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TETRAHEDRON

Efficient Synthesis of Carbohydrate-containing Carbocyclic Compounds Based on Palladium-catalyzed Vinylation of Sugars and Subsequent Diels-Alder Reaction

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Abstract: In the presence of catalytic amount of Pd(dba)$_2$ and P(o-tol)$_3$, the reaction of 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal with ethylene proceeded smoothly to afford the conjugated dieno-pyranoside in high yield. The Diels-Alder reaction of this carbohydrate-derived diene with some dienophiles constructed chiral carbocyclic system. © 1999 Elsevier Science Ltd. All rights reserved.

***Keywords:** carbohydrates, Diels-Alder reaction, palladium and compounds*

INTRODUCTION

The Diels-Alder reactions of carbohydrate derivatives have become a significant tool for the construction of chiral carbocyclic ring systems in natural product synthesis.[1] Approaches towards the biologically active compounds such as Olivin,[2] Actinobolin,[3] Forskolin[4] and Dehydromevinolin[5] rely on the stereoselective [4+2] cycloaddition of sugar dienes or dienophiles. Especially, conjugated carbohydrate-derived dienes have been found to be excellent building blocks for annulated sugars.[6] Therefore the development of efficient syntheses of such sugar dienes has been strongly desired. Lopez and Lukacs reported the preparation of pyranoid conjugated dienes through a dithiane-based method followed by a Wittig reaction.[7] Giuliano also reported the synthesis of a series of carbohydrate-derived dienes by Wittig alkenylation of carbohydrate-derived enals.[8] These methods require several steps for the synthesis of conjugated dieno-pyranosides. More recently, Voelter and co-workers reported a method for the introduction of a vinyl function into the 3-position of pyranose.[9] They used the reaction of enol triflate pyranoses with vinyltributylstannane in the presence of tetrakis(triphenylphosphine)palladium and lithium chloride according to the Stille method.

In this paper, we would like to report the direct introduction of a vinyl substituents to 2-bromo-D-glucal by palladium-catalyzed reaction and the following Diels-Alder reaction of the obtained conjugated dieno-pyranosides with some dienophiles which lead to the straightforward synthesis of chiral carbocyclic compounds.

RESULTS AND DISCUSSION

We first examined the reaction of 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal (**1**)[10] with vinyltributylstannane in

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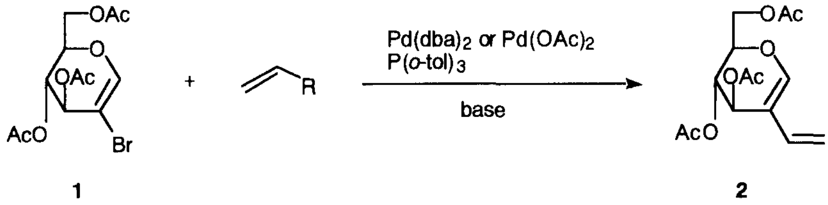
the presence of a palladium catalyst (Stille condition: entry 1–3 in Table 1). After screening of the effect of palladium precursors, solvent, and additives we found the use of $[Pd_2(dba)_3.dba]$ (dba = dibenzylideneacetone)[12] as a catalyst precursor and acetonitrile as a solvent was essential to realize a highly efficient reaction. The use of $Pd(OAc)_2$ instead of $Pd(dba)_2$ resulted in only 28% yield. DMF was also usable as a solvent in this Stille reaction. Under the optimized reaction conditions (10 mol% palladium catalyst, in CH_3CN, at 80 °C), the yield of the product was raised up to 86% (entry 2). Furthermore, we found ethylene can be used as vinyl source. The operational simplicity should be noted. That is, ethylene gas was bubbled into a mixture of bromo-glucal **1**, $Pd(dba)_2$ (5 mol%), $P(o\text{-tol})_3$ (10 mol%), and diisopropylethylamine for 5 min at room temperature, and then the ampule was sealed. After the mixture was stirred at 80 °C for 20 h, filtration of the mixture through short silica-gel afforded the dieno-pyranoside **2** in 76% yield (entry 6). In a case of the present Heck reaction using ethylene, the use of DMF resulted in only low yield.



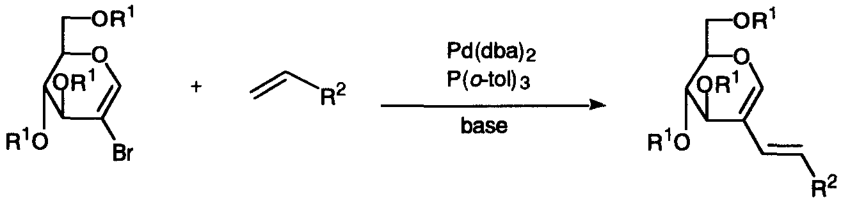
(eq. 1)

