3.89 (s, 1 H), 3.82 (dd, 1 H, *J* = 3.0, 11.8 Hz), 3.75 (dd, 1 H, *J* = 4.1, 11.8 Hz), 3.65 (m, 1 H), 2.79 (br s, 1 H), 2.25 (br s, 1 H), 1.87 (br s, 2 H), 1.70 (bs, 2 H), 1.39-1.19 (m, 5 H); ¹³C NMR (125 Hz, CDCl₃) δ 137.0, 128.6, 128.1, 128.0, 103.4, 87.0, 86.9, 75.3, 74.8, 71.8, 62.7, 33.6, 31.4, 25.6, 24.1, 23.9; HRMS calc. for $[C_{18}H_{26}O_5Na]^+$: 345.1678, found: 345.1662. **10β**: White crystalline solid. Mp 100.8 °C; $R_f =$ 0.2 (Hexanes-ethyl acetate 1:1); $[\alpha]_D$ −91.2 (*c*, 1.0, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.38-7.30 (m, 5 H), 5.05 (d, 1 H, *J* = 4.5 Hz), 4.66 (d, 1 H, *J* = 11.6 Hz), 4.56 (d, 1 H, *J* = 11.6 Hz), 4.48 (t, 1 H, *J* = 7.3 Hz), 3.93-3.88 (m, 2 H), 3.75 (dd, 1 H, *J* = 3.0, 11.8 Hz), 3.65 (dd, 1 H, *J* = 3.7, 11.8 Hz), 3.50 (m, 1 H), 2.45 (br s, 2 H), 1.91 (m, 2 H). 1.75 (m, 2 H), 1.55 (m, 1 H), 1.45-1.10 (m, 5 H); ¹³C NMR (125 Hz, CDCl₃) δ 137.7, 128.6, 128.1, 128.1, 98.7, 84.5, 82.1, 73.5, 72.5, 62.9, 33.8, 32.2, 25.5, 24.4, 24.3; HRMS calc. for $[C_{18}H_{26}O_5Na]^+$: 345.1678, found: 345.1667.

Activation of Thioglycoside 6 with Diphenyl Sulfoxide and Trifluoromethanesulfonic Anhydride (Method B)

Thioglycoside **6** (53 mg, 0.12 mmol), diphenyl sulfoxide (74 mg, 0.37 mmol), TTBP (182 mg, 0.73 mmol) and crushed activated 4 Å molecular sieves (100 mg) were dried in vacuo and dissolved in CH₂Cl₂ (3 mL) under argon, then stirred at rt for 1 h prior to cooling it to −72 ° C. After 15 min. Tf₂O was added and after an additional 30 min. cyclohexanol (39 µL, 0.37 mmol) was added. The reaction was allowed to warm to −30 °C with stirring, then was treated with several drops of Et₃N, filtered and concentrated in vacuo. Purification by silica gel chromatography and removal of the benzylidene acetal by exposure to trifluoroacetic acid as described in method A gave **10α** (12.8 mg) and **10β** and (10 mg) (58 % combined yield).

Methyl 6-*O*-(2-*O*-benzyl-α-ᴅ-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-ᴅ-glucopyranoside (13α) and Methyl 6-*O*-(2-*O*-benzyl-β-ᴅ-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-ᴅ-glucopyranoside (13β)

Thioglycoside **6** (60 mg, 0.14 mmol), BSP (40 mg, 0.19 mmol), TTBP (206 mg, 0.83 mmol) and crushed activated 4 Å molecular sieves (100 mg) were dried in vacuo and dissolved in CH₂Cl₂ (4 mL) under argon, then stirred at rt for 1 h prior to cooling to −56 °C. After 15 min. Tf₂O (28 µL, 0.17 mmol) was added and after additional 15 min. methyl 2,3,4-tri-O-benzyl-α-ᴅ-glucopyranoside (128 mg, 0.28 mmol) in CH₂Cl₂ (1 mL) was added. The reaction mixture was allowed to warm to −40 °C then was treated with several drops of Et₃N, filtered and concentrated in vacuo. The crude mixture was purified by flash chromatography (Hexanes-CH₂Cl₂ 1:1) to give methyl 6-*O*-(2-*O*-benzyl-3,5-di-*O*-benzylidene-α-ᴅ-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-ᴅ-glucopyranoside (**12α**) (21 mg) and methyl 6-*O*-(2-*O*-benzyl-3,5-di-*O*-benzylidene-β-ᴅ-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-ᴅ-glucopyranoside (**12β**) (20 mg) β (35 % combined yield) as colorless syrups. Further characterization was not attempted and both products were exposed to trifluoroacetic acid (1 drop) in CH₂Cl₂ (1 mL) for 1 min. The reaction mixtures were concentrated and purified by flash chromatography to give **13α** (6 mg) and **13β** (10 mg). **13α**: Colorless syrup; $R_f = 0.3$ (hexanes-ethyl acetate 3:1); $[\alpha]_D$ +44 (*c*, 0.9, CHCl₃); lit.[13c] $[\alpha]_D$ +31 (*c*, 0.9, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.36-7.15 (m, 20 H), 4.94 (d, 1 H, *J* = 10.9 Hz), 4.89 (d, 1 H, *J* = 4.4 Hz), 4.83 (d, 1 H, *J* = 11.2 Hz), 4.78 (d, 1 H, *J* = 10.7 Hz), 4.76 (d, 1 H, *J* = 11.2 Hz), 4.71-4.63 (m, 6 H), 4.57 (d, 1 H, J = 11.9 Hz), 3.98-3.75 (m, 9 H), 3.61-3.57 (m, 2 H), 3.38 (s, 3 H); ¹³C NMR (125 Hz, CDCl₃) δ 138.8, 138.5, 138.1, 137.6, 128.4, 128.4, 128.3, 128.3, 128.0, 127.9, 127.8, 127.6, 127.5, 127.4, 99.4, 98.2, 84.4, 82.5, 81.7, 80.4, 75.6, 74.9, 73.5, 72.4, 72.0, 69.7, 66.2, 61.4, 55.0. **13β**: Colorless syrup; $R_f = 0.25$ (hexanes-ethyl acetate 3:1); $[\alpha]_D$ −17.3 (*c*, 1.0, CHCl₃); ¹H NMR(500 MHz, CDCl₃) δ 7.36-7.17 (m, 20 H), 4.94 (d, 1 H, *J* = 10.9 Hz), 4.89

(d, 1 H, J = 4.4 Hz), 4.83 (d, 1 H, J = 11.2 Hz), 4.78 (d, 1 H, J = 10.7 Hz), 4.76 (d, 1 H, J = 11.2 Hz), 7.70 (d, 1H, J = 3.5 Hz), 4.68-4.63 (m, 4 H) 4.57 (d, 1 H, J = 11.9 Hz), 3.98-3.75 (m, 8 H), 3.60 (dd, 1 H, J = 2.6, 9.2 Hz), 5.57 (dd, 1 H, J = 3.5, 7.1 Hz), 3.38 (s, 3 H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 138.8, 138.5, 138.1, 137.6, 128.4, 128.4, 128.3, 128.3, 128.0, 127.9, 127.8, 127.6, 127.5, 127.4, 99.4, 98.2, 84.4, 82.5, 81.7, 80.4, 75.6, 74.9, 73.5, 72.4, 72.0, 69.7, 66.2, 61.4, 55.5; HRMS calc. for $[C_{40}H_{46}O_{10}Na]^+$: 709.2989, found: 709.2983.

