C-Arylglycosides via a Benzannulation Mediated by Fischer Chromium Carbene Complexes

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C-arylglycosides, part of the general *C*-glycoside family, are carbohydrates with an aromatic ring directly attached to the anomeric carbon.[1] These compounds, with an inherently stable carbon−carbon glycosidic linkage show a broad range of useful antitumor, antifungal, and antibiotic properties that, encourages the development of synthetic methodologies targeted toward this class of natural products.[2] Vineomycin B2 (**1**), medermycin (**2**), and mederrhodin A (**3**) represent two of the four classes of naturally occurring *C*-arylglycosides each based on the regiochemistry of the glycosylated aromatic ring (Figure 1).[3] In each of these compounds there is an ortho relationship between a sugar moiety and a phenolic hydroxyl of the aromatic ring. This is common to many of the naturally occurring *C*-arylglygosides and any synthetic approach toward these compounds must address this point.

Methods available for the formation of *C*-arylglycosides fall into one of the following categories: (1) activation of the anomeric center, providing an electrophilic oxonium ion followed by capture with an aromatic nucleophile,[1,2] (2) addition of a metalated aromatic to a glycosyl halide or lactone,[4] (3) addition of an anomeric carbanion to an electrophilic aromatic equivalent,[5] and (4) transition-metal-mediated cross-coupling between suitably functionalized glycosyl and aromatic coupling partners.[6] Each of these involve formation of the C−C bond between the aromatic and the carbohydrate. In addition, strategies that involve cycloaddition between aromatic aldehydes and activated dienes offer de novo approaches to *C*-arylglycosides.[7] Less common are benzannulation strategies based on assembling the glycosylated aromatic ring from suitably functionalized carbohydrate precursors. For example, *C*-arylglycosides result from the aromatization of products derived from carbohydrate β-polyketides,[8] addition of carbohydrate C-1 silyl enol ethers to quinones,[9] and Bradsher cyclization of isoquinolinium salts.[10] Recently McDonald and co-workers reported an alkyne cyclotrimerization as an example of a benzannulation approach for constructing the aromatic moiety from acyclic precursors.[11] In the following report we describe a strategy toward *C*-arylglycosides that utilizes a benzannulation reaction between Fischer alkenyl carbene complexes and acetylenic sugars. The resulting products are envisaged as intermediates in synthetic approaches to *C*-arylglycoside antibiotics.

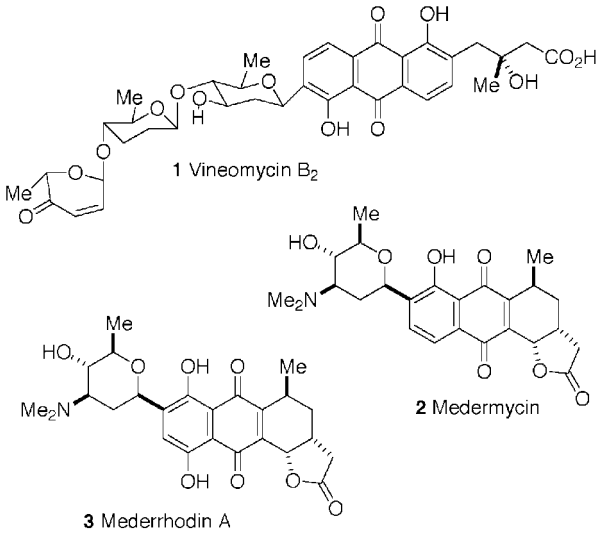

Figure 1. Representative *C*-arylglycosides.

Unsaturated Fischer chromium carbene complexes undergo what is formally a [3+2+1] cycloaddition (the Dötz reaction) with alkynes. The reaction is key to a number of natural product syntheses requiring diversely substituted aromatic rings.[12] Theory and experiment support a mechanism consistent with rate-limiting loss of CO and insertion into an alkyne resulting in a η^1,η^3-vinylcarbene intermediate which after CO insertion and cyclization affords a phenol after demetalation.[13,14] Our interest in the synthesis of *C*-arylglycosides led to a method that involves reacting a *C*-alkynylglycoside **A**[15] with a alkenyl carbene complex **B** or reacting a *C*-glycosylated carbene complex **C** with an alkyne to afford *C*-arylglycosides (Scheme 1). We are aware of only one

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(11) McDonald, F. E.; Zhu, H. Y. H.; Holmquist, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 6605.