Table 1. Reaction of 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal (**1**) with vinyltributylstannane or ethylene [a,b]

entry	R	palladium precursor (mol%)	solvent	base	conditions temp/°C	conditions time/h	% yield[c]
1	$SnBu_3$	$Pd(OAc)_2$ (10)	CH_3CN	none	80	22	28
2	$SnBu_3$	$Pd(dba)_2$ (10)	CH_3CN	none	80	22	86
3	$SnBu_3$	$Pd(dba)_2$ (10)	DMF	none	80	20	74
4	H	$Pd(OAc)_2$ (10)	CH_3CN	Et_3N	80	22	28 (21)[d]
5	H	$Pd(dba)_2$ (5)	CH_3CN	Et_3N	80	43	61
6	H	$Pd(dba)_2$ (5)	CH_3CN	$i\text{-}Pr_2NEt$	80	20	76
7	H	$Pd(dba)_2$ (10)	DMF	Et_3N	80	15	15(63)[d]

[a] Two equiv. of $P(o\text{-tol})_3$ per Pd was used. [b] $Pd(dba)_2$ was prepared according to the reported procedure.[11] Isolated yield after silica-gel column chromatography. [d] The values in the parenthesis indicate the percent of the recovery of starting material.

3,4,6-tri-*O*-Acetyl-2-bromo-D-glucal **1** was also coupled with a variety of acrylic acid and its derivatives such as methyl acrylate[12] and acrylonitrile (eq. 2). Some of the results obtained are summarized in Table 2. In all cases we examined, the uses of $Pd(dba)_2$–$P(o\text{-tol})_3$ as a catalyst system and CH_3CN as a solvent afforded the best results. It should be noted that the reaction of **1** with methyl acrylate in aqueous solvent such as CH_3CN–H_2O (5:1) and DMF–H_2O (5:1) using the same catalyst system proceeded smoothly to give the product **4** in up to 84% yield. The reaction of **1** with acrylonitrile was rather sluggish, so 20 mol% of $Pd(dba)_2$ was necessary to obtain the product in satisfactory yield (base: Et_3N, 62%, *E*/*Z* = 78/22; $i\text{-}Pr_2NEt$, 77%, *E*/*Z* = 60/40). Furthermore, unprotected substrate was also usable in this reaction. That is, the reaction of 2-bromo-D-glucal **3** with methyl acrylate gave the product **5** in 62% yield.



(eq. 2)

1; R^1 = Ac
3; R^1 = H

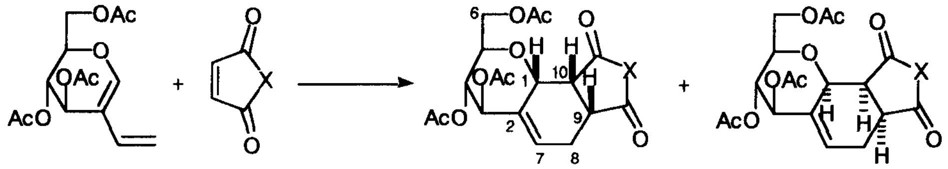
4; R^1 = Ac, R^2 = CO_2CH_3
5; R^1 = H, R^2 = CO_2CH_3
6; R^1 = Ac, R^2 = CO_2H
7; R^1 = Ac, R^2 = CN

Table 2. Reaction of 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal (**1**) and 2-bromo-D-glucal (**3**) with acrylic acid derivatives [a,b]

entry	substrate	R^2	palladium precursor (mol%)	solvent	base	conditions temp/°C	time/h	% yield[c]
1	**1**	CO_2CH_3	$Pd(dba)_2$ (2.5)	CH_3CN	Et_3N	60	18	90
2	**1**	CO_2CH_3	$Pd(dba)_2$ (2.5)	CH_3CN-H_2O (5:1)	Et_3N	80	22	64
3	**1**	CO_2CH_3	$Pd(dba)_2$ (5)	DMF–H_2O (5:1)	Et_3N	80	17	84
4	**1**	CO_2H	$Pd(dba)_2$ (5)	CH_3CN	*i*-Pr_2NEt	80	47	55
5	**1**	CN	$Pd(dba)_2$ (20)	CH_3CN	Et_3N	80	40	62[d]
6	**1**	CN	$Pd(dba)_2$ (20)	CH_3CN	*i*-Pr_2NEt	80	43	77[e]
7	**3**	CO_2CH_3	$Pd(dba)_2$ (5)	CH_3CN	Et_3N	80	21	62

[a] Two equiv. of $P(o\text{-tol})_3$ per Pd was used. [b] $Pd(dba)_2$ was prepared according to the reported procedure.[11] Isolated yield after silica-gel column chromatography. [d] *E/Z* = 78/22. [e] *E/Z* = 60/40.

