The preparation of *C*-aryl glucals via palladium-catalyzed cross-coupling methods

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The *C*-aryl glucals **17–31** have been prepared by the palladium-catalyzed cross coupling of 1-tributylstannyl-3,4,6-tri-*O*-(*tert*-butyldimethylsilyl)-D-glucal (**11**) and aryl bromides. The major by-product in all of these reactions is the dimer **33**, the product of homocoupling of **11**. Alternatively, the *C*-aryl glucals **34–40** can be obtained from the palladium-catalyzed coupling of 1-iodo-3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (**16**) and a variety of metalated aromatics, including ArZnCl, $ArB(OH)_2$, and $ArB(OMe)_2$. The advantages of the latter procedure include superior coupling yields under milder reaction conditions and the high yielding preparation of **16** directly from 3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (**12**) by a metalation–iodination sequence.

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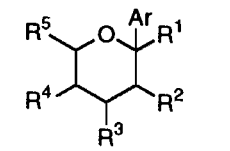
On a préparé les *C*-aryl glucals **17–31** par un couplage croisé catalysé par le palladium du 1-tributylstannyl-3,4,6-tri-*O*-(*tert*-butyldiméthylsilyl)-D-glucal (**11**) et des bromures d'aryle. Le sous-produit principal de toutes ces réactions est le dimère **33**, le produit d'homocouplage du produit **11**. On peut aussi obtenir les *C*-aryl glucals **34–40** par un couplage catalysé par le palladium du 1-iodo-3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (**16**) avec une variété de produits aromatiques métallés comportant le ArZnCl, le $ArB(OH)_2$ et $ArB(OMe)_2$. Les avantages de la dernière méthode incluent des rendements supérieurs de couplage dans des conditions plus douces et la préparation avec un rendement élevé du composé **16** directement à partir du 3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (**12**) par une séquence de métallation et d'iodation.

[Traduit par la Rédaction]

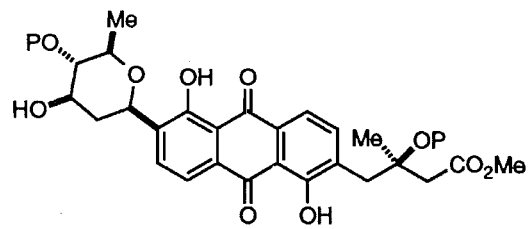
Introduction

The class of natural products known as the *C*-aryl glycosides (1, 2) has recently received a great deal of attention in the synthetic community since many of these compounds exhibit unique antibiotic and (or) antitumor activity. Although the key structural unit that identifies these compounds is the novel carbon–carbon bond that unites the carbohydrate and aromatic fragments, a further subclassification can be made based upon the type of substitution at C1 and C2 of the carbohydrate moiety. Three broad groupings of naturally occurring *C*-aryl glycosides made on this basis can be illustrated in general terms by **1–3** with representative examples including vineomycinone B2 methyl ester (3), chaetiacandin (4, 5), and papulacandin D (6, 7), respectively. Synthetic strategies directed toward the preparation of any of these classes must address not only the method of creating the key carbon–carbon bond with a large array of substituted aromatics, but also must be concerned with its stereoselective formation with respect to the various substituents at C1–C5 on the carbohydrate framework. Previously reported strategies directed toward the synthesis of *C*-aryl glycosides[2] address, for the most part, the preparation of only one of the three main *C*-aryl glycoside subclasses (8).

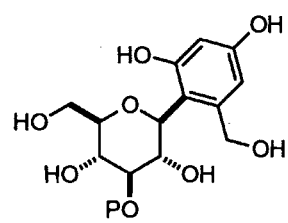
We became interested in developing a rapid, facile, and general route to *C*-aryl glycosides that would be relatively flexible with respect to aromatic substitution pattern and type and with respect to the availability of the range of *C*-aryl glycoside subclasses as described above (9–12). The fundamental difference between our anticipated route to *C*-aryl glycosides and previous results is that the functionalization of C1 and C2, and the determination of the anomeric carbon stereogenicity, would occur subsequent to the key C—C bond-forming reaction by the regio- and stereoselective functionalization of the enol ether double bond in a *C*-aryl glucal **8**. The general strategy that we



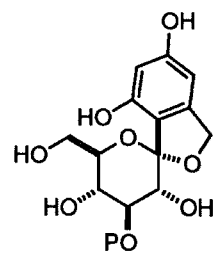
1 $R^1 = R^2 = H$
2 $R^1 = H$, R^2 = alkoxy
3 $R^1 = R^2$ = alkoxy



Vineomycinone B2 methyl ester
(P = carbohydrate)



Chaetiacandin
(P = 6-O-acyl-galactopyranosyl)



Papulacandin D (P = acyl)

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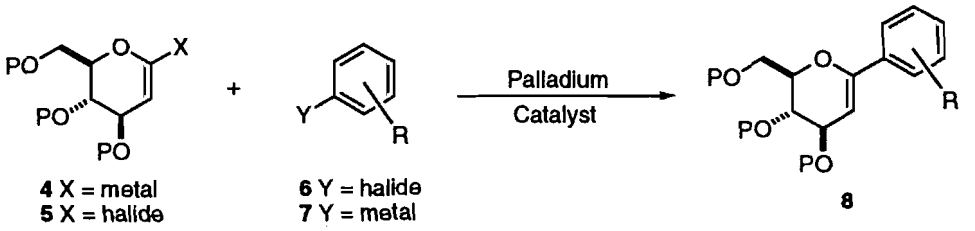
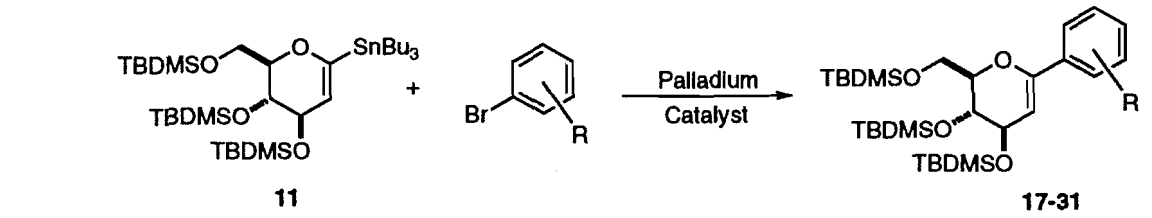
[2]An excellent review of recent methods for *C*-glycoside formation, including *C*-aryl glycosides, is found in ref. 8. For alternative methods for preparing *C*-aryl glycosides, see ref. 8 as well as the extensive summaries of references found in refs. 9, 20, and 21.



SCHEME 1



SCHEME 2

envisaged for the preparation of **8** was the palladium-catalyzed reaction (13, 14) of suitably derivatized organometallic and organic halide coupling partners (**4** + **6** → **8** or **5** + **7** → **8**) (see Scheme 1). Herein, we deail the results of our investigations that have led to the facile and efficient preparation of *C*-aryl glucals **8**, the key intermediates with respect to a general entry into the synthesis of *C*-aryl glycosides.[3]

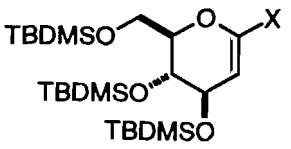
Results and discussion

*(a) Palladium-catalyzed coupling reactions of 1-tributylstannyl-3,4,6-tri-O-(tert-butyldimethylsilyl)-D-glucal (**11**) and 1-tributylstannyl-3,4,6-tri-O-(triisopropylsilyl)-D-glucal (**14**)*

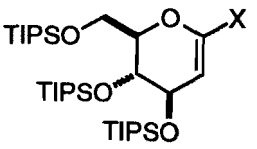
At the time we began this study, there was some indication in the literature that simple metalated enol ethers related to those illustrated by **4** (X = tin, zinc) would undergo palladium- catalyzed coupling reactions with aryl halides (22, 23). In addition, the preparation of stynnylated glucal **4** (X = *n*-Bu_3Sn) had been described by several groups (24–26). Therefore, it was the strategy illustrated by **4** + **6** → **8** (Scheme 1) that received our initial attention.

Previous reports from this laboratory have detailed the preparation of 1-tributylstannyl-3,4,6-tri-*O*-(*tert*-butyldimethylsilyl)-D-glucal (**11**) and 1-tributylstannyl-3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (**14**) (27). These compounds were prepared from the corresponding C1-unsubstituted silylated glucals **9** (TDMS = *tert*-butyldimethylsilyl) and **12** (TIPS = triisopropylsilyl), respectively, via metalation (*t*-BuLi, ether, 0°C) and trapping of the derived vinyl anions **10** and **13** with *n*-Bu_3SnCl. The problems that we have encountered in the preparation of **11**, due to competing metalation α to silicon on one or more of the *tert*-butyldimethylsilyl (TBDMS) protecting groups, have been documented (27).[4] As a result, the optimum yield in the preparation of **11** via this method is 30%. Conversely, the C1-metalation of **12** proceeds cleanly and **14** is readily obtained in 70–90% yield (27).

We now report the full details of a study involving the palladium-catalyzed coupling reactions of 1-tributylstannyl-



9 X = H
10 X = Li
11 X = *n*-Bu_3Sn



12 X = H
13 X = Li
14 X = *n*-Bu_3Sn
15 X = ZnCl
16 X = I

3,4,6-tri-*O*-(*tert*-butyldimethylsilyl)-D-glucal (**11**) with aryl bromides (Scheme 2, Table 1).[5] The initial investigation was concerned with the coupling of the simplest substrate, bromobenzene, and involved systematic variation of the typical palladium catalysts (14, 22, 23), solvent, and temperature. A representative sampling of the results is found in Table 1, entries 1–7. The optimum reaction conditions for the preparation of the *C*-phenyl glycal **17** (R = H) by the coupling of glucal **11** and bromobenzene were realized in refluxing THF (0.06 M in **11**), using $Pd(Ph_3P)_4$ as catalyst (Table 1, entry 3). Employing these conditions, **17** was produced very cleanly along with a small amount (ca. 10%) of a single by-product (vide infra).