Activation of Thioglycoside 8 with 1-Benzenesulfinyl Piperidine and Trifluoromethanesulfonic Anhydride (Method C)

BSP (1.4 equiv.), TTBP (3 equiv.), the thioglycoside, and 4 Å powdered molecular sieves were dissolved in CH$_2$Cl$_2$ (5 mL/100 mg) and stirred for 1 h under argon, before cooling to −55 °C. After 30 min. Tf$_2$O (1.2 equiv.) was added and the reaction mixture was allowed to stir for 10 min. before the acceptor (2 equiv) in 1 mL CH$_2$Cl$_2$ was added. The solution then was stirred for 30 min. at −55 °C before it was allowed to reach 0 °C and basified with Et$_3$N. The crude reaction mixture was filtered, concentrated in vacuo, and purified by flash chromatography on silica gel.

Activation of Thioglycoside 8 with Diphenyl Sulfoxide and Trifluoromethanesulfonic Anhydride (Method D)

Diphenyl sulfoxide (3 equiv.), TTBP (3 equiv.), thioglycoside **8**, and 4 Å powdered molecular sieves were dissolved CH$_2$Cl$_2$ (5 mL/100 mg) and stirred for 1 h before cooling to −78 °C. After 30 min. Tf$_2$O (1.2 equiv.) was added and the reaction mixture was allowed to stir for 20 min. before the acceptor (2 equiv) in CH$_2$Cl$_2$ (1 mL) was added. The solution was allowed to reach 0 °C before it was basified with Et$_3$N, then filtered, concentrated in vacuo, and purified by flash chromatography on silica gel.

Modified Procedure for the Activation of Thioglycoside 8 with 1-Benzenesulfinyl Piperidine and Trifluoromethanesulfonic Anhydride (Method E)

BSP (1.4 equiv.), TTBP (3 equiv.), and thioglycoside **8** were dissolved in CH$_2$Cl$_2$ (5 mL/100 mg) and cooled to −55 °C under argon. After 30 min. Tf$_2$O (1.2 equiv.) was added and the reaction mixture was allowed to warm to −25 °C over 2h during which the color of the reaction mixture changed from red-brown to pale yellow. After 30 min. −25 °C the reaction was recooled to −70 °C and the acceptor (1.5 equiv) in CH$_2$Cl$_2$ (1 mL) was added. The reaction was allowed to reach rt before it was quenched with Et$_3$N, filtered, concentrated, and purified by flash chromatography on silica gel.

Activation of Thioglycoside 8 with *N*-Iodosuccinimide and Silver Trifluoromethanesulfonate (Method F)

The donor **8** (101 mg, 0.21 mmol) and methyl 2,3,4-tri-*O*-benzyl-α-$_D$-glucopyranoside (97 mg, 0.21 mmol) were coevaporated with toluene 4 times and dried under vacuum together with 4 Å ms, then dissolved in CH$_2$Cl$_2$ (5 mL) and stirred 1 h prior to cooling the reaction mixture to −30 °C under argon. After stirring for 30 min. NIS (58 mg, 0.26 mmol) and AgOTf (11 mg, 41 µmol) were added. The reaction was then allowed to warm rt before it was filtered, diluted with CH$_2$Cl$_2$ (20 mL), washed with 5% aqueous sodium thiosulfate, brine, dried (Na$_2$SO$_4$), and concentrated in vacuo to give **17** (137 mg, 80 %) as a mixture of anomers containing <10% of the β-anomer as determined by ^{1}H NMR spectroscopy of the crude reaction mixture. Treatment of the crude product (100 mg) with tetrabutylammonium fluoride as described below gave **13α** (69 mg, 82%) identical with the sample described above.

General Procedure for Removal of the 3,5-Di-*O*-(di-*tert*-butylsilylene) Acetal

The silylene acetal was dissolved in THF (4 mL/100 mg) and tetrabutylammonium fluoride (2.2 equiv. of 1 M THF solution) was added at rt. The reaction was monitored by TLC (Ethyl acetate) and stopped when the substrate was converted to a single more polar compound, typically within 3 h at rt. The crude reaction mixture was then evaporated and purified by flash chromatography on silica gel.

Methyl 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-α-ᴅ-arabinofuranoside (14α)

Colorless syrup; R_f = 0.8 (CH_2Cl_2); $[α]_D$ +41.3 (*c*, 0.9, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.41-7.28 (m, 5 H), 4.84 (d, 1 H, *J* = 2.9 Hz), 4.80 (d, 1 H, *J* = 11.8 Hz), 4.65 (d, 1 H, *J* = 11.8 Hz), 4.36 (m, 1 H), 4.12 (dd, 1 H, *J* = 7.2, 9.0 Hz), 3.98-3.92 (m, 3 H), 3.37 (s, 3 H) 1.08 (s, 9 H), 1.01 (s, 9 H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 137.8, 128.4, 128.0, 127.8, 108.2, 87.9, 81.6, 73.8, 72.1, 67.6, 55.9, 27.5, 22.7, 20.2; HRMS calc. for $[C_{21}H_{34}O_5Si]^+$: 394.2176, found: 394.2192.

Methyl 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-β-ᴅ-arabinofuranoside (14β)

Colorless syrup; R_f = 0.8 (CH_2Cl_2); $[α]_D$ −49.5 (*c*, 1.0, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.2 Hz 2 H), 7.36 (t, 2 H, *J* = 7.2 Hz), 7.31 (t, 2 H, *J* = 7.2 Hz), 4.86 (d, 1 H, *J* = 12.3 Hz), 4.81 (d, 1 H, *J* = 12.3 Hz), 4.79 (d, 1 H, *J* = 5.4 Hz), 4.35 (t, 1 H, *J* = 9.1 Hz), 4.30 (dd, 1 H, *J* = 5.1, 9.0 Hz), 3.93 (d, 1 H, *J* = 9.2), 3.91 (dd, 1 H, *J* = 5.0, 9.0 Hz), 3.65 (ddd, 1 H, *J* = 5.0, 9.4, 10.2 Hz), 3.40 (s, 31 3 H), 1.08 (s, 9H), 1.00 (s, 9H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 137.7, 128.41, 128.35, 127.8, 101.4, 80.2, 78.8, 73.7, 71.9, 68.5, 55.9, 27.58, 27.2, 22.6, 20.1; HRMS calc. for $[C_{21}H_{34}O_5SiNa]^+$: 417.2074, found: 417.2084.

Cyclohexyl 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-α-ᴅ-arabinofuranoside (15α)

Colorless syrup; R_f = 0.8 (CH_2Cl_2); $[α]_D$ +41.9 (*c*, 0.9, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.27 (m, 5 H), 5.11 (d, 1 H, *J* = 3.08 Hz), 4.78 (d, 1 H, *J* = 12 Hz), 4.66 (d, 1 H, *J* = 12 Hz), 4.34 (dd, 1 H, *J* = 4.4, 8.4 Hz), 4.08 (dd, 1 H, *J* = 7.4, 9.0 Hz), 4.00-3.87 (m, 3 H), 3.50 (m, 1 H), 1.88 (m, 2H), 1.73 (m, 2 H), 1.53 (m, 1 H), 1.40-1.10 (m, 5 H), 1.07 (s, 9 H), 1.00 (s, 9 H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 138.1, 128.4, 127.8, 127.7, 105.1, 88.2, 814, 73.7, 72.0, 67.8, 33.9, 31.8, 27.5, 27.2, 25.7, 24.3, 21.2, 22.7, 20.2; HRMS calc. for $[C_{26}H_{42}O_5SiNa]^+$: 485.2700, found: 485.2704.