Next, we examined the Diels-Alder reaction of dieno-pyranoside **2** with some dienophiles such as maleic anhydride and *N*-phenylmaleimide (NPM) (eq. 3). The reactions were carried out in benzene at 80 °C. Hereby of the four products possible for Diels-Alder reaction of **2** with dienophiles, the endo-product **8**–**11** were obtained exclusively as a mixture of anti and syn adducts in 68% and 74% yield, respectively. The ratios between the isomers were 5:1 (**8**:**9**) and 6:1 (**10**:**11**) respectively, favouring the addition of the dienophile to the face of the diene opposite the allylic acetoxy group at C-3. This diastereofacial selectivity would be due to the desire of such electronegative groups in pyranosidic allyl positions to adopt a maximum axial orientation, resulting in an anti-directing effect.[6c,8] Significant NOE effects revealed a all-cis relationship between the two



(eq. 3)

2

X = O, NPh

8; X = O
10; X = NPh

9; X = O
11; X = NPh

hydrogens of the former maleic C-C double bond, the hydrogen at the former anomeric center (C-1) and the C-6 methylene group.

The reaction of 2-bromoglucal **1** with bis(trimethylsilyl)acetylene did not proceed under the same conditions.

CONCLUSION

In conclusion, the above mentioned method represents an efficient and straightforward access to carbohydrate-containing carbocyclic systems, which should be interesting chiral synthons for the construction of optically active polyannulated carbocycles

Experimental Section

General and Materials. All melting points were uncorrected. ^{1}H NMR spectra were recorded on a BRUKER AVANCE 400S at 400 MHz or Varian Unity 500 with tetramethylsilane used as an internal standard. The chemical shifts are reported in ppm on δ scale downfield from tetramethylsilane, and signal patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad peak. ^{13}C NMR spectra were recorded on a BRUKER NMR spectrometer at 100.6 MHz. The chemical shifts are reported in ppm with chloroform-δ (77.0 ppm) or tetramethylsilane as an internal standard. The numbering of the proton and carbon in the assignments are indicated according to the number in eq. (3). IR spectra were measured on Nicolet Impact 410. Optical rotations were measured by SEPA-300 (HORIBA) in solution in a 1-dm cell. Elemental analyses were performed on Yanaco CHN CORDER MT-5 or Perkin Elmer 2400II CHNS/O. Preparative column chromatography was carried out on a Fuji-Davison BW-820 or Wacogel-300 column. Thin layer chromatography (TLC): Foil plates, silica gel 60 F_{254} (Merck; layer thickness 0.2 mm). Acetonitrile was distilled from CaH_2. $Pd(OAc)_2$ was purchased from Wako and used without further purification. [$Pd_2(dba)_3$.dba] was prepared according to the reported procedure.[11]

Reaction of 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal with vinyltributylstannane: [$Pd_2(dba)_3$.dba] (48.9 mg, 0.085 mmol), P(*o*-tol)$_3$ (51.6 mg, 0.17 mmol) and CH_3CN (1.5 mL) were placed under argon in an ampule equipped with a magnetic stirring bar and a Young valve. After being stirred for 1 h at 80 °C, 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal (**1**) (300 mg, 0.85 mmol) in CH_3CN (1.5 mL) was added at room temperature, then vinyltributylstannane (0.50 mL, 1.7 mmol) was added into the above mixture. The ampule was sealed and stirred at 80 °C for 22 h. After confirmation of the completion of the reaction by TLC, the mixture was passed through short silica-gel and the filtrate was concentrated. The residue was chromatographed on silica-gel to give the dieno-pyranoside **2** (218.8 mg, 86%) as a pale yellow syrup. R_f 0.61 (hexane–ethyl acetate 1:1). $[\alpha]_D = +4.7$ ($c = 1.0$, $CHCl_3$). IR (neat): υ_{max} (cm^{-1}) 2962, 1743, 1646, 1428, 1370, 1229, 1164, 1049, 1025, 989, 913, 896, 762, 684 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 2.08, 2.09, 2.10 (each s, 9H, CH_3CO- x 3), 4.18 (dd, $J_{H\text{-}6'\text{-}H6} = 11.2$ Hz, $J_{H6'\text{-}H5} = 3.3$ Hz, 1H, $H_{6'}$), 4.41 (ddd, $J_{H\text{-}5\text{-}H6} = 7.3$ Hz, $J_{H5\text{-}H6'} = 3.3$ Hz, $J_{H5\text{-}H4} = 3.7$ Hz, 1H, H_5), 4.45 (dd, $J_{H\text{-}6\text{-}H6'} = 11.2$ Hz, $J_{H6\text{-}H5} = 7.3$ Hz, 1H, H_6), 4.90 (d, $J_{Hc\text{-}Ha} = 11.2$ Hz, 1H, CH=CH_2), 4.91 (d, $J_{Hb\text{-}Ha} = 17.6$ Hz, 1H, CH=C*H*$_2$), 5.15 (dd, $J_{H4\text{-}H3}$ = 3.5 Hz, $J_{H4\text{-}H5}$ = 3.7 Hz, 1H, H$_4$), 5.64 (br d, $J_{H3\text{-}H4}$ = 3.5 Hz, 1H, H$_3$), 6.15 (dd, $J_{Ha\text{-}Hb}$ = 17.6 Hz, $J_{Ha\text{-}Hc}$ = 11.2 Hz, 1H, C*H*=CH$_2$), 6.68 (s, 1H, H$_1$). ^{13}C NMR (CDCl$_3$) δ 20.4, 20.5, 20.6 (*C*H$_3$CO-), 61.0 (C6), 63.2 (C3), 66.8 (C4), 73.4 (C5), 109.8 (CH=*C*H$_2$), 110.5 (C2), 131.5 (*C*H=CH$_2$), 146.0 (C1), 169.3, 169.9, 170.2 (CH$_3$*C*O-). Anal. Calcd for $C_{14}H_{18}O_7$: C, 56.37; H, 6.08. Found: 56.70; H, 6.13.