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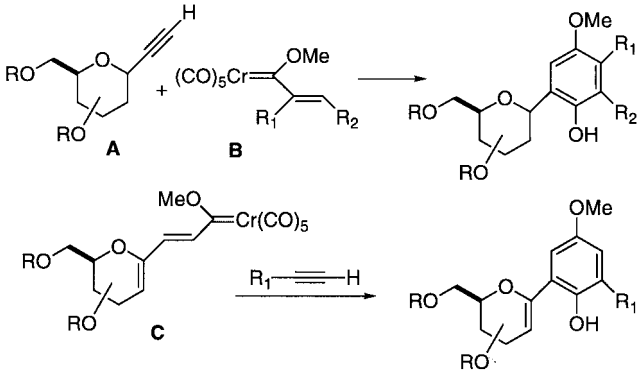
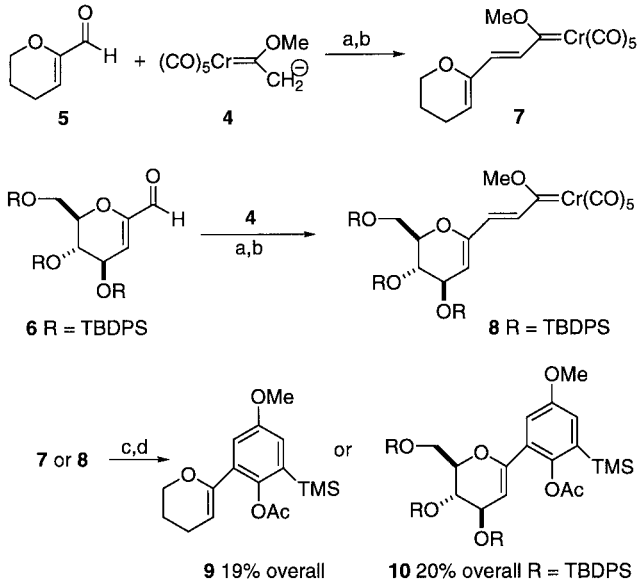
Scheme 1. Two Complementary Approaches



previous example of this strategy in which the authors had limited success in a model reaction directed toward the synthesis of nogalarol using aryl carbene complexes and functionalized alkynes.[16] The difficulty was attributed to the presence of the propargylic oxygen such as that found in *C*-alkynylglycosides. Our methodology is the first report of the formation of *C*-arylglycosides using alkenyl carbene complexes such as **B** or the novel glycosylated carbenes **C**.[17]

Our initial effort involves the benzannulation between α,β-unsaturated glycosylated chromium carbene complexes **7** and **8** and trimethylsilylacetylene (Scheme 2). Metalation of dihydropyran or tri-OTBDPS-D-glucal with *tert*-butyllithium followed by the addition of DMF gives the required C-1 glycosyl aldehydes **5** and **6**.[18] Aldol condensation with the anion of [(methyl)(methoxy)carbene]pentacarbonylchromium(0) **4** gives the desired glycosylated carbene complexes.[19] Complexes **7** and **8** can be isolated by silica gel chromatography. However, it is more convenient to carry the crude complexes on to the

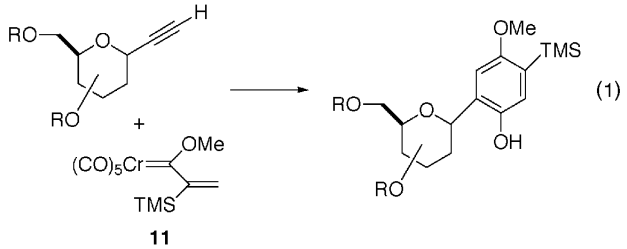
Scheme 2. Synthesis of Glycosylated Carbenes and Cycloaddition[a]



[a] (a) $BF_3 \cdot Et_2O$ or $TiCl_4$ 1:1 complex with aldehyde (3 equiv), (b) pyridine followed by SiO_2, (c) (trimethylsilyl)acetylene (4 equiv), (d) Ac_2O, pyridine, DMAP.

annulation reaction. Heating a THF solution of the carbene complexes and TMS−acetylene, followed by air oxidation to remove the chromium, and subsequent acetylation result in the desired model *C*-arylglycosides as the acetates **9** and **10** in a modest 20% overall yield from the aldehydes. In each case we observe a single regioisomer in accordance with the accepted mechanism for the Dötz reaction. It is important to point out that the observed regiochemistry establishes the phenolic OH (derived from CO) ortho to the C−C linkage to the carbohydrate. Incorporation of the trimethylsilyl group onto the aromatic provides an opportunity to introduce electrophiles onto the ring for further elaboration.[20]

Having established precedent for achieving *C*-arylglycosides via the Dötz benzannulation between glycosylated carbenes and alkynes, we turned our attention to the benzannulation between chromium carbene complex **11** and alkynylglycosides (eq 1). The advantages of this



(1)

method are the availability of the alkenyl carbene complexes and access to a number of alkynylglycosides with various substitution patterns and stereochemistry.[15]

We chose alkynylglycosides **12**−**16** to determine the generality of the annulation with respect to structural variation. The preparation of the alkynylglycosides proceeded according to the following (Scheme 3): React-

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(16) (a) Semmelhack, M. F.; Jeong, N. *Tetrahedron Lett.* **1990**, *31*, 605. (b) Semmelhack, M. F.; Jeong, N.; Lee, G. L. *Tetrahedron Lett.* **1990**, *31*, 609.

