JOC*Article*

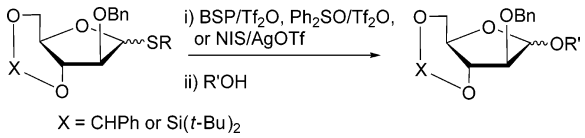
On the Use of 3,5-*O*-Benzylidene and 3,5-*O*-(Di-*tert*-butylsilylene)-2-*O*-benzylarabinothiofuranosides and Their Sulfoxides as Glycosyl Donors for the Synthesis of *β*-Arabinofuranosides: Importance of the Activation Method

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

Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607-7061, and Department of Chemistry, University of Aarhus, Langelandsgade 140, DK-8000 Aarhus C, Denmark

dcrich@uic.edu

Received July 11, 2006



A 2-*O*-benzyl-3,5-*O*-benzylidene-α-D-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 −55 °C, reaction with glycosyl acceptors affords anomeric mixtures with little or no selectivity. The analogous 2-*O*-benzyl-3,5-*O*-(di-*tert*-butylsilylene)-α-D-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-*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 L-version being very common in plants where it occurs mostly in the α-furanoside form. *β*-L-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 D-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]

In contrast to the α-arabinofuranosides, which are readily obtained through neighboring group participation, the synthesis of *β*-arabinofuranosides with a high degree of stereocontrol is problematic.[4] In early work on the methanolysis of α-D-arabinofuranosyl chlorides carrying nonparticipating O2 protecting groups, Fletcher and Glaudemans obtained primarily the

† University of Illinois at Chicago.
‡ University of Aarhus.

(1) Houseknecht, J. B.; Lowary, T. L. *Curr. Opin. Chem. Biol.* **2001**, *5*, 677.

(2) (a) Allen, A. K.; Desai, N. N.; Neuberger, A. *Biochem. J.* **1978**, *171*, 665. (b) Ashford, D.; Desai, N. N.; Allen, A. K.; Neuberger, A. *Biochem. J.* **1982**, *201*, 199.

(3) (a) Lowary, T. L. *Curr. Opin. Chem. Biol.* **2003**, *7*, 749. (b) Lowary, T. L. *J. Carb. Chem.* **2002**, *21*, 691. (c) Lowary, T. L. In *Glycoscience*: *Chemistry and Chemical Biology*; Fraser-Reid, B., Tatsuta, K., Thiem, J., Eds.; Springer: Berlin, Germany, 2001; Vol.3, p 2005.

(4) Lowary, T. L. In *Glycochemistry*: *Principles, Synthesis, and Applications*; Wang, P. G., Bertozzi, C. R., Eds.; Dekker: New York, 2001; p 133.

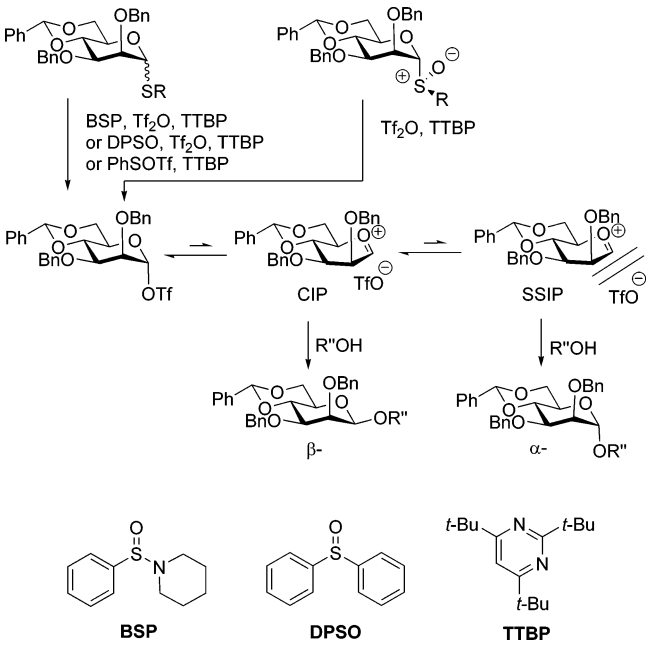
10.1021/jo061440x CCC: $37.00
Published on Web 02/08/2007

β-anomer and proposed a mechanism involving an ion pair.[5] Working with trimethylsilyl 2,3,5-tri-*O*-benzyl-D-arabinofuranoside as donor Mukaiyama and co-workers 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 co-workers 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 intramolecular 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-D-lyxofuranosyl thioglycoside donor, with subsequent, regioselective epoxide opening to give the β-D-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-D-mannosides,[16] β-D-rhamnosides,[17] and β-D-glycero-D-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.

SCHEME 1. Selective β-Mannosylation



The generally excellent results in the mannose series prompted the investigation that we describe here into the applicability of a 3,5-*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 co-workers.

(5) (a) Glaudemans, C. P.; Fletcher, H. G. *J. Am. Chem. Soc.* **1965**, *87*, 2456. (b) Glaudemans, C. P.; Fletcher, H. G. *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, F. W.; Lowary, T. L. *J. Org. Chem.* **2002**, *67*, 892.

(8) Li, Y.; Singh, G. T. *Tetrahedron Lett.* **2001**, *42*, 6615.

(9) Lee, Y. J.; Lee, K.; Jung, E. H.; Jeon, H. B.; Kim, K. S. *Org. Lett.* **2005**, *7*, 3263.

(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, R. R.; Callam, C. S.; Lowary, T. L. *Org. Lett.* **2001**, *3*, 607. (b) Callam, C. S.; Gadikota, R. R.; Lowary, T. L. *J. Org. Chem.* **2001**, *66*, 4549. (c) Gadikota, R. R.; Callam, C. S.; Wagner, T.; Fraino, B. D.; Lowary, T. L. *J. Am. Chem. Soc.* **2003**, *125*, 4155. (d) Cociorva, O. M.; Lowary, T. L. *Tetrahedron* **2004**, *60*, 1481.