Reaction of 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal with ethylene: [Pd$_2$(dba)$_3$.dba] (24.4 mg, 0.0425 mmol), P(*o*-tol)$_3$ (25.8 mg, 0.85 mmol) and CH$_3$CN (1.0 mL) were placed under argon in an ampule equipped with a magnetic stirring bar and a Young valve. After addition of diisopropylethylamine (0.59 mL, 3.4 mmol), the mixture was stirred for 1 h at 80 °C. 3,4,6-Tri-*O*-acetyl-2-bromo-D-glucal (**1**) (300 mg, 0.85 mmol) in CH$_3$CN (1.5 mL) was added and ethylene gas was bubbled in to the above mixture at room temperature for 5 min. Then the ampule was sealed and stirred at 80 °C for 20 h. After confirmation of the completion of the reaction by TLC, the mixture was passed through short silica-gel and the filtrate was concentrated. The residue was chromatograped on silica-gel to give the dieno-pyranoside **2** (193 mg, 76%) as a pale yellow syrup. All spectral data are in full agreement with those of obtained above. $[\alpha]_D$ = +4.6 (*c* = 1.0, CHCl$_3$).

Reaction of 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal with methyl acrylate: [Pd$_2$ (dba)$_3$.dba] (204 mg, 0.356 mmol), P(*o*-tol)$_3$ (216 mg, 0.712 mmol) and CH$_3$CN (2 mL) were placed under argon in an ampoule equipped with a magnetic stirring bar and a Young valve. After addition of triethylamine (5.76 g, 57.0 mmol), the mixture was stirred for 1 h at 80 °C. 3,4,6-Tri-*O*-acetyl-2-bromo-D-glucal (**1**) (5.0 g, 14.3 mmol) in CH$_3$CN (8 mL), and methyl acrylate (3.85 mL, 42.8 mmol) were then added and stirred for 18 h at 80 °C. After confirmation of the completion of the reaction by TLC, the mixture was passed through short silica-gel and the filtrate was concentrated. The residue was chromatograped on silica-gel to give the product **4** (4.6g, 90%) as a pale yellow oil. R_f = 0.31 (hexane/ethyl acetate 2:1). $[\alpha]_D$ = +8.9 (*c* = 1.0, CHCl$_3$). IR (neat): υ_{max} (cm^{-1}) 1742, 1629, 1491, 1443, 1369, 1231, 1167, 1029, 936, 774, 695. ^{1}H NMR (CDCl$_3$) δ 2.09, 2.10 (each s, 9H, C*H*$_3$CO- x 3), 3.73 (s, 3H, CO$_2$C*H*$_3$), 4.20 (dd, $J_{H6\text{-}H6'}$ = 7.3 Hz, $J_{H6\text{-}H5}$ = 3.7 Hz, 1H, H$_6$), 4.4–4.6 (m, 2H, H$_5$, H$_{6'}$), 5.17 (dd, $J_{H4\text{-}H3}$ = 4.3 Hz, $J_{H4\text{-}H5}$ = 4.3 Hz, 1H, H$_4$), 5.60 (d, $J_{H3\text{-}H4}$ = 4.3 Hz, H$_3$), 5.64 (d, *J* = 15.9 Hz, 1H, CH=C*H*CO$_2$Me), 7.00 (s, 1H, H$_1$), 7.22 (d, *J* = 15.9 Hz, 1H, C*H*=CHCO$_2$Me). ^{13}C NMR (CDCl$_3$) δ 20.7, 20.8 (*C*H$_3$CO-), 51.3 (CO$_2$*C*H$_3$), 61.0 (C6), 62.9 (C3), 66.4 (C4), 74.4 (C5), 109.4 (C2), 113.8 (CH=*C*HCO$_2$Me), 140.9 (*C*H=CHCO$_2$Me), 152.1 (C1), 167.2, 169.1, 169.7, 170.0 (CH$_3$*C*O-, *C*O$_2$CH$_3$). Anal. calcd for $C_{16}H_{20}O_9$: C, 53.93; H, 5.66. Found: C, 53.96; H, 5.64.