(17) For recent examples of carbene complex functionalized sugars, see: (a) Dötz, K. H.; Straub, W.; Ehlenz, R.; Peseke, K.; Meisel, R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1856 and references therein. (b) Ehlenz, R.; Neub, O.; Teckenbrock, M.; Dötz, K. H. *Tetrahedron* **1997**, *53*, 5143. (c) Dötz, K. H.; Ehlenz, R.; Paetsch, D. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2376.

(18) (a) Friesen, R. W.; Trimble, L. A. *J. Org. Chem.* **1996**, *61*, 1165. (b) Friesen, R. W.; Sturino, C. F.; Daljeet, A. K.; Kolaczewska, A. *J. Org. Chem.* **1991**, *56*, 1944. (b) Paquette, L. A.; Schulze, M. M.; Bolin, D. G. *J. Org. Chem.* **1994**, *59*, 2043.

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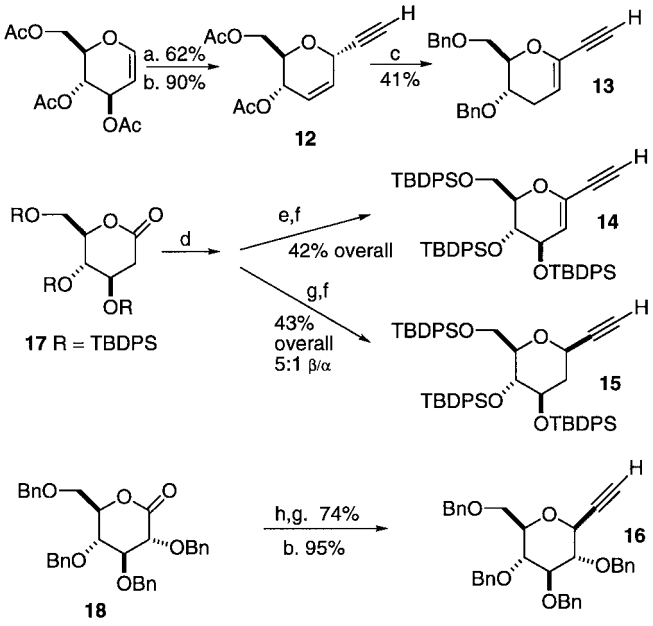
(20) (a) Wilbur, D. S.; Stone, W. E.; Anderson, K. W. *J. Org. Chem.* **1983**, *48*, 1542. (b) Mills, R. J.; Snieckus, V. *Tetrahedron Lett.* **1984**, *25*, 483. (c) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599.

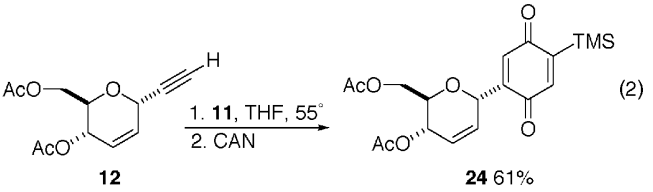
Scheme 3. Synthesis of *C*-Alkynylglycosides[a]



[a] (a) Bis(trimethylsilyl)acetylene, $SnCl_4$; (b) TBAF; (c) (i) K_2CO_3/MeOH; (ii) NaH, DMSO, BnCl; (d) 2-(trimethylsilyl)ethynylmagnesium bromide; (e) $POCl_3$, pyridine; (f) $BnEt_3NCl$, CH_2Cl_2/CH_3CN, 50% aq NaOH; (g) Et_3SiH, $BF_3{\cdot}Et_2O$; (h) 2-(trimethylsilyl)ethynyllithium.

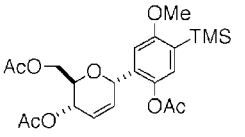
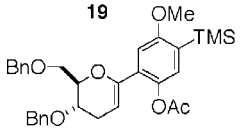
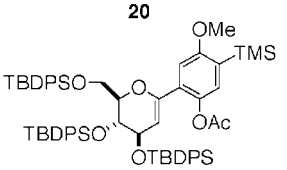
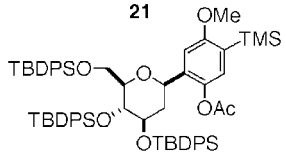
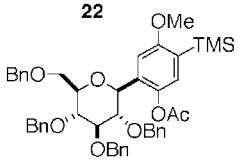
ing bistrimethylsilylacetylene with tri-O-acetyl-D-glucal in the presence of $SnCl_4$,[15] followed by TBAF-induced desilylation, or base-induced conjugation, followed by benzylation, gave alkynylglycosides **12** (α isomer) and **13**. Addition of 2-(trimethylsilyl)ethynylmagnesium bromide to 2-deoxy-D-glucolactone **17** followed by $POCl_3$/pyridine[11] or $BF_3{\cdot}OEt_2/Et_3SiH$[4] and selective desilylation gave alkynylglycosides **14** and **15**. The alkyne **15** was obtained as a inseparable 5:1 mixture of anomers. Addition of 2-(trimethylsilyl)ethynyllithium to the tetra-*O*-benzyl-D-glucolactone **18** followed by reductive deoxygenation and desilylation yields the *β* anomer of alkynylglycoside **16**.