(14) (a) Crich, D.; Sun, S. *J. Org. Chem.* **1996**, *61*, 4506. (b) Crich, D.; Sun, S. *Tetrahedron* **1998**, *54*, 8321.

(15) Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2002**, *124*, 8867.

(16) Crich. D.; Banerjee, A.; Yao, Q. *J. Am. Chem. Soc.* **2004**, *126*, 14930.

(17) Crich, D.; Bowers, A. *J. Org. Chem.* **2006**, *71*, 3452.

(18) Crich, D.; Banerjee, A. *J. Am. Chem. Soc.* **2006**, *128*, 8078.

(19) Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015.

(20) Crich, D.; Sun, S. *J. Am. Chem. Soc.* **1998**, *120*, 435.

(21) Codée, J. D. C.; van den Bos, L. J.; Litjens, R. E. J. N.; Overkleeft, H. S.; van Boeckel, C. A. A.; van Boom, J. H.; van der Marel, G. A. *Tetrahedron* **2004**, *60*, 1057.

(22) Crich, D.; Smith, M.; Yao, Q.; Picione, J. *Synthesis* **2001**, 323.

(23) Crich, D.; Lim, L. B. L. *Org. React.* **2004**, *64*, 115.

(24) Crich, D.; Sun, S. *J. Am. Chem. Soc.* **1997**, *119*, 11217.

(25) Crich, D.; Chandraskera, N. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 5386.

(26) Fraser-Reid, B.; Wu, Z.; Andrews, C. W.; Skowronski, E. J. *J. Am. Chem. Soc.* **1991**, *113*, 1434.

(27) (a) Jensen, H. H.; Nordstrøm, L. U.; Bols, M. *J. Am. Chem. Soc.* **2004**, *126*, 9205. (b) For computational work in this area see: Nukuda, T.; Bérces, A.; Wang, L.; Zgierski, M. Z.; Whitfield, D. M. *Carbohydr. Res.* **2005**, *340*, 841.

(28) (a) Rao, Y.; Zhu. X.; Boons, G. J. *Abstracts of Papers*; 231st National Meeting of the American Chemical Society, Atlanta, 2006; American Chemical Society: Washington, DC, 2006; CARB-030. (b) Rao, Y.; Zhu, X.; Boons, G. J. *Abstracts of Papers*; 23rd International Carbohydrate Symposium, Whistler, 2006; PS.44. (c) Zhu, X.; Kawatkar, S. P.; Rao, Y.; Boons, G. J. *J. Am. Chem. Soc.* **2006**, *128*, 11948.

(29) (a) Ishiwata, A.; Akao, H.; Ito, Y. *Abstracts of Papers*; 23rd International Carbohydrate Symposium, Whistler, 2006; PS.20. (b) Ishiwata, A.; Akao, H.; Ito, Y. *Org. Lett.* **2006**, *8*, 5525.

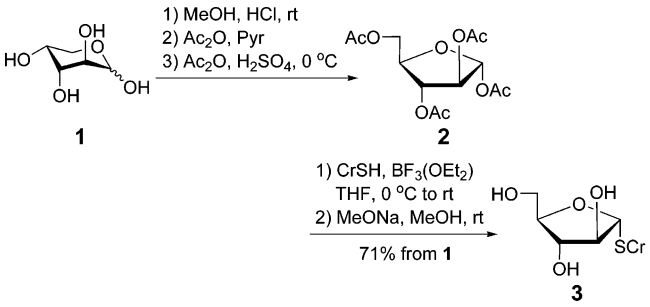
Results

Donor Synthesis. The literature on the existence and use of 3,5-*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-*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-*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]

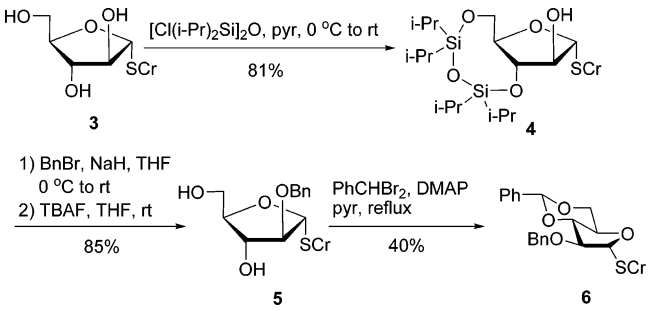
The synthesis of the 3,5-*O*-benzylidene protected donor **6** began with the preparation of the triol **3**, which was obtained from D-arabinose. Among the various literature protocols for the synthesis of the methyl arabinofuranoside investigated,[36] the one of Lowary and co-workers was optimal.[37] The methyl arabinofuranoside so-obtained was esterified under standard conditions and then transformed into the glycosyl acetate **2** with sulfuric acid in acidic acetic anhydride. The corresponding *p*-cresyl thioglycoside was obtained by Lewis acid hydrolysis in the 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 furanose ring giving multiple products, and resolved to protect O2 before attempted introduction of the acetal (Scheme 3). Thus, **3** was converted

SCHEME 2. Thioglycoside Synthesis



SCHEME 3. Synthesis of Benzylidene Acetal 6



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 catalyzed 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