Reaction of unprotected glucal. A mixture of [Pd$_2$ (dba)$_3$.dba] (51.0 mg, 0.088 mmol) and P(*o*-tol)$_3$ (54.0 mg, 0.18 mmol) in CH$_3$CN (1 mL) was stirred at 20 °C for 30 min under argon in an ampoule equipped with a magnetic stirring bar and a Young valve. 2-bromo-D-glucal (**3**) (400 mg, 1.78 mmol) in CH$_3$CN (1 mL), and methyl acrylate (0.48 mL, 5.34 mmol) were then added and stirred for another 30 min, and the whole mixture was stirred at 80 °C for 21 h. After confirmation of the completion of the reaction, the mixture was passed through short silica-gel using ethyl acetate as an eluent and the filtrate was concentrated. The residue was triturated with benzene to give the product **5** (254 mg, 62%) as a colorless solid. mp.148–153 °C. R_f = 0.32 (ethyl acetate). $[\alpha]_D^{28}$ = +180 (*c* = 1.0, C_2H_5OH). IR (KBr): υ_{max} (cm^{-1}) 3287, 1724, 1619, 1429, 1320, 1296, 1271, 1251, 1166, 985, 869, 782. ^1H NMR (DMSO-d_6) δ 3.63 (s, 3H, CO_2CH_3), 3.6–3.7 (m, 3H, H_5, H_6, $H_{6'}$), 3.94 (dd, $J_{H4\text{-}H3}$ = 4.9 Hz, $J_{H4\text{-}H5}$ = 9.8 Hz, 1H, H_4), 4.03 (d, $J_{H3\text{-}H4}$ = 4.9 Hz, 1H, H_3), 4.8 (br s, 1H, O*H*), 5.3 (br s, 2H,2 x O*H*), 5.90 (d, *J* = 15.8 Hz, 1H, CH=C*H*CO_2Me), 7.11 (s, 1H, H_1), 7.20 (d, *J* = 15.8 Hz, 1H, C*H*=CHCO_2Me). ^{13}C NMR (DMSO-d_6) δ 50.8 (CO_2CH_3), 59.8 (C6), 64.9 (C3), 68.1 (C4), 80.8 (C5), 111.6 (C2), 113.6 (CH=*C*HCO_2Me), 144.0 (*C*H=CHCO_2Me), 152.2 (C1), 167.1 (*C*O_2CH_3). Anal. calcd for $C_{10}H_{14}O_6$ .1/4 H_2O: C, 51.17; H, 6.22. Found: C, 51.19; H, 6.13.

Reaction of 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal with acrylic acid: [Pd_2 $(dba)_3$.dba] (82.0 mg, 0.143 mmol), P(*o*-tol)$_3$ (86.4 mg, 0.285 mmol) and CH_3CN (1 mL) were placed under argon in an ampoule equipped with a magnetic stirring bar and a Young valve. After addition of diisopropylethylamine (1.47 g, 11.4 mmol), the mixture was stirred for 1 h at 80 °C. 3,4,6-Tri-*O*-acetyl-2-bromo-D-glucal (**1**) (1.0 g, 2.85 mmol) in CH_3CN (2 mL), and acrylic acid (0.59 mL, 8.55 mmol) were then added and stirred for 47 h at 80 °C. After confirmation of the completion of the reaction by TLC, the mixture was passed through short silica-gel and the filtrate was concentrated. The residue was chromatograped on silica-gel to give the product **6** (536.6 mg, 55%) as a pale yellow syrup. R_f = 0.31 (hexane/ethyl acetate 1:2). $[\alpha]_D$ = +19.7 (*c* = 1.0, $CHCl_3$). IR (neat): υ_{max} (cm^{-1}) 2969, 1750, 1624, 1368, 1227, 1169, 1054, 1022, 677. ^1H NMR ($CDCl_3$) δ 2.09, 2.10 (each s, 9H, CH_3CO- x 3), 4.20 (dd, $J_{H6\text{-}H6'}$ = 11.6 Hz, $J_{H6\text{-}H5}$ = 3.7 Hz, 1H, H_6), 4.48 (dd, $J_{H6\text{-}H6'}$ = 11.6 Hz, $J_{H6'\text{-}H5}$ = 7.3 Hz, 1H, $H_{6'}$), 4.51--4.53 (m, 1H, H_5), 5.19 (dd, $J_{H4\text{-}H3}$ = 3.7 Hz, $J_{H4\text{-}H5}$ = 3.7 Hz, 1H, H_4), 5.60 (d, $J_{H3\text{-}H4}$ = 3.7 Hz, H_3), 5.63 (d, *J* = 15.9 Hz, 1H, CH=C*H*CO_2H), 7.04 (s, 1H, H_1), 7.30 (d, *J* = 15.9 Hz, 1H, C*H*=CHCO_2H). ^{13}C NMR ($CDCl_3$): δ 20.6, 20.7, 20.8 (*C*H_3CO-), 61.0 (C6), 62.7 (C3), 66.3 (C4), 74.6 (C5), 109.4 (C2), 113.2 (CH=*C*HCO_2H), 143.3 (*C*H=CHCO_2H), 153.2 (C1), 169.4, 170.0, 170.4, 172.1 (CH_3*C*O-, *C*O_2H). Anal. calcd for $C_{15}H_{18}O_9$: C, 52.63; H, 5.30. Found: C, 52.30; H, 5.39.