In each case the unoptimized benzannulation between alkynylglycosides **12**−**16** and alkenyl carbene complex **11** proceeds smoothly to afford *C*-arylglycosides **19**−**23** (Table 1). The reactions are done at 50−55 °C at 0.05 M with 1.2 equiv of alkynylglycoside followed by simple air oxidation to give the phenol products. However, it is generally more convenient to protect the phenol with Ac_2O prior to isolation. Alternatively an oxidative workup with Ce(IV) results in the quinone **24** (eq 2).[21]



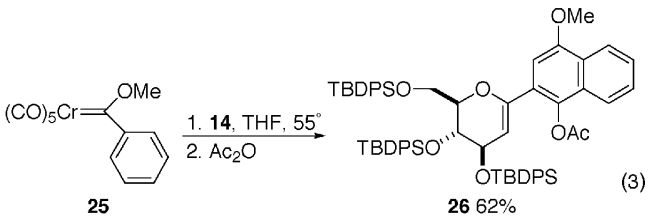
Annulations with carbene complex **11** complement the annulations of complexes **7** and **8** in that the TMS group is now positioned ortho to the methoxy group instead of the phenol derived from CO. This regiochemistry is consistent with the accepted mechanism and positions the phenol OH ortho to the carbohydrate portion of the molecule.[13]

Table 1. Reaction of Carbene 11 with Alkynylglycosides 12−16

Alkyne	Carbene	Product[a]	(%) Yield[b]
12	**11**	 **19**	59[c]
13	**11**	 **20**	53
14	**11**	 **21**	56
15	**11**	 **22**	32[d]
16	**11**	 **23**	54[c]

[a] All reactions were carried out with 1.2 equiv of the alkyne, THF, at 50−55 °C. [b] Isolated purified yield of a single regioisomer after cycloaddition, air oxidation, and protection of the phenol with Ac_2O. [c] Single anomer. [d] Isolated as a 7:1 *β*/α mixture of anomers.

The most convergent approach to *C*-arylglycosides with potential biological activity would involve directly appending the complete aromatic skeleton to the carbohydrate. Semmelhack reported that aryl-substituted carbene complexes were inefficient in their reaction with propargylic ether substituted alkynes to give the desired 4-methoxy-1-naphthols.[16] However, given our success with the alkenyl carbene complexes (vide supra), we began to investigate the methoxy phenyl carbene complex **25** in the benzannulation of our alkynylglycosides. Despite the potential problems, the methoxy phenyl carbene complex **25** reacts with alkynylglycoside **14** to give the desired naphthol **26** as a single regioisomer in 62% yield as the acetate (eq 3). Encouraged by this initial result



we pursued the reaction of **25** with alkynylglycosides **12** and **15**. However, except for **14**, these reactions were problematic, yielding only limited amounts of the desired

(21) Wulff, W. D.; Chan, K.-S.; Tang, P.-C. *J. Org. Chem.* **1984**, *49*, 2293.

naphthols. ^{1}H NMR analysis of the crude reaction mixtures indicated the presence of furan and indene side products; however, these were not isolated to verify this point.[16] Apparently, the oxygen-substituted eneyne functionality of **14** balances the steric and electronic effects in the Dötz benzannulation to favor formation of the desired naphthol product. We are currently investigating the generality of *C*-alkynylglycals such as **14** in their reaction with arylcarbene complexes in an effort to achieve a convergent approach to *C*-arylglycosides.

In conclusion, we have shown that *C*-arylglycosides are available via two complementary approaches utilizing the Dötz benzannulation reaction between Fischer alkenyl chromium carbene complexes and alkynes. We envisage that both the phenols and the quinones will allow for further elaboration of the aromatic moiety of these molecules. Optimization of the convergent naphthol approach and application of the methodology to synthetic efforts are in progress.

Experimental Section

General. All air- or moisture-sensitive reactions were carried out in oven-dried (at 120 °C) or flame-dried glassware under an argon atmosphere. Solvents were degassed and purified by distillation under nitrogen from standard drying reagents. Flash chromatography was carried out using 230−400 mesh silica gel with technical grade solvents distilled prior to use. Radial chromatography was performed on plates prepared from silica gel 60 with PF_{254} indicator. NMR chemical shifts are reported in δ vs Me_4Si assigning the $CDCl_3$ resonance in ^{13}C spectra to be at 77.00 ppm. Elemental analyses were performed by M−H−W Laboratories (Phoenix, AZ). High-resolution mass spectra were obtained in-house or from Washington University Resource for Biomedical/Bio-organic Mass Spectrometry (St. Louis, MO). Compounds **5**,[18b] **11**,[22] **12**,[15] **14**,[11] **16**,[23] **17**,[24] **18**,[25] and **25**[26] were all prepared from literature procedures.