(30) de Belder, A. N. *Adv. Carbohydr. Chem. Biochem.* **1977**, *34*, 179.
(31) The exceptions are the xylofuranosides which readily form 3,5-*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, R. J.; Hatton, L. R. *Carbohydr. Res.* **1967**, *5*, 132. (b) von Schuching, S.; Frye, G. H. *J. Org. Chem.* **1965**, *30*, 1288 and references cited therein.
(32) (a) Borrachero, P.; Cabrera-Escribano, F.; Carmona, A. T.; 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, C. L.; Goodman, J. M. *Tetrahedron Lett.* **2001**, *42*, 7091.
(34) (a) Rhee, J. U.; Bliss, B. I.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2003**, *125*, 1492. (b) Rhee, J. U.; Bliss, B. I.; RajanBabu, T. V. *Tetrahedron: Asymmetry* **2003**, *14*, 2939.
(35) Harvey, J. F.; Raw, S. A.; Taylor, R. J. K. *Org. Lett.* **2004**, *6*, 2611.
(36) (a) Schneider, R. F.; Engelhardt, E. L.; Stobbe, C. C.; Fenning, M. C.; Chapman, J. D. *J. Labelled Compd. Radiopharm.* **1997**, *39*, 541. (b) Wright, R. S.; Khorana, H. G. *J. Am. Chem. Soc.* **1958**, *80*, 1994. (c) Morota, T.; Sasaki, H.; Nishimura, H.; Sugama, K.; Chin, M.; Mitsuhashi, H. *Phytochemistry* **1989**, *28*, 2149.
(37) (a) Callam, C. S.; Lowary, T. L. *J. Chem. Ed.* **2001**, *78*, 73. (b) Czernecki, S.; Diguarher, T. L. *Synthesis*, **1991**, 683. (c) D'Souza, F. W.; Cheshev, P. E.; Ayers, J. D.; Lowary, T. L. *J. Org. Chem.* **1998**, *63*, 9037.
(38) Ayers, J. D.; Lowary, T. L.; Morehouse, C. B.; Besra, G. S. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 437.
(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-*O*-benzylidene derivative of a furanose form. Grindley, T. B.; Szarek, W. A. *Carbohydr. Res.* **1972**, *25*, 187.
(40) D'Souza, F. W.; Ayers, J. D.; McCarren, P. R.; Lowary, T. L. *J. Am. Chem. Soc.* **2000**, *122*, 1251.
(41) Yin, H.; Lowary, T. L. *Tetrahedron Lett.* **2001**, *42*, 5829.
(42) Adinolfi, M.; Barone, G.; De Napoli, L.; Iadonisi, A.; Piccialli, G. *Tetrahedron Lett.* **1996**, *37*, 5007.

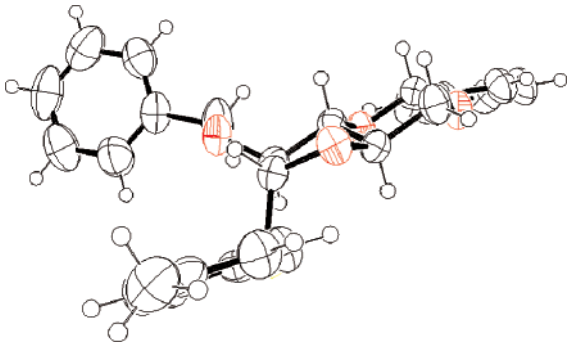
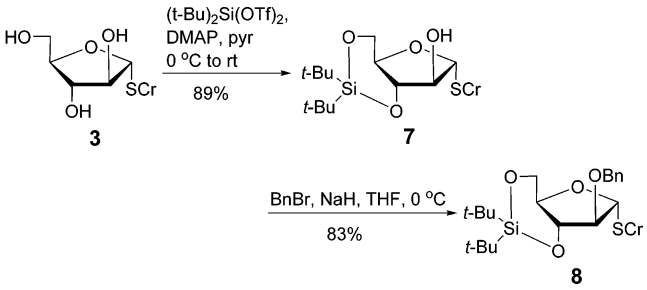


FIGURE 1. X-ray crystal structure of **6** showing the E_4 conformation.

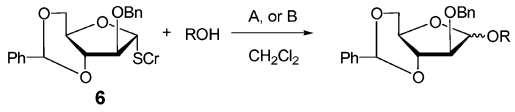
SCHEME 4. Synthesis of the Silylene Protected Donor 8



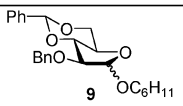
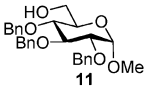
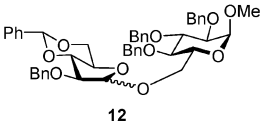
anticipated significant downfield shift of the H2 resonance in the ^{1}H NMR spectrum was observed, and by correlations of subsequent products with literature data as described below. Benzylation of **7** with sodium hydride and benzyl bromide afforded the glycosyl donor **8**, with THF again proving 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 upfield relative to its α-counterpart.[44] Furthermore, the *β*-anomer showed a significantly larger (3−5 Hz) $^3J_{H1-H2}$ 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 favor 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 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

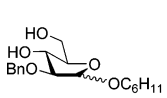
TABLE 1. Glycosylation with Benzylidene Protected Donor 6

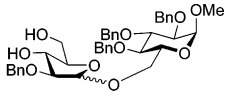


(A) BSP, TTBP, -55 °C, Tf_2O, then ROH; (B) DPSO, TTBP, Tf_2O, then ROH, -72 °C → -25 °C.

Entry	Acceptor	Method	Product (% yield),[a] α:β ratio
1	Cyclohexanol		 **9**
		A	**9** (82%), 1:1.1
		B	**9** (58%), 1:0.8
2	 **11**		 **12**
		A	**12** (35%), 1:1

[a] Isolated yields.


10


13

of the stereochemistry was provided by comparison of the spectral data of the known α-diol **13** with that found in the literature.[13c]

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 that 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.