Reaction of 3,4,6-tri-*O*-acetyl-2-bromo-D-glucal with acrylonitrile: [Pd_2 $(dba)_3$.dba] (328 mg, 0.57 mmol), P(*o*-tol)$_3$ (346 mg, 1.14 mmol) and CH_3CN (2 mL) were placed under argon in an ampoule equipped with a magnetic stirring bar and a Young valve. After addition of diisopropylethylamine (1.47 g, 11.4 mmol), the mixture was stirred for 1 h at 80 °C. 3,4,6-Tri-*O*-acetyl-2-bromo-D-glucal (**1**) (1.0 g, 2.85 mmol) in CH_3CN (1 mL), and acrylonitrile (0.56 mL, 8.55 mmol) were then added and stirred for 18 h at 43 °C. After confirmation of the completion of the reaction by TLC, the mixture was passed through short silica-gel and the filtrate was concentrated. The residue was chromatograped on silica-gel to give the product **7** (709 mg, 77%) as an *E*/*Z* (60/40) mixture. *E*-isomer; R_f = 0.42 (hexane/ethyl acetate 2:1). $[\alpha]_D$ = +39.0 (*c* = 1.0, $CHCl_3$). IR (neat): υ_{max} (cm^{-1}) 3067, 2963, 2213, 1742, 1638, 1621, 1433, 1371, 1221, 1054, 967, 921, 825, 791. ^1H NMR ($CDCl_3$) δ 2.10, 2.10, 2.11 (each s, 9H, C*H*$_3$CO- x 3), 4.19 (dd, $J_{H6\text{-}H6'}$ = 12.1 Hz, $J_{H6\text{-}H5}$ = 4.3 Hz, 1H, H_6), 4.4–4.5 (dd, $J_{H6'\text{-}H6}$ = 12.1 Hz, $J_{H6'\text{-}H5}$ = 7.6 Hz, 1H, $H_{6'}$), 4.5–4.6 (m, 1H, H_5), 5.10 (d, *J* = 16.4 Hz, 1H, CH=C*H*CN), 5.14 (dd, $J_{H4\text{-}H3}$ = 3.5 Hz, $J_{H4\text{-}H5}$ = 3.4 Hz, 1H, H_4), 5.57 (dd, $J_{H3\text{-}H4}$ = 3.5 Hz, $J_{H3\text{-}H5}$ = 1.6 Hz, 1H, H_3), 6.86 (d *J* = 15.5 Hz, 1H, C*H*=CHCN), 6.98 (s, 1H, H_1). ^{13}C NMR ($CDCl_3$) δ 20.6, 20.7, 20.8

(*C*H$_3$CO-), 60.9 (C6), 61.7 (C3), 66.2 (C4), 74.7 (C5), 92.0 (CH=*C*HCN), 109.5 (C2), 118.5 (CN), 146.4 (*C*H=CHCN), 152.7 (C1), 169.3, 169.8, 170.3 (CH$_3$*C*O-). Anal. calcd for $C_{15}H_{17}NO_7$: C, 55.73; H, 5.30; N, 4.33. Found: C, 55.94; H, 5.50; N, 4.49. *Z*-isomer; R_f = 0.31 (hexane/ethyl acetate 2:1). mp. 169--170 °C. $[\alpha]_D$ = +89.0 (*c* = 1.0, CHCl$_3$). IR (neat): υ_{max} (cm^{-1}) 3079, 2954, 2208, 1754, 1619, 1368, 1267, 1231, 1197, 1172, 1058, 1024, 907, 762, 608. ^{1}H NMR (CDCl$_3$) δ 2.10, 2.10, 2.12 (each s, 9H, C*H*$_3$CO- x 3), 4.15 (dd, $J_{H6\text{-}H6'}$ = 11.9 Hz, $J_{H6\text{-}H5}$ = 4.6 Hz, 1H, H_6), 4.4–4.5 ($J_{H6'\text{-}H6}$ = 11.9 Hz, $J_{H6'\text{-}H5}$ = 7.8 Hz, 1H, $H_{6'}$), 4.5–4.6 (m, 1H, H_5), 5.09 (d, J = 12.2 Hz, 1H, CH=C*H*CN), 5.35 (dd, $J_{H4\text{-}H3}$ = 3.0 Hz, $J_{H4\text{-}H5}$ = 3.1 Hz, 1H, H_4), 5.58 (dd, $J_{H3\text{-}H4}$ = 3.0 Hz, $J_{H3\text{-}H5}$ = 1.5 Hz, 1H, H_3), 6.48 (d J = 12.2 Hz, 1H, C*H*=CHCN), 7.16 (s, 1H, H_1). ^{13}C NMR (CDCl$_3$) δ 20.7, 20.8, 21.2 (*C*H$_3$CO-), 60.8 (C6), 64.0 (C3), 65.5 (C4), 74.3 (C5), 90.5 (CH=*C*HCN), 109.0 (C2), 117.2 (CN), 144.6 (*C*H=CHCN), 153.3 (C1), 169.2, 170.0, 170.3 (CH$_3$*C*O-). Anal. calcd for $C_{15}H_{17}NO_7$: C, 55.73; H, 5.30; N, 4.33. Found: C, 56.04; H, 5.26; N, 4.36.