General Benzannulation Procedure A. To a THF (0.2 M) solution of methyl(methoxy)chromium carbene (1.0 equiv), at −78 °C, was added *n*-BuLi (1.0 equiv), and the mixture stirred for 20 min. This solution was cannulated to a CH_2Cl_2 (0.2 M) solution of a 1:1 complex of the aldehyde and Lewis acid (3.0 equiv) at −78 °C. Reaction progress was monitored by TLC, and when starting carbene was consumed, dry pyridine (5 equiv) was added dropwise. After stirring for 45 min, SiO_2 (1 g/100 mg carbene) was added and the mixture stirred for another 15 min. The reaction was filtered through Celite and the filtrate washed with water. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the glycosylated carbene as a red/orange oil. This crude carbene complex was dissolved in THF (0.05 M) and TMS-acetylene (4 equiv) was introduced. The solution was freeze−thaw−degassed (−196 to 25 °C, three cycles) and then heated to 55 °C and stirred under positive argon pressure. When the starting carbene was consumed (TLC) the reaction flask was cooled to room temperature and subsequently stirred in the open air for 0.5 h. Removal of the solvent under reduced pressure and redissolving in CH_2Cl_2 (0.1 M based on starting carbene) preceded the treatment with Ac_2O (2 equiv), pyridine (2 equiv), and a catalytic amount of DMAP. The reaction mixture was stirred at room temperature (16−24 h) until acetylation was complete. The crude reaction was filtered through Celite, and solvents were removed under reduced pressure. Chromatography by standard methods on silica gel gave the pure acetylated phenols.

1-*O*-Acetyl-2-(1′-dihydropyranyl)-4-methoxy-6-trimethylsilylbenzene (9). Following general procedure A, **5** (200 mg, 1.8 mmol), $TiCl_4$ (0.20 mL, 1.8 mmol), methyl(methoxy)chromium carbene anion (150 mg, 0.6 mmol), pyridine (0.25 mL, 3.1 mmol), and 2 g of dry SiO_2 were reacted. The glycosylated carbene **7** was treated with (trimethylsilyl)acetylene (0.25 mL, 1.8 mmol). The solution was degassed, heated under argon to 55 °C, and stirred for 22 h. Subsequent air oxidation, acetylation, and purification by radial chromatography (5−10% EtOAc/hexane) gave 37 mg (19%) of **9** as a single regioisomer: R_f = 0.47 (15% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (d, J = 3.1 Hz, 1H), 6.92 (d, J = 3.1 Hz, 1H), 5.07 (t, J = 3.9 Hz, 1H), 4.10 (t, J = 5.1 Hz, 2H), 3.80 (s, 3H), 2.24 (s, 3H), 2.17 (m, 2H), 1.8 (m, 2H), 0.26 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 169.44, 156.64, 150.72, 145.85, 133.93, 130.48, 120.64, 114.77, 100.99, 66.55, 55.51, 22.12, 21.19, 20.80, −0.80; IR (neat) 2956, 2847, 1766, 1658, 1581, 1428, 1176 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{17}H_{24}O_4Si$ 320.1444, found 320.1445.

1-*O*-Acetyl-2-(2′-deoxy-3′,4′,6′-tri-*O*-*t*-butyldiphenylsilyl-1′-D-glucal)-4-methoxy-6-trimethylsilylbenzene (10). Following general procedure A, **6** (232 mg, 0.216 mmol), $BF_3{\cdot}Et_2O$ (0.027 mL, 0.216 mmol), and methyl(methoxy)chromium carbene anion (33 mg, 0.131 mmol) in 2.5 mL of THF were reacted. In this case the reaction mixture was quenched after 15 min with a pH 7 buffer and extracted with ether (2 × 10 mL). The combined organic layers were dried over $MgSO_4$, and concentration gave an orange oil that was dissolved in ether and stirred with dry SiO_2 (2 g). The glycosylated carbene **8** was treated with (trimethylsilyl)acetylene (0.055 mL, 0.393 mmol). This solution was degassed, heated under argon to 55 °C, and stirred for 28 h. Subsequent air oxidation, acetylation, and purification by radial chromatography (5% EtOAc/hexane) gave 26 mg (20%) of **10** as a single regioisomer: R_f = 0.36 (5% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57−7.55 (m, 6H), 7.45−7.17 (m, 24H), 6.95 (m, 2H), 4.89 (dd, J = 5.5, 1.3 Hz, 1H), 4.41−4.38 (m, 1H), 4.19 (dd, J = 11.5, 7.8 Hz, 1H), 4.06 (d, J = 1.7 Hz, 1H), 3.92−3.90 (m, 1H), 3.83 (dd, J = 11.5, 4.3 Hz, 1H), 3.66 (s, 3H), 1.91 (s, 3H), 1.00 (s, 9H), 0.92 (s, 9H), 0.75 (s, 9H), 0.24 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 169.65, 161.67, 148.02, 141.36, 135.74, 135.72, 135.64, 135.63, 135.55, 135.50, 133.73, 133.67, 133.50, 133.48, 133.39, 133.23, 130.85, 129.76, 129.66, 129.59, 129.56, 129.51, 129.48, 129.15, 127.63, 127.57, 127.56, 127.48, 110.14, 100.36, 80.52, 69.74, 66.15, 62.33, 55.36, 26.87, 26.74, 20.75, 19.17, 19.15, 18.88, −1.17; IR (neat) 3071, 3052, 2960, 2933, 2895, 2859, 1657, 1607, 1478, 1769, 1210, 1116 cm^{-1}; $[\alpha]^{20}_D$ −80.3° (c = 0.66, CH_2Cl_2); HRMS *m*/*z* calcd for $C_{66}H_{80}O_7Si_4$ 1096.4981, found 1096.4979.