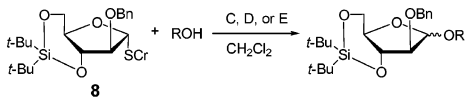
At this stage in our investigation we became aware of the work of Boons and co-workers in the enantiomeric series in which activation of the *S*-phenyl thioglycoside **24** with *N*-iodosuccinimide and silver triflate in dichloromethane at −30 °C afforded *β*-selective couplings to a range of acceptors, 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

(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 pseudorotation, 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.

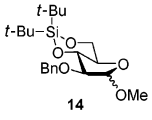
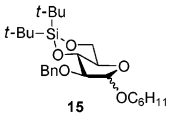
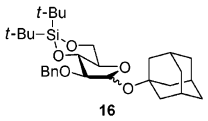
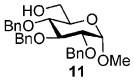
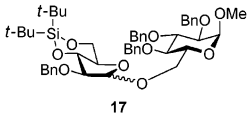
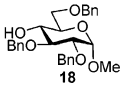
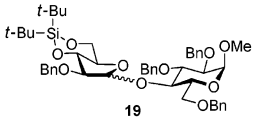
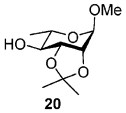
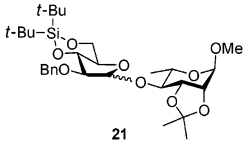
(45) Crich, D.; Li, H. *J. Org. Chem.* **2000**, *56*, 801.

TABLE 2. Coupling Reactions with Silylene Protected Donor 8



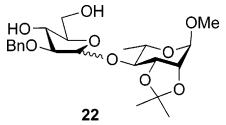
8

(C) BSP, TTBP, -55 °C, Tf_2O, then ROH; (D) DPSO, TTBP, Tf_2O, -78 °C, then ROH; (E) BSP, TTBP, -55 °C, Tf_2O, → -25 °C, 30 min, → -55 °C, then ROH.

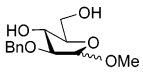
Entry	Acceptor	Method	Product (% yield),[a] α:β ratio
1	Methanol		 **14**
		C	**14** (79%), 1:1
		D	**14** (93%), 1:0.7
		E[b]	**14** (-), 1:3
2	Cyclohexanol		 **15**
		C	**15** (78%), 1:1.3
		D[c]	**15** (67%), 1:1.2
		D	**15** (88%), 1:0.8
		E	**15** (57%), 1:2.5
3	1-Adamantanol		 **16**
		C	**16** (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 equiv of DPSO. [d] Acceptor added before Tf_2O.

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.



22



23

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 ^1H 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 **14**α and **17**α to the diols **23**α and **13**α, 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 the Supporting Information). In the 4,6-*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-*O*-silylene acetal protected thioglycoside **8**, activation at −55 °C with the BSP/trifluoromethanesulfonic anhydride combination in CD_2Cl_2 was surprisingly complex and provided several apparent anomeric resonances. On gradual warming to approximately 0 °C, these signals collapsed in favor 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_2Cl_2 (Supporting Information) with the exception that the apparent anomeric

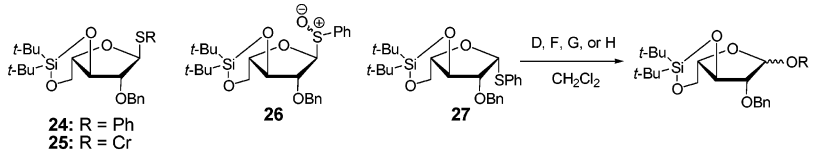
(46) Correlations of the type described here should only be used determining configuration of compounds exhibiting closely related conformations to the examples presented.

(47) Duus, J. Ø.; Gotfredsen, C. H.; Bock, C. *Chem. Rev.* **2000**, *100*, 4589.

(48) Hudson, C. S. *J. Am. Chem. Soc.* **1916**, *38*, 1566.

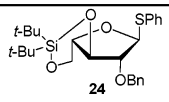
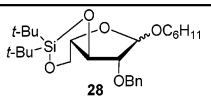
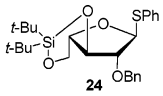
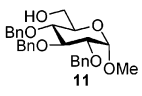
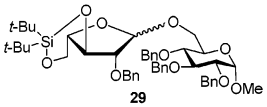
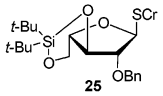
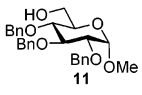
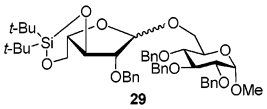
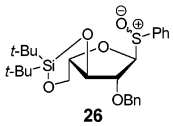
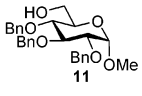
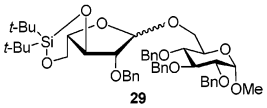
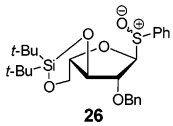
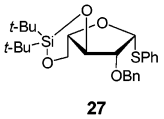
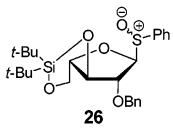
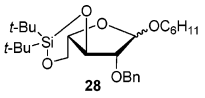
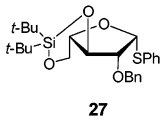
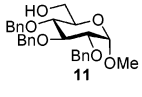
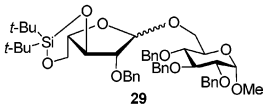
(49) Along with glycal type products, this product is typical of the kind observed in previous variable-temperature NMR studies of glycosyl triflates.[17,23]

TABLE 3. Coupling Reactions with Silylene Protected Donors 24−27



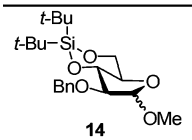
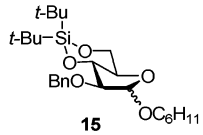
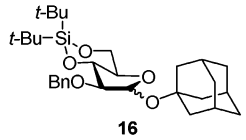
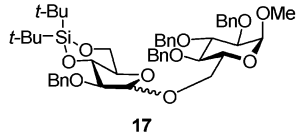
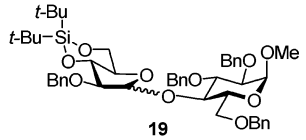
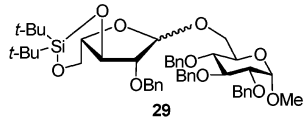
(D) DPSO, TTBP, Tf_2O, -78 °C, then ROH; (F) NIS/AgOTf, -30 °C, → rt.