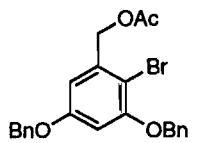
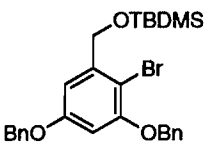
While the coupling of bromobenzene proceeded readily under these "standard" conditions, similar reactions of glucal **11** with substituted bromobenzenes (1-bromo-4-nitrobenzene and 4-bromoanisole) were not reproducible and often failed completely under apparently identical reaction conditions. Similarly, attempts at using aryl iodides or aryl triflates (31, 32) in these coupling reactions gave poor and irreproducible results. After a great deal of experimentation, it was found that concentration, temperature, and catalyst all play an important role in the success or failure of the coupling reaction of **11** with substituted aryl bromides. The reaction conditions that appear to be

[3]Similar palladium-catalyzed coupling strategies (15–18) and alternative strategies (19–21) have been directed toward the preparation of *C*-aryl glycals.

[4]There have been other reports describing the problems associated with the vinylic deprotonation of a variety of highly substituted cyclic vinyl ethers containing silyl protecting groups (28–30). For example, Crich and Ritchie isolated a phenylthio derivative of **9** that had been formed upon metalation of **9** followed by trapping with $(PhS)_2$. They proposed that the phenylthio moiety had been introduced into the TBDMS group at C6 although no evidence in support of this proposal was given (30).

[5]For a prelminary account of this work, see ref. 9.

TABLE 1. Palladium-catalyzed coupling of the stannylated glucal **11** and aryl bromides[a]

Entry	ArX (1.1–2 equiv.)	Reaction conditions (catalyst/solvent/time)	Coupled product yield, % (dimer)[b]
1	PhBr	$Pd(Ph_3P)_4$/PhH/15 h	**17** 50[c]
2	PhBr	$Pd(Ph_3P)_4$/DMF[d]/15 h	**17** 34[c]
3	PhBr	$Pd(Ph_3P)_4$/THF/15 h	**17** 70[c]
4	PhBr	$Pd(Ph_3P)_4$/MeCN/15 h	**17** NR
5	PhBr	$Pd(Ph_3P)_2Cl_2$/PhH/15 h	**17** 52[c]
6	PhBr	$Pd(OAc)_2$/PhH/15 h	**17** Trace[c]
7	PhBr	$Pd(PhCN)_2Cl_2$/PhH/15 h	**17** Trace[c]
8	4-$NO_2C_6H_4Br$	$Pd(Ph_3P)_2Cl_2$/PhMe/30 min	**18** 78 (4)
9	4-CNC_6H_4Br	$Pd(Pd_3P)_2Cl_2$/PhMe/20 min	**19** 81 (8)
10	1-Bromonaphthalene	$Pd(Ph_3P)_2Cl_2$PhMe[d]/2 h	**20** 59 (15)[e]
11	4-$MeO_2CC_6H_4Br$	$Pd(Ph_3P)_2Cl_2$/PhMe/15 h	**21** 56 (8)
12	2-$MeO_2CC_6H_4Br$	$Pd(Ph_3P)_2Cl_2$/PhMe/15 h	**22** 48 (5)
13	4-ClC_6H_4Br	$Pd(Ph_3P)_2Cl_2$/PhMe/45 min	**23** 49 (8)
14	2-MeC_6H_4Br	$Pd(Ph_3P)_2Cl_2$/PhMe/2 h	**24** 49 (11)
15	2-$AcOCH_2C_6H_4Br$	$Pd(Ph_3P)_2Cl_2$/PhMe/2 h	**25** 46 (15)
16	PhBr	$Pd(Ph_3P)_2Cl_2$/PhMe/30 min	**17** 41 (12)
17	2-$AcOC_6H_4Br$	$Pd(Ph_3P)_2Cl_2$/PhMe/1 h	**26** 40 (11)
18	2-$BnOC_6H_4Br$	$Pd(Ph_3P)_2Cl_2$/PhMe/1 h	**27** 44 (4)
19	4-$MeOC_6H_4Br$	$Pd(Ph_3P)_2Cl_2$/PhMe[d]/2 h	**28** 30 (13)
20	2,5-$(MeO)_2C_6H_3Br$	$Pd(Ph_3P)_2Cl_2$/PhMe[d]/1 h	**29** 65 (9)
21		$Pd(Ph_3P)_2Cl_2$/PhMe/15 h	**30** 36 (18)
22		$Pd(Ph_3P)_2Cl_2$/mesitylene/1 h	**30** 51[c]
23		$Pd(Ph_3P)_2Cl_2$/PhH/15 h	**30** 85[c,f]
24		$Pd(Ph_3P)_2Cl_2$/PhMe/15 h	**31** 56 (13)
25	4-CNC_6H_4Br	$Pd(Ph_3P)_4$/mesitylene/30 min	**32** 66[c]

[a]See Scheme 2; 5 mol% catalyst. Approximate concentration **11** in refluxing solvent unless stated otherwise: 0.05 M for entries 1–7 and 0.2–1 M for entries 8–25.

[b]Yields of isolated, chromatographically pure products. Numbers in parentheses refer to the isolated yield of dimer **33**. Note that a 10% yield of dimer **33** involves the consumption of 20% of **11**.

[c]Dimer yield not measured.

[d]Reaction done at 100°C.

[e]The yield is based on an ^1H NMR integrated ratio of a chromatographically pure mixture of **20** and **33**. A small amount of pure **20** was isolated and characterized.

[f]Four equivalents of **11** used with respect to aryl bromide.

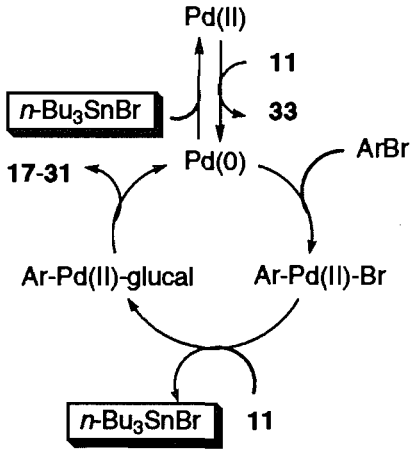
[g]Reaction carried out with glucal **14**.

universally successful involve refluxing toluene solutions of the stannyl glucal **11**, at concentrations of 0.2–1.0 M in **11**, in the presence of $Pd(Ph_3P)_2Cl_2$ (5 mol%) and the aryl bromide (1.1–2 equiv.).

Employing the revised "standard" reaction conditions, a wide variety of substituted aryl bromides were coupled successfully (Table 1, entries 8–24). Included in this list are aryl bromides containing electron-withdrawing and -donating substituents along with several highly substituted aromatics (see Table 1, entries 21–24). In all cases, the crude reaction mixtures were quite clean, providing the expected *C*-aryl glucals **17–31** in moderate to good yields. Several trends and additional points of interest regarding this coupling reaction are worth noting.

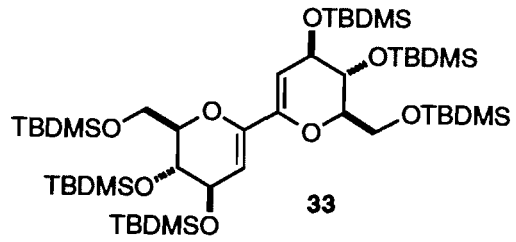
Firstly, the conditions of choice for the preparations of the unsubstituted *C*-phenyl glucal **17** are the original "standard" reaction conditions (compare Table 1, entries 3 and 16). For reasons that we cannot explain, bromobenzene is the sole example in which satisfactory coupling reactions take place under conditions of $Pd(Ph_3P)_4$ catalysis in THF. Secondly, the isolated yields of the *C*-aryl glucals reflect, at least qualitatively, an ordering based on the electronic properties of the aromatic substituent. In most cases, electron-poor aryl bromides (X = CN, NO_2, CO_2R) provide higher yields of coupled products than those aryl bromides with electron-donating substituents (X = alkyl, OR).[6] In addition, a general trend towards greater forma-

[6]A similar ordering, based on electron-withdrawing properties, has been observed in the palladium-catalyzed rate (not yield) of reaction of organostannanes with substituted aryl bromides (33) and terminal acetylenes (34, 35).



SCHEME 3

tion of the by-products (vide infra) is observed with electron-rich aryl bromides. Thirdly, more efficient coupling reactions could be effected in some cases by using an excess (with respect to the aryl bromide) of the stannyl glucal **11** and considering the aryl bromide as the limiting reagent (compare Table 1, entries 21 and 23).[7] However, due to the difficulties associated with obtaining significant quantities of **11** (vide supra), we have generally used **11** as the limiting reagent in our coupling reactions. The entries in Table 1 result from an optimization of the reaction conditions in light of this limitation. Finally, the major by-product that is produced in all of the reactions that we have performed results from the homocoupling of **11** (36). This dimer **33** accounts for the consumption of up to



36% of the starting material **11** (Table 1, entry 21) and in many cases proved to be extremely difficult to separate from the desired *C*-aryl glucal. A variety of reaction modifications were considered in order to decrease the production of this dimer. None of these attempts, including employing nickel catalysts or using the vinyl zinc glucal derived from **10**, met with success.

Several established synthetic procedures for the preparation of 1,3-dienes involve the Pd(II) mediated homocoupling of vinylsilanes (37) or vinylstannanes (38). The mechanism that has been postulated to account for the dimerization reaction in the presence of Pd(II) suggests that dimerization of the organometallic reagent should proceed to an extent equal to the amount of Pd(II) used (Scheme 3).[8] Indeed, when stannylated glucal **11** is treated solely with $Pd(Ph_3P)_2Cl_2$ in refluxing toluene, dimer formation is observed, while repeating the same reaction using $Pd(Ph_3P)_4$ as catalyst produces no dimer. Thus, it is the presence of Pd(II) that is responsible for dimer formation. In our work, this dimerization mechanism would limit the yield of dimer **33** to a maximum of 5%. However, from Table 1 we see that many of the cited reactions result in the production of more dimer than would be expected based on the use of 5 mol% of Pd(II) catalyst. A possible explanation for these results involves the oxidation of the catalytically active Pd(0) species back to Pd(II) by one of two processes. Either advantitious molecular oxygen is responsible or, alternatively, the oxidation of Pd(0) to a Pd(II) is being mediated by Bu_3SnBr, the by-product that is formed in the catalytic cross-coupling cycle.[9] Support for the latter hypothesis can be found by treating stannylated glucal **11** solely with $Pd(Ph_3P)_4$ and *n*-Bu_3SnCl in the absence of aryl bromide. The formation of dimer **33** takes place after several hours. Regardless of which mechanism is operative, the additional Pd(II) that is produced can lead to excessive dimer formation. Furthermore, the latter experiment suggests that dimerization of **11** is unavoidable under the conditions that we are using.

