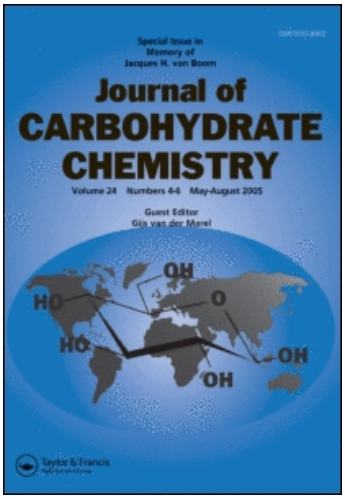

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

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Online publication date: 12 March 2003

To cite this Article Darwish, Omar S. , Callam, Christopher S. , Hadad, Christopher M. and Lowary, Todd L.(2003) 'Regioselectivity in Alkylation Reactions of 1,2-*O*-Stannylene Acetals of d-Arabinofuranose', Journal of Carbohydrate Chemistry, 22: 9, 963 — 981
To link to this Article: DOI: 10.1081/CAR-120026604
URL: http://dx.doi.org/10.1081/CAR-120026604

JOURNAL OF CARBOHYDRATE CHEMISTRY
Vol. 22, No. 9, pp. 963–981, 2003

Regioselectivity in Alkylation Reactions of 1,2-*O*-Stannylene Acetals of D-Arabinofuranose

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ABSTRACT

The synthesis of β-arabinofuranosides via alkylation of 1,2-*O*-stannylene acetal intermediates has been studied. With reactive alkyl halides (benzyl bromide, allyl bromide, and *p*-methoxybenzyl chloride), the method provides a mixture of β-arabinofuranosides and 2-*O*-alkylated lactols in ratios of 4:1 to 1:1.5. However, with carbohydrate-derived electrophiles, no alkylated products are produced. It appears, therefore, that the method is limited to the preparation of β-arabinofuranosides of simple alcohols. Through the use of computational chemistry, we have explored the conformational properties of one of these stannylene acetals and propose that these species exist in more than one conformation in solution and that this contributes to the relatively poor regioselectivity in these reactions.

Key Words: Stannylene acetal; β-arabinofuranosides; Glycosylation; Alkylation.

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DOI: 10.1081/CAR-120026604
0732-8303 (Print); 1532-2327 (Online)

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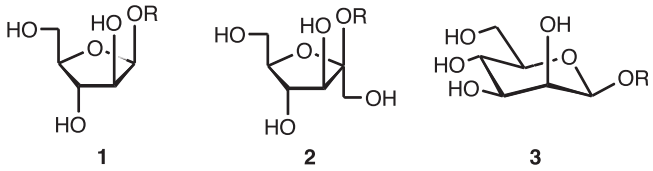

Scheme 1. Representative examples of a β-arabinofuranoside (**1**), a β-fructofuranoside (**2**) and a β-mannopyranoside (**3**).

INTRODUCTION

Polysaccharides containing β-arabinofuranosyl residues (**1**, Scheme 1) are important structural components of the mycobacterial cell wall.[1,2] Recent interest[3,4] in identifying inhibitors of the enzymes involved in the biosynthesis of these glycans has prompted the development of new methods for the synthesis of β-arabinofuranosides,[5–10] as convenient access to fragments of these polysaccharides is needed for fundamental biochemical investigations aimed ultimately at drug and vaccine development.[11–15] The stereoselective synthesis of β-arabinofuranosides, as well as the related β-fructofuranosides (**2**), is plagued by the same problems that complicate the preparation of the stereochemically analogous β-mannopyranosides (**3**).[16,17] However, in contrast to the significant body of work that has addressed the stereoselective synthesis of β-mannopyranosides,[16,17] the preparation of 1,2-*cis*-β-furanosides has received relatively little attention until recently.[5–10,18–20]

Shown in Figure 1 is a straightforward approach for the synthesis of β-mannopyranosides (or β-rhamnopyranosides) that was developed by Hodosi and Kovac.[21,22] The method involves the treatment of a reducing sugar (**4**) with dibutyltin oxide to produce the corresponding stannylene acetal (**5**), which is subsequently reacted with an electrophile to generate the β-glycoside (**6**) in a stereoselective fashion. This work extends earlier investigations on the alkylation of 1,2-*O*-stannylene acetals with simple alkyl halides, which led to the production of β-mannopyranosides,[23,24] α-glucopyranosides,[23] and α-ribofuranosides.[25] The simplicity of this approach, coupled with the ready availability of 3,5-protected arabinofuranose derivatives (e.g., **7**, Figure 2), prompted us to explore this method for the synthesis of β-arabinofuranosides.

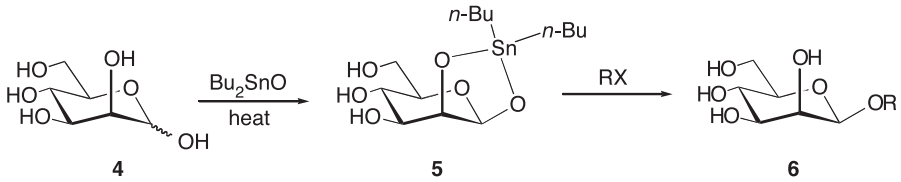

Figure 1. Stannylene acetal approach to β-mannopyranosides developed by Hodosi and Kovác.

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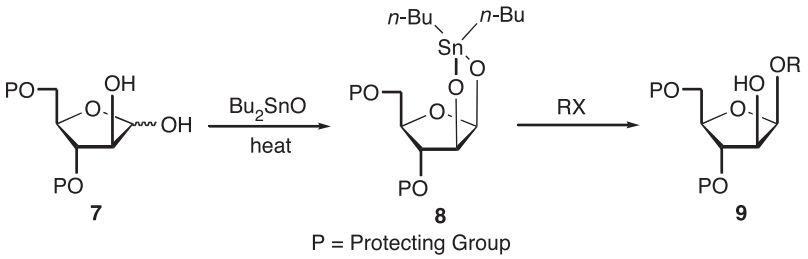


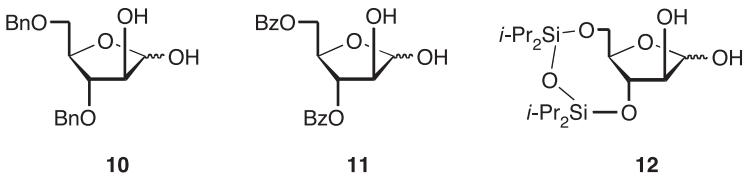
Figure 2. Proposed synthesis of β-arabinofuranosides via the stannylene acetal approach.

RESULTS AND DISCUSSION

In exploring the potential of the route shown in Figure 2 for the synthesis of β-arabinofuranosides, we chose to probe the effect that the O-3 and O-5 protecting groups had on the outcome of the reaction. We therefore chose diols **10**–**12** (Scheme 2) as substrates. Compounds **10**[26] and **11**[27] were synthesized as previously reported. The preparation of **12** (Figure 3) was achieved from the known thioglycoside **13**,[28] upon treatment with *N*-iodosuccinimide and silver triflate in wet acetonitrile. This reaction afforded **12** in 78% yield as a 1:2.3 α:β mixture of isomers.

With all three substrates in hand, we explored the synthesis of simple alkyl glycosides via the route outlined in Figure 2. A number of reaction conditions were explored, and we found that the best results were obtained when the glycosylation was carried out by heating a solution of the diol (e.g., **10**) with dibutyltin oxide in toluene at reflux for 30 minutes, followed by addition of the electrophile and *n*-Bu_4NBr. The progress of the reaction was monitored by TLC and was stopped after no change was observed. In our initial series of reactions, we employed *p*-methoxybenzyl chloride, benzyl bromide, or allyl bromide as the electrophile. The results of these reactions are presented in Table 1; the structures of the products are provided in Scheme 3.