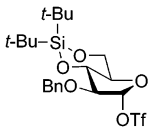
(G) Tf_2O, -78 ° → -50 → -78 °C, 30 min, then ROH; (H) Tf_2O 78 °, 30 min, then ROH.

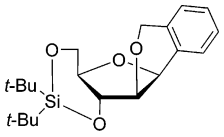
Entry	Donor	Acceptor	Method	Product (% yield),[a] β:α ratio
1		Cyclohexanol		
			F	**28** (89%), 1.5:1
2				
			D	**29** (56%), 1.1:1
			F	**29** (92%), 6.5:1
3				
			F[b]	**29** (90%), β-only
4				
			G	**29** (83%), 9.0:1
5		Thiophenol		
			H	**27** (70%), 6.3:1
6		Cyclohexanol		
			H	**28** (60%),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

[a] Isolated yields. [b] 2 equiv of acceptor **11** were employed.

TABLE 4. Comparison of Chemical Shifts and Coupling Constants in Anomeric Arabinofuranosides

R	$^3J_{H1-H2}$ (Hz)		$^1J_{C1-H1}$ (Hz)		^{13}C-NMR C1 (ppm)		^{1}H-NMR H1 (ppm)		^{1}H-NMR H4 (ppm)		$[\alpha]_D$	
	α	β	α	β	α	β	α	β	α	β	α	β
 **14**	2.9	5.4	171.2	172.5	108.2	101.4	4.84	4.79	3.95	3.65	+41.3	-49.5
 **15**	3.1	5.4	171.2	168.7	105.1	99.0	5.11	5.08	3.95	3.59	+41.9	-66.8
 **16**	3.6	5.7	168.7	168.7	100.4	93.5	5.34	5.37	3.99	3.53	+28.5	-64.9
 **17**	2.9	5.4	172.5	172.5	107.3	100.9	5.04	5.01	~4.0	3.60	+43.8	-19.3
 **19**	3.0	5.8	177.6	173.7	107.6	102.2	5.87	5.01	3.85	3.44	+30.5	-13.1
 **29**	3.5	5.5	169.2	172.5	108.0	100.8	5.00	5.06	3.98	3.64	+2.9	+59.4


30


31

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).

(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-*O*-benzylidene acetal.

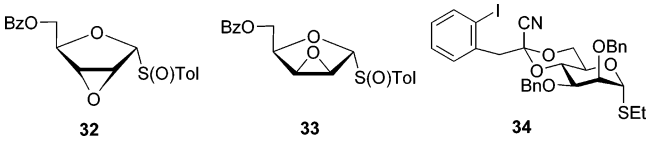
Discussion

It is apparent from the results presented in Table 3 that the stereoselectivity of the NIS/AgOTf-mediated glycosylations reported originally by Boons and co-workers[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/trifluoromethanesulfonic anhydride combination previously, suggest that it is slow activation of the thioglycosides by the BSP/trifluoromethanesulfonic anhydride that is the problem.

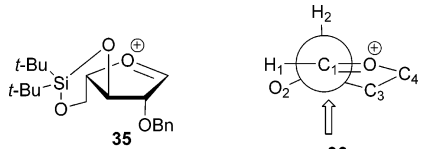
Furanose sugars are generally thermodynamically less stable than the isomeric pyranoses for most configurations as is clear from the relative populations of the five- and six-membered rings under equilibrating conditions.[51] Furanosides are also generally more reactive, and display different kinetic 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-*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 co-workers[54] and the comparably slow activation of certain mannosyl thioglycosides bearing electron-deficient 4,6-*O*-alkylidene groups such as in **34**.[17]



32 **33** **34**

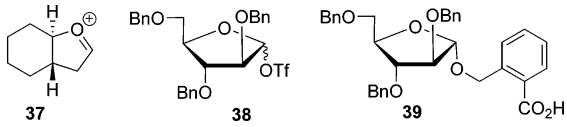
The parallel between the slow activation observed for **32** and **33** by Lowary and co-workers and that observed here for **6** and **8** is striking. It is unlikely that the epoxide in **32** and **33** is unusually strongly electron withdrawing, just as it is improbable that the acetals in the donors studied here are more electron withdrawing than the 4,6-*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** serve 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.



35 **36**

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



37 **38** **39**

nucleophiles, contrasts with the observations of Kim and co-workers, 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 that with carbon nucleophiles and other factors need to be taken into consideration, perhaps including hydrogen bonding of the incoming alcohol to the donor.

Conclusion

In conclusion a somewhat acid sensitive 3,5-*O*-benzylidene protected arabinofuranosyl system may be prepared provided

(51) (a) Zhu, Y.; Zajicek, J.; Serianni, A. S. *J. Org. Chem.* **2001**, *66*, 6244. (b) Angyal, S. J. *Adv. Carbohydr. Chem. Biochem.* **1991**, *49*, 19. (c) Angyal, S. J. *Adv. Carbohydr. Chem. Biochem.* **1984**, *42*, 15.

(52) (a) Capon, B. *Chem. Rev.* **1969**, *69*, 407. (b) BeMillar, J. N. *Adv. Carbohydr. Chem. Biochem.* **1967**, *22*, 25.