Although the preparation of *C*-aryl glucals **17–31** via this method is fairly efficient and broad in scope, there are several problems that are evident. The first is the limited availability of the stannylated glucal **11** via vinylic metalation/stannylation methods (27). This problem is especially evident if one is considering using **11** in excess with respect to the aryl bromide, a set of conditions that is desirable when the aryl bromide is the more difficult reaction partner to obtain.[7] In addition, we are faced with poor yields in the coupling reactions of **11** with electron-rich aromatic bromides as well as the consumption of the stannylated glucal **11** by an apparently unavoidable dimerization process.

The first of these problems has been overcome by the facile and high-yielding formation of 1-tributylstannyl-3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (**14**) (27). Therefore, it was imperative that we demonstrate that this stannylated glucal could be utilized in the key palladium-catalyzed cross-coupling reaction with aryl bromides.

It soon became evident that the apparently simple change from TBDMS to TIPS protecting groups on the stannylated glucal was in fact a major and detrimental modification. Whereas the *C*-aryl glucal **19** was efficiently prepared (81% yield) by the coupling of **11** and 4-bromobenzonitrile (Table 1, entry 9), the best yield that we could achieve in the coupling of **14** and 4-bromobenzonitrile was 67% (Table 1, entry 25). Results with other substituted aryl bromides including 4-bromo anisole and methyl 2-bromobenzoate were similarly discouraging, in many cases providing no coupled material.

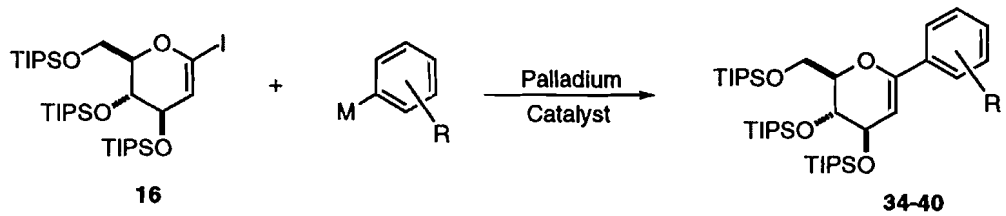
The mechanism that has been proposed for the Stille reaction (see Scheme 3) (40) involves a rapid oxidative addition of Pd(0) to the organic halide (here ArBr), followed by a slow transmetalation step with the organometallic partner to provide a diorgano-Pd(II) species.[10] We attributed the disappointing results that were observed in the attempted coupling reactions of

[7]We have used this observation to our advantage in the synthesis of the tricyclic spiroketal core of the papulacandins, a synthesis that involves the intermediacy of glucal **30** (10).

[8]For those cases in which the diene was the desired product, an added oxidant such as Cu(II) or *t*-BuOOH was used to reoxidize the Pd(0) that was produced in the reaction back to Pd(II) to make the reactions catalytic in Pd(II). In our reactions, it is this dimerization process that produces Pd(0), the species that is catalytically active in the desired cross-coupling process.

[9]In a subsequent but related study, Tius et al. noted that the rigorous exclusion of oxygen minimized the dimerization of a zinc glucal during palladium-mediated coupling reactions with aryl bromides (17). In addition, the oxidative addition of Pd(0) to a Six—X bonds has been reported (39).

[10]Detailed mechanistic investigations into the related reactions with platinum have been described (41, 42).



SCHEME 4

stannylated glucal **14** and aryl bromides to a decrease in the rate of an already slow transmetalation step. Although not initially obvious, but clearly seen from molecular models, the protecting group change from TBDMS to TIPS dramatically increases the steric bulk around the C1 position of the glucal. We believe that it is this protecting group change from TBDMS to TIPS that manifests itself in decreasing the rate of the slow transmetalation step, leading to inferior results in the cross-coupling reaction. Therefore, we reasoned that if we could reverse the sense of the coupling reaction by making the carbohydrate moiety the more reactive organic halide partner, we might be able to overcome this steric bias. The initial rapid oxidation addition of Pd(0) to a 1-haloglucal would be much less susceptible to steric factors (14) and the slow transmetalation step would then take place on the metal centre of a glucal-Pd(II)-halide, remote from the sterically encumbered C1 position of the glucal.

*(b) Preparation and palladium-catalyzed coupling of 3,4,6-tri-O-(triisopropylsilyl)-1-iodo-D-glucal (**16**) with metalated aromatics*

The readily available stannylated glucal **14** was converted into the iodo glucal **16**[11] (89–100% yield) by treatment of a CH_2Cl_2 solution of **14** with I_2 in CH_2Cl_2 (43–45). Based on the success of the coupling reaction of the iodo glucal **16** with metalated aromatics (vide infra), we sought a more direct pre-paration of **16** that would bypass the intermediacy of **14** and the use of toxic tributyltin chloride that is required in this method.

Reaction of the easily generated vinyl lithium intermediate **13** (27) with *N*-iodosuccinimide (NIS) met with limited success. The optimum conditions provided **16** in 30% yield along with 25% of recovered **12**. The preparation of other organometallic species from **13** (vinyl copper, vinyl silane, vinyl Grignard) followed by the attempted trapping of these intermediates with an iodonium source (I_2 or NIS) were similarly unsuccessful. However, metalation of **12** with *t*-BuLi (27) followed by transmetalation of the derived lithio derivative **13** with $ZnCl_2$ (approximately 4 equiv., ether solution) and subsequent quenching of the reaction mixture with either NIS (4.4 equiv.) or I_2 (3.7 equiv.), provided the iodo glucal **16** in yields of 67 and 81%, respectively, along with recoverable starting material (27 and 6%, respectively). It was imperative in this preparation of **16** that an excess of $ZnCl_2$ (with respect to the amount of *t*-BuLi that was used initially to metalate **12**) be used to generate **15** from **13**, presumably to convert the excess *t*-BuLi into the less reactive *t*-BuZnCl. In the event that less $ZnCl_2$ was used, the *t*-BuLi remaining in the reaction mixture would simply react (metal–halogen exchange) with the iodo glucal **16** that was produced.

Although a variety of metalated aromatics (such as zinc halides (46, 47) and boronic acids (48, 49)) have been demonstrated to undergo palladium-catalyzed cross-coupling reactions with organic halides, the use of 1-alkoxy-1-iodo alkenes as the organic halide partner in a Stille coupling reaction with organometallics had not been documented prior to our initial report (12). To test the utility of the iodo glucal **16** in the coupling reaction, **16** and a variety of metalated benzenes were treated with a palladium catalyst under appropriate reaction conditions (Scheme 4; Table 2, entries 1–13).[12] The optimum isolated yields of the *C*-phenyl glucal **34** (R = H) were obtained using phenylboronic acid (81%), dimethyl phenylboronate[13] (87–90%), and phenylzinc chloride (90%) as coupling partners. Inferior results were observed with PhLi, *n*-Bu_3SnPh, and PhMgBr (Table 2, entries 1–3). The coupling reactions in the former cases were extremely clean. The only by-product that was observed was biphenyl, arising from the now expected dimerization of the metalated benzene. The palladium catalyst is necessary in these reactions since, in its absence, no cross coupling is observed (Table 2, entry 10). A noteworthy exception is the reaction of **16** with the higher-order mixed cuprate reagent $Ph_2Cu(CN)Li_2$ (Table 2, entry 5) that produced **34** in low yield in the absence of palladium (51). While the reaction with phenylzinc chloride proceeds quickly and cleanly at room temperature in THF with $Pd(Ph_3P)_2Cl_2$ as catalyst, the reaction occurs much more slowly and in lower yield using $Pd(Ph_3P)_4$ (compare Table 2, entries 12 and 13). It appears that 4 equivalents of PhZnCl, with respect to the iodo glucal **16**, is the ratio required for an optimum coupling reaction. When 2 equivalents of PhZnCl were utilized, there was incomplete consumption of **16** after 24 h (compare Table 2, entries 11 and 13). Similarly, 2–4 equivalents of $PhB(OH)_2$ or $PhB(OMe)_2$ are required for high-yielding coupling reactions. The ability to use the boronate esters in the coupling reaction[13] under a variety of reaction conditions (see Table 2, entries 6–9) is noteworthy since the (sometimes) problematic isolation of the boronic acids (derived from the esters by hydrolysis) can now be avoided.

The coupling reaction using iodo glucal **16** can be extended to include substituted arylboronic acids, dimethyl arylboronates, and arylzinc chlorides as well (Table 2, entries 14–21). The isolated yields of the *C*-aryl glucals **35–40** obtained under these mild reaction conditions are superior to those that we had observed for every analogous example in the coupling of tin glucal **11** and aryl bromides (compare Table 1, entries 3, 9, 10, 14, and 19 with Table 2, entries 9, 14, 20, 21, and 15, respectively). For example, the poorest substrates in the coupling

[11]An iodo glucal analogous to **16** was obtained as an unexpected product (75%) in the attempted cross coupling of a C-1 stannylated glucal with 3-iodo-2-propyn-1-ol (16). The isolable vinyl iodide **16** is stable for several months when stored under vacuum in the dark. We have only stored the iodide **16** for this length of time although it may be stable for longer storage periods since no decomposition was noted under these conditions. However, if **16** is stored in the presence of light, or even under argon in the dark, decomposition to a dark red mixture of unidentified compounds is rapid.

[12]For a preliminary account of this work, see ref. 12.

[13]Boronate esters can be used in the coupling reaction without prior hydrolysis to, or isolation of, the boronic acids (50).