Cyclohexyl 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-β-ᴅ-arabinofuranoside (15β)

Colorless syrup; R_f = 0.7 (CH_2Cl_2); $[α]_D$ −66.8 (*c*, 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.42-7.27 (m, 5 H), 5.08 (d, 1 H, *J* = 5.4 Hz), 4.77 (s, 2 H), 4.34 (t, 1 H, *J* = 9.1 Hz), 4.29 (dd, 1 H, *J* = 5.0, 9.0 Hz), 3.91 (dd, 1 H, *J* = 9.2, 10.6 Hz), 3.88 (d, 1 H, *J* = 4.3, 9.0 Hz), 3.59 (ddd, 1H, *J* = 5.0, 9.3, 10.5 Hz), 3.47 (m, 1 H), 1.90 (m, 2H), 1.74 (m, 2 H), 1.53 (m, 1H), 1.45-1.10 (m, 5 H), 1.07 (s, 9 H), 0.99 (s, 9 H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 138.2, 128.3, 127.9, 127.6, 99.0, 80.7, 78.7, 77.6, 73.3, 71.6, 68.6, 33.8, 32.2, 27.6, 27.2, 26.6, 24.5, 24.4, 22.6; HRMS calc. for $[C_{26}H_{42}O_5SiNa]^+$: 485.2700, found: 485.2713.

Adamantyl 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-α-ᴅ-arabinofuranoside (16α)

Colorless syrup; R_f = 0.6 (CH_2Cl_2); $[α]_D$ +28.5 (*c*, 1.1, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.45-7.27 (m, 5 H), 5.34 (d, 1 H, *J* = 3.59 Hz), 4.79 (d, 1 H, *J* = 12.1 Hz), 4.69 (d, 1 H, *J* = 12.1 Hz), 4.32 (dd, 1 H, *J* = 4.9, 9.0 Hz), 4.06 (dd, 1 H, *J* = 7.4, 9.5 Hz), 3.99 (dt, 1 H, *J* = 4.9, 10.2 Hz), 3.95 (dd, 1 H, *J* = 3.6, 7.4 Hz), 3.89 (dd, 1 H, *J* = 9.1, 10.2 Hz), 2.14 (br s, 3 H), 1.84 (br d, 3 H, *J* = 11.6 Hz), 1.75 (br d, 3 H, *J* = 11.6 Hz),1.61 (br s, 6 H), 1.07 (s, 9 H), 1.00 (s, 9 H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 138.3, 128.3, 127.7, 127.6, 100.4, 88.5, 80.9, 74.6, 73.6,

71.9, 68.0, 42.7, 36.3, 30.6, 27.5, 27.2, 22.7, 20.2; HRMS calc. for $[C_{30}H_{46}O_5Si]^+$: 514.3115, found: 514.3099.

Adamantyl 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-β-ᴅ-arabinofuranoside (16β)

Colorless syrup; R_f = 0.7 (CH$_2$Cl$_2$); [α]$_D$ −64.9 (*c*, 0.9, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.42 (d, 2 H, *J* = 7.3 Hz), 7.35 (t, 2 H, *J* = 7.3 Hz), 7.28 (t, 1 H, *J* = 7.3 Hz), 5.37 (d, 1 H, *J* = 5.7 Hz), 4.79 (d, 1 H, *J* = 12.1 Hz), 4.72 (d, 1 H, *J* = 12.1 Hz), 4.32 (t, 1 H, *J* = 9.0 Hz), 4.28 (dd, 1 H, *J* = 5.0, 9.1 Hz), 3.94 (dd, 1 H, *J* = 9.3, 10.4 Hz), 3.86 (dd, 1 H, *J* = 5.7, 8.8 Hz), 3.53 (ddd, 1 H, *J* = 5.0, 9.6, 10.3 Hz), 2.14 (br s, 3H), 1.85 (br d, 3 H, *J* = 11.5 Hz), 1.79 (br d, 3 H, *J* = 11.5 Hz),1.61 (br s, 6 H), 1.07 (s, 9 H), 0.99 (s, 9 H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 138.4, 128.3, 127.8, 127.5, 93.5, 80.8, 79.1, 74.8, 72.9, 71.4, 68.6, 42.7, 36.3, 30.7, 27.6, 27.2, 22.6, 20.1; HRMS calc. for $[C_{30}H_{46}O_5SiNa]^+$: 537.3013, found: 537.3010.

Methyl 6-*O*-(2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-α-ᴅ-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-ᴅ-glucopyranoside (17α)

Colorless syrup; R_f = 0.15 (CH$_2$Cl$_2$); [α]$_D$ +43.8 (*c*, 1.0, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.37-7.26 (m, 20 H), 5.04 (d, 1 H, *J* = 2.9 Hz), 4.98 (d, 1 H, *J* = 10.8 Hz), 4.87 (d, 1 H, J = 10.7 Hz), 4.83 (d, 1 H, *J* = 10.8 Hz), 4.78 (d, 1 H, *J* = 12.1 Hz), 4.75 (d, 1 H, *J* = 11.8 Hz), 4.68-4.60 (m, 4 H), 4.18 (dd, 1 H, *J* = 3.4, 7.6 Hz), 4.08 (dd, 1 H, *J* = 7.3, 9.0 Hz), 4.05-3.95 (m, 3 H), 3.93-3.86 (m, 2 H), 3.75 (ddd, 1 H, *J* = 1.9, 3.6, 10.1 Hz), 3.64-3.57 (m, 2 H), 3.53 (dd, 1 H, *J* = 3.5, 9.6 Hz), 3.36 (s, 3 H), 1.05 (s, 9 H), 0.95 (s, 9 H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 138.8, 138.3, 138.2, 137.8, 128.8, 128.7, 128.6, 128.5, 128.4, 128.1, 127.9, 127.8, 127.8, 127.7, 107.3, 98.1, 87.8, 82.1, 81.6, 80.0, 77.7, 75.1, 74.0, 73.9, 73.4, 71.9, 69.9, 67.5, 66.8, 55.2, 27.5, 27.1, 27.0, 26.9, 22.6, 20.1; HRMS calc. for $[C_{48}H_{62}O_{10}SiNa]^+$: 849.4010, found: 849.3991.

Methyl 6-*O*-(2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-β-ᴅ-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-ᴅ-glucopyranoside (17β)

Colorless syrup; R_f = 0.1 (CH$_2$Cl$_2$); [α]$_D$ −19.3 (*c*, 0.9, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.39-7.21 (m, 20 H), 5.01 (d, 1 H, *J* = 5.4 Hz), 4.97 (d, 1 H, *J* = 10.9 Hz), 4.85 (d, 1 H, *J* = 11.1 Hz), 4.81-4.76 (m, 3 H), 4.75 (d, 1 H, *J* = 12.2 Hz), 4.65 (d, 1 H, *J* = 12.1 Hz), 4.60 (d, 1 H, *J* = 11.1 Hz), 4.58 (d, 1 H, *J* = 3.5 Hz), 4.28 (t, 1 H, *J* = 9.1 Hz), 4.27 (dd, 1 H, *J* = 5.0, 9.1 Hz), 3.98 (t, 1 H, *J* = 9.3 Hz), 3.78 (br dd, 1 H, *J* = 5.1, 10.0 Hz), 3.69 (dd, 1 H, *J* = 5.3, 11.1 Hz), 3.60 (ddd, 1 H, *J* = 5.0, 9.4, 10.4 Hz), 3.53-3.48 (m, 2 H), 3.32 (s, 3 H), 1.05 (s, 9 H), 0.98 (s, 9 H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 138.8, 138.4, 138.2, 138.0, 130.7, 128.8, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.7, 127.6, 127.3, 101.0, 97.9, 82.1, 80.7, 79.9, 79.0, 77.9, 75.7, 74.9, 73.4, 73.4, 71.5, 70.3, 68.3, 67.4, 55.1, 47.0, 27.5, 27.2, 22.6, 20.1; HRMS calc. for $[C_{48}H_{62}O_{10}SiNa]^+$: 849.4010, found: 849.3983.