(53) (a) Brown, H. C.; Brewster, J. H.; Schechter, H. *J. Am. Chem. Soc.* **1954**, *76*, 467. (b) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; and references therein.

(54) Callam, S. C.; Gadikota, R. R.; Krein, D. M.; Lowary, T. L. *J. Am. Chem. Soc.* **2003**, *125*, 13112.

(55) (a) Smith, D. M.; Tran, M. B.; Woerpel, K. A. *J. Am. Chem. Soc.* **2003**, *125*, 14149. (b) Larsen, C. H.; Ridgway, B. H.; Shaw, J. T.; Woerpel, K. A. *J. Am. Chem. Soc.* **1999**, *121*, 12208. (c) Schmitt, A.; Reissig, H.-U. *Eur. J. Org. Chem.* **2000**, 3893.

(56) Larsen, C. H.; Ridgway, B. H.; Shaw, J. T.; Smith, D. M.; Woerpel, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 10879.

that O2 is protected before attempted introduction of the acetal. The corresponding 3,5-*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-*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-D-arabinofuranoside (3).**[13c,37] A suspension of D-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_2Cl_2/MeOH 4:1) showed full conversion of **1** (R_f 0.1) to two new spots (R_f 0.5 and 0.6). The reaction mixture was quenched with pyridine, evaporated, then coevaporated with CH_2Cl_2 to give a crude product that 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 and the reaction was diluted with CH_2Cl_2 (300 mL) and finally washed thoroughly with water, 1 M HCl (aq), $NaHCO_3$ (sat), and brine. The organic phase was dried (Na_2SO_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_2SO_4 (5 mL) were added dropwise. 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_2Cl_2. The organic layer was separated and washed thoroughly with additional $NaHCO_3$ (sat) and brine, dried (Na_2SO_4), and concentrated in vacuo to give a crude product (15.45 g). The crude product was dissolved in dry CH_2Cl_2 (150 mL) and cooled to 0 °C when $BF_3{\cdot}OEt_2$ (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_3N and diluted to 300 mL with CH_2Cl_2, washed with water and brine, dried (Na_2SO_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) then 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_2Cl_2−MeOH 10:1) to give 4.06 g (71%) of the title triol. R_f 0.3 (EtOAc); $[\alpha]_D$ +235.6 (*c* 1.0, $CHCl_3$), lit.[37] $[\alpha]_D$ +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-D-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×), $NaHCO_3$ (sat), and brine, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (hexanes−CH_2Cl_2 1:1, then CH_2Cl_2) to give the 3,5-*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 portionwise with NaH (60% dispersion in oil, 370 mg, 9.2 mmol). After 8 h at rt an additional 1 equiv (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 that 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_2Cl_2 then CH_2Cl_2−EtOAc 1:1) to give **5** (1.08 g, 69% for 2 steps) as a colorless syrup. R_f 0.25 (CH_2Cl_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 (br d, 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-*O*-benzylidene-1-thio-α-D-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_3N (180 μL, 1.3 mmol). After 1 h additional 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_2Cl_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_2Cl_2); $[\alpha]_D$ +177 (*c* 1.0, CH_2Cl_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 calcd for $[C_{26}H_{26}O_4S]^+$ 434.1552, found 434.1547.

***p*-Cresyl 3,5-*O*-(Di-*tert*-butylsilylene)-1-thio-α-D-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_2Cl_2); $[\alpha]_D$ +196 (*c* 1.0, CH_2Cl_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 calcd for $[C_{20}H_{32}O_4SSi]^+$ 396.1791, found 396.1791.

***p*-Cresyl 2-*O*-Acetyl-3,5-*O*-(di-*tert*-butylsilylene)-1-thio-α-D-arabinofuranoside (7-*O*-Ac).** Microscale acetylation of **7** with pyridine and acetic anhydride gave **7-*O*-Ac** quantitatively as a white crystalline solid. Mp 72 °C; R_f 0.8 (CH_2Cl_2); $[\alpha]_D$ +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 calcd for $[C_{22}H_{34}O_5SSiNa]^+$ 461.1794, found 461.1772.

***p*-Cresyl 2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-1-thio-α-D-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 portionwise 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_2Cl_2) to give **8** (1.19, 83%) as a white crystalline solid. Mp 80 °C; R_f 0.8 (CH_2Cl_2); $[\alpha]_D$ +154 (*c* 1.0, CH_2Cl_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 calcd for $[C_{27}H_{38}O_4SSi]^+$ 486.2260, found 486.2257.

Activation of Thioglycoside 6 with 1-Benzenesulfinyl Piperidine and Trifluoromethanesulfonic Anhydride (Method A): Cyclohexyl 2-*O*-Benzyl-*β*-D-arabinofuranoside (10*β*) and Cyclohexyl 2-*O*-Benzyl-α-D-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_2Cl_2 (4 mL) under argon, then stirred at rt for 1 h prior to cooling to −55 °C. After 15 min Tf_2O (21 μL, 0.13 mmol) was added 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_3N, filtered, and concentrated in vacuo. The crude mixture was purified by flash chromatography on silica gel (hexanes−CH_2Cl_2 1:1) to give cyclohexyl 2-*O*-benzyl-3,5-*O*-benzylidene-α-D-arabinofuranoside (**9**α) (17 mg) and cyclohexyl 2-*O*-benzyl-3,5-*O*-benzylidene-α-D-arabinofuranoside (**9***β*) (18 mg) (82% combined yield) as colorless syrups. **9**α: ^{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). **9***β*: ^{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_2Cl_2 (1 mL) at room temperature for 1 min. Concentration and purification by flash chromatography on silica gel gave cyclohexyl 2-*O*-benzyl-α-D-arabinofuranoside (**10**α) (6 mg) and cyclohexyl 2-*O*-benzyl-*β*-D-arabinofuranoside (**10***β*) (10 mg). **10**α: Colorless syrup. R_f 0.3 (hexanes−ethyl acetate 1:1); $[\alpha]_D$ +70.1 (*c* 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) 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 (br s, 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 (br s, 2 H), 1.39−1.19 (m, 5 H); ^{13}C NMR (125 Hz, $CDCl_3$) 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 calcd for $[C_{18}H_{26}O_5Na]^+$ 345.1678, found 345.1662. **10***β*: White crystalline solid. Mp 100 °C; R_f 0.2 (hexanes−ethyl acetate 1:1); $[\alpha]_D$ −91.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 Hz, $CDCl_3$) 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 calcd 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 CH_2Cl_2 (3 mL) under argon, then stirred at rt for 1 h prior to cooling to −72 °C. After 15 min Tf_2O 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 Et_3N, 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 **10**α (12.8 mg) and **10***β* (10 mg) (58% combined yield).