TABLE 2. Palladium-catalyzed coupling of iodo glucal **16** and metalated aromatics[a]

Entry	ArM[b] (equiv.)	Reaction conditions (solvent/temp/time)	Coupled product (yield, %)[c]
1	PhLi (4)	THF/rt[d]	NR
2	$PhSnBu_3$ (4)	THF/reflux/24 h[d]	**34** 20
3	PhMgBr (4)	PhMe/reflux/10 h[e]	**34** 25
4	$PhB(OH)_2$ (4)	THF – aq.Na_2CO_3/75°C/1.5 h[d]	**34** 81
5	$Ph_2Cu(CN)Li_2$ (3)	THF/–20°C/15 h[f]	**34** 25
6	$PhB(OMe)_2$ (2)	THF – aq.Na_2CO_3/70°C/4 h	**34** 84
7	$PhB(OMe)_2$ (2)	THF – aq.Na_2CO_3/rt/72 h[d]	**34** 80
8	$PhB(OMe)_2$ (4)	THF – aq.Na_2CO_3/rt/72 h[g]	**34** 87
9	$PhB(OMe)_2$ (4)	THF – aq.Na_2CO_3/rt/15 h[d]	**34** 90
10	PhZnCl (4)	THF/rt/24 h[f]	NR
11	PhZnCl (2)	THF/rt/24 h[d]	INC
12	PhZnCl (4)	THF/rt/16 h[e]	**34** 74
13	PhZnCl (4)	THF/rt/30 min[d]	**34** 90
14	$4\text{-}NCC_6H_4B(OMe)_2$ (2)	THF – aq.Na_2CO_3/70°C/15 h	**35** 90
15	$4\text{-}MeOC_6H_4B(OH)_2$ (2)	THF – aq.Na_2CO_3/75°C/40 min[d]	**36** 81
16	$4\text{-}MeOC_6H_4ZnCl$ (4)	THF/rt/15 min	**36** 73
17	2-FurylZnCl (4)	THF/rt/30 min	**37** 79
18	2-FurylB(OMe)_2 (2)	THF – aq.Na_2CO_3/60°C/40 min	**37** 78
19	$2,5\text{-}Cl_2C_6H_3B(OH)_2$ (2)	THF – aq.Na_2CO_3/75°C/15 min[d]	**38** 79
20	1-NaphthylB$(OH)_2$ (2)	THF – aq.Na_2CO_3/75°C/90 min[d]	**39** 75
21	$2\text{-}MeC_6H_4ZnCl$ (4)	THF/rt/15 min	**40** 68
22	$CH_2CHB(OMe)_2$ (4)	THF – aq.Na_2CO_3/65°C/5.5 h	**41** 60
23	$(CH_2CH)_4Sn$ (2)	THF/reflux/8 h[d]	**41** 67

[a]See Scheme 4. $Pd(Ph_3P)_2Cl_2$ catalyst (5 mol%) unless stated otherwise. Reactions of $ArB(OH)_2$ and $ArB(OMe)_2$ use 2 equivalents of 2 M Na_2CO_3 per mole of ArM.

[b]The metalated aromatics were commercially available or were prepared according to literature procedures from the corresponding aryl bromides (see Experimental). Numbers in parentheses refer to the number of equivalents of ArM used with respect to **16**.

[c]Yield of chromatographically purified product. NR indicates no reaction. INC indicates incomplete reaction.

[d]$Pd(Ph_3P)_2Cl_2$ catalyst (10 mol%).

[e]$Pd(Ph_3P)_4$ catalyst (10 mol%).

[f]No Pd catalyst.

[g]$Pd(Ph_3P)_2Cl_2$ catalyst (2 mol%).

reaction with the tin glucal **11** are electron-rich aromatic bromides. Thus, the improved yield in the preparation of the anisole derivative **36** (Table 2, entries 15 and 16 (73–81%)) compared with the yield for the preparation of **28** (Table 1, entry 19 (30%)) was gratifying since many of the naturally occurring *C*-aryl glycosides are oxygen-substituted aromatics (1, 2). As expected, there was no evidence for the production of the glucal dimer that previously had been the major by-product (up to 18%) in all of our coupling reactions with stannyl glucal **11**. Furthermore, purification of the glucals **34–40** is more easily accomplished than in the original procedure since the presence of the dimer **33** had, in some cases, hampered chromatographic isolation (see Table 1, entry 10). Finally, the reaction is not limited to the coupling of metalated benzenes but can be extended to include metalated heteroaromatics such as furan (Table 2, entries 17 and 18) as well as metalated olefins such as tetravinyltin or dimethyl vinylboronate (Table 2, entries 19 and 20). Each of the resulting *C*-glucal products **37** and **41**, respectively, have the potential for further synthetic manipulation. For example, *C*-furyl glucals such as **37** have been demonstrated to be useful synthetic equivalents for the preparation of C1-carboxyl glycosides (52) while dienes related to **41** undergo stereoselective Diels–Alder reactions (53).

Summary

A wide range of novel *C*-aryl glucals have been prepared by two complementary and operationally simple two-step procedures. The first process involves the vinylic metalation/stannylation of a suitably protected glucal followed by a palladium-catalyzed coupling of the resulting stannylated glucal with an aryl bromide (Scheme 2), while the second process calls for the initial preparation of an iodo glucal followed by coupling with a metalated aromatic (Scheme 4). This latter procedure is noteworthy since it does not require the use of stannylated intermediates and provides *C*-aryl glucals in an efficient three-step procedure from D-glucal (protection, metalation/iodination, coupling). We feel that the wide range of substituted aromatic moieties that can be appended onto the carbohydrate nucleus, creating the unique carbon–carbon bond present in the *C*-aryl glycosides, makes this an attractive method for the preparation of this class of compounds. The preliminary investigations that have been reported from our laboratories (10, 11) and from other groups (15, 17, 19–21) addressing the synthetic capabilities of the remaining enol ether double bond in the *C*-aryl glucals are encouraging. Indeed, several stereoselective procedures have been developed, resulting in an important and general method for the preparation of *C*-aryl glycosides.

Experimental

General information

^1H NMR spectra were recorded at 200 MHz in $CDCl_3$ unless stated otherwise. Broad band proton-decoupled ^{13}C NMR spectra were recorded at 50 MHz in $CDCl_3$ unless stated otherwise. IR spectra were recorded on neat samples unless stated otherwise. Work-up procedures involving the drying of organics was done with $MgSO_4$. The prepara-

tion of 1-tributylstannyl-3,4,6-tri-*O*-(*tert*-butyldimethylsilyl)-D-glucal (**11**), 3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (**12**), 1-tributylstannyl-3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (**14**), and other general experimental procedures have been described elsewhere (27). **Note:** Compounds for which high-resolution mass measurements are given exhibited one spot by TLC analysis.

*General procedure A: coupling of 1-tributylstannyl-3,4,6-tri-*O-(tert-*butyldimethylsilyl)-D-glucal (**11**) and aryl bromides*

A flame-dried 5 mL round-bottom flask was charged with the stannylglucal **11**, the appropriate aryl bromide (1.1–2 equiv.) and the reaction solvent (0.2–1 M in **11**). The palladium catalyst (5 mol%) was added and the reaction mixture was heated at the temperature and for the times indicated in Table 1. When TLC analysis indicated the disappearance of **11**, the reaction mixture was cooled to room temperature and the solvent was removed in vacuo. The crude reaction mixture was subjected to flash column chromatography on silica gel to provide the corresponding aryl *C*-glucal and the dimer **33**.

*1-C-Phenyl-3,4,6-tri-*O-(tert-*butyldimethylsilyl)-D-glucal (**17**)*

Following general procedure A, **11** (84.2 mg, 0.108 mmol) was reacted with bromobenzene (0.054 mL). After chromatography (elution with 50:1 hexanes:Et_2O v/v), **17** (42.4 mg, 70%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −20.5 (*c* 1.2); IR: 2956, 2856, 2803, 1652, 1483, 1153, 813, 669 cm^{-1}; ^1H NMR (400 MHz) δ: 0.00 (s, 3H), 0.03 (s, 3H), 0.10 (s, 6H), 0.11 (s, 6H), 0.868 (s, 9H), 0.873 (s, 9H), 0.89 (s, 9H), 3.84 (m, 2H), 3.96 (dd, 1H, *J* = 4.3, 6.9 Hz), 4.14 (m, 2H), 5.23 (dd, 1H, *J* = 0.9, 4.2 Hz), 7.30 (m, 3H), 7.60 (m, 2H); ^{13}C NMR δ: −5.6, −5.5, −4.9, −4.4, −4.3, −4.2, 18.0, 18.2, 25.7, 25.8, 25.9, 61.6, 69.0, 70.3, 80.4, 98.1, 125.4, 128.2, 128.5, 135.7, 150.8. Exact Mass calcd. for $C_{29}H_{53}O_4Si_3$ $(M - CH_3)^+$: 549.3251; found: 549.3245.

*1-C-(4-Nitrophenyl)-3,4,6-tri-*O-(tert-*butyldimethylsilyl)-D-glucal (**18**)*

Following general procedure A, **11** (93.2 mg, 0.12 mmol) was reacted with 1-bromo-4-nitrobenzene (24 mg). After chromatography (elution with 50:1 hexanes:Et_2O v/v), **18** (56.8 mg, 78%) was obtained as a yellow solid (mp 50–52°C); $[\alpha]_D^{25}$ −17.1 (*c* 0.40); IR ($CHCl_3$): 2956, 2930, 2893, 1651, 1344, 1257, 765, 750 cm^{-1}; ^1H NMR (400 MHz) δ: −0.01 (s, 3H), 0.01 (s, 3H), 0.10 (s, 6H), 0.12 (s, 6H), 0.86 (s, 18H), 0.90 (s, 9H), 3.79 (m, 1H), 3.87 (t, 1H, *J* = 3.2 Hz), 3.98 (dd, 1H, *J* = 7.6, 11.2 Hz), 4.11 (t, 1H, *J* = 3.2 Hz), 4.21 (m, 1H), 5.43 (d, 1H, *J* = 4.4 Hz), 7.75 (d, 2H, *J* = 8.8 Hz), 8.17 (d, 2H, *J* = 8.8 Hz). Exact Mass calcd. for $C_{26}H_{46}NO_6Si_3$ $(M - C_4H_9)^+$: 552.2633; found: 552.2630. Anal. calcd. for $C_{30}H_{55}NO_6Si_3$: C 59.07, H 9.09; found: C 59.24, H 9.06.