From the data presented in Table 1 it is clear that this approach is of limited utility for the stereocontrolled synthesis of β-arabinofuranosides in high yield. As hoped, the reaction produces the desired β-glycoside (e.g., **14**) and none of the corresponding α-glycoside was detected. However, in all cases, the reaction also produces significant quantities of the isomeric 2-*O*-alkylated product (e.g., **15**) as a byproduct. These lactol byproducts were each isolated as an α/β mixture that was inseparable by chromatography.



Scheme 2. Glycosyl donors **10**–**12**.

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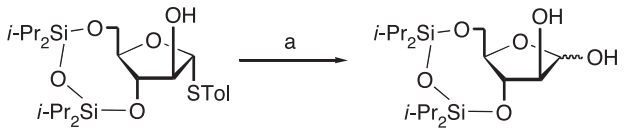
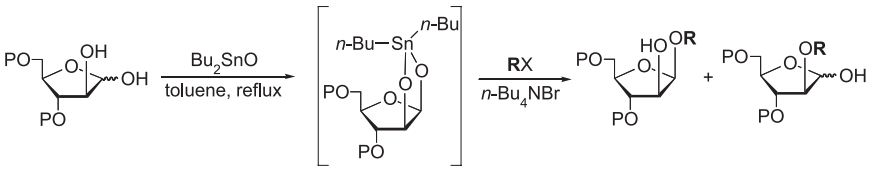


Figure 3. Synthesis of **12**, (a) NIS, AgOTf, CH_3CN, H_2O, 0 °C, 78%.

^1H and ^{13}C NMR spectroscopy were used to determine the structures of the products. In the ^1H NMR spectra of the β-glycosides, the resonance for the anomeric hydrogen appeared as a doublet ($J \sim 4.5$ Hz) between 5.0 and 5.2 ppm. The ^{13}C NMR spectra of these compounds showed a resonance for the anomeric carbon in the range of 99–102 ppm. Both of these features are diagnostic for β-arabinofuranosides.[29] Had the α-glycosides been produced, the resonances for the anomeric hydrogens would have appeared in the ^1H NMR spectra as singlets, or doublets with a smaller coupling constant ($J \sim 1.5$ Hz) and the resonances for the anomeric carbons would have been found in the ^{13}C NMR spectra above 105 ppm.[29] The identity of the lactols was easily ascertained from ^{13}C NMR spectra, which showed two resonances in the region

Table 1. Use of 1,2-*O*-stannylene acetals in the synthesis of β-arabinofuranosides.



Substrate	Alkyl halide	Reaction time (h)	Isolated yield (%)	Products (ratio)[a]
10	AllBr	3	52	**14**:**15** (1.7:1)
10	BnBr	1	61	**16**:**17** (1.8:1)
10	PMBCl	0.25	72	**18**:**19** (1:1)
11	AllBr	3	20	**20**:**21** (2:1)
11	BnBr	3	42	**22**:**23** (4:1)
11	PMBCl	3	59	**24**:**25** (1.5:1)
12	AllBr	7	59	**26**:**27** (1:1.5)
12	BnBr	7	73	**28**:**29** (1.3:1)
12	PMBCl	7	81	**30**:**31** (1.3:1)

[a]Ratio determined from mass of isolated products.

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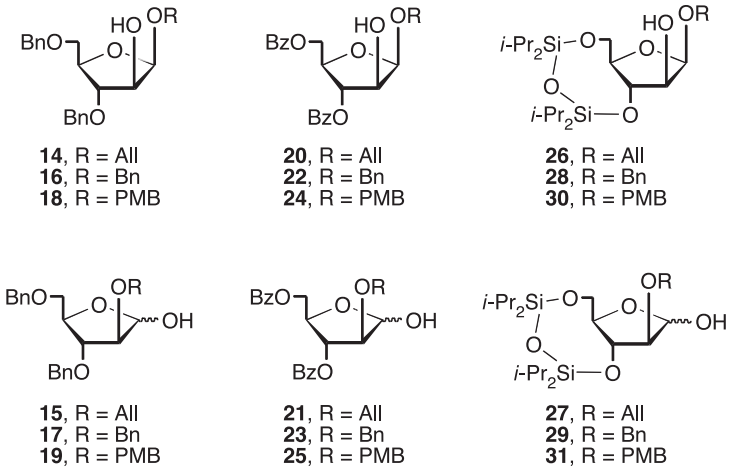
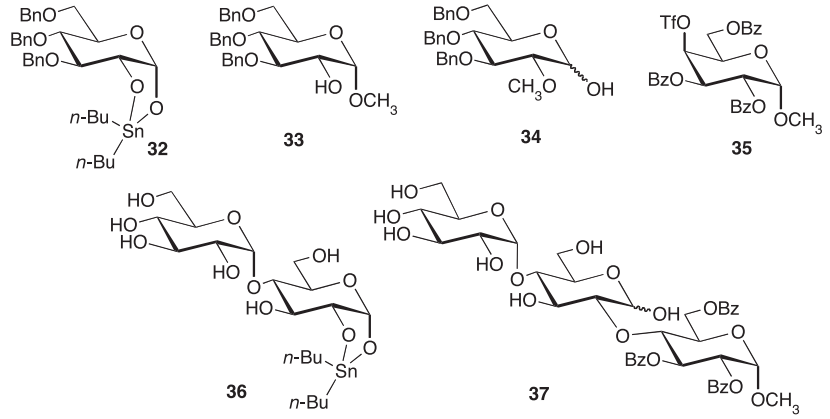


Scheme 3. Structures of products produced in alkylation reactions.

between 94 and 102 ppm, corresponding to C-1 in the α and β reducing sugars. The presence of the two isomers was also clearly visible in the ^{1}H NMR spectrum; however, due to spectral overlap it was sometimes difficult to assign the signals arising from the anomeric hydrogen in both anomers. In the case of **17**, further proof for the structure was obtained by comparison with the ^{1}H and ^{13}C NMR data for the known compound,[30] which is commercially available.

The overall alkylation yields ranged from 20–80% and the best results were obtained when *p*-methoxybenzyl chloride was used as the electrophile. With regard to the donor substrates, the benzylated and silylated donors **10** and **12** gave modest to good combined yields of the alkylated products. The yields were slightly better with **12** as compared to **10**; however, the regioselectivity in favor of the β-glycoside was marginally higher when **10** was used as the donor. It is perhaps not unexpected that the benzoylated substrate, **11**, gave the lowest overall yields. The electron-withdrawing ability of the ester protecting groups on **11** would be expected to reduce the nucleophilicity of the stannylene acetal oxygens through an inductive effect.

To rationalize the regioselectivity of these reactions, we considered first the factors that govern alkylations of stannylene acetals. In reactions involving stannylene acetals formed from non-anomeric *cis*-diols on pyranose rings, the equatorial oxygen is almost always the site of predominant reaction.[31,32] Although these stannylene acetals are known to aggregate in solution, when halide salts are added to promote the reaction (as in the present case), it is believed that they react through their monomeric forms.[31] An important consideration is that the relative rigidity of the pyranose ring ensures that the molecule adopts a single major conformation in solution, at least with respect to the relative orientation of O-1 and O-2, and thus the regioselectivity is generally high. However, anomalous results have been obtained. For example, Srivastava and Schuerch reported[23] that reaction of methyl iodide with stannylene acetal **32** (Scheme 4) provided a 7:3 mixture of α-glycoside **33** and the 2-*O*-alkylated lactol **34**. It was subsequently shown[22] that treatment of triflate **35** with the maltose-derived stannylene

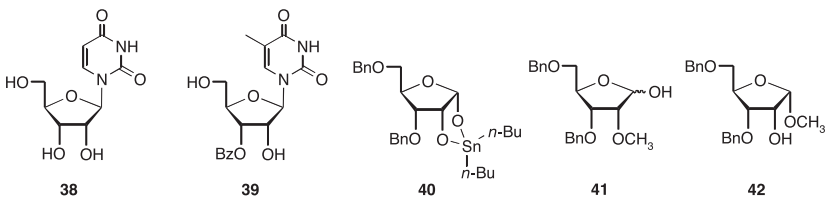


Scheme 4. Compounds **32–37**.

acetal **36** yielded the 2-*O* alkylated product **37** in 75% yield and no mention was made of the formation of the corresponding glycoside.