Methyl 4-*O*-(2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-α-ᴅ-arabinofuranosyl)-2,3,6-tri-*O*-benzyl-α-ᴅ-glucopyranoside (19α)

Colorless syrup; R_f = 0.15 (CH$_2$Cl$_2$); [α]$_D$ +30.5 (*c*, 1.7, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.32-7.21 (m, 20 H), 5.87 (d, 1 H, *J* = 3.0 Hz), 4.87 (d, 1 H, *J* = 10.1), 4.82 (d, 1 H, *J* = 10.1 Hz), 4.77 (d, 1 H, *J* = 11.6 Hz), 4.75 (d, 1 H, *J* = 10.8 Hz), 4.64 (d, 1 H, *J* = 11.7), 4.60 (d, 1 H, *J* = 9.9 Hz), 4.58 (br s, 1 H), 4.57 (d, 1 H, *J* = 12.0 Hz), 4.48 (d, 1 H, *J* = 11.9 Hz), 4.13-4.08 (m, 2 H), 3.99 (dd, 1 H, *J* = 3, 7.2 Hz), 3.94 (t, 1 H, *J* = 9.2 Hz), 3.89-3.80 (m, 2 H), 3.77 (ddd, 1 H, *J* = 1.7, 5.3, 10.0 Hz), 3.73 (dd, 1 H, *J* = 1.9, 10.6 Hz), 3.67 (dd, 1 H, *J* = 9.0, 9.8 Hz), 3.60 (dd, 1 H, *J* = 5.6, 10.6 Hz), 3.49 (dd, 1 H, *J* = 3.5, 9.7 Hz), 3.39 (s, 3 H), 1.06 (s, 9 H), 1.00 (s, 9 H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 138.5, 138.2, 138.1, 137.6, 128.5, 128.3, 128.2, 128.2, 127.9, 127.7, 127.6, 127.5, 107.6, 97.9, 87.5, 81.9, 81.8, 79.8, 75.8, 75.5,

74.0, 73.7, 73.4, 71.7, 69.5, 69.4, 67.4, 55.2, 27.5, 27.2, 22.6, 20.1; HRMS calc. for $[C_{48}H_{62}O_{10}SiNa]^+$: 849.4010, found: 849.4035.

Methyl 4-*O*-(2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-β-ᴅ-arabinofuranosyl)-2,3,6-tri-*O*-benzyl-α-ᴅ-glucopyranoside (19β)

Colorless syrup; R_f = 0.1 (CH$_2$Cl$_2$); [α]$_D$ −13.1 (*c*, 0.8, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.38-7.21 (m, 20 H), 5.01 (d, 1 H, *J* = 5.8 Hz), 4.92 (d, 1 H, *J* = 10.6 Hz), 4.81 (d, 1 H, *J* = 12.4 Hz), 4.81 (d, 1 H, *J* = 10.3 Hz), 4.75 (d, 1 H, *J* = 12.3 Hz), 4.70 (d, 1 H, *J* = 12.2 Hz), 4.60 (d, 1 H, *J* = 12.3 Hz), 4.56 (d, 1 H, *J* = 3.6 Hz), 4.51 (d, 1 H, *J* = 12.1 Hz), 4.28-4.24 (m, 2 H), 4.11 (dd, 1 H, *J* = 5.0, 9.2 Hz), 3.94 (m, 1 H), 3.85 (br d, 1 H, *J* = 10.6 Hz), 3.75-3.71 (m, 3 H), 3.67-3.64 (m, 2 H), 3.47 (dd, 1 H, *J* = 3.5, 9.6 Hz), 3.44 (ddd, 1 H, *J* = 5.0, 9.3, 10.5 Hz), 3.36 (s, 3 H), 1.06 (s, 9 H), 0.99 (s, 9 H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 139.1, 138.3, 138.1, 137.8, 128.5, 128.4, 128.4, 128.2, 127.9, 127.8, 127.7, 127.6, 127.3, 102.2, 98.3, 80.2, 80.1, 79.6, 79.4, 79.3, 75.4, 73.6, 73.2, 72.8, 71.7, 70.0, 68.2, 68.1, 55.2, 27.6, 27.2, 22.6, 20.1; HRMS calc. for $[C_{48}H_{62}O_{10}SiNa]^+$: 849.4010, found: 849.4006.

Methyl 4-*O*-(2-*O*-benzyl-ᴅ-arabinofuranosyl)-2,3-di-*O*-isopropylidene-α-ʟ-rhamnopyranoside (22)

The arabinopyranoside **21** was obtained in the form of an inseparable α,β-mixture. R_f = 0.3 (CH$_2$Cl$_2$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.45-7.29 (m, 5 H), 5.47 (d, 0.65 H, *J* = 5.0 Hz, H$_{1β}$), 5.30 (s, 1 H, H$_{1'}$), 5.14 (d, 0.35 H, *J* = 2.8 Hz, H$_{1α}$), 4.87-4.77 (m, 3 H), 4.66 (d, 0.35 H, *J* = 12.0 Hz, α), 4.37-4.28 (m, 2 H), 4.22 (dd, 0.65 H, *J* = 5.7, 7.4 Hz, β), 4.14 (dd, 0.35 H, *J* = 5.7, 7.0 Hz, α), 4.11-4.02 (m, 1.65 H), 3.98-3.85 (m, 2.35 H), 3.74-3.60 (m, 2 H), 3.51 (dd, 0.65 H, *J* = 7.5, 10.0 Hz, β), 3.39 (d, 0.35 H, *J* = 7.3, 9.9 Hz), 3.36 (s, 1.05 H, α), 3.34 (s, 1.95 H, β), 1.52 (s, 1.95 H, β), 1.49 (s, 1.05 H, α), 1.35 (s, 1.95, β), 1.33 (s, 1.05 H, α), 1.26 (d, 1.95 H, J = 6.6 Hz, β), 1.25 (d, 1.05 H, J = 35 6.4 Hz, α), 1.07 (s, 9 H), 1.00 (s, 3.15 H, α), 0.98 (s, 5.85 H, β). **21α**: ^{13}C NMR (125 Hz, CDCl$_3$) δ 137.7, 128.3, 127.9, 127.6, 127.3, 109.1, 106.8, 98.0, 81.6, 80.0, 78.4, 75.8, 73.8, 71.9, 67.6, 64.6, 54.7, 53.4, 27.9, 27.5, 27.1, 26.4, 22.6, 20.1, 17.7. **21β**: ^{13}C NMR (125 Hz, CDCl$_3$) δ 137.9, 128.3, 127.9, 127.7, 109.3, 99.3, 97.9, 80.3, 78.4, 78.3, 78.1, 76.0, 74.0, 71.6, 68.5, 63.9, 54.8, 54.7, 28.0, 27.5, 27.1, 26.4, 22.6, 20.1, 17.7. Owing to the inseparable nature of this mixture of isomers it was partially deprotected to **22** without further charcterization. Compound **22** also was obtained in the form of an inseparable α,β-mixture. R_f = 0.4 (CH$_2$Cl$_2$ EtOAc 3:1); HRMS calc. for $[C_{22}H_{32}O_9Na]^+$: 463.1944, found: 463.1943; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.40-7.30 (m, 5 H), 5.48 (d, 0.65 H, *J* = 4.5 Hz, H$_{1β}$), 5.21 (s, 0.35 H, H$_{1α}$), 4.84 (s, 1 H, H$_{1'}$), 4.80 (d, 0.65 H, *J* = 11.7 Hz, β), 4.65 (d, 0.35 H, *J* = 11.7 Hz, α), 4.60 (d, 0.65 H, *J* = 11.7 Hz, β), 4.55 (d, 0.35 H, *J* = 11.7 Hz, α), 4.37-4.31 (m, 1 H), 4.23 (dd, 0.65 H, *J* = 5.8, 7.5 Hz, β), 4.13 (bd, 0.35 H, *J* = 3.4 Hz, α), 5.78 (m, 1 H), 4.02 (dd, 0.35 H, *J* = 5.5, 7.3 Hz, α), 3.92-3.89 (m, 1 H), 3.85-3.51 (m, 5 H), 3.36 (s, 1.95 H, β), 3.35 (s, 1.05 H, α), 1.54 (s, 3 H), 1.34 (s, 1.95 H, β), 1.33 (1.05 H, α), 1.30 (d, 1.95 H, *J* = 6.3 Hz, β), 1.25 (d, 1.05 H, *J* = 6.1 Hz, α). **22α**: ^{13}C NMR (125 Hz, CDCl$_3$) δ 137.0, 128.6, 128.1, 127.9, 109.5, 105.2, 98.0, 87.6, 86.5, 76.9, 76.0, 75.6, 71.9, 64.9, 62.5, 54.9, 27.7, 26.4, 18.4. **22β**: ^{13}C NMR (125 Hz, CDCl$_3$) δ 137.7, 128.5, 128.1, 128.0, 109.4, 98.8, 97.9, 83.7, 81.3, 79.5, 77.8, 76.0, 73.7, 72.4, 63.7, 63.4, 54.8, 28.0, 26.3, 17.8.