*1-C-(4-Cyanophenyl)-3,4,6-tri-*O-(tert-*butyldimethylsilyl)-D-glucal (**19**)*

Following general procedure A, **11** (148.5 mg, 0.19 mmol) was reacted with 4-bromobenzonitrile (35 mg). After chromatography (elution with 50:1 hexanes:Et_2O v/v), **19** (90.7 mg, 81%) was obtained as a yellow oil; $[\alpha]_D^{25}$ −20.2 (*c* 0.60); IR: 2954, 2929, 2886, 2228, 1650, 1471, 1250, 777, 672 cm^{-1}; ^1H NMR (400 MHz) δ: −0.02 (s, 3H), 0.00 (s, 3H), 0.10 (s, 6H), 0.11 (s, 6H), 0.86 (s, 18H), 0.89 (s, 9H), 3.78 (dd, 1H, *J* = 3.7, 11.4 Hz), 3.86 (m, 1H), 3.96 (dd, 1H, *J* = 7.4, 11.4 Hz), 4.09 (m, 1H), 4.19 (m, 1H), 5.37 (dd, 1H, *J* = 1.0, 4.6 Hz), 7.61 (m, 2H), 7.69 (m, 2H). Exact Mass calcd. for $C_{27}H_{46}NO_4Si_3$ $(M - C_4H_9)^+$: 532.2734; found: 532.2726.

*1-C-(1-Naphthyl)-3,4,6-tri-*O-(tert-*butyldimethylsilyl)-D-glucal (**20**)*

Following general procedure A, **11** (50.3 mg, 0.065 mmol) was reacted with 1-bromonaphthalene (20 mg). After chromatography (elution with 50:1 hexanes:Et_2O v/v), a mixture of **20** and **33** was obtained. Integration of the ^1H NMR spectrum of the mixture indicated a 59% yield of **20** and a 15% yield of **33**. A small amount of pure **20** was isolated by drip column chromatography (elution with 100:1 hexanes:Et_2O v/v) as a colorless oil; $[\alpha]_D^{25}$ −15.7 (*c* 0.80); IR: 2954, 2929, 2886, 1662, 1472, 1463, 1256, 775, 667 cm^{-1}; ^1H NMR (400 MHz) δ: 0.00 (s, 3H), 0.02 (s, 3H), 0.099 (s, 3H), 0.103 (s, 3H), 0.146 (s, 3H), 0.150 (s, 3H), 0.86 (s, 9H), 0.91 (s, 9H), 0.94 (s, 9H), 3.93 (dd, 1H, *J* = 2.4, 11.3 Hz), 3.97 (m, 1H), 4.08 (dd, 1H, *J* = 7.3, 11.2 Hz), 4.15 (m, 1H), 4.26 (m, 1H), 5.01 (dd, 1H, *J* = 1.1, 4.8 Hz), 7.43 (m, 4H), 7.80 (m, 2H), 8.30 (m, 1H). Exact Mass calcd. for $C_{33}H_{55}O_4Si_3$ $(M - CH_3)^+$: 599.3408; found: 599.3394.

*1-C-(4-Carbomethoxyphenyl)-3,4,6-tri-*O-(tert-*butyldimethylsilyl)-D-glucal (**21**)*

Following general procedure A, **11** (129.1 mg, 0.166 mmol) was reacted with methyl 4-bromobenzoate (39 mg). After chromatography (elution with 30:1 hexanes:Et_2O v/v), **21** (57.8 mg, 56%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −17.5 (*c* 2.1); IR: 2954, 2930, 2857, 1728, 1651, 1472, 1463, 1277, 1256 cm^{-1}; ^1H NMR (400 MHz) δ: −0.02 (s, 3H), 0.01 (s, 3H), 0.10 (s, 6H), 0.11 (s, 3H), 0.12 (s, 3H), 0.86 (s, 18H), 0.89 (s, 9H), 3.81 (dd, 1H, *J* = 3.6, 11.4 Hz), 3.87 (m, 1H), 3.90 (s, 3H), 3.98 (dd, 1H, *J* = 7.2, 11.3 Hz), 4.12 (m, 1H), 4.17 (m, 1H), 5.36 (d, 1H, *J* = 4.4 Hz), 7.66 (m, 2H), 7.98 (m, 2H); ^{13}C NMR δ: −5.6, −5.5, −4.9, −4.5, −4.4, −4.3, 17.9, 18.2, 25.6, 25.7, 52.0, 61.4, 68.5, 70.1, 80.6, 100.0, 125.2, 129.5, 129.9, 140.0, 149.8, 167.2. Exact Mass calcd. for $C_{31}H_{55}O_6Si_3$ $(M - CH_3)^+$: 607.3306; found: 607.3293.

*1-C-(2-Carbomethoxyphenyl)-3,4,6-tri-*O-(tert-*butyldimethylsilyl)-D-glucal (**22**)*

Following general procedure A, **11** (124.0 mg, 0.159 mmol) was reacted with methyl 2-bromobenzoate (42 mg). After chromatography (elution with 30:1 hexanes: Et_2O v/v), **22** (47.3 mg, 48%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −43.8 (*c* 0.021); IR: 2954, 2929, 2857, 1735, 1665 cm^{-1}; ^1H NMR (400 MHz) δ: −0.05 (s, 3H), −0.02 (s, 3H), 0.11 (s, 6H), 0.115 (s, 3H), 0.121 (s, 3H), 0.83, 0.89, 0.91 (s each, 9H each), 3.83 (s, 3H), 3.83–3.96 (m, 4H), 4.27 (m, 1H), 4.94 (d, 1H, *J* = 3.7 Hz), 7.34 (m, 1H), 7.41 (m, 2H), 7.62 (m, 1H). Exact Mass calcd. for $C_{31}H_{55}O_6Si_3$ $(M - CH_3)^+$: 607.3306; found: 607.3315.

*1-C-(4-Chlorophenyl)-3,4,6-tri-*O-(tert-*butyldimethylsilyl)-D-glucal (**23**)*

Following general procedure A, **11** (142.1 mg, 0.183 mmol) was reacted with 4-chlorobromobenzene (40.7 mg). After chromatography (elution with 150:1 hexanes: Et_2O v/v), **23** (52.6 mg, 49%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −17.7 (*c* 1.3); IR ($CHCl_3$): 2955, 2929, 2857, 1654, 1472, 1463, 1255 cm^{-1}; ^1H NMR (400 MHz) δ: −0.01 (s, 3H), 0.02 (s, 3H), 0.10 (s, 6H), 0.11 (s, 6H), 0.869 (s, 9H), 0.873 (s, 9H), 0.89 (s, 9H), 3.79 (m, 2H), 3.97 (dd, 1H, *J* = 7.2, 11.4 Hz), 4.15 (m, 2H), 5.23 (dd, 1H, *J* = 1.0, 4.5 Hz), 7.27 (m, 2H), 7.53 (m, 2H). Exact Mass calcd. for $C_{29}H_{52}ClO_4Si_3$ $(M - CH_3)^+$: 583.2862; found: 583.2861.

*1-C-(2-Methylphenyl)-3,4,6-tri-*O-(tert-*butyldimethylsilyl)-D-glucal (**24**)*

Following general procedure A, **11** (113.0 mg, 0.145 mmol) was reacted with 2-bromotoluene (30 μL). After chromatography (elution with 50:1 hexanes: Et_2O v/v), **24** (40.3 mg, 48%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −23.5 (*c* 0.80); IR: 2955, 2929, 2857, 1663, 1463, 1360, 1346, 777, 760 cm^{-1}; ^1H NMR (400 MHz) δ: 0.00 (s, 3H), 0.04 (s, 3H), 0.08 (s, 3H), 0.09 (s, 3H), 0.10 (s, 3H), 0.11 (s, 3H), 0.86 (s, 9H), 0.89 (s, 9H), 0.90 (s, 9H), 2.37 (s, 3H), 3.88 (m, 2H), 3.97 (dd, 1H, *J* = 7.2, 11.1 Hz), 4.08 (m, 1H), 4.79 (dd, 1H, *J* = 0.9, 4.6 Hz), 7.19 (m, 4H). Exact Mass calcd. for $C_{27}H_{49}O_4Si_3$ $(M - C_4H_9)^+$: 521.2938; found: 521.2940.

*1-C-(2-Acetyloxymethylphenyl)-3,4,6-tri-*O-(tert-*butyldimethylsilyl)-D-glucal (**25**)*

Following general procedure A, **11** (104.6 mg, 0.134 mmol) was reacted with 2-acetoxymethylbromobenzene (38 mg). After chromatography (elution with 50:1 hexanes: Et_2O v/v), **25** (38.7 mg, 46%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −20.4 (*c* 0.50); IR: 3068, 3030, 2929, 1747, 1661, 1472, 1463, 1253 cm^{-1}; ^1H NMR (400 MHz) δ: 0.00 (s, 6H), 0.088 (s, 3H), 0.093 (s, 3H), 0.10 (s, 3H), 0.11 (s, 3H), 0.86 (s, 9H), 0.88 (s, 9H), 0.89 (s, 9H), 2.07 (s, 3H), 3.87 (m, 2H), 3.97 (dd, 1H,

J = 7.1, 11.2 Hz), 4.08 (m, 1H), 4.15 (m, 1H), 4.90 (dd, 1H, J = 1.0, 4.6 Hz), 5.24 (d, 1H, J = 12.9 Hz), 5.28 (d, 1H, J = 12.9 Hz), 7.31 (m, 4H); ^{13}C NMR δ: −5.7, −4.9, −4.5, −4.4, 17.8, 18.1, 20.9, 25.6, 25.8, 61.6, 64.1, 67.9, 69.5, 80.9, 101.6, 127.9, 128.7, 129.3, 134.6, 136.3, 151.7, 170.9. Exact Mass calcd. for $C_{29}H_{51}O_6Si_3$ $(M - C_4H_9)^+$: 579.2993; found: 579.2974.