The paucity of previous investigations on organotin-mediated reactions on furanose rings makes it difficult to draw substantially on literature precedence when proposing an explanation for the regioselectivity observed in the alkylation reactions of these arabinofuranose systems. Although some of the first demonstrated examples of stannylene acetals in protecting group chemistry were carried out on nucleosides,[33] relatively little additional work has been done on these systems to date.[25,34,35] In the initial paper by Moffat and coworkers,[33] acylations of ribonucleosides (e.g., **38**, Scheme 5) via stanylene acetals were investigated. In general, alkylation of O-3 predominated (e.g., **39**), however, determining the inherent regioselectivity of the process was complicated by the tendency of the acyl group on O-2 to migrate to O-3. A paper more directly relevant to the present work describes the alkylation of stannylene acetal **40**.[36,37] When methyl iodide was used as the electrophile, a mixture of 2-*O*-methyl lactol (**41**) and α-glycoside (**42**) were produced in 1:1 ratio, whereas benzyl bromide afforded the α-glycoside as the major product over the corresponding lactol (83%:13%).

Furanose rings are inherently more flexible than their pyranose counterparts, and the substituents on a five membered ring adopt pseudo-axial or pseudo-equatorial orientations rather than classical axial or equatorial arrangements. Mindful of this issue,



Scheme 5. Compounds **38–42**.

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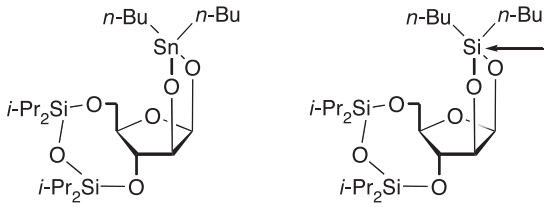


43 **44**

Scheme 6. Comparison of **43** and **44**.

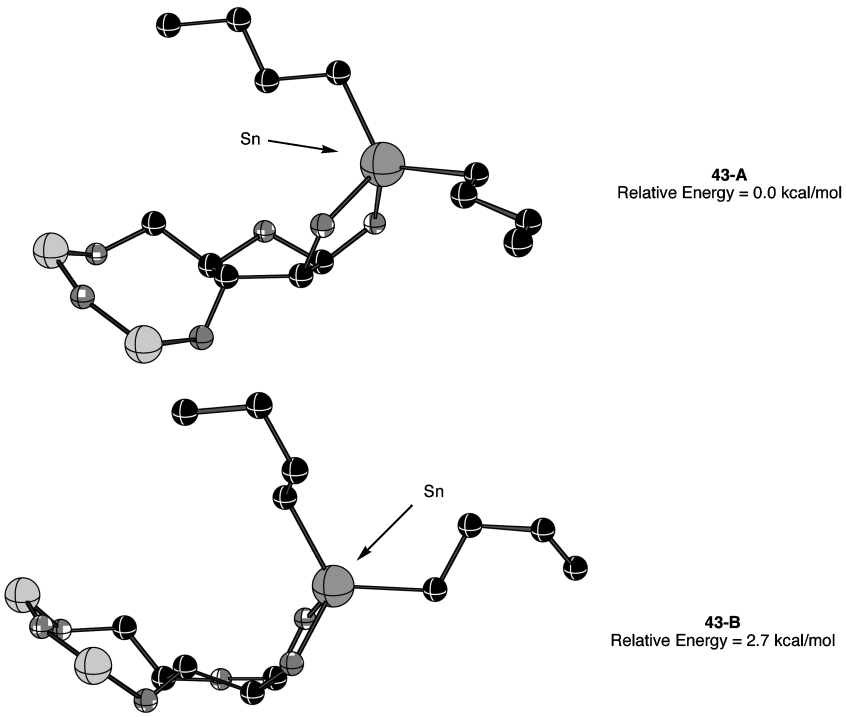
we envisioned two possible explanations for the poor regioselectivity observed in these alkylation reactions. One possibility is that in the stannylene acetal intermediate the pseudo-axial/pseudo-equatorial placement of both oxygens does not lead to sufficient steric differentiation and therefore they compete for the electrophile. Another plausible explanation is that the stannylene acetal adopts two or more low energy conformations in which the relative orientations of O-1 and O-2 differ, e.g., O-1 is pseudo-axial in one conformer and pseudo-equatorial in another. An erosion in regioselectivity would be expected to result from the reaction of both conformers with the electrophile. Under either scenario, it could be expected that changes in reaction conditions (e.g., protecting groups on the donor, the electrophile used) would influence the regioselectivity of the reaction, as is observed in the results presented in Table 1.

In an effort to probe these hypotheses we carried out density functional theory[36,37] calculations on stannylene acetal, **43** (Scheme 6), the species formed upon reaction of **12** with dibutyltin oxide. This substrate was chosen as the yields of these reactions were the best of the three donors explored. The general flexibility of the ring was of concern and so we began by generating a diverse family of conformers using the Systematic Pseudo Monte Carlo (SPMC) search protocol as implemented in MacroModel version 6.5.[38,39] A limitation in the application of MacroModel to this problem is that it is not parameterized for tin and therefore the SPMC search was carried out on an analog (**44**, Scheme 6) in which the tin atom was replaced with silicon. As the purpose of the search was simply to generate diverse geometries for higher level calculations, we viewed the tin/silicon replacement as a reasonable alternative to the manual generation of a large number of initial starting geometries via an approach that would necessarily be biased by intuition.

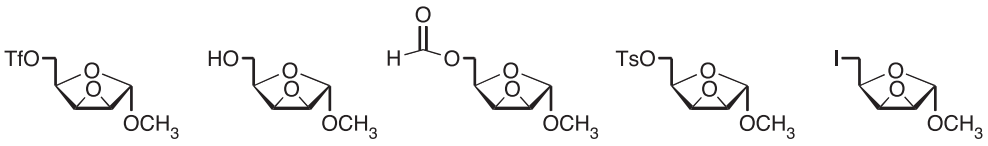
A total of 10,000 structures of **44** were generated by the SPMC search, which were then minimized in the gas phase at the AM1[40] level of theory, yielding a family of 113 conformers, all of which were within 32 kcal/mol of the lowest energy structure. Clustered around the global minimum was a group of four structures that all possessed similar furanose ring conformations. A second family of six conformers, all possessing a common furanose ring conformation, was present $\sim$ 1.1 kcal/mol above the global minimum (see Experimental Section for additional details). The other 103 conformers obtained after AM1 optimization were more than 3.0 kcal/mol above the global minimum structure. The lowest AM1 energy structures from each of these two families of conformers were then taken, the silicon atom connecting O-1 and O-2 replaced with tin, and the resulting structures were subjected to higher level calculations as outlined in the Experimental section. The optimized geometries for these conformers (**43**-**A** and

43-**B**) are shown in Scheme 7 (all hydrogens and the alkyl groups on the siloxane moiety are omitted for clarity). The furanose ring in **43**-**A** adopts an ^{O}E conformation, which places O-1 pseudo-equatorial and O-2 pseudo-axial; in **43**-**B** the ring is in a $^{3}T_{2}$ conformation, in which O-2 is pseudo-equatorial and O-1 is pseudo-axial. Thus, the orientation of O-1 and O-2 differ in these two structures. Based upon our calculations, these two conformers differ by 2.7 kcal/mol, with **43**-**A** being of lower energy.