Methyl 2-*O*-benzyl-α-ᴅ-arabinofuranoside (23)

Colorless syrup; R_f = 0.25 (hexanes - EtOAc 1:1); [α]$_D$ +60.5 (*c*, 1, CHCl$_3$); lit.[7] [α]$_D$ +60 (*c*, 0.5, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.37-7.28 (m, 5 H), 4.97 (s, 1 H), 4.63 (d, 1 H, *J* = 11.6 Hz), 4.57 (d, 1 H, *J* = 11.7 Hz), 4.13 (dd, 1 H, *J* = 2.0, 4.0 Hz), 4.10 (dd, 1 H, *J* = 4.0, 7.5 Hz), 3.90 (d, 1 H, *J* = 2.0 Hz), 3.82 (dd, 1 H, *J* = 3.3, 11.9 Hz), 3.74 (dd, 1 H, *J* = 4.3, 11.9 Hz), 3.38 (s, 3 H), 2.46 (br s, 2 H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 137.0, 128.6, 128.1, 127.9, 106.9, 87.5, 85.9, 75.4, 71.9, 62.4, 54.9.

p-Cresyl 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-1-thio-α-ʟ-arabinofuranoside (25)

Compound **25** was prepared analogously to its enantiomer **8**, starting from ʟ-arabinose. All spectral data matched that of compound **8**. $[\alpha]_D$ −153.4 (*c*, 1.0, CHCl₃).

S-Phenyl 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-1-thio-α-ʟ-arabinofuranoside *S*-oxide (26)

Compound **24** (0.76 g) was dissolved in CH_2Cl_2 (40 mL) and cooled to −78 °C under inert atmosphere, and *m*CPBA (0.476 g, 70 wt. %, ~1.9 mmol, 1.2 equiv) was added portionwise. The reaction mixture was warmed to room temperature over 1 h, at which time TLC showed dissappearance of starting material in favor of two significantly more polar compounds. The sulfoxide **26** (0.621 g, 1.3 mmol, 79% yield) was obtained as a mixture of diastereomers after column chromatography on silica gel. Colorless syrup; R_f = 0.19 and 0.28 (hexanes - EtOAc 10:1); ¹H NMR (500 MHz, CDCl₃) δ 7.59-7.64 (m, 4H), 7.48-7.54 (m, 6H), .24-7.38 (m, 8H), 6.97-6.99 (m, 2H), 4.79 (d *J* = 11.5 Hz, 1H), 4.69 (d *J* = 5.0 Hz, 1H), 4.63 (d *J* = 11.0 Hz, 1H) < 4.62 (d *J* = 10.0 Hz, 1H), 4.60 (d *J* = 5.0 Hz, 1H), 4.55 (d *J* = 11.0 Hz, 1H), 4.42 (dd *J* = 3.5, 7.5 Hz, 1H), 4.37 (dd *J* = 5.5, 9.5 Hz, 1H), 4.31-4.33 (m, 1H), 4.21-4.29 (m, 3H), 4.05-4.10 (m, 1H), 3.84-3.92 (m, 3H), 1.06 (s, 18H), 1.01 (s, 9H), 0.96 (s, 9H); ¹³C NMR (125 Hz, CDCl₃) δ 139.8, 139.6, 137.2, 131.6, 131.1, 129.19, 129.15, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 125.5, 124.4, 99.4, 98.2, 82.1, 81.5, 81.1, 78.5, 77.1, 76.7, 76.6, 72.3, 71.9, 67.3, 67.2, 27.4, 27.1, 27.0, 22.6, 20.2, 20.0; HRMS calc. for $[C_{26}H_{36}O_5SSiNa]^+$: 511.1945, found: 511.1955.

Activation of Sulfoxide 26 with Trifluoromethanesulfonic Anhydride (Method G)

Donor **26** (1.0 equiv.) and TTBP (2.0 equiv.) were dissolved in dry CH_2Cl_2 (0.04 M) together with crushed 4Å molecular sieves under argon and cooled to −78 °C. Tf₂O (1.2 equiv.) was added and the solution was allowed to stir for ~10 min., before being warmed to −50 °C for ~15 min. and subsequently recooled to −78 °C. The acceptor (0.63 equiv) in CH_2Cl_2 (0.1 M) was then added drop-wise. The reaction mixture was allowed to warm to −30 °C, when it was quenched by addition of Et₃N and filtered through Celite. The solvent was removed and the crude mixture directly purified by column chromatography on silica gel.

Modified Method for Activation of Sulfoxide 26 with Trifluoromethanesulfonic Anhydride (Method H)

All conditions and equivalents for method H are the same as those employed in Method G, save that the reaction mixture was not warmed to −50 °C after the addition of Tf₂O.

S-Phenyl 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-1-thio-β-ʟ-arabinofuranoside (27)

According to the general procedure for sulfoxide couplings, **26** (0.35 g, 0.71 mmol) was combined with thiophenol (0.15 mL, 1.42 mmol, 2.0 equiv.) in presence of 1-octene (3 mL). On column chromatography on silica gel **24** (0.032 g, 0.07 mmol, 9%) eluted first, followed closely by **27** (0.205 g, 0.43 mmol, 61%). **27:** Colorless syrup; R_f = 0.47 (hexanes - EtOAc 30:1); $[\alpha]_D$ +79.6 (*c*, 1.0, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.52 (d *J* = 7.0 Hz, 2H), 7.46 (d *J* = 7.0 Hz, 2H), 7.37 (t *J* = 7.5 Hz, 2H), 7.23-7.32 (m, 4H), 5.64 (d *J* = 7.0 Hz, 1H), 4.89 (d *J* = 13.0 Hz, 1H), 4.82 (d *J* = 12.5 Hz, 1H), 4.34 (dd *J* = 5.0, 9.0 Hz, 1H), 4.28 (t *J* = 7.5 Hz, 1H), 4.21 (t *J* = 9.0 Hz, 1H), 4.00 (t *J* = 10.0 Hz, 1H), 3.66 (m, 1H), 1.06 (s, 9H), 0.99 (s, 9H); ¹³C NMR (125 Hz, CDCl₃) δ 137.7, 134.5, 131.8, 128.8, 128.4, 127.7, 127.3, 88.2, 81.6, 80.9, 74.7, 71.9, 68.0, 27.5, 27.1, 22.6, 20.1; HRMS calc. for $[C_{26}H_{36}O_4SSiNa]^+$: 495.2002, found: 495.1999.