*1-C-(2-Acetyloxyphenyl)-3,4,6-tri-O-(tert-butyldimethylsilyl)-D-glucal (**26**)*

Following general procedure A, **11** (92.5 mg, 0.119 mmol) was reacted with 2-bromophenyl acetate (31.4 mg). After chromatography (elution with 30:1 hexanes: Et_2O v/v), **26** (29.6 mg, 40%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −21.3 (*c* 0.70); IR: 2954, 2923, 2857, 1772, 1660, 1488, 1212, 1190 cm^{-1}; ^{1}H NMR (400 MHz) δ: −0.01 (s, 3H), 0.01 (s, 3H), 0.08 (s, 3H), 0.09 (s, 3H), 0.10 (s, 6H), 0.86 (s, 9H), 0.88 (s, 9H), 0.89 (s, 9H), 2.25 (s, 3H), 3.89 (m, 3H), 4.05 (m, 1H), 4.11 (m, 1H), 5.02 (dd, 1H, J = 1.0, 4.5 Hz), 7.01 (dd, 1H, J = 1.2, 8.0 Hz), 7.25 (m, 2H), 7.49 (dd, 1H, J = 1.8, 7.7 Hz). Exact Mass calcd. for $C_{31}H_{55}O_6Si_3$ $(M - CH_3)^+$: 607.3306; found: 607.3296.

*1-C-(2-Benzyloxyphenyl)-3,4,6-tri-O-(tert-butyldimethylsilyl)-D-glucal (**27**)*

Following general procedure A, **11** (97.4 mg, 0.125 mmol) was reacted with 2-benzyloxybromobenzene (36 mg). After chromatography (elution with 30:1 hexanes: Et_2O v/v), **27** (36.9 mg, 44%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −3.1 (*c* 1.1); IR: 2953, 2856, 1648, 1254, 1222, 1158 cm^{-1}; ^{1}H NMR (400 MHz) δ: −0.02 (s, 3H), −0.01 (s, 3H), 0.00 (s, 3H), 0.03 (s, 3H), 0.10 (s, 6H), 0.84 (s, 9H), 0.86 (s, 9H), 0.87 (s, 9H), 3.90 (m, 3H), 4.12 (m, 2H), 5.10 (s, 2H), 5.23 (dd, 1H, J = 0.8, 4.3 Hz), 6.91 (m, 2H), 7.18 (m, 1H), 7.31 (m, 3H), 7.40 (m, 2H), 7.63 (dd, 1H, J = 1.8, 7.8 Hz); ^{13}C NMR δ: −5.5, −4.9, −4.5, −4.5, 17.9, 18.2, 25.8, 61.5, 69.0, 70.2, 70.6, 80.3, 103.1, 113.4, 120.8, 125.6, 127.4, 127.8, 128.6, 129.2, 129.5, 137.4, 147.7, 156.4. Exact Mass calcd. for $C_{33}H_{53}O_5Si_3$ $(M - C_4H_9)^+$: 613.3200; found: 613.3205.

*1-C-(4-Methoxyphenyl)-3,4,6-tri-O-(tert-butyldimethylsilyl)-D-glucal (**28**)*

Following general procedure A, **11** (122.1 mg, 0.157 mmol) was reacted with 4-bromoanisole (32 mg). After chromatography (elution with 50:1 hexanes: Et_2O v/v), **28** (26.5 mg, 30%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −19.9 (*c* 0.70); IR: 2954, 2929, 2885, 1653, 1252, 1175, 1104 cm^{-1}; ^{1}H NMR (400 MHz) δ: 0.00 (s, 3H), 0.03 (s, 3H), 0.09 (s, 3H), 0.10 (s, 3H), 0.11 (s, 6H), 0.87 (s, 9H), 0.88 (s, 9H), 0.89 (s, 9H), 3.79 (s, 3H), 3.85 (m, 2H), 3.96 (dd, 1H, J = 6.7, 11.3 Hz), 4.12 (m, 2H), 5.12 (d, 1H, J = 4.0 Hz), 6.84 (m, 2H), 7.53 (m, 2H). Exact Mass calcd. for $C_{30}H_{55}O_5Si_3$ $(M - CH_3)^+$: 579.3357; found: 579.3324.

*1-C-(2,5-Dimethoxyphenyl)-3,4,6-tri-O-(tert-butyldimethylsilyl)-D-glucal (**29**)*

Following general procedure A, **11** (101.8 mg, 0.131 mmol) was reacted with 2,5-dimethoxybromobenzene (33 mg). After chromatography (elution with 50:1 hexane:Et_2O v/v), **29** (52.4 mg, 65%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −5.0 (*c* 0.70); IR ($CHCl_3$): 2993, 2953, 2886, 1650, 1500, 1471, 812, 778 cm^{-1}; ^{1}H NMR (400 MHz) δ: 0.02 (s, 3H), 0.04 (s, 3H), 0.106 (s, 3H), 0.111 (s, 3H), 0.12 (s, 6H), 0.87 (s, 9H), 0.90 (s, 9H), 0.91 (s, 9H), 3.75 (s, 3H), 3.77 (s, 3H), 3.87 (m, 1H), 3.92 (s, 1H), 3.93 (d, 1H, J = 0.8 Hz), 4.03 (m, 1H), 4.23 (m, 1H), 5.62 (d, 1H, J = 3.5 Hz), 6.79 (m, 2H), 7.20 (d, 1H, J = 3.0 Hz); ^{13}C NMR δ: −5.5, −4.9, −4.2, 17.9, 18.1, 18.2, 25.8, 25.9, 55.7, 56.3, 61.9, 70.2, 70.4, 80.4, 103.8, 113.3, 114.0, 114.7, 125.4, 147.6, 151.7, 153.6. Exact Mass calcd. for $C_{28}H_{51}O_6Si_3$ $(M - C_4H_9)^+$: 567.2993; found: 567.2973.

*1-C-(6-Acetyloxymethyl-2,4-dibenzyloxyphenyl)-3,4,6-tri-O-(tert-butyldimethylsilyl)-D-glucal (**30**)*

Following general procedure A, **11** (139.2 mg, 0.179 mmol) was reacted with 1-acetyloxymethyl-2-bromo-3,5-dibenzyloxybenzene (7) (86.8 mg) in mesitylene. After chromatography (elution with 9:1 hexanes: EtOAc v/v), **30** (72.2 mg, 51%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −23.8 (*c* 1.45); IR: 2953, 2930, 2885, 1743, 1671 cm^{-1}; ^{1}H NMR (400 MHz) δ: −0.059, −0.056, 0.05, 0.08, 0.10, 0.11 (s each, 3H each), 0.83, 0.87, 0.89 (s each, 9H each), 2.07 (s, 3H), 3.73 (dd, 1H, J = 5.6, 10.3 Hz), 4.00–4.09 (m, 4H), 4.81 (dd, 1H, J = 1.1, 4.7 Hz), 4.99 (s, 2H), 5.00 (s, 2H), 5.13 (d, 1H, J = 12.9 Hz), 5.19 (d, 1H, J = 12.9 Hz), 6.48 (d, 1H, J = 2.3 Hz), 6.57 (d, 1H, J = 2.3 Hz), 7.34–7.37 (m, 10H); ^{13}C NMR δ: −5.63, −5.58, −5.0, −4.7, −4.5, 17.8, 17.9, 18.0, 20.8, 25.6, 25.7, 61.1, 63.6, 67.7, 69.3, 70.0, 80.4, 100.6, 103.0, 105.8, 119.2, 127.1, 127.6, 127.7, 128.1, 128.5, 128.7, 136.8, 137.1, 137.9, 146.8, 157.9, 170.7. Exact Mass calcd. for $C_{47}H_{72}O_8Si_3$ (M^+): 848.4534; found: 848.4573. Anal. calcd. for $C_{47}H_{72}NO_8Si_3$: C 66.46, H 8.54; found: C 66.31, H 8.53.

*1-C-(6-tert-Butyldimethylsiloxymethyl-2,4-dibenzyloxyphenyl)-3,4,6-tri-O-(tert-butyldimethylsilyl)-D-glucal (**31**)*

Following general procedure A, **11** (135.6 mg, 0.174 mmol) was reacted with 1-*tert*-butyldimethylsilyloxymethyl-2-bromo-3,5-dibenzyloxybenzene (107 mg). After chromatography (elution with 10:1 hexanes: EtOAc v/v), **31** (89.9 mg, 56%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −17.1 (*c* 1.38); IR: 2959, 2931, 2854, 1680, 1602, 1469, 1258, 1159, 1061, 836 cm^{-1}; ^{1}H NMR (400 MHz) δ: −0.08, −0.07, 0.03, 0.04, 0.05, 0.06, 0.09 (s, each, 3H each), 0.82, 0.86, 0.89, 0.91 (s each, 9H each), 3.69 (m, 1H), 4.02–4.10 (m, 4H), 4.70–4.81 (m, 3H), 4.96–5.04 (m, 4H), 6.41 (d, 1H, J = 2.4 Hz), 6.82 (d, 1H, J = 2.4 Hz), 7.22–7.39 (m, 10H); ^{13}C NMR δ: −5.6, −5.5, −5.4, −4.9, −4.6, −4.5, −4.4, 17.90, 17.96, 18.02, 18.1, 25.7, 25.8, 61.1, 62.1, 68.1, 69.5, 69.9, 70.4, 80.1, 99.8, 102.6, 103.6, 117.0, 127.2, 127.6, 127.7, 128.0, 128.5, 128.7, 137.2, 137.5, 143.4, 147.1, 157.6, 160.0. Exact Mass calcd. for $C_{51}H_{85}O_7Si_4$ $(M + H)^+$: 920.5294; found: 920.5303.