These calculations suggest that the furanose ring in stannylene acetal **43** exists in (at least) two conformations in which the relative pseudo-axial/pseudo-equatorial orientations of O-1 and O-2 differ. Moreover, the differences in energy between these conformers, **43**-**A** and **43**-**B**, are relatively small and, given the relatively low interconversion barriers typically seen for furanose rings,[41] it is reasonable to expect that these isomers interconvert rapidly, especially under the elevated temperatures at which these reactions are carried out. Taken together, these data suggest that the low regioselectivity observed in the alkylation reactions in these systems is the result of the presence of more than one stannylene acetal conformer, which react with electrophiles at O-1 and O-2 to varying degrees. We note that we have examined only the thermodynamically most stable conformers and it is possible (likely) that other reactive conformers may also be present. Under these conditions, it is plausible that the regioselectivity of the reaction is influenced not only by these conformational effects, but also by the donor substrates and reaction conditions. For example, in the results presented in Table 1, the benzoylated



Scheme 7. B3LYP-optimized geometries of **43-A** and **43-B**. For clarity, all hydrogen atoms as well as carbon atoms of the siloxane acetal and butyl groups have been deleted.



45 **46** **47** **48** **49**

Scheme 8. Compounds **45–49**.

donor **11** gave the highest regioselectivity in the alkylation reactions. The electron-withdrawing ability of the benzoyloxy group at C-3 can be invoked to rationalize this observation. The closer proximity of this protecting group to O-2 would be expected to decrease the nucleophilicity of this oxygen relative to O-1.

Despite the relatively modest results in the alkylation reactions with the simple electrophiles, we explored the possibility of synthesizing oligosaccharides via this approach. As a simple model carbohydrate electrophile, we chose triflate **45** (Scheme 8), which was prepared from the known alcohol **46**[42] upon treatment with triflic anhydride and pyridine. However, upon reaction of **45** with the stannylidene acetal generated from **12**, no alkylated products could be isolated. Earlier reports[22] have demonstrated that polar solvents can also be used to promote these alkylation reactions. The reaction was therefore repeated by generating the stannylene acetal and then adding **45** and DMF. However, when these conditions were used, no disaccharide was formed; rather, the formate ester **47** was produced in modest (39%) yield. The production of formate esters as byproducts in these reactions has been previously reported[22] and has been minimized by carrying out the reaction at reduced temperatures. However, in our hands, cooling the reaction mixture to room temperature led to the formation of no alkylated products. As a final attempt to prepare a disaccharide, we synthesized the iodide **49** (via tosylate **48**) and reacted it with stannylene acetal **12** and *n*-Bu_4NBr in toluene at reflux. However, no alkylated products were produced.

CONCLUSIONS

In conclusion, the stereoselective synthesis of β-arabinofuranosides in high yields was shown to be unsuccessful via of the 1,2-*O*-stannylene approach. Although the formation of the α-glycoside was avoided, our results with simple electrophiles demonstrated that the reactivity difference between the O-1 and O-2 is small. We propose that in these furanose ring systems, more than one reactive stannylene acetal conformer is present and they collectively contribute to the decrease in regioselectivity observed in these alkylation reactions. This contrasts to the application of this method to the synthesis of β-mannopyranoside or β-rhamnopyranosides, where the rigid nature of the pyranose ring orients the tin acetal oxygen atoms in distinctly different steric environments. In the course of our investigations, Oscarsson and coworkers reported a study in which the stereoselective synthesis of β-fructofuranosides (e.g., **2**, Scheme 1) via stannylene acetals was explored.[18] When a benzylated species analogous to **10** was

used as the donor and allyl bromide was employed as the electrophile, the desired fructofuranosides were produced as a 1:4.6 α/β mixture. Interestingly, no products arising from alkylation at the non-anomeric oxygen were reported; however, as in our investigations, the use of carbohydrate electrophiles gave no disaccharide products. These results, together with ours and earlier work by Klein[25] and coworkers, suggest the 1,2-*O*-stannylene acetal glycosylation methodology is of limited utility for the stereocontrolled synthesis of 1,2-*cis*-furanosides in high yield.

EXPERIMENTAL

Solvents were distilled from the appropriate drying agents before use. Unless stated otherwise, all reactions were carried out under a positive pressure of argon and were monitored by TLC on silica gel 60 F_{254} (0.25 mm, E. Merck). Spots were detected under UV light, by charring with 10% H_2SO_4 in ethanol, or by charring with anisaldehyde in ethanol. Solvents were evaporated under reduced pressure and below 40°C (bath). Column chromatography was performed on silica gel 60 (40–60 μM). The ratio between silica gel and crude product ranged from 100 to 50:1 (w/w). Optical rotations were measured at 21 ± 2°C. ^{1}H NMR spectra were recorded at 400 or 500 MHz, and chemical shifts are referenced to TMS (0.0, $CDCl_3$). ^{13}C NMR spectra were recorded at 100 or 125 MHz, and ^{13}C chemical shifts are referenced to $CDCl_3$ (77.00, $CDCl_3$). Elemental analyses were performed by Atlantic Microlab Inc., Norcross, GA. Electrospray mass spectra were recorded on samples suspended in THF or CH_3OH with added NaCl.

3,5-*O*-(Tetraisopropylsiloxane-1,3-diyl)-D-arabinofuranose (12). Thioglycoside **13** (990 mg, 2.0 mmol) was dissolved in acetonitrile (10 mL) and water (2 mL) and the mixture was cooled to 0°C. *N*-iodosuccinimide (0.49 g, 2.2 mmol) and silver triflate (0.13 g, 0.5 mmol) were added to the reaction mixture and, after stirring for 5 min, triethylamine (1.0 mL) was added and the mixture was filtered through Celite. The filtrate was diluted with CH_2Cl_2, washed with water, and the organic layer was dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (hexane/EtOAc, 2:1) to give **12** (600 mg, 78%) as a clear syrup: R_f 0.3 (hexane/EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 5.25 (d, 0.7 H, J = 4.7 Hz), 5.22 (d, 0.3 H, J = 2.8 Hz), 4.31–3.63 (m, 6 H), 2.70 (br s, 1 H), 1.10–0.94 (m, 28 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 101.9, 95.0, 82.8, 81.7, 78.6, 78.4, 78.1, 73.0, 66.3, 65.3, 17.9 (2), 17.80 (2), 17.7 (3), 17.5 (2), 17.4 (4), 13.9, 13.6, 13.2, 12.9 (2).

Anal. Calcd for $C_{17}H_{36}O_6Si_2$ (398.1366): C, 52.00; H, 9.24. Found: C, 51.98; H, 9.21.

General procedure for glycosylation reactions. A mixture of the diol (1.3 mmol), and dibutyltin oxide (1.5 mmol) was heated at reflux in toluene (15 mL) for 30 min. The electrophile (1.9 mmol) and *n*-Bu_4NBr (1.2 mmol) were then added and stirring with heating continued until there was no change in the progress of the reaction as monitored by TLC. The reaction mixture was cooled, concentrated, and the products were purified by column chromatography.