Methyl 6-*O*-(2-*O*-Benzyl-α-D-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (13α) and Methyl 6-*O*-(2-*O*-Benzyl-*β*-D-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (13*β*). 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 CH_2Cl_2 (4 mL) under argon, then stirred at rt for 1 h prior to cooling to −56 °C. After 15 min Tf_2O (28 μL, 0.17 mmol) was added and after an additional 15 min methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (128 mg, 0.28 mmol) in CH_2Cl_2 (1 mL) was added. The reaction mixture was allowed to warm to −40 °C then was treated with several drops of Et_3N, filtered, and concentrated in vacuo. The crude mixture was purified by flash chromatography (hexanes−CH_2Cl_2 1:1) to give methyl 6-*O*-(2-*O*-benzyl-3,5-*O*-benzylidene-α-D-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**12**α) (21 mg) and methyl 6-*O*-(2-*O*-benzyl-3,5-*O*-benzylidene-*β*-D-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**12***β*) (20 mg) (35% combined yield) as colorless syrups. Further characterization was not attempted and both products were exposed to trifluoroacetic acid (1 drop) in CH_2Cl_2 (1 mL) for 1 min. The reaction mixtures were concentrated and purified by flash chromatography to give **13**α (6 mg) and **13***β* (10 mg). **13**α: Colorless syrup; R_f 0.3 (hexanes−ethyl acetate 3:1); $[\alpha]_D$ +44 (*c* 0.9, $CHCl_3$), lit.[13c] $[\alpha]_D$ +31 (*c* 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{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, 55.0. **13***β*: Colorless syrup; R_f 0.25 (hexanes−ethyl acetate 3:1); $[\alpha]_D$ −17.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR(500 MHz, $CDCl_3$) 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 calcd 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_2Cl_2 (5 mL/100 mg) and stirred for 1 h under argon, before cooling to −55 °C. After 30 min Tf_2O (1.2 equiv) was added and the reaction mixture was allowed to stir for 10 min before the acceptor (2 equiv) in 1 mL of CH_2Cl_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_3N. 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 in CH_2Cl_2 (5 mL/100 mg) and stirred for 1 h before cooling to −78 °C. After 30 min Tf_2O (1.2 equiv) was added and the reaction mixture was allowed to stir for 20 min before the acceptor (2 equiv) in CH_2Cl_2 (1 mL) was added. The solution was allowed to reach 0 °C before it was basified with Et_3N, 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_2Cl_2 (5 mL/100 mg) and cooled to −55 °C under argon. After 30 min Tf_2O (1.2 equiv) was added and the reaction mixture was allowed to warm to −25 °C over 2 h during which the color of the reaction mixture changed from red-brown to pale yellow. After 30 min at −25 °C the reaction was recooled to −70 °C and the acceptor (1.5 equiv) in CH_2Cl_2 (1 mL) was added. The reaction was allowed to reach rt before it was quenched with Et_3N, 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 molecular sieves, then dissolved in CH_2Cl_2 (5 mL) and stirred 1 h prior to cooling the reaction mixture to −30 °C under argon. After the reaction was stirred for 30 min NIS (58 mg, 0.26 mmol) and AgOTf (11 mg, 41 μmol) were added. The reaction was then allowed to warm to rt before it was filtered, diluted with CH_2Cl_2 (20 mL), washed with 5% aqueous sodium thiosulfate and brine, dried (Na_2SO_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 **13**α (69 mg, 82%) identical with the sample described above.

General Procedure for Removal of the 3,5-*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-*O*-(di-*tert*-butylsilylene)-α-D-arabinofuranoside (14α). Colorless syrup; R_f 0.8 (CH_2Cl_2); $[\alpha]_D$ +41.3 (*c* 0.9, $CHCl_3$); ^{1}H 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 calcd for $[C_{21}H_{34}O_5Si]^+$ 394.2176, found 394.2192.

Methyl 2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-β-D-arabinofuranoside (14β). Colorless syrup; R_f 0.8 (CH_2Cl_2); $[\alpha]_D$ −49.5 (*c* 1.0, CH_2Cl_2); ^{1}H 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, 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 calcd for $[C_{21}H_{34}O_5SiNa]^+$ 417.2074, found 417.2084.

Cyclohexyl 2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-α-D-arabinofuranoside (15α). Colorless syrup; R_f 0.8 (CH_2Cl_2); $[\alpha]_D$ +41.9 (*c* 0.9, $CHCl_3$); ^{1}H 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 calcd for $[C_{26}H_{42}O_5SiNa]^+$ 485.2700, found 485.2704.