Diels-Alder reaction of dieno-pyranoside 2 with maleic anhydride: A solution of dieno-pyranoside **2** (870 mg, 2.9 mmol) and maleic anhydride (341 mg, 3.5 mmol) in benzene (5 mL) was heated at 80 °C for 18 h. The mixture was concentrated and the remaining solvent was removed *in vacuo*, and the obtained residue was column chromatographed on silica-gel to afford 782 mg (68%) of a 5:1 ratio of inseparatable cycloadducts of **8** (anti) and **9** (syn) as a colorless solid. R_f 0.69 (ethyl acetate); mp 25--27 °C; [α] +19.6 (*c* 1.0. CHCl$_3$); IR (KBr) 2958, 1864, 1788, 1747, 1433, 1370, 1230, 1223, 1135, 1101, 1037, 980, 962, 950, 925, 720 cm^{-1}; ^{1}H NMR (**8**, CDCl$_3$) δ 2.07, 2.11, 2.13 (each s, 9H, C*H*$_3$CO- x 3), 2.34 (ddd, $J_{H8'\text{-}H8}$ = 19.0 Hz, $J_{H8'\text{-}H7}$ = 6.7 Hz, $J_{H8'\text{-}H9}$ = 1.7 Hz, 1H, $H_{8'}$), 2.92 (ddd, $J_{H8\text{-}H8'}$ = 19.0 Hz, $J_{H8\text{-}H9}$ = 6.6 Hz, $J_{H8\text{-}H7}$ = 5.3 Hz, 1H, H_8), 3.38 (ddd, $J_{H9\text{-}H10}$ = 8.1 Hz, $J_{H9\text{-}H8}$ = 6.6 Hz, $J_{H9\text{-}H8'}$ = 1.7 Hz, 1H, H_9), 3.64 (dd, $J_{H10\text{-}H1}$ = 8.4 Hz, $J_{H10\text{-}H9}$ = 8.1 Hz, 1H, H_{10}), 3.97 (dd, $J_{H6\text{-}H6'}$ = 12.1 Hz, $J_{H6\text{-}H5}$ = 3.8 Hz, 1H, H_6), 4.0--4.1 (m, 1H, H_5), 4.76 (br d, $J_{H1\text{-}H10}$ = 8.4 Hz, 1H, H_1), 4.83 (dd, $J_{H4\text{-}H3}$ = 4.1 Hz, $J_{H4\text{-}H5}$ = 4.0 Hz, 1H, H_4), 4.8–4.9 (m, 1H, $H_{6'}$), 5.35 (d, $J_{H3\text{-}H4}$ = 4.1 Hz, 1H, H_3), 6.11 (br d, $J_{H7\text{-}H8'}$ = 6.7 Hz, 1H, H_7). ^{13}C NMR (**8**, CDCl$_3$) δ 20.5, 20.7, 20.8 (*C*H$_3$CO-), 21.0 (C8), 37.7 (C9), 43.8 (C10), 59.9 (C6), 61.5 (C1), 69.1 (C4), 71.8 (C3), 74.2 (C5), 127.5 (C7), 130.1 (C2), 168.0, 169.1, 169.6 170.8, 172.5 (CH$_3$*C*O-, C=O). Anal. Calcd for $C_{24}H_{25}NO_9$: C, 61.14; H, 5.34; N, 2.97. Found: C, 61.12; H, 5.36 N, 3.02.

Diels-Alder reaction of dieno-pyranoside 2 with *N*-phenylmaleimide: A solution of **2** (870 mg, 2.9 mmol) and *N*-phenylmaleimide (550 mg, 3.19 mmol) in benzene (5 mL) was heated at 80 °C for 18 h. The mixture was concentrated and the remaining solvent was removed *in vacuo*, and the obtained residue was column chromatographed on silica-gel to afford 1.01 g (74%) of a 6:1 ratio of inseparatable cycloadducts of **10** (anti) and **11** (syn). R_f 0.64 (ethyl acetate); mp 44--45 °C; [α] +13.3 (*c* 1.0, CHCl$_3$); IR (KBr) 2958, 1758, 1716, 1598, 1499, 1384, 1231, 1049, 1035, 916, 759, 695 cm^{-1}; ^{1}H NMR (**10**, CDCl$_3$) δ 2.03, 2.08, 2.11 (each s, 9H, C*H*$_3$CO- x 3), 2.27 (ddd, $J_{H8\text{-}H8'}$ = 17.0 Hz, $J_{H8\text{-}H7}$ = 1.6 Hz, $J_{H8\text{-}H9}$ = 7.6 Hz, 1H, H_8), 2.99 (ddd, $J_{H8'\text{-}H8}$ = 17.0 Hz, $J_{H8'\text{-}H7}$ = 6.1 Hz, $J_{H8'\text{-}H9}$ = 2.0 Hz, 1H, $H_{8'}$), 3.28 (ddd, $J_{H9\text{-}H10}$ = 8.7 Hz, $J_{H9\text{-}H8}$ = 7.6 Hz, $J_{H9\text{-}H8'}$ = 2.0 Hz, 1H, H_9), 3.57 (dd, $J_{H10\text{-}H1}$ = 7.7 Hz, $J_{H10\text{-}H9}$ = 8.7 Hz, 1H, H_{10}), 4.1--4.15 (m, 2H, H_5, H_6), 4.6–4.65 (m, 1H, $H_{6'}$), 4.78 (dd, $J_{H1\text{-}H10}$ = 7.7 Hz, $J_{H1\text{-}H3}$ = 1.6 Hz, 1H, H_1), 4.90 (dd, $J_{H4\text{-}H3}$ = 6.0 Hz, $J_{H4\text{-}H5}$ =