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Allyl 3,5-di-*O*-benzyl-β-D-arabinofuranoside (14) and 2-*O*-Allyl-3,5-di-*O*-benzyl-D-arabinofuranose (15). The crude mixture resulting from the reaction of **10** and allyl bromide was purified by chromatography (hexane/EtOAc, 5:1) to give **14** (39%) and **15** (24%) as clear oils. **14**: R_f 0.5 (hexane/EtOAc, 2:1); $[\alpha]_D$ − 34.9° (*c* 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 7.33–7.27 (m, 10 H), 5.88–5.81 (m, 1 H), 5.23 (ddd, 1 H, *J* = 17.2, 3.1, 1.6 Hz), 5.17 (ddd, 1 H, *J* = 10.4, 2.7, 1.3 Hz), 5.00 (d, 1 H, *J* = 4.7 Hz), 4.75 (d, 1 H, *J* = 11.9 Hz), 4.65 (d, 1 H, *J* = 12.3 Hz), 4.60–4.52 (m, 2 H), 4.26 (m, 2 H), 4.14 (dd, 1 H, *J* = 11.3, 5.6 Hz), 4.04–3.99 (m, 1 H), 3.86 (t, 1 H, *J* = 5.8 Hz), 3.53 (d, 2 H, *J* = 5.7 Hz), 2.62 (br d, 1 H, *J* = 7.9 Hz); ^{13}C NMR (100 MHz $CDCl_3$, δ_C) 138.5 (2), 134.2, 129.0, 128.8. 128.2, 128.1, 118.1, 101.2, 85.2, 81.3, 78.5, 73.7, 72.5, 72.3, 69.1.

Anal. Calcd for $C_{22}H_{26}O_5$ (370.18): C, 71.33; H, 7.07. Found: C, 71.39; H, 7.10.

15: R_f 0.4 (hexane/EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 7.35–7.25 (m, 10 H), 5.91–5.79 (m, 1 H), 5.34–5.16 (m, 3 H), 4.62–4.45 (m, 4 H), 4.11–3.89 (m, 5 H), 3.80 (d, 0.4 H, *J* = 6.0 Hz), 3.58–3.49 (m, 2 H), 3.32 (d, 0.6 H, *J* = 7.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 138.5, 138.3, 137.9, 137.7, 134.4, 134.3, 128.9, 128.8, 128.4, 128.3, 128.2 (2), 128.1, 118.3, 117.9, 101.5, 96.6, 86.8, 84.5, 83.1, 82.4, 82.2, 80.8, 74.0, 73.8, 72.5, 72.4, 71.7, 71.1, 70.9, 70.6. HRMS (ESI) Calcd for $C_{22}H_{26}O_5$ $[M + Na]^+$ 393.1672. Found 393.1709.

Benzyl 3,5-di-*O*-benzyl-β-D-arabinofuranoside (16) and 2,3,5-Tri-*O*-benzyl-D-arabinofuranose (17). The crude mixture resulting from the reaction of **10** and benzyl bromide was purified by chromatography (hexane/EtOAc, 4:1) to give **16** (39%) as a clear oil and **17**[27] (22%) as a white solid. **16**: R_f 0.5 (hexane/EtOAc, 2:1); $[\alpha]_D$ − 40.2° (*c* 0.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 7.35–7.19 (m, 15 H), 5.07 (d, 1 H, *J* = 4.7 Hz), 4.78 (d, 1 H, *J* = 8.0 Hz), 4.75 (d, 1 H, *J* = 8.3 Hz), 4.63–4.48 (m, 4 H), 4.27 (t, 1 H, *J* = 5.4 Hz), 4.17 (dd, 1 H, *J* = 11.3, 5.6 Hz), 3.89 (t, 1 H, *J* = 5.9 Hz), 3.56 (d, 2 H, *J* = 5.7 Hz), 2.58 (br s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 138.0 (2), 137.1, 128.5, 128.4 (2), 128.2, 128.0, 127.8, 127.7 (2), 100.8, 84.7, 81.0, 78.1, 73.3, 72.0 (2), 69.7.

Anal. Calcd for $C_{26}H_{28}O_5$ (420.19): C, 74.26; H, 6.71. Found: C, 74.05; H, 6.66.

17: R_f 0.3 (hexane/EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 7.34–7.24 (m, 15 H), 5.38 (d, 0.2 H, *J* = 7.7 Hz), 5.32 (dd, 0.8 H, *J* = 9.9, 4.3 Hz), 4.66–4.44 (m, 6 H), 4.17–4.14 (m, 0.8 H), 4.10–4.07 (m, 0.8 H), 4.02–3.97 (m, 1.4 H), 3.85 (d, 0.8 H, *J* = 10.0 Hz), 3.62–3.49 (m, 2 H), 3.23 (d, 0.2 H, *J* = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 138.5, 138.3, 137.86, 137.9, 137.7, 129.0, 128.9, 128.8, 128.5, 128.4, 128.3 (2), 128.2 (2), 128.1, 101.6, 96.7, 86.9, 84.5, 83.1, 82.5, 82.3, 81.0, 77.8, 74.0, 73.8, 72.7, 72.5, 72.4, 72.2, 71.0, 70.6. HRMS (ESI) Calcd for $C_{26}H_{28}O_5$ $[M + Na]^+$ 443.1834. Found 443.1829.

***p*-Methoxybenzyl 3,5-di-*O*-benzyl-β-D-arabinofuranoside (18) and 3,5-Di-*O*-benzyl-2-*O*-*p*-methoxybenzyl-D-arabinofuranose (19).** The crude mixture resulting from the reaction of **10** and *p*-methoxybenzyl chloride was purified by chromatography (hexane/EtOAc, 3:1) to give **18** (36%) and **19** (36%) both as white solids. **18**: R_f 0.3

(hexane/EtOAc, 2:1); mp 41–44°C; $[\alpha]_D$ − 25.5° (*c* 0.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ_H) 7.33–7.25 (m, 10 H), 7.18 (d, 2 H, *J* = 8.4 Hz), 6.83 (d, 2 H, *J* = 8.4 Hz), 5.04 (d, 1 H, *J* = 4.6 Hz), 4.75 (d, 1 H, *J* = 11.9 Hz), 4.70 (d, 1 H, *J* = 11.2 Hz), 4.62–4.55 (m, 3 H), 4.42 (d, 1 H, *J* = 11.2 Hz), 4.27–4.23 (m, 1 H), 4.17 (dd, 1 H, *J* = 11.2, 5.6 Hz), 3.87 (t, 1 H, *J* = 5.9 Hz), 3.78 (s, 3 H), 3.56 (d, 2 H, *J* = 5.6 Hz), 2.62 (d, 1 H, *J* = 9.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 159.9, 138.5 (2), 130.4, 129.6, 128.9, 128.8, 128.2, 128.1 (2), 114.3, 101.0, 85.1, 81.3, 78.5, 73.8, 72.5, 72.3, 69.8, 55.7.

Anal. Calcd for $C_{27}H_{30}O_6$ (450.20): C, 71.98; H, 6.71. Found: C, 71.87; H, 6.68.

19: R_f 0.2 (hexane/EtOAc, 2:1); ^1H NMR (500 MHz, $CDCl_3$, δ_H) 7.40–7.30 (m, 10 H), 7.24 (d, 1 H, *J* = 6.9 Hz), 6.96–6.91 (m, 3 H), 5.40–5.35 (m, 1 H), 4.66–4.54 (m, 6 H), 4.52–4.42 (m, 1 H), 4.20–4.12 (m, 1 H), 4.06–3.95 (m, 1 H), 3.86 (s, 3 H), 3.66–3.52 (m, 2 H), 3.40 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 160.0, 159.9, 159.7, 138.5, 138.3, 137.9, 137.8, 133.6, 130.2, 129.9, 129.8, 129.1, 128.9, 128.9, 128.8, 128.4, 128.3 (3), 128.2, 128.20, 128.1, 114.4 (2), 101.6, 96.7, 86.7, 84.1, 83.2, 82.4, 82.3, 80.9, 74.0, 73.78, 72.4 (2), 71.9, 71.0, 70.7, 65.4, 55.7 (2). HRMS (ESI) Calcd for $C_{27}H_{30}O_6$ $[M + Na]^+$ 473.1940. Found 473.1941.