Cyclohexyl 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-α-ʟ-arabinofuranoside (28α) and Cyclohexyl 2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-β-ʟ-arabinofuranoside (28β) had

spectral data identical to the enantiomers (**15α** and **15 β**). (**28α**): $[\alpha]_D$ −41.1 (*c*, 1.0, CHCl$_3$); $[\alpha]_D$ +65.7 (*c*, 1.0, CHCl$_3$).

Methyl 6-*O*-(2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-α-ʟ-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-ᴅ-glucopyranoside (29α)

Colorless syrup; R$_f$ = 0.42 (hexanes - EtOAc 5:1); $[\alpha]_D$ +2.9 (*c*, 1.0, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.22-7.38 (m, 20 H), 5.00 (d *J* = 3.5 Hz, 1H), 4.99 (d *J* = 11.0 Hz, 1H), 4.88 (d *J* = 10.5 Hz, 1H), 4.82 (d *J* = 11.0 Hz, 1H), 4.80 (d *J* = 12.5 Hz, 1H), 4.77 (d *J* = 12.0 Hz,1 H), 4.67 (d *J* = 13.5 Hz, 1H), 4.64 (d *J* = 11.5 Hz, 1H), 4.61 (d *J* = 3.5 Hz, 1H), 4.57 (d *J* = 11.0 Hz, 1H), 4.31 (dd *J* = 4.5, 8.5 Hz, 1H), 4.11 (dd *J* = 7.0, 9.0 Hz, 1H), 4.04 (dd *J* = 3.0, 7.0 Hz, 1H), 3.89-4.02 (m, 4H), 3.77 (dd *J* = 4.5, 10.0 Hz, 1H), 3.62 (dd *J* = 5.5, 11.5 Hz, 1H), 3.5-3.55 (m, 2H), 3.36 (s, 3H), 1.07 (s, 9H), 0.99 (s, 9H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 138.7, 138.2, 137.7, 128.5, 128.4, 128.3, 128.2, 128.1, 128.04, 128.02, 127.9, 127.8, 127.73, 127.70, 127.67, 127.59, 108.0 ($^1J_{C-H}$ = 169.2 Hz), 98.1 ($^1J_{C-H}$ = 167.3), 87.2, 82.1, 81.4, 79.9, 77.2, 77.1, 76.9, 76.6, 75.8, 75.1, 74.0, 73.3, 72.0, 70.0, 67.9, 67.6, 55.1, 27.527.1, 20.1; HRMS calc. for [C$_{48}$H$_{62}$O$_{10}$SiNa]$^+$: 849.4005, found: 849.4036.

Methyl 6-*O*-(2-*O*-benzyl-3,5-di-*O*-(di-*tert*-butylsilylene)-β-ʟ-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-ᴅ-glucopyranoside (29β)

Colorless syrup; R$_f$ = 0.34 (hexanes - EtOAc 5:1); $[\alpha]_D$ +59.4 (*c*, 1.0, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.66 (dd *J* = 2.0, 8.0 Hz, 2H), 7.24-7.49 (m, 18H), 5.06 (d *J* = 5.5 Hz, 1H), 4.96 (d *J* = 11.0 Hz, 1H), 4.83 (d *J* = 10.5 Hz, 1H), 4.81 (d *J* = 10.5 Hz, 1H), 4.77 (d *J* = 12.0 Hz, 1H), 4.74 (s, 2H), 4.67 (d *J* = 11.5 Hz, 1H), 4.64 (d *J* = 12.0 Hz, 1H), 4.59 (d *J* = 3.5 Hz, 1H), 4.34 (t *J* = 9.0 Hz, 1H), 4.24 (dd *J* = 5.0, 9.5 Hz, 1H), 4.04 (dd *J* = 4.0, 11.5 Hz, 1H), 3.97 (t *J* = 9.5 Hz, 1H), 3.93 (dd *J* = 5.0, 8.5 Hz, 1H), 3.81 (t *J* = 10.5 Hz, 1H), 3.76 (dd *J* = 2.5, 10.0 Hz, 1H), 3.63-3.68 (m, 3H), 3.47 (dd *J* = 4.0, 9.5 Hz, 1H), 3.36 (s, 3H), 1.03 (s, 9H), 0.99 (s, 9H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 18.9, 138.4, 138.3, 131.1, 129.4, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 124.8, 100.8 ($^1J_{C-H}$ = 172.5 Hz), 98.1 ($^1J_{C-H}$ = 164.9 Hz), 82.1, 80.9, 80.0, 78.6, 77.8, 77.3, 75.8, 75.1, 73.6, 73.5, 71.5, 70.1, 68.4, 67.2, 55.2, 27.5, 27.2, 22.6 HRMS calc. for [C$_{48}$H$_{62}$O$_{10}$SiNa]$^+$: 849.4005, found: 849.4029.

Variable Temperature NMR Experiments

The donor (20 mg, 41 µmol), BSP (12 mg, 58 µmol) and TTBP (20 mg, 82 µmol) were dried overnight in dessicator, then dissolved in CD$_2$Cl$_2$ (1 mL) under argon. The NMR tube was then cooled to −55 °C and a spectrum was recorded. Tf$_2$O (8.3 µL, 50 µmol) was added at −60 °C and the reaction mixture warmed in 10 °C increments, with monitoring by ^{1}H NMR.

Decompostion Product 31

The pooled reaction mixtures from several VT-NMR experiments were purified by flash chromatography on silica gel (toluene) to give **31** as a colorless syrup. R$_f$ = 0.4 (toluene); $[\alpha]_D$ −123.1 (*c*, 1.0, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.41-7.26 (m, 4 H), 5.33 (d, 1 H, *J* = 5.1 Hz), 4.77 (d, 1 H, *J* = 11.9 Hz), 4.68 (d, 1 H, *J* = 11.9 Hz), 4.38 (t, 1 H, *J* = 9.2 Hz), 4.25 (dd, 1 H, *J* = 5.0, 8.9 Hz), 3.97 (dd, 1 H, *J* = 5.1, 8.9 Hz), 3.80 (dd, 1 H, *J* = 9.1, 10.6 Hz), 3.68 (ddd, 1 H, *J* = 4.9, 9.3, 10.6 Hz), 1.00 (s, 9 H), 0.97 (s, 9H); ^{13}C NMR (125 Hz, CDCl$_3$) δ 138.1, 128.3, 128.3, 127.7, 127.5, 127.4, 96.8, 80.5, 77.9, 74.0, 71.1, 68.4, 27.5, 27.2, 22.5, 20.1; HRMS calc. for [C$_{20}$H$_{31}$O$_4$Si]$^+$: 363.1992, found: 363.1994 (M+H).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgment

References

1. Houseknecht JB, Lowary TL. Curr. Opin. Chem. Biol 2001;5:677. [PubMed: 11738178]

2. (a) Allen AK, Desai NN, Neuberger A. Biochem J 1978;171:665. [PubMed: 666730] (b) Ashford D, Desai NN, Allen AK, Neuberger A. Biochem. J 1982;201:199. [PubMed: 7082284]

3. (a) Lowary TL. Curr. Opin. Chem. Biol 2003;7:749. [PubMed: 14644185] (b) Lowary TL. J. Carb. Chem 2002;21:691.Lowary, TL. Glycoscience: Chemistry and Chemical Biology. Fraser-Reid, B.; Tatsuta, K.; Thiem, J., editors. vol 3. Springer, Berlin: 2001. p. 2005

4. Lowary, TL. Glycochemistry: Principles, Synthesis, and Applications. Wang, PG.; Bertozzi, CR., editors. New York: Dekker; 2001. p. 133

5. (a) Glaudemans CP, Fletcher HG. J. Am. Chem. Soc 1965;87:2456. (b) Glaudemans CP, Fletcher HG. J. Am. Chem. Soc 1965;87:4636.