*Dimer **33***

The isolated yields of **33** from each individual experiment can be found in Table 1. Colorless oil; $[\alpha]_D^{25}$ −35.4 (*c* 0.50); IR: 2954, 2936, 1623, 1251, 1105 cm^{-1}; ^{1}H NMR (400 MHz) δ: 0.01 (s, 6H), 0.03 (s, 6H), 0.06 (s, 18H), 0.07 (s, 6H), 0.84 (s, 18H), 0.86 (s, 18H), 0.87 (s, 18H), 3.71 (dd, 2H, J = 3.7, 11.3 Hz), 3.8 (m, 2H), 3.86 (dd, 2H, J = 7.0, 11.4 Hz), 3.98 (m, 2H), 4.03 (m, 2H), 5.80 (dd, 2H, J = 1.5, 4.8 Hz); ^{13}C NMR δ: −5.7, −5.4, −4.9, −4.6, −4.6, −4.4, 17.8, 18.2, 25.6, 25.7, 25.8, 61.5, 67.7, 70.2, 80.5, 98.6, 145.8. Exact Mass calcd. for $C_{48}H_{102}O_8Si_6$ (M^+): 974.6190; found: 974.6194.

*Preparation of 1-iodo-3,4,6-tri-O-(triisopropylsilyl)-D-glucal (**16**) from **14***

Tin glucal **14** (15) (2.0 g, 2.3 mmol) was dissolved in CH_2Cl_2 (10 mmol) under an argon atmosphere. To this colorless mixture was added a solution of iodine (0.5 g) in CH_2Cl_2 (10 mL) dropwise until a persistent red color, indicating an excess of iodine, remained. The complete consumption of **14** was confirmed by TLC and saturated aqueous $Na_2S_2O_3$ was then added. The mixture was subsequently extracted with CH_2Cl_2, and the combined organic phases were dried and concentrated. Column chromatography of the residual oil on silica gel (5% ether in hexanes or 10% CH_2Cl_2 in hexanes) yielded **16** (1.5 g, 89%) as a colorless oil; $[\alpha]_D^{25}$ −23.6 (*c* 0.30); IR: 1463, 1624, 2866-2958 cm^{-1}; ^{1}H NMR δ: 1.03–1.05 (m, 63H), 3.82–3.91 (m, 2H), 4.06–4.15 (m, 2H), 4.30–4.37 (m, 1H), 5.38 (dd, 1H, J = 1.5, 5.5 Hz); ^{13}C NMR δ: 12.2, 12.5, 12.6, 18.2, 61.9, 68.2, 69.7, 86.2, 107.8, 111.9. Exact Mass calcd. for $C_{30}H_{62}O_4Si_3I$ $(M - C_3H_7)^+$: 697.3001; found: 697.3013.

*Preparation of 1-iodo-3,4,6-tri-O-(triisopropylsilyl)-D-glucal (**16**) from **12***

To a solution of **12** (15) (1.8595 g, 3.0 mmol) in THF (9 mL, 0.35 M) at −78°C was added *t*-BuLi (7.2 mL of a 1.7 M solution in pentane, 12.0 mmol) dropwise. The mixture was stirred for 1.25 h at 0°C and then $ZnCl_2$ (15.1 mL of a 1.0 M solution in Et_2O, 15.0 mmol) was added and the mixture was stirred at room temperature for 40 min. I_2 (1.4 g, 11.1 mmol) was added as a solid and the resulting solution was stirred for 2 h at room temperature. Work-up and chromatography as above provided **16** (1.8238 g, 81%) and the starting material **12** (0.1085 g, 6%).

*General procedure B: preparation and coupling of arylzinc chlorides with 1-iodo-3,4,6-tri-O-(triisopropylsilyl)-D-glucal (**16**)*

A solution of 4-bromoanisole (0.41 mL, 3.3 mmol) in THF (1 mL) at −78°C was treated dropwise with *n*-BuLi (2.0 mL of a 1.6 M solution in hexane) and the resulting white mixture was stirred for 1 h at −78°C. $ZnCl_2$ (3.2 mL of a 1.0 M solution in ether) was then slowly added, and the mixture was warmed to room temperature and stirred for a further 30 min. The ensuing two-phase mixture was concentrated in vacuo and the viscous residue containing 4-methoxyphenylzinc chloride was then dissolved in 1 mL THF to yield a 1.4 M solution of the arylzinc chloride.

4-Methoxyphenylzinc chloride (0.67 mL of a 1.4 M solution in THF) was added dropwise to a solution of **16** (162.1 mg, 0.21 mmol) and $Pd(PPh_3)_2Cl_2$ (7.7 mg, 0.01 mmol) in THF (0.5 mL). The light yellow mixture was stirred at room temperature until the color of the solution changed to dark red (15 min). The consumption of **16** was then confirmed by TLC analysis and the solvent was removed on the rotovap. The crude reaction mixture was purified by column chromatography on silica gel (4:1 hexanes:benzene) to yield 1-*C*-(4-methoxy)phenyl-3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (**36**) (115.3 mg, 73%, Table 2, entry 16) as a colorless oil. This material exhibited: $[\alpha]_D^{25}$ −0.8 (*c* 0.99); IR: 1651, 2866-2945 cm^{-1}; ^1H NMR δ: 1.01–1.06 (m, 63H), 3.79–3.91 (m, 4H), 4.08–4.18 (m, 3H), 4.39–4.44 (m, 1H), 5.22 (dd, 1H, *J* = 1.4, 5.4 Hz) 6.81–6.87 (m, 2H), 7.52–7.59 (m, 2H); ^{13}C NMR δ: 12.2, 12.6, 12.7, 18.2, 18.3, 18.4, 55.6, 62.3, 67.2, 70.5, 81.6, 95.6, 113.7, 127.2, 129.6, 150.6, 160.3. Exact Mass calcd. for $C_{40}H_{76}O_5Si_3$ (M^+): 720.5001; found: 720.4988.

*1-C-Phenyl-3,4,6-tri-O-(triisopropylsilyl)-1-D-glucal (**34**)*

Following general procedure B, **16** (108.4 mg, 0.15 mmol) was reacted with phenylzinc chloride (Table 2, entry 13). After chromatography (elution with 0.5% EtOAc in hexanes), **34** (91.3 mg, 90%) was obtained as a colorless oil: $[\alpha]_D^{25}$ −8.2 (*c* 0.77); IR: 1463, 1495, 1650, 2866–2964 cm^{-1}; ^1H NMR δ: 1.02–1.08 (m, 63H), 3.90 (dd, 1H, *J* = 4.3, 11.1 Hz), 4.06–4.20 (m, 3H), 4.43–4.48 (m, 1H), 5.35 (dd, 1H, *J* = 1.5, 5.3 Hz); ^{13}C NMR δ: 12.2, 12.6, 12.7, 18.2, 18.3, 18.4, 62.3, 67.1, 70.4, 81.7, 97.1, 125.9, 128.4, 128.7, 136.9, 150.9. Exact Mass calcd. for $C_{39}H_{74}O_4Si_3$ (M^+): 690.4895; found: 690.4885. Anal. calcd. for $C_{39}H_{74}O_4Si_3$: C 67.76, H 10.79; found: C 67.43, H 11.00.

*1-O-(2-Furyl)3,4,6-tri-O-(triisopropylsilyl)-D-glucal (**37**)*

Following general procedure B, **16** (91.5 mg, 0.12 mmol) was reacted with 2-furylzinc chloride (Table 2, entry 17). After chromatography (elution with 20% benzene in hexanes), **37** (66.2 mg, 79%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −8.3 (*c* 0.41); IR: 1463, 1492, 1667, 2868–2963 cm^{-1}; ^1H NMR δ: 1.02–1.06 (m, 63H), 3.88 (dd, 1H, *J* = 4.4, 11.2 Hz), 4.02–4.19 (m, 4H), 4.35–4.40 (m, 1H), 5.39 (dd, 1H, *J* = 1.5, 5.3 Hz), 6.37 (dd, 1H, *J* = 1.8, 3.4 Hz), 6.50 (d, 1H, *J* = 3.4 Hz), 7.33 (s, 1H); ^{13}C NMR δ: 12.2, 12.6, 12.7, 18.2, 18.3, 18.4, 62.3, 66.4, 70.6, 81.6, 95.9, 107.4, 111.4, 142.5, 143.6, 150.8. Exact Mass calcd. for $C_{37}H_{72}O_5Si_3$ (M^+): 680.4688; found: 680.4700. Anal. calcd. for $C_{37}H_{72}O_5Si_3$: C 65.24, H 10.65; found: C 64.79, H 10.55.

*1-C-(2-Methylphenyl)-3,4,6-tri-O-(triisopropylsilyl)-D-glucal (**40**)*

Following general procedure B, **16** (101.8 mg, 0.14 mmol) was reacted with 2-methylphenylzinc chloride (Table 2, entry 21). After chromatography (elution with 10% benzene in hexanes), **40** (66.2 mg, 68%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −24.9 (*c* 0.33); IR: 681, 1463, 1658, 2866–2958 cm^{-1}; ^1H NMR δ: 1.00–1.06 (m, 63H), 2.39 (s, 3H), 3.97 (dd, 1H, *J* = 4.8, 11 Hz), 4.10–4.19 (m, 3H), 4.36–4.40 (m, 1H), 4.89 (dd, 1H, *J* = 2.2, 4.8 Hz), 7.11–7.27 (m, 4H); ^{13}C NMR δ: 12.2, 12.6, 18.2, 18.3, 20.1, 62.4, 66.7, 69.8, 82.0, 99.8, 125.8, 128.8, 129.6, 130.6, 137.4, 137.7, 153.4. Exact Mass calcd. for $C_{40}H_{76}O_4Si_3$ (M^+): 704.5051; found: 704.5048.