General Benzannulation Procedure B. A Schlenk reaction vessel was charged with the carbene complex and *C*-alkynylglycoside and diluted with THF to make the concentration 0.05 M (based on carbene). The solution was freeze−thaw−degassed (−196 to 25 °C, three cycles) and the reaction vessel filled with dry argon. The reaction mixture was heated to 55 °C while being stirred under positive argon pressure. When the starting carbene was consumed (TLC, 16−36 h), the reaction flask was cooled to room temperature and stirred in the open air for 0.5 h. The solvent was removed under reduced pressure and the residue dissolved in CH_2Cl_2 (0.1 M based on starting carbene), treated with Ac_2O (2 equiv), pyridine (2 equiv), and a catalytic amount of DMAP, and stirred under argon at room temperature (16−24 h). The crude reaction was filtered through Celite, and were solvents removed under reduced pressure. Chromatography on silica gel gave the pure acetylated phenols.

1-*O*-Acetyl-2-(4′,6′-di-*O*-acetyl-2′,3′-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-4-methoxy-5-trimethylsilylbenzene (19). Following general procedure B, **12** (120 mg, 0.50 mmol), **11** (152 mg, 0.46 mmol), THF (1 mL), 55 °C for 24 h, air oxidation, acetylation, and radial chromatography (25% EtOAc/hexane) gave 134 mg (59%) of **19**: R_f = 0.5 (33% EtOAc/hexanes); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.01 (s, 1H), 6.85 (s, 1H), 6.12−5.98 (m, 2H), 5.39 (dd, J = 3.8, 1.9 Hz, 1H), 5.30−5.26 (m, 1H), 4.34 (dd, J = 12.0, 5.7 Hz, 1H), 4.03 (dd, J = 12.0, 3.4 Hz, 1H), 3.92 (ddd, J = 9.6, 3.4, 3.4 Hz, 1H), 3.81 (s, 3H), 2.30 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 0.25 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 170.73, 170.32, 170.07, 161.70, 142.60, 132.14, 131.18, 129.98, 129.17, 125.10, 110.00, 70.04, 69.02, 64.75, 62.39, 55.47, 21.00, 20.88, 20.75, −1.22; IR (neat) 2958, 2905, 1747, 1607, 1465, 1371, 1239 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{22}H_{30}O_8Si$ 450.1710, found 450.1728; $[\alpha]^{20}_D$ −30.0° (c = 2.28, CH_2Cl_2).

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1-*O*-Acetyl-2-(4′,6′-di-*O*-benzyl-3′-deoxy-1′-D-glucal)-4-methoxy-5-trimethylsilylbenzene (20). Following general procedure B, **13** (50 mg, 0.15 mmol), **11** (45 mg, 0.14 mmol), THF (1 mL), 55 °C for 24 h, air oxidation, acetylation, and radial chromatography (5%EtOAc/hexane) gave 41 mg (53%) of **20**: R_f = 0.2 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.27 (m, 10H), 6.94 (s, 1H), 6.89 (s, 1H), 5.06 (dd, J = 5.0, 3.0 Hz, 1H), 4.68−4.57 (m, 4H), 4.03 (ddd, J = 12.5, 8.1, 3.9 Hz, 1H), 3.90−3.85 (m, 3H), 3.75 (s, 3H), 2.52 (ddd, J = 17.1, 5.5, 5.5 Hz, 1H), 2.26 (ddd, J = 17.1, 8.3, 3.0 Hz, 1H), 2.18 (s, 3H), 0.23 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 169.95, 161.69, 149.45, 141.14, 138.29, 138.27, 130.40, 129.60, 128.98, 128.38, 128.30, 127.70, 127.68, 127.52, 109.86, 98.49, 77.76, 73.51, 71.24, 70.25, 69.20, 55.41, 27.91, 20.98, −1.19; IR (neat) 3031, 2956, 2902, 2864, 1763, 1603, 1397, 1372, 1207, 1177 cm^{-1}; HRMS (EI) m/z calcd for $C_{32}H_{38}O_6Si$ 546.2438, found 546.2409; $[\alpha]^{20}_D$ 92.1° (c = 0.33, CH_2Cl_2).