6. Mukaiyama T, Yamada M, Suda S, Yokomizo Y, Kobayashi S. Chem. Lett 1992;21:1401.

7. Yin H, D'Souza FW, Lowary TL. J. Org. Chem 2002;67:892. [PubMed: 11856034]

8. Li Y, Singh GT. Tetrahedron Lett 2001;42:6615.

9. Lee YJ, Lee K, Jung EH, Jeon HB, Kim KS. Org. Lett 2005;7:3263. [PubMed: 16018636]

10. Ito Y, Ogawa T. Angew. Chem. Int. Ed. Engl 1994;33:1765.

11. Bamhaoud T, Sanchez S, Prandi J. Chem Commun 2000:569.

12. Sanchez S, Bamhaoud T, Prandi . J. Tetrahedron Lett 2000;41:7447.

13. (a) Gadikota RR, Callam CS, Lowary TL. Org. Lett 2001;3:607. [PubMed: 11178837] (b) Callam CS, Gadikota RR, Lowary TL. J. Org. Chem 2001;66:4549. [PubMed: 11421773] (c) Gadikota RR, Callam CS, Wagner T, Fraino BD, Lowart TL. J. Am. Chem. Soc 2003;125:4155. [PubMed: 12670238] (d) Cociorva OM, Lowary TL. Tetrahedron 2004;60:1481.

14. (a) Crich D, Sun S. J. Org. Chem 1996;61:4506. [PubMed: 11667369] (b) Crich D, Sun S. Tetrahedron 1998;54:8321.

15. Crich D, Smith M. J. Am. Chem. Soc 2002;124:8867. [PubMed: 12137540]

16. Crich D, Banerjee A, Yao Q. J. Am. Chem. Soc 2004;126:14930. [PubMed: 15535720]

17. Crich D, Bowers A. J. Org. Chem 2006;71:3452. [PubMed: 16626126]

18. Crich D, Banerjee A. J. Am. Chem. Soc 2006;128:8078. [PubMed: 16771524]

19. Crich D, Smith M. J. Am. Chem. Soc 2001;123:9015. [PubMed: 11552809]

20. Crich D, Sun S. J. Am. Chem. Soc 1998;120:435.

21. Codée JDC, van den Bos LJ, Litjens REJN, Overkleeft HS, van Boeckel CAA, van Boom JH, van der Marel GA. Tetrahedron 2004;60:1057.

22. Crich D, Smith M, Yao Q, Picione J. Synthesis 2001:323.

23. Crich D, Lim LBL. Org. React 2004;64:115.

24. Crich D, Sun S. J. Am. Chem. Soc 1997;119:11217.

25. Crich D, Chandraskera NS. Angew Chem. Int. Ed 2004;43:5386.

26. Fraser-Reid B, Wu Z, Andrews CW, Skowronski EJ. J. Am. Chem. Soc 1991;113:1434.

27. Jensen HH, Nordstrøm LU, Bols M. J. Am. Chem. Soc 2004;126:9205. [PubMed: 15281809]For computational work in this area seeNukuda T, Bérces A, Wang L, Zgierski MZ, Whitfield DM. Carbohydr. Res 2005;340:841. [PubMed: 15780250]

28. Rao, Y.; Zhu, X.; Boons, GJ. Abstracts of Papers; 231st Nat. Meeting Am. Chem. Soc.; Atlanta. 2006. CARB-030Rao, Y.; Zhu, X.; Boons, GJ. Abstracts of Papers; 23rd Int. Carbohydr. Symp.; Whistler. 2006. PS.44 (c) Zhu X, Kawatkar SP, Rao Y, Boons GJ. J. Am. Chem. Soc 2006;128:11948. [PubMed: 16953636]

29. Ishiwata, A.; Akao, H.; Ito, Y. Abstracts of Papers; 23rd Int. Carbohydr. Symp.; Whistler. 2006. PS. 20 (b) Ishiwata A, Akao H, Ito Y. Org. Lett 2006;8:5525. [PubMed: 17107063]

30. de Belder AN. Adv. Carbohydr. Chem. Biochem 1977;34:179.

31. The exceptions are the xylofuranosides which readily form 3,5-di-*O*-benzylidene acetals and related cyclohexylidene derivatives. However, it should be noted that these xylofuranoside derivatives have a *cis*-fused ring junction unlike the *trans*-fused one in the corresponding arabinofuranosides. See(a) Ferrier RJ, Hatton LR. Carbohydr. Res 1967;5:132. (b) von Schuching S, Frye GH. J. Org. Chem 1965;30:1288.and references therein

32. (a) Borrachero P, Cabrera-Escribano F, Carmona AT, Gómez-Guillén M. Tetrahedron: Asymmetry 2000;11:2927. (b) Vera-Ayoso Y, Borrachero P, Cabrera-Escribano F, Gómez-Guillén M. Tetrahedron: Asymmetry 2005;16:889.

33. Winn CL, Goodman JM. Tetrahedron Lett 2001;42:7091.

34. (a) Rhee JU, Bliss BI, RajanBabu TV. J. Am. Chem. Soc 2003;125:1492. [PubMed: 12568605] (b) Rhee JU, Bliss BI, RajanBabu TV. Tetrahedron: Asymmetry 2003;14:2939.

35. Harvey JF, Raw SA, Taylor RJK. Org. Lett 2004;6:2611. [PubMed: 15255703]

36. (a) Schneider RF, Engelhardt EL, Stobbe CC, Fenning MC, Chapman JD. J. Label. Compds. Radiopharm 1997;39:541. (b) Wright RS, Khorana HG. J. Am. Chem. Soc 1957;80:1994. (c) Morota T, Sasaki H, Nishimura H, Sugama K, Chin M, Mitsuhashi H. Phytochemistry 1989;28:2149.

37. (a) Callam CS, Lowary TL. J. Chem. Ed 2001;78:73. (b) Czernecki S, Diguarher TL. Synthesis 1991:683. (c) D'Souza FW, Cheshev PE, Ayers JD, Lowary TL. J. Org. Chem 1998;63:9037.

38. Ayers JD, Lowary TL, Morehouse CB, Besra GS. Bioorg. Med. Chem. Lett 1998;8:437. [PubMed: 9871594]

39. This observation parallels the numerous products obtained on condensation of ribose with benzaldehyde under a variety of conditions, none of which were a 3,5-di-*O*-benzylidene derivative of a furanose formGrindley TB, Szarek WA. Carbohydr. Res 1972;25:187.

40. D'Souza FW, Ayers JD, McCarren PR, Lowary TL. J. Am. Chem. Soc 2000;122:1251.

41. Yin H, Lowary TL. Tetrahedron Lett 2001;42:5829.

42. Adinolfi M, Barone G, De Napoli L, Iadonisi A, Piccialli G. Tetrahedron Lett 1996;37:5007.

43. The effect of conformational constraint on furanosides is evident in the magnitude of the anomeric effect. Thus, while it may be considered that the anomeric effect is reduced in furanosides because of the ease of pseudo-rotation, it has been demonstrated that in conformationally restricted furanosides the anomeric effect has a comparable magnitude to that observed in pyranosides:Ellervik U, Magnusson G. J. Am. Chem. Soc 1994;116:2340.