*General procedure C: preparation and coupling of arylboronate esters with 1-iodo-3,4,6-tri-O(triisopropylsilyl)-D-glucal (**16**)*

A solution of distilled bromobenzene (60 μL, 0.5 mmol) in THF (0.5 mL) at −78°C was treated with *n*-BuLi (0.2 mL of a 2.5 M solution in hexanes, 0.5 mmol) and the resulting solution was stirred for 1.25 h. Trimethylborate (60 μL, 0.5 mmol) was then added dropwise and the resulting milky white solution was warmed to room temperature and stirred a further 30 min. Iodo glucal **16** (185.1 mg, 0.25 mmol) dissolved in THF (2 mL), Na_2CO_3 (0.5 mL of a 2.0 M aqueous solution), and $PdCl_2(PPh_3)_2$ (7.8 mg, 0.0125 mmol) were added to the solution. The reaction temperature was then raised to 70°C and stirring was continued for another 4 h. The crude mixture was concentrated and the residual material was subjected to column chromatography (eluting with 5% benzene in hexanes) to afford 1-*C*-phenyl-3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (**34**) (145.6 mg, 84%, Table 2, entry 6) as a colorless oil.

*1-C-(4-Cyanophenyl)-3,4,6-tri-O-(triisopropylsilyl)-1-D-glucal (**35**)*

Following general procedure C, **16** (187.8 mg, 0.25 mmol) was reacted with the boronate ester generated from 4-bromobenzonitrile (Table 2, entry 14). After chromatography (elution with 20% benzene in hexanes), **35** (162.4 mg, 90%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −8.2 (c 0.27); IR: 1646, 1650, 2229, 2866–2959 cm^{-1}; ^1H NMR δ: 1.03–1.05 (m, 63H), 3.84 (dd, 1H, *J* = 3.8, 11.4 Hz), 4.07–4.20 (m, 3H), 4.47–4.53 (m, 1H), 5.49 (dd, 1H, *J* = 1.4, 5.4 Hz), 7.68 (dd, 4H, *J* = 8.7, 25.6 Hz); ^{13}C NMR δ: 11.8, 12.2, 12.3, 17.8, 17.9, 18.0, 61.7, 66.3, 69.8, 81.7, 99.6, 111.7, 119.1, 125.9, 132.0, 140.6, 148.7. Exact Mass calcd. for $C_{40}H_{73}O_4Si_3N$ (M^+): 715.4847; found: 715.4808. Anal. calcd. for $C_{40}H_{73}O_4Si_3N$: C 67.07, H 10.27; found: C 67.12, H 10.19.

*1-C-(2-Furyl)-3,4,6-tri-O-(triisopropylsilyl)-D-glucal (**37**)*

Following general procedure C, **16** (134.9 mg, 0.18 mmol) was reacted with the boronate ester generated from furan (Table 2, entry 18). After chromatography (elution with 5% benzene in hexanes), **37** (96.1 mg, 78%) was obtained as a colorless oil.

*1-C-Ethenyl-3,4,6-tri-O-(triisopropylsilyl)-D-glucal (**41**)*

Following general procedure C, **16** (119.1 mg, 0.16 mmol) was reacted with the boronate ester generated from vinyl magnesium bromide (Table 2, entry 22). After chromatography (elution with 5% benzene in hexanes), **41** (61.1 mg, 60%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −34.2 (*c* 0.64); IR: 1600, 1658, 2866–2958 cm^{-1}; ^1H NMR δ: 1.03 (s, 63H), 3.81 (dd, 1H, *J* = 3.7, 11.3 Hz), 3.95–4.04 (m, 3H), 4.30–4.34 (m, 1H), 4.81 (t, 1H, *J* = 3.2 Hz), 5.08 (d, 1H, *J* = 10.8 Hz), 5.62 (dd, 1H, *J* = 1.6, 17.2), 6.03 (dd, 1H, *J* = 10.7, 17.5); ^{13}C NMR δ: 12.2, 12.5, 12.7, 18.2, 18.3, 62.4, 66.9, 70.5, 81.2, 101.6, 115.2, 133.2, 149.6. Exact Mass calcd. for $C_{35}H_{72}O_4Si_3$ (M^+): 640.4738; found: 640.4747. Anal. calcd. for $C_{35}H_{72}O_4Si_3$: C 65.56, H 11.32; found: C 65.96, H 11.57.

*General procedure D: preparation and coupling of arylboronic acids with 1-iodo-3,4,6-tri-O-(triisopropylsilyl)-D-glucal (**16**)*

A solution of the Grignard reagent derived from the reaction of 1-bromonaphthalene (0.7 mL, 5 mmol) and magnesium turnings (136.4 mg, 5.5 mmol) in ether (5 mL) was added over 45 min to a solution of trimethylborate in ether (15 mL) at −78°C. The reaction mixture was stirred at this temperature overnight and then treated with 10% H_2SO_4 (10 mL). The mixture was extracted with ether and then the ether extract was acidified with concentrated H_2SO_4. The ether phase was washed with saturated brine and water and was then concentrated to provide 1-naphthylboronic acid, which was used as such.

To a solution of 1-naphthylboronic acid (25.8 mg, 0.15 mmol), **16** (54.3 mg, 0.073 mmol), and $Pd(PPh_3)_2Cl_2$ (5 mg, 0.007 mmol) in THF (0.5 mL) was added Na_2CO_3 (0.15 mL, 2 M aqueous solution) and the resulting two-phase mixture was stirred at 75°C for 90 min. The consumption of **16** was confirmed by TLC analysis, the mixture was cooled to room temperature, and water was added. The crude mixture was extracted with ether, and the combined organic phases were dried and concentrated. Column chromatography of the residual oil on silica gel (1% EtOAc in hexanes) yielded 1-*C*-(1-naphthyl)-3,4,6-tri-*O*-(triisopropylsilyl)-D-glucal (**39**) (40.7 mg, 75%, Table 2, entry 20) as a

colorless oil; $[\alpha]_D^{25}$ −8.8 (*c* 0.16); IR: 1666, 2867–2945 cm^{-1}; ^1H NMR δ: 1.02–1.11 (s, 63H), 4.06 (dd, 1H, *J* = 4.8, 11 Hz), 4.20–4.29 (m, 3H), 4.47–4.51 (m, 1H), 5.10 (t, 1H, *J* = 3.4 Hz), 7.36–7.47 (m, 4H), 7.77–7.82 (m, 2H), 8.34–8.39 (m, 1H); ^{13}C NMR δ: 12.2, 12.6, 12.7, 18.2, 18.4, 62.5, 66.8, 69.8, 82.2, 101.1, 125.5, 126.2, 126.3, 126.4, 126.9, 127.0, 128.3, 129.2, 132.1, 134.0, 152.8. Exact Mass calcd. for $C_{43}H_{76}O_4Si_3$ (M^+): 740.5051; found: 740.5007.

1-C-Phenyl-3,4,6-tri-O-(triisopropylsilyl)-1-D-glucal (34)

Following general procedure D, **16** (98.4 mg, 0.13 mmol) was reacted with phenylboronic acid (Table 2, entry 4). After chromatography (elution with 1% EtOAc in hexanes), **34** (72.8 mg, 81%) was obtained as a colorless oil.

1-C-(4-Methoxyphenyl)-3,4,6-tri-O-(triisopropylsilyl)-1-D-glucal (36)

Following general procedure D, **16** (29 mg, 0.04 mmol) was reacted with 4-methoxyphenylboronic acid (Table 2, entry 15). After chromatography (elution with 1% EtOAc in hexanes), **36** (22.9 mg, 81%) was obtained as a colorless oil.

1-C-(2,4-Dichlorophenyl)-3,4,6-tri-O-(triisopropylsilyl)-1-D-glucal (38)

Following general procedure D, **16** (58.9 mg, 0.08 mmol) was reacted with 2,5-dichlorophenylboronic acid (Table 2, entry 19). After chromatography (elution with 1% EtOAc in hexanes), **38** (49.8 mg, 79%) was obtained as a colorless oil; $[\alpha]_D^{25}$ −18.9 (*c* 0.35); IR: 1463, 1492, 1662, 1666, 2867–2945 cm^{-1}; ^1H NMR δ: 1.02–1.06 (m, 63H), 3.96 (dd, 1H, *J* = 4.7, 11.1 Hz), 4.10–4.19 (m, 3H), 4.37–4.41 (, 1H), 5.11 (dd, 1H, *J* = 2.5, 4.3 Hz), 7.18 (dd, 1H, *J* = 1.9, 8.3 Hz), 7.35 (d, 1H, *J* = 1.9 Hz) 7.36 (d, 1H, *J* = 8.3 Hz); ^{13}C NMR δ: 12.2, 12.5, 12.6, 18.2, 18.3, 62.1, 66.5, 69.8, 82.2, 102.2, 127.2, 130.2, 132.1, 134.0, 134.9, 135.0, 149.0. Exact Mass calcd. for $C_{36}H_{65}O_4Si_3Cl_2$ $(M-C_3H_7)^+$: 715.3568; found: 715.3560.

1-C-Phenyl-3,4,6-tri-O-(triisopropylsilyl)-1-D-glucal (34) from higher order mixed cuprate and 1-iodo-3,4,6-tri-O-(triisopropylsilyl)-D-glucal (16)

To a slurry of CuCN (90.2 mg, 1.0 mmol) in THF (2 mL) at −78°C was added phenyllithium (5.8 mL of a 0.35 M solution in ether) and the resulting mixture was warmed to −20°C for 5 min. After recooling to −78°C, a solution of **16** (241.5 mg, 0.33 mmol) in THF (2 mL) was added and the resulting mixture was stirred at −20°C for 15 h. Saturated NH_4Cl was added and the mixture extracted with ether. The ether phase was washed with water and saturated brine, dried, and concentrated. Flash chromatography as described above provided **34** (55.3 mg, 25%, Table 2, entry 5) as a colorless oil together with 109.7 mg of recovered **16**.

1-C-Ethenyl-3,4,6-tri-O-(triisopropylsilyl)-D-glucal (41) from tetravinyltin *and 1-iodo-3,4,6-tri-O-(triisopropylsilyl)-D-glucal (16)*

A mixture of tetravinyltin (0.024 mL, 0.13 mmol), **16** (45 mg, 0.061 mmol), and $Pd(PPh_3)_2Cl_2$ (4.3 mg, 0.006 mmol) in THF (0.5 mL) was refluxed for 8 h. The mixture was concentrated and column chromatography of the residual oil on silica gel (5% CH_2Cl_2 in hexanes) yielded **41** (26.1 mg, 67%, Table 2, entry 23) as a colorless oil.

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