Allyl 3,5-di-*O*-benzoyl-β-D-arabinofuranoside (20) and 2-*O*-Allyl-3,5-di-*O*-benzoyl-D-arabinofuranose (21). The crude mixture resulting from the reaction of **11** and allyl bromide was purified by chromatography (hexane/EtOAc, 5:1) to give **20** (13%) and **21** (7%) as white solids. **20**: R_f 0.4 (hexane/EtOAc, 2:1); mp 60–64°C; $[\alpha]_D$ − 54.1° (*c* 0.03, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ_H) 8.06–8.04 (m, 4 H), 7.61–7.37 (m, 2 H), 7.47–7.37 (m, 4 H), 5.94–5.84 (m, 1 H), 5.49 (t, 1 H, *J* = 6.0 Hz), 5.28 (ddd, 1 H, *J* = 17.2, 2.9, 1.4 Hz), 5.20 (dd, 1 H, *J* = 10.4 Hz), 5.15 (d, 1 H, *J* = 4.7 Hz), 4.67 (dd, 1 H, *J* = 11.7, 4.5 Hz), 4.55 (dd, 1 H, *J* = 11.7, 6.5 Hz), 4.50 (dd, 1 H, *J* = 6.5, 4.7 Hz), 4.43–4.39 (m, 1 H), 4.34–4.29 (m, 1 H), 4.12–4.07 (m, 1 H), 2.55 (br s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 166.5, 166.2, 133.5, 133.4, 133.0, 129.9 (2), 129.8, 129.2, 128.5, 128.4, 118.2, 100.5, 79.9, 79.3, 76.7, 69.0, 65.6.

Anal. Calcd for $C_{22}H_{22}O_7$ (398.1366): C, 66.32; H, 5.57. Found: C, 66.08; H, 5.70.

21: R_f 0.3 (hexane/EtOAc, 2:1); ^1H NMR (400 MHz, $CDCl_3$, δ_H) 8.09–8.04 (m, 4 H), 7.59–7.40 (m, 6 H), 5.94–5.87 (m, 1 H), 5.57–5.20 (m, 4 H), 4.73–4.55 (m, 3 H), 4.26–4.12 (m, 3 H), 3.90 (d, 0.3 H, *J* = 9.6 Hz), 2.77 (d, 0.7 H, *J* = 4.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 166.2, 166.1, 134.1 (2), 133.7, 133.9, 133.5, 130.3, 130.2, 129.0 (2), 128.8 (2), 118.3, 102.1, 88.7, 88.5, 87.7, 87.4, 78.6, 71.4, 65.5, 64.9.

Anal. Calcd for $C_{22}H_{22}O_7$ (398.1366): C, 66.32; H, 5.57. Found: C, 66.06; H, 5.70.

Benzyl 3,5-di-*O*-benzoyl-β-D-arabinofuranoside (22) and 3,5-di-*O*-benzoyl-2-*O*-benzyl-D-arabinofuranose (23). The crude mixture resulting from the reaction of **11** and benzyl bromide was purified by chromatography (hexane/EtOAc, 5:1) to give **22** (34%) and **23** (8%) both as white solids. **22**: R_f 0.5 (hexane/EtOAc, 2:1); mp 85–87°C; $[\alpha]_D$ − 48.1° (*c* 0.04, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ_H) 8.05–8.03 (m, 4 H), 7.59–7.29 (m, 11 H), 5.51 (t, 1 H, *J* = 6.1 Hz), 5.19 (d, 1 H, *J* = 4.7 Hz), 4.86 (d, 1

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H, J = 11.7 Hz), 4.68 (dd, 1 H, J = 11.7, 4.4 Hz), 4.60 (d, 1 H, J = 11.7 Hz), 4.58 (dd, 1 H, J = 11.7, 6.6 Hz), 4.50 (ddd, 1 H, J = 10.1, 5.4, 3.6 Hz), 4.44–4.40 (m, 1 H), 2.94 (d, 1 H, J = 10.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 166.8, 166.6, 137.0, 133.9, 133.5, 130.3 (2), 129.7, 129.0, 128.9, 128.8, 128.7, 128.6, 100.9, 80.2, 79.8, 77.1, 70.5, 66.1.

Anal. Calcd for $C_{26}H_{24}O_7$ (448.1522): C, 69.63; H, 5.39. Found: C, 69.37; H, 5.53.

23: R_f 0.4 (hexane/EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 8.06–8.03 (m, 4 H), 7.48–7.25 (m, 11 H), 5.60–5.46 (m, 2 H), 4.89–4.56 (m, 5 H), 4.38–4.34 (m, 0.3 H), 4.20 (br s, 0.4 H), 4.12 (dd, 0.3 H, J = 4.0, 2.7 Hz), 3.90 (br s, 0.3 H), 2.80 (br s, 0.7 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 166.8, 166.3, 137.6, 137.0, 134.1, 134.0, 133.4, 130.3, 130.2 (2), 129.7, 129.1, 129.0 (2), 128.9, 128.8, 128.7, 128.6, 128.4, 128.3, 102.1, 97.7, 87.6, 81.9, 81.5, 79.5, 78.5, 77.1, 73.3, 72.5, 65.5, 64.8. HRMS (ESI) Calcd for $C_{26}H_{24}O_7$ $[M + Na]^+$ 471.1320. Found 471.1432.

***p*-Methoxybenzyl-3,5-di-*O*-benzoyl-β-D-arabinofuranoside (24) and 3,5-Di-*O*-benzoyl-2-*O*-*p*-methoxybenzyl-D-arabinofuranose (25).** The crude mixture resulting from the reaction of **11** and *p*-methoxybenzyl chloride was purified by chromatography (hexane/EtOAc, 5:1) to give **24** (35%) and **25** (24%) both as white solids. **24**: R_f 0.3 (hexane/EtOAc, 2:1); mp 60–64°C; $[\alpha]_D$ − 42.2° (c 0.03, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.11–8.09 (m, 4 H), 7.63 (t, 1 H, J = 7.4 Hz), 7.58 (t, 1 H, J = 7.4 Hz), 7.49 (t, 2 H, J = 7.8 Hz), 7.42 (t, 2 H, J = 7.8 Hz), 7.30 (d, 2 H, J = 8.6 Hz), 6.90 (d, 2 H, J = 8.5 Hz), 5.54 (t, 1 H, J = 6.0 Hz), 5.23 (d, 1 H, J = 4.7 Hz), 4.85 (d, 1 H, J = 11.3 Hz), 4.73 (dd, 1 H, J = 11.7, 4.3 Hz), 4.64 (dd, 1 H, J = 11.7, 6.7 Hz), 4.59 (d, 1 H, J = 11.3 Hz), 4.54 (dd, 1 H, J = 6.4, 4.8 Hz), 4.49–4.45 (m, 1 H), 3.84 (s, 3 H), 2.67 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 166.8, 166.6, 160.0, 133.9, 133.4 (2), 130.3, 130.2, 129.7, 129.1, 128.9, 128.8, 114.4, 100.6, 80.3, 79.9, 77.1, 70.2, 66.1, 55.7. HRMS (ESI) Calcd for $C_{27}H_{26}O_8$ $[M + Na]^+$ 501.1525. Found 501.1521.