1-*O*-Acetyl-2-(3′,4′,6′-tri-*O*-*t*-butyldiphenylsilyl-1′-D-glucal)-4-methoxy-5-trimethylsilylbenzene (21). Following general procedure B, **14** (51 mg, 0.057 mmol), **11** (18 mg, 0.054 mmol), THF (1 mL), 55 °C for 24 h, air oxidation, acetylation, and radial chromatography (2% EtOAc/hexane) gave 33 mg (56%) of **21**: R_f = 0.42 (5% EtOAc/hexane); ^{1}H NMR (250 MHz, CDCl3) δ 7.58−7.15 (m, 30H), 6.96 (s, 2H), 4.89 (dd, J = 5.4, 1.4 Hz, 1H), 4.39 (m, 1H), 4.19 (dd, J = 11.3, 7.7 Hz, 1H), 4.07 (d, J = 1.7 Hz, 1H), 3.92 (m, 1H), 3.83 (dd, J = 11.3, 4.2 Hz, 1H), 3.66 (s, 3H), 1.91 (s, 3H), 1.01 (s, 9H), 0.92 (s, 9H), 0.75 (s, 9H), 0.24 (s, 9H); ^{13}C NMR (62.9 MHz, CDCl3) δ 169.61, 161.68, 148.04, 141.38, 135.73, 135.64, 135.54, 135.50, 133.74, 133.68, 133.52, 133.50, 133.41, 133.25, 130.85, 129.76, 129.65, 129.55, 129.50, 129.15, 127.62, 127.57, 127.48, 110.16, 100.37, 80.54, 69.76, 66.17, 62.35, 55.37, 26.88, 26.75, 20.74, 19.16, 18.87, −1.17; IR (neat) 3073, 2961, 2930, 2860, 1757, 1433, 1210, 1117 cm^{-1}; $[\alpha]^{20}_D$ −65.2° (c = 1.46, CH_2Cl_2). Anal. calcd for $C_{66}H_{80}O_7Si_4$ C, 72.22; H, 7.35. Found: C, 71.99; H, 7.53.

1-*O*-Acetyl-2-(2′-deoxy-3′,4′,6′-tri-*O*-*t*-butyldiphenylsilyl-1′-β-D-glucose)-4-methoxy-5-trimethylsilylbenzene (22). Following general procedure B, **15** (65 mg, 0.073 mmol), **11** (22 mg, 0.066 mmol), THF (1.3 mL), 55 °C for 22 h, air oxidation, acetylation, and radial chromatography (5% EtOAc/hexane) gave 23 mg (32%) of **22** as a 7:1 mixture of anomers enriched during chromatography. The anomeric ratio was determined by integration of the methyl resonance of the acetate at 2.26 ppm for the minor and 2.12 ppm for the major. The following data is for the major β anomer: R_f = 0.28 (5% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70−7.16 (m, 30H), 6.88 (s, 1H), 6.85 (s, 1H), 4.70 (dd, J = 10.6, 4.2 Hz, 1H), 4.19 (dd, J = 11.1, 5.5 Hz, 1H), 4.02 (appt, J = 4.4 Hz, 1H), 3.96−3.92 (m, 1H), 3.78 (dd, J = 10.5, 6.3 Hz, 1H), 3.63 (dd, J = 10.5, 4.3 Hz, 1H), 3.55 (s, 3H), 2.12 (s, 3H), 2.03 (ddd, J = 13.9, 6.0, 4.2 Hz, 1H), 1.64 (ddd, J = 16.0, 10.7, 5.5 Hz, 1H), 0.96 (m, 18H), 0.77 (s, 9H), 0.23 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 169.64, 162.17, 140.51, 136.71, 135.81, 135.73, 135.68, 135.66, 135.42, 134.37, 134.03, 133.73, 133.67, 133.62, 129.60, 129.36, 129.33, 129.30, 127.98, 127.85, 127.61, 127.57, 127.53, 127.44, 127.41, 107.78, 82.87, 72.54, 71.95, 68.59, 65.48, 55.34, 38.55, 31.59, 27.00, 26.92, 26.83, 22.65, 20.89, 19.37, 19.22, 18.97, 11.71, −1.14; IR (neat) 3073, 2960, 2933, 2860, 1765, 1609, 1477, 1430, 1200, 1114 cm^{-1}; HRMS m/z calcd for $C_{66}H_{82}O_7Si_4$ 1098.5138, found 1098.5136.

1-*O*-Acetyl-2-(2′,3′,4′,6′-tetra-*O*-benzyl-1′-β-D-glucose)-4-methoxy-5-trimethylsilyl benzene (23). Following general procedure B, **16** (163 mg, 0.297 mmol), **11** (90 mg, 0.27 mmol), THF (1 mL), 55 °C for 16 h, air oxidation, acetylation, and radial chromatography (5% EtOAc/hexane) gave 111 mg (54%) of **23**: R_f = 0.32 (10% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.14 (m, 18H), 7.02 (s, 1H), 6.85 (s, 1H), 6.84 (s, 1H), 6.71 (s, 1H), 4.97−4.90 (m, 3H), 4.69 (d, J = 10.7 Hz, 1H), 4.58 (d, J = 11.9 Hz, 1H), 4.49 (m, 2H), 4.22 (d, J = 9.5 Hz, 1H), 3.95 (d, J = 10.5 Hz, 1H), 3.89−3.82 (m, 2H), 3.80−3.70 (m, 3H), 3.66 (s, 3H), 3.49−3.47 (m, 1H), 2.16 (s, 3H), 0.27 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 170.13, 161.66, 142.58, 138.60, 138.28, 138.09, 137.57, 131.85, 129.69, 129.56, 128.50, 128.47, 128.43, 128.31, 128.11, 127.89, 127.83, 127.75, 127.69, 127.64, 127.56, 111.20, 86.98, 81.59, 80.16, 79.32, 78.00, 75.82, 75.10, 74.81, 73.49, 68.92, 55.31, 21.00, −1.17, −1.18; IR (neat) 3089, 3034, 2956, 2904, 2865, 1766, 1610, 1457, 1368, 1199, 1069 cm^{-1}; $[\alpha]^{20}_D$ −4.70° (c = 2.00, CH_2Cl_2). Anal. calcd for $C_{46}H_{52}O_8Si$ C, 72.60; H, 6.89. Found: C, 72.56; H, 6.76.