44. Mizutani K, Kasai R, Nakamura M, Tanaka O, Matsuura H. Carbohydr. Res 1989;185:27.

45. Crich D, Li H. J. Org. Chem 2000;56:801. [PubMed: 10814013]

46. Correlations of the type described here should only be used determining configuration of compounds exhibiting closely related conformations to the examples presented.

47. Duus JØ, Gotfredsen CH, Bock C. Chem. Rev 2000;100:4589. [PubMed: 11749359]

48. Hudson CS. J. Am. Chem. Soc 1916;38:1566.

49. Along with glycal type products, this product is typical of the kind observed in previous variable temperature NMR studies of glycosyl triflates.[17,23]

50. The higher decomposition temperature observed in the silylene acetal as compared to the benzylidene acetal should not be over interpreted as it may be coupled with decomposition of the highly acid sensitive 3,5-di-*O*-benzylidene acetal.

51. (a) Zhu Y, Zajicek J, Serianni AS. J. Org. Chem 2001;66:6244. [PubMed: 11559169] (b) Angyal SJ. Adv. Carbohydr. Chem. Biochem 1991;49:19. (c) Angyal SJ. Adv. Carbohydr. Chem. Biochem 1984;42:15.

52. (a) Capon B. Chem. Rev 1969;69:407. (b) BeMillar JN. Adv. Carbohydr. Chem. Biochem 1967;22:25. [PubMed: 4890502]

53. (a) Brown HC, Brewster JH, Schechter H. J. Am. Chem. Soc 1954;76:467.Eliel, EL.; Wilen, SH. Stereochemistry of Organic Compounds. New York: Wiley; 1994. and references therein

54. Callam SC, Gadikota RR, Krein DM, Lowary TL. J. Am. Chem. Soc 2003;125:13112. [PubMed: 14570484]

55. (a) Smith DM, Tran MB, Woerpel KA. J. Am. Chem. Soc 2003;125:14149. [PubMed: 14611253] (b) Larsen CH, Ridgway BH, Shaw JT, Woerpel KA. J. Am. Chem. Soc 1999;121:12208. (c) Schmitt A, Reissig H-U. Eur. J. Org. Chem 2000:3893.

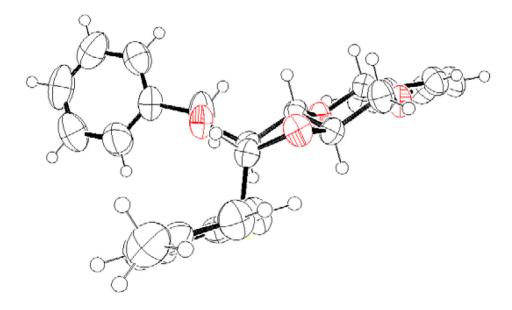56. Larsen CH, Ridgway BH, Shaw JT, Smith DM, Woerpel KA. J. Am. Chem. Soc 2005;127:10879. [PubMed: 16076193]

Figure 1.
X-ray crystal structure of **6** showing the E_4 conformation

Scheme 1.
Selective β-Mannosylation

Scheme 2.
Thioglycoside Synthesis

Scheme 3.
Synthesis of Benzylidene Acetal 6

Scheme 4.
Synthesis of the Silylene Protected Donor 8

Table 1

Glycosylation with Benzylidene Protected Donor 6.

(A) BSP, TTBP, −55 °C, Tf₂O, then ROH; (B) DPSO, TTBP, Tf₂O, then ROH, −72 °C → −25 °C.

Entry	Acceptor	Method	Product (% yield),^{a} α:β ratio
1	Cyclohexanol		
		A	9 (82%), 1:1.1
		B	9 (58%), 1:0.8
2			
		A	12 (35%), 1:1.

$^{a)}$Isolated yields

Table 2

Coupling Reactions with Silylene Protected Donor 8

(C) BSP, TTBP, −55 °C, Tf$_2$O, then ROH; (D) DPSO, TTBP, Tf$_2$O, −78 °C, then ROH; (E) BSP, TTBP, −55 °C, Tf$_2$O, → −25 °C, 30 min., → −55 °C, then ROH.

Entry	Acceptor	Method	Product (% yield),[a] α:β ratio
1	Methanol		**14**
		C	14 (79%), 1:1
		D	14 (93%), 1:0.7
		E[b]	14 (−), 1:3
2	Cyclohexanol		**15**
		C	15 (78%), 1:1.3
		D[c]	15 (67%), 1:1.2
		D	15 (88%), 1:0.8
		E	15 (57%), 1:2.5
3	1-Adamantanol		**16**
		C	16 (95%), 1:0.6
		D	16 (84%), 1:0
		D[d]	16 (68%), 1:0.6
4	**11**		**17**
		C	17 (65%), 1:1.5
		E	17 (85%), 1:1.1
5	**18**		**19**
		C[b]	19 (−), 1:2
		D	19 (86%), 1:0.7
		E	19 (58%), 1:3
6	**20**		**21**
		E	21 (84), 1:1.9

[a] Isolated yields

[b] Taken from NMR experiments

[c)]1.4 eq. DPSO

[d)]Acceptor added before Tf$_2$O.

Table 3

Coupling Reactions with Silylene Protected Donors 24–27

24: R = Ph
25: R = Cr

26

27

(D) DPSO, TTBP, Tf$_2$O, −78 °C, then ROH; (F) NIS/AgOTf, CH$_2$Cl$_2$, −30 °C, → rt. (G) Tf$_2$O, −78 ° → −50 → −78 °C, 30 min., then ROH; (H) Tf$_2$O 78 °, 30 min., then ROH.

Entry	Donor	Acceptor	Method	Product (% yield)^a, β:α ratio
1	**24**	Cyclohexanol		**28**
2	**24**	**11**	F	**28** (89%), 1.5:1
			D	**29** (56%), 1.1:1
3	**25**	**11**	F	**29** (92%), 6.5:1
4	**26**	**11**	F^b	**29** (90%), β-only
5	**26**	Thiophenol	G	**29** (83%), 9.0:1
				27
6	**26**	Cyclohexanol	H	**27** (70%), 6.3:1
				28
7	**27**	**11**	H	**28** (60%), 10.0:1
				29
			F	**29** (72%), 5.0:1

$^{a)}$Isolated yields

$^{b)}$2 equivalent of acceptor **11** were employed.

Table 4

Comparison of Chemical Shifts and Coupling Constants in Anomeric Arabinofuranosides

R	$^3J_{H1\text{-}H2}$ (Hz) α	β	$^1J_{C1\text{-}H1}$ (Hz) β	α	^{13}C-NMR C1 (ppm) β	α	^{1}H-NMR H1 (ppm) α	β	^{1}H-NMR H4 (ppm) α	β	$[\alpha]_D$ α	β
14	2.9	5.4	171.3	170.0	101.4	108.2	4.84	4.79	3.95	3.65	+41.3	−49.5
15	3.1	5.4	167.5	170.0	99.0	105.1	5.11	5.08	3.95	3.59	+41.9	−66.8
16	3.6	5.7	167.5	167.5	93.5	100.4	5.34	5.37	3.99	3.53	+28.5	−64.9
17	2.9	5.4	171.3	171.3	100.9	107.3	5.04	5.01	~4.0	3.60	+43.8	−19.3
19	3.0	5.8	172.5	176.3	102.2	107.6	5.87	5.01	3.85	3.44	+30.5	−13.1
29	3.5	5.5	172.5	169.2	100.8	108.0	5.00	5.06	3.98	3.64	+2.9	+59.4