5.3 Hz, 1H, H_4), 5.52 (dd, $J_{H3\text{-}H4}$ = 6.0 Hz, $J_{H3\text{-}H1}$ = 1.6 Hz, 1H, H_3), 6.00 (dd, $J_{H7\text{-}H8'}$ = 6.1 Hz, $J_{H7\text{-}H8}$ = 1.6 Hz, 1H, H_7), 7.25–7.3 (m, 2H, aromatic protons), 7.4–7.5 (m, 3H, aromatic protons). ^{13}C NMR (**10**, $CDCl_3$) δ 20.5, 20.6, 20.7 (CH_3CO-), 22.2 (C8), 37.8 (C9), 43.3 (C10), 60.9 (C6), 66.0 (C1), 69.6 (C4), 71.4 (C3), 76.7 (C5), 125.6 (C7), 126.2, 128.4, 128.9, 129.0, 131.7 (aromatic carbon), 131.9 (C2), 169.3, 169.6, 170.6 (CH_3*C*O-), 174.0, 177.3 (C=O). Anal. Calcd for $C_{24}H_{25}NO_9$: C, 61.14; H, 5.34; N, 2.97. Found: C, 61.13; H, 5.34; N, 2.77.

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References and Notes

1. Giuliano, R. M. In Cycloaddition Reactions in Carbohydrate Chemistry; American Chemical Society, Washington 1992.
2. Franck, R.W.; John, T. V. *J. Org. Chem.* **1983**, *48*, 3269–3276.
3. Rahman, M. A.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1985**, *107*, 5576–5578.
4. (a) Tsang, R; Fraser-Reid, B. *J. Org. Chem.* **1992**, *57*, 1065–1067: (b) Mukhopadhyay, A.; Ali, S. M.; Husain, M.; Suryawanshi, S. N.; Bhakuni, D. S. *Tetrahedron Lett.* **1989**, *30*, 1853–1856.
5. Herscovici, J.; Delatre, S.; Antonakis, K. *Tetrahedron Lett.* **1991**, *32*, 1183–1186.
6. (a) Lopez J, C.; Lameignère, E.; Burnouf, C.; Laborde, M.A.; Ghini, A. A.; Olesker, A.; Lukacs, G.; *Tetrahedron* **1993**, *49*, 7701–7722: (b) Giuliano, R. M.; Buzby, J. H.; Macropulos, N.; Springer, J. P. *J. Org. Chem.* **1990**, *55*, 3555–3562: (c) Burnouf, C.; Lopez, J. C.; Calvo-Flores, F. G.; Laborde, M. A.; Olesker, A.; Lukacs, G. *J. Chem. Soc., Chem. Commun.* **1990**, 823–825: (d) Lipshutz, B. H.; Nguyen, S. L.; Elworthy, T. R. *Tetrahedron* **1988**, *44*, 3355–3364: (e) Lopez, J. C.; Lameignère, E.; Lukacs, G. *J. Chem. Commun., Chem. Commun.* **1988**, 706–707: (f) Giuliano, R. M.; Buzby, J. H. *Carbohydr. Res.* **1986**, *158*, C1–C4.
7. Lopez, J. C.; Lameignère, E.; Lukacs, G. *J. Chem. Soc., Chem. Commun.* **1988**, 514–515.
8. Giuliano, R. M.; Jordan, Jr. A. D.; Gauthier, A. D.; Hoogsteen, K. *J. Org. Chem.* **1993**, *58*, 4979–4988.
9. Al-Abed, Y.; Al-Tel, T. H.; Schröder, C.; Voelter, W. *Angew. Chem.* **1994**, *106*, 1568–1571; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1499–1501.
10. Fogh, A.; Lundt, I.; Pedersen, C.; Rasmussen, P. *Acta Chem. Scand. B.* **1977**, *31*, 768–770.
11. (a) Takahashi, Y.; Ito, T.; Sakai, S.; Ishii, Y. *Chem. Commun.* **1970**, 1065–1066: Ukai, T.: (b) Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253–256.
12. Preliminary results for the reaction of **1** with methyl acrylate; Hayashi, M.; Amano, K.; Tsukada, K.; Lamberth, C. *J. Chem. Soc., Perkin Trans 1* **1999**, 239–240.