25: R_f 0.2 (hexane/EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 8.06–8.03 (m, 4 H), 7.47–7.26 (m, 8 H), 6.86–6.83 (m, 2 H), 5.56–5.44 (m, 2 H), 4.81–4.55 (m, 4.5 H), 4.37–4.33 (m, 0.5 H), 4.17 (s, 0.6 H), 4.09 (dd, 0.5 H, J = 4.0, 2.6 Hz), 3.96 (br d, 0.4 H J = 8.2 Hz), 3.77 (s, 3 H), 2.92 (br s, 0.5 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 166.3, 165.9, 159.4, 133.6, 133.5, 133.1, 133.0, 129.9 (2), 129.8, 129.6, 129.3 (2), 129.2, 128.7, 128.6 (2), 128.5, 128.4, 128.3, 114.1, 113.9, 101.8, 97.3, 86.9, 81.4, 80.7, 79.12, 78.17, 76.73, 72.62, 71.79, 65.1, 64.5, 55.3. HRMS (ESI) Calcd for $C_{27}H_{26}O_8$ $[M + Na]^+$ 501.1525. Found 501.1520.

Allyl 3,5-*O*-(tetraisopropylsiloxane-1,3-diyl)-β-D-arabinofuranoside (26) and 3,5-*O*-(tetraisopropylsiloxane-1,3-diyl)-2-*O*-benzyl-D-arabinofuranose (27). The crude reaction mixture resulting from the reaction of **12** and allyl bromide was purified by chromatography (hexane/EtOAc, 6:1) to give **26** (23%) and **27** (36%) as clear oils. **26**: R_f 0.8 (hexane/EtOAc, 2:1); $[\alpha]_D$ − 58.1° (c 0.04, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 5.94–5.84 (m, 1 H), 5.27 (ddd, 1 H, J = 17.2, 3.1, 1.5 Hz), 5.20 (ddd, 1 H, J = 10.4, 2.7, 1.3 Hz), 4.90 (d, 1 H, J = 4.7 Hz), 4.26–4.20 (m, 2 H), 4.16–4.10 (m, 1

H), 4.03–3.99 (m, 1 H), 3.95 (dd, 1 H, J = 10.7, 3.2 Hz), 3.88–3.83 (m, 1 H), 3.78 (dd, 1 H, J = 10.7, 8.8 Hz), 2.30 (d, 1 H, J = 10.3 Hz), 1.11–0.94 (m, 28 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 134.3, 117.9, 99.9, 82.6, 80.0, 79.1, 68.8, 66.4, 18.0, 17.9, 17.80, 17.5, 17.4 (2), 13.9, 13.7, 13.72, 13.3, 12.9.

Anal. Calcd for $C_{20}H_{40}O_6Si_2$ (432.24): C, 55.52; H, 9.32. Found: C, 55.67; H, 9.32.

27: R_f 0.7 (hexane/EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 5.96–5.85 (m, 1 H), 5.36–5.32 (m, 1 H), 5.32–5.28 (m, 1 H), 5.25–5.18 (m, 1 H), 4.34 (t, 0.5 H, J = 6.2 Hz), 4.26 (dd, 0.5 H, J = 6.9, 5.0 Hz), 4.19–4.05 (m, 2.5 H), 4.03–3.98 (m, 1 H), 3.93–3.84 (m, 2 H), 3.81–3.77 (m, 0.5 H), 3.32 (d, 0.5, J = 6.2 Hz), 2.82 (d, 0.5 H, J = 5.2 Hz), 1.10–1.02 (m, 28 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 134.3, 134.0, 117.9, 117.1, 100.5, 94.3, 89.5, 84.7, 81.8, 81.2, 76.7, 76.5, 72.0, 71.4, 65.5, 62.4, 17.4 (5), 17.1 (4), 17.0, 13.5 (2), 13.1, 13.0, 12.9, 12.6, 12.5. HRMS (ESI) Cald for $C_{20}H_{40}O_6Si_2$ $[M + Na]^+$ 455.2256. Found 455.2236.

Benzyl 3,5-*O*-(tetraisopropylsiloxane-1,3-diyl)-β-D-arabinofuranoside (28) and 3,5-*O*-(Tetraisopropylsiloxane-1,3-diyl)-2-*O*-benzyl-D-arabinofuranose (29). The crude mixture resulting from the reaction of **12** and benzyl bromide was purified by chromatography (hexane/EtOAc, 6:1) to give **28**[43] (36%) as a white solid and **29** (37%) as a clear oil. **28**: R_f 0.8 (hexane/EtOAc, 2:1); $[\alpha]_D$ − 113.2° (c 0.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 7.38–7.29 (m, 5 H), 4.97 (d, 1 H, J = 4.7 Hz), 4.77 (d, 1 H, J = 11.5 Hz), 4.50 (d, 1 H, J = 11.5 Hz), 4.26 (dd, 1 H, J = 7.4, 6.0 Hz), 4.17–4.12 (m, 1 H), 3.97 (dd, 1 H, J = 10.8, 3.2 Hz), 3.90–3.86 (m, 1 H), 3.81 (dd, 1 H, J = 10.8, 8.7 Hz), 2.30 (d, 1 H, 10.5 Hz), 1.09–0.94 (m, 28 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 137.1, 128.5, 128.2, 128.0, 99.6, 82.2, 79.6, 78.7, 69.6, 66.0, 17.6, 17.5, 17.4 (2), 17.2, 17.0 (3), 13.5, 13.3, 12.9, 12.5.

Anal. Calcd for $C_{24}H_{42}O_6Si_2$ (482.25): C, 59.71; H, 8.77. Found: C, 59.95; H, 8.77.

29: R_f 0.7 (hexane/EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 7.36–7.30 (m, 5 H), 5.34 (dd, 0.7 H, J = 6.6, 2.5 Hz), 5.23 (dd, 0.3 H, J = 7.7, 5.5 Hz), 4.75–4.60 (m, 2 H), 4.43 (t, 0.3 H, J = 7.6 Hz), 4.34 (dd, 0.7 H, J = 8.5, 6.0 Hz), 4.15–4.09 (m, 0.8 H), 4.06 (d, 0.3 H), 4.03–3.98 (m, 1.7 H), 3.92–3.86 (m, 1 H), 3.86–3.80 (m, 0.2 H), 3.33 (d, 0.3 H, J = 6.2 Hz), 2.83 (d, 0.7 H, J = 5.3 Hz). 1.10–0.91 (m, 28 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 138.2, 137.7, 128.9, 128.8, 128.5, 128.3, 128.1 (2), 100.9, 94.7, 89.9, 85.1, 82.5, 81.8, 77.8, 77.1, 73.2, 72.7, 66.0, 62.9, 17.9, 17.8 (3), 17.5 (4), 17.4 (2), 13.9 (2), 13.7, 13.5, 13.3, 13.0. HRMS (ESI) Calcd for $C_{24}H_{42}O_6Si_2$ $[M + Na]^+$ 505.2412. Found 505.2432.

***p*-Methoxybenzyl 3,5-*O*-(tetraisopropylsiloxane-1,3-diyl)-β-D-arabinofuranoside (30) and 3,5-*O*-(Tetraisopropylsiloxane-1,3-diyl)-2-*O*-*p*-methoxybenzyl-D-arabinofuranose (31).** The crude mixture resulting from the reaction of **12** and *p*-methoxybenxyl chloride was purified by chromatography (hexane/EtOAc, 6:1) to give **30** (45%) and **31** (36%) as clear oils. **30**: R_f 0.7 (hexane/EtOAc, 2:1); $[\alpha]_D$ − 80.9° (c 0.09, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 7.26–7.23 (m, 2 H), 6.89–6.87 (m, 2 H), 4.95 (d, 1 H, J = 4.7 Hz), 4.70 (d, 1 H, J = 11.2 Hz), 4.43 (d, 1 H, J = 11.2 Hz), 4.23 (dd, 1 H, J = 7.3, 5.9 Hz), 4.15–4.09 (m, 1 H), 3.97 (dd, 1 H, J = 10.7, 3.2 Hz),

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3.89–3.85 (m, 1 H), 3.81 (s, 3 H), 3.80 (dd, 1 H, J = 10.7, 8.8 Hz), 2.28 (d, 1 H, J = 10.4 Hz), 1.10–0.95 (m, 28 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 159.9, 130.3, 129.6, 114.3, 99.7, 82.6, 80.1, 79.1, 69.7, 66.5, 55.7, 18.0, 17.8 (2), 17.4 (3), 13.9, 13.7, 13.3, 12.9.