2-(4′,6′-di-*O*-acetyl-2′,3′-deoxy-α-D-*erythro*-hex-2-enopyranosyl)-5-trimethylsilyl-1,4-benzoquinone (24). Following general procedure B, **12** (260 mg, 1.09 mmol), **11** (331 mg, 0.991 mmol), and THF (20 mL) were freeze−thaw−degassed and then reacted at 55 °C for 18 h. Upon completion of the reaction (TLC), 7.0 mL of CAN (3.5 mmol, 0.5 M in HNO_3) was added and stirring continued for 0.5 h at room temperature. The reaction mixture was diluted with brine and extracted with Et_2O (2 × 20 mL), and the combined organic layers were dried over $MgSO_4$. The volatiles were removed under reduced pressure followed by flash chromatography (25% EtOAc/hexane) to give 228 mg (61%) of **24** as a deep orange oil: R_f = 0.62 (25% EtOAc/hexanes); ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.88 (m, 2H), 6.13 (ddd, J = 10.4, 2.9, 1.5 Hz, 1H), 5.93 (ddd, J = 10.4, 2.7, 2.7 Hz, 1H), 5.33 (ddd, J = 6.6, 4.4, 2.3 Hz, 1H), 5.19 (m, 1H), 4.31−4.18 (m, 2H), 3.97 (ddd, J = 10.5, 4.0, 4.0 Hz, 1H), 2.13 (s, 3H), 2.09 (s, 3H), 0.25 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 190.90, 185.93, 170.63, 170.18, 152.35, 144.47, 143.55, 133.39, 129.21, 125.64, 70.85, 68.06, 64.56, 62.69, 20.92, 20.73, −1.84; IR (neat) 2961, 2905, 1747, 1656, 1586, 1368, 1242 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{24}O_7Si$ 392.1291, found 392.1234; $[\alpha]^{20}_D$ −49.1° (c = 1.64, CH_2Cl_2).

1-*O*-Acetyl-2-(3′,4′,6′-tri-*O*-*t*-butyldiphenylsilyl-1′-D-glucal)-4-methoxynaphthalene (26). Following general procedure B, **14** (60 mg, 0.068 mmol), **25** (18 mg, 0.058 mmol), THF (1 mL), 55 °C for 36 h, air oxidation, acetylation, and flash chromatography (5% EtOAc/hexane) gave 42.5 mg (62%) of **26**: R_f = 0.32 (10% EtOAc/hexanes); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.23−8.19 (m, 1H), 7.72−7.69 (m, 1H), 7.61−7.16 (m, 32H), 6.92 (s, 1H), 4.99 (d, J = 4.9 Hz, 1H), 4.44−4.41 (m, 1H), 4.28 (dd, J = 11.3, 7.9 Hz, 1H), 4.08 (s, 1H), 4.01−3.98 (m, 1H), 3.86−3.81 (m, 4H), 2.07 (s, 3H), 1.02 (s, 9H), 0.94 (s, 9H), 0.76 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.40, 153.03, 148.37, 137.59, 135.76, 135.67, 135.56, 135.51, 133.74, 133.66, 133.51, 133.41, 133.26, 129.68, 129.58, 129.53, 128.00, 127.65, 127.60, 127.50, 127.09, 126.23, 125.95, 125.56, 122.23, 121.73, 103.88, 100.96, 80.63, 69.91, 66.32, 62.34, 55.59, 32.59, 26.89, 26.78, 22.65, 20.60, 19.19, 18.89, 14.11; IR (neat) 3071, 2960, 2932, 2894, 1771, 1657, 1599, 1462, 1430, 1111 cm^{-1}; HRMS m/z calcd for $C_{67}H_{74}O_7Si_3$ 1074.4742, found 1074.4721; $[\alpha]^{20}_D$ −63.5° (c = 1.39, CH_2Cl_2).

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Supporting Information Available: Experimental procedures for compounds **6**, **13**, and **15** and ^{1}H/ ^{13}C NMR spectra of compounds **6**, **9**, **10**, **13**, **15**, **19**, **20**, **22**, **24**, and **26** (23 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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