Cyclohexyl 2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-β-D-arabinofuranoside (15β). Colorless syrup; R_f 0.7 (CH_2Cl_2); $[\alpha]_D$ −66.8 (*c* 1.0, $CHCl_3$); ^{1}H 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 calcd for $[C_{26}H_{42}O_5SiNa]^+$ 485.2700, found 485.2713.

Adamantyl 2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-α-D-arabinofuranoside (16α). Colorless syrup; R_f 0.6 (CH_2Cl_2); $[\alpha]_D$ +28.5 (*c* 1.1, $CHCl_3$); ^{1}H 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 calcd for $[C_{30}H_{46}O_5Si]^+$ 514.3115, found 514.3099.

Adamantyl 2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-β-D-arabinofuranoside (16β). Colorless syrup; R_f 0.7 (CH_2Cl_2); $[\alpha]_D$ −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 calcd for $[C_{30}H_{46}O_5SiNa]^+$ 537.3013, found 537.3010.

Methyl 6-*O*-(2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-α-D-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (17α). Colorless syrup; R_f 0.15 (CH_2Cl_2); $[\alpha]_D$ +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 calcd for $[C_{48}H_{62}O_{10}SiNa]^+$ 849.4010, found 849.3991.

Methyl 6-*O*-(2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-*β*-D-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (17*β*). Colorless syrup; R_f 0.1 (CH_2Cl_2); $[\alpha]_D$ −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 calcd for $[C_{48}H_{62}O_{10}SiNa]^+$ 849.4010, found 849.3983.

Methyl 4-*O*-(2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-α-D-arabinofuranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (19α). Colorless syrup; R_f 0.15 (CH_2Cl_2); $[\alpha]_D$ +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 calcd for $[C_{48}H_{62}O_{10}SiNa]^+$ 849.4010, found 849.4035.

Methyl 4-*O*-(2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-*β*-D-arabinofuranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (19*β*). Colorless syrup; R_f 0.1 (CH_2Cl_2); $[\alpha]_D$ −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 calcd for $[C_{48}H_{62}O_{10}SiNa]^+$ 849.4010, found 849.4006.

Methyl 4-*O*-(2-*O*-Benzyl-D-arabinofuranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (22). The arabinopyranoside **21** was obtained in the form of an inseparable α,*β*-mixture. R_f 0.3 (CH_2Cl_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, $H_{1\beta}$), 5.30 (s, 1 H, $H_{1'}$), 5.14 (d, 0.35 H, J = 2.8 Hz, $H_{1\alpha}$), 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 = 6.4 Hz, α), 1.07 (s, 9 H), 1.00 (s, 3.15 H, α), 0.98 (s, 5.85 H, *β*). **21**α: ^{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. **21***β*: ^{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 characterization. Compound **22** also was obtained in the form of an inseparable α,*β*-mixture. R_f 0.4 (CH_2Cl_2 EtOAc 3:1); HRMS calcd 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, $H_{1\beta}$), 5.21 (s, 0.35 H, $H_{1\alpha}$), 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 (br d, 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). **22**α: ^{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. **22***β*: ^{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-D-arabinofuranoside (23). Colorless syrup; R_f 0.25 (hexanes−EtOAc 1:1); $[\alpha]_D$ +60.5 (*c* 1, $CHCl_3$), lit.[7] $[\alpha]_D$ +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-*O*-(di-*tert*-butylsilylene)-1-thio-α-L-arabinofuranoside (25).** Compound **25** was prepared analogously to its enantiomer **8**, starting from L-arabinose. All spectral data matched those of compound **8**. $[\alpha]_D$ −153.4 (*c* 1.0, $CHCl_3$).

***S*-Phenyl 2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-1-thio-α-L-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); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59−7.64 (m, 4H), 7.48−7.54 (m, 6H), 0.24−7.38 (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); ^{13}C NMR (125 Hz, $CDCl_3$) 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 calcd 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. Tf_2O (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 dropwise. The reaction mixture was allowed to warm to −30 °C, when it was quenched by addition of Et_3N 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 Tf_2O.

***S*-Phenyl 2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-1-thio-*β*-L-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 the 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, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 Hz, $CDCl_3$) 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 calcd for $[C_{26}H_{36}O_4SSiNa]^+$ 495.2002, found 495.1999.

Cyclohexyl 2-*O*-benzyl-3,5-*O*-(di-*tert*-butylsilylene)-α-L-arabinofuranoside (28α) and cyclohexyl 2-*O*-benzyl-3,5-*O*-(di-*tert*-butylsilylene)-*β*-L-arabinofuranoside (28*β*) had spectral data identical with those of the enantiomers (**15**α and **15**β). **28**α: $[\alpha]_D$ −41.1 (*c* 1.0, $CHCl_3$); $[\alpha]_D$ +65.7 (*c* 1.0, $CHCl_3$).

Methyl 6-*O*-(2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-α-L-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-D-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 calcd for $[C_{48}H_{62}O_{10}SiNa]^+$ 849.4005, found 849.4036.

Methyl 6-*O*-(2-*O*-Benzyl-3,5-*O*-(di-*tert*-butylsilylene)-*β*-L-arabinofuranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (29*β*). 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 calcd 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 a desiccator, then dissolved in CD_2Cl_2 (1 mL) under argon. The NMR tube was then cooled to −55 °C and a spectrum was recorded. Tf_2O (8.3 μL, 50 μmol) was added at −60 °C and the reaction mixture was warmed in 10 deg 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 calcd for $[C_{20}H_{31}O_4Si]^+$ 363.1992, found 363.1994 (M+H).

Acknowledgment. We thank the Lundbeck Foundation and the NIH (GM62160) for financial support, and Professor Geert-Jan Boons for a helpful exchange of information.

Supporting Information Available: Copies of NMR spectra for all compounds, copies of the VT-NMR spectra, and the crystallographic CIF file for compound **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO061440X