Anal. Calcd for $C_{25}H_{44}O_7Si_2$ (512.26): C, 58.56; H, 8.65. Found: C, 58.38; H, 8.59.

31: R_f 0.5 (hexane/EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 7.29–7.25 (m, 2 H), 6.89–6.86 (m, 2 H), 5.30 (dd, 0.6 H, J = 6.6, 2.4 Hz), 5.16 (t, 0.4 H, J = 3.8 Hz), 4.65–4.55 (m, 2 H), 4.37 (t, 0.4 H, J = 7.6 Hz), 4.29 (dd, 0.6 H, J = 8.4, 6.0 Hz), 4.09–4.03 (m, 1 H), 4.01–3.97 (m, 1 H), 3.95–3.93 (m, 1 H), 3.88–3.83 (m, 1 H), 3.81 (s, 3 H), 3.33 (d, 0.4 H, J = 6.2 Hz), 2.83 (d, 0.6 H, J = 5.4 Hz), 1.08–0.94 (m, 28 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 160.0, 159.7, 130.2, 130.1, 129.8, 114.3, 114.2, 101.0, 94.8, 89.6, 84.9, 82.7, 81.8, 77.9, 77.2, 77.1, 73.0, 72.5, 65.9, 63.1, 55.7 (2), 18.0, 17.9, 17.8 (3), 17.6, 17.5 (2) 17.4, 13.9, 13.7 (2), 13.4, 13.0, 12.9. HRMS (ESI) Calcd for $C_{25}H_{44}O_7Si_2$ $[M + Na]^+$ 535.2518. Found 535.2494.

Methyl 2,3-anhydro-5-*O*-toluenesulfonyl-α-D-lyxofuranoside (34). Alcohol **32** (0.90 g, 6.2 mmol) and *p*-TsCl (2.41 g, 12.7 mmol) were dissolved in pyridine and stirred overnight at room temperature. The mixture was diluted with CH_2Cl_2, washed with water, and the organic layer was dried ($MgSO_4$) and concentrated. Column chromatography (hexane/EtOAc, 2:1) of the residue gave **34** (1.55 g, 83%) as a white solid: R_f 0.4 (hexane/EtOAc, 2:1); mp 74–76°C.[44] ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 7.81 (d, 2 H, J = 8.3 Hz), 7.36 (d, 2 H, J = 8.0 Hz), 4.88 (s, 1 H), 4.21 (t, 1 H, J = 6.3 Hz), 4.14–4.12 (m, 2 H), 3.72 (d, 1 H, J = 2.8 Hz), 3.64 (d, 1 H, J = 2.8 Hz), 3.37 (s, 3 H), 2.45 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 145.1, 132.6, 130.0, 128.0, 102.3, 73.7, 67.5, 56.5, 55.7, 53.7, 21.7.

Methyl 2,3-anhydro-5-deoxy-5-iodo-α-D-lyxofuranoside (35). Tosylate **34** (1.18 g, 3.9 mmol) and *n*-Bu_4I (3.03 g, 8.2 mmol) were dissolved in toluene (20 mL) and heated at reflux for 7 h. The mixture was concentrated and the residue was dissolved in CH_2Cl_2, washed with water and a saturated aqueous solution of $NaHSO_3$. The organic layer was dried ($MgSO_4$) and concentrated. Column chromatography (hexane/EtOAc, 4:1) of the residue gave **35** (0.86 g, 86%) as a white solid: R_f 0.6 (hexane/EtOAc, 2:1). $[\alpha]_D$ + 68.7° (c 0.2, $CHCl_3$); mp 74–76°C; ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 5.05 (s, 1 H), 4.28 (t, 1 H, J = 7.2 Hz), 3.90 (d, 1 H, J = 2.8 Hz), 3.68 (d, 1 H, J = 2.8 Hz), 3.42 (s, 3 H), 3.24 (s, 1 H), 3.23 (d, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 102.3, 76.7, 56.3, 55.0, 54.4, 0.6. HRMS (ESI) Calcd for $C_6H_9IO_3$ $[M + Na]^+$ 278.9489. Found 278.9481.

Methyl 2,3-anhydro-5-*O*-formyl-α-D-lyxofuranoside (37). A mixture of **12** (0.15 g, 0.38 mmol) and dibutyltin oxide (0.10 g, 0.41 mmol) in toluene (12 mL) was heated at reflux for 20 min. Triflate **33** (0.31 g, 1.12 mmol) was added and stirring continued at reflux for 6 h before DMF (2 mL) was added. After 1 h, a new product was detected by TLC, and the reaction mixture was then cooled and concentrated. The residue was dissolved in CH_2Cl_2, washed with water, and the organic layer was dried

(Na_2SO_4), and concentrated. The residue was purified by chromatography (hexane/EtOAc, 6:1) to give **38** (77 mg, 39%) as a white solid: R_f 0.4 (hexane/EtOAc, 2:1); $[\alpha]_D$ + 13.8° (*c* 0.02, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ_H) 8.10 (d, 1 H, *J* = 0.7 Hz,), 4.98 (s, 1 H), 4.37 (d, 2 H, *J* = 6.2 Hz), 4.23 (t, 1 H, *J* = 5.9 Hz), 3.74 (dd, 1 H, *J* = 2.8, 0.7 Hz), 3.68 (d, 1 H, *J* = 2.8 Hz), 3.43 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, δ_C) 160.9, 102.8, 74.2, 62.5, 56.6, 56.2, 54.2. HRMS (ESI) Calcd for $C_7H_{10}O_5$ $[M + Na]^+$ 197.0420. Found 197.0424.

Computational studies on 43. Because many force fields for stochastic searching do not effectively handle tin as an element, a surrogate approach using silicon as a mimic was employed. Thus, the SPMC search protocol available in MacroModel Version 6.5 was used to generate an initial family of 10,000 conformers of **44**. Each conformer was then minimized in the gas phase using AM1,[40] which generated 113 unique conformers, all of which were within 32 kcal/mol of the global minimum. Two families of structures were present. One family (four conformers) was clustered at the global minimum and the other (6 conformers) $\sim$ 1.1 kcal/mol above the global minimum. Within each family of structures, the furanose ring adopted the same conformation, and the geometrical differences were only in the orientations about the bonds in the siloxane moeity. The two lowest energy conformers in each family were subsequently optimized at the B3LYP level of theory after replacement of the surrogate silicon atom with tin. The basis set used for the full geometry optimization was 3-21G* for silicon, oxygen, carbon, and hydrogen and the basis set for tin was the SDD effective core potential.[45] Single-point energy calculations were subsequently performed at the B3LYP level of theory[46–48] using a 6-31G* basis set for silicon, oxygen, carbon, and hydrogen and the SDD effective core potential for tin. All DFT calculations utilized 6 Cartesian d functions and were performed using Gaussian 98.[49]

ACKNOWLEDGMENTS

This work was supported by The National Institutes of Health and the Ohio Supercomputer Center. OSD thanks the Ohio State University College of Arts and Science for a senior Honors Thesis Scholarship.

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Received May 20, 2003
Accepted August 7, 2003