A Rapid Synthesis of Pyranoid Glycals Promoted by β-Cyclodextrin and Ultrasound

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A convenient and environmentally benign procedure for the synthesis of glycals from glycosyl bromides with very low zinc dust loading (1.5 equiv.) is described. The process is activated by *β*-cyclodextrin and ultrasound. Based on 19 samples, this method has been demonstrated to be highly effective for a broad range of glycosyl bromides, including acid- or base-sensitive and disaccharide glycosyl bromides. A yield of 85%—96% of glycals was obtained.

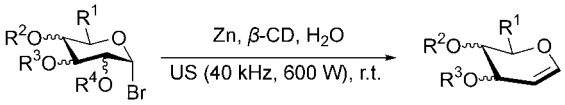
Keywords ultrasound, *β*-cyclodextrin, glycal, znic, glycosyl bromide, carbohydrate

Introduction

Glycals are useful substrates in the synthesis of biologically active carbohydrates and their analogs.[1] Due to the double bond between C-1 and C-2, glycals show remarkable properties in glycosidation, and can react with various aglycons to provide *O*-glycosides,[2] *C*-glycosides,[3] *S*-glycosides,[4] *N*-glycosides,[5] cyclopropanated carbohydrates[6] and 2-amino sugars.[7] The preparation of glycals is generally based on the radical-induced elimination of glycosyl bromides, glycosyl chlorides, 1-thioglycosides and their S-oxides, and 1-telluroglycosides, using agents such as zinc dust, titanium(III), chromium(II), and aluminum amalgam. The classic Fischer-Zach glycal synthesis, which treats glycosyl bromide with zinc in acetic acid, has been one of the most popular methods, it has been widely investigated and modified. Usually, large amounts of zinc dust or toxic, expensive metal reagents are used under vigorous conditions to enhance the activity of zinc.[8] Recently, the Fischer-Zach procedure was found to be feasible in neutral PEG-600/H_2O at room temperature using a slight excess of zinc dust (2.0 equiv.).[9]

β-Cyclodextrin (*β*-CD) is a torus-shaped molecule with a hydrophobic interior cavity and a hydrophilic surface. It has been used in reactions requiring covalent catalysis, general acid-base catalysis, or non-covalent catalysis.[10] It has attracted interests of synthetic chemists in recent years.[11] Ultrasound, which minimizes waste production and the use of hazardous reagents by enhancing the rate, yield, and selectivity of reactions, has emerged as an environmentally benign technology.[12] Protected glycopyranosyl bromides are readily transformed to the high yields of the corresponding glycals, using more than 10 equiv. of zinc dust in phosphate buffer at room temperature. Under these conditions, a longer reaction time is necessary to support conversion.[13] Herein, a highly efficient alternative procedure for Fischer-Zach glycal synthesis is proposed. The procedure involved only 1.5 equiv. of zinc dust, and the transformation was promoted by the combined effects of *β*-CD and ultrasound in water at room temperature (Scheme 1). This procedure is especially efficient for the synthesis of disaccharide glycals.

Scheme 1 Synthesis of glycals promoted by *β*-CD and ultrasound



R^1 = H, CH_3, CH_2OAc, CH_2OBz, CH_2OMs, CH_2OTs, CH_2N_3
R^2 = Ac, Bz, Bn, glycosyl
R^3 = Ac, Bz, Bn
R^4 = Ac, Bz

Experimental

General methods

Sonochemical reactions were carried out in a commercially available ultrasound cleaning bath (40 kHz, 600 W) equipped with an automatic thermally regulated heating/cooling circulation system. Reactions were

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Received March 1, 2011; revised April 11, 2011; accepted May 10, 2011.
Project supported by the Project of Science and Technology of Shanxi Province (No. 20100311069) and the Scientific Research Foundation of Shanxi Agricultural University (No. XB2009013).

monitored by thin layer chromatography using silica gel HSGF254 plates. Flash chromatography was performed using silica gel HG/T2354-92. ^{1}H NMR and ^{13}C NMR (600 and 150 MHz, respectively) spectra were recorded in $CDCl_3$. ^{1}H NMR chemical shifts are reported in δ relative to tetramethylsilane (TMS), with the solvent resonance employed as the internal standard ($CDCl_3$, δ=7.26). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), integration, and coupling constants (Hz). ^{13}C NMR chemical shifts are reported from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$, δ=77.0). ESI-HRMS spectra were recorded on a BioTOF Q instrument. Optical rotations were examined on a Perkin Elmer-341 digital polarimeter. Glycals **2**, **21**—**37** are known compounds and their ^{1}H NMR data matched the literature data.[14,15] *D*-Glucose, *D*-mannose, *D*-galactose, *D*-arabinose, *L*-rhamnose, *D*-maltose, *D*-lactose, and *D*-cellobiose were commercially available and used without further purification. Glycopyranosyl bromide **1**, **3**—**20** were prepared according to the reported procedure.[16]

General procedure

β-Cyclodextrin (0.2 mmol) and zinc dust (1.5 mmol) were added to a solution of glycopyranosyl bromide (1 mmol) in H_2O (20.0 mL) under ultrasound irradiation. TLC was used to monitor the reaction. Usual workup and purification provided the corresponding compounds.

3,6,2',3',4',6'-Hexa-*O*-acetyl-*α*-*D*-maltal (2) Colorless syrup, $[\alpha]_D^{25}$ +169 (*c* 0.6, $CHCl_3$) [lit.[14a] $[\alpha]_D^{25}$ +66 (*c* 1.0, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ: 2.01 (s, 3H), 2.03 (s, 3H), 2.05 (s, 3H), 2.06 (s, 3H), 2.10 (s, 3H), 2.13 (s, 3H), 4.03—4.05 (m, 2H), 4.11 (dd, *J*=12.3, 2.0 Hz, 1H), 4.23 (dd, *J*=12.3, 4.1 Hz, 1H), 4.29—4.32 (m, 1H), 4.33—4.39 (m, 2H), 4.82—4.84 (m, 2H), 5.06 (dd, *J*=10.0, 9.9 Hz, 1H), 5.18 (dd, *J*=4.2, 4.1 Hz, 1H), 5.41 (dd, *J*=10.0, 9.9 Hz, 1H), 5.50 (d, *J*=4.0 Hz, 1H), 6.44 (d, *J*=6.2 Hz, 1H).

3,6,2',3',4',6'-Hexa-*O*-acetyl-*α*-*D*-cellobial (21)[14b] Colorless syrup, $[\alpha]_D^{25}$ −4 (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 2.00 (s, 3H), 2.02 (s, 3H), 2.05 (s, 3H), 2.06 (s, 3H), 2.09 (s, 3H), 2.12 (s, 3H), 3.68—3.70 (m, 1H), 3.99 (dd, *J*=7.4, 5.6 Hz, 1H), 4.07 (dd, *J*=12.3, 2.2 Hz, 1H), 4.13—4.16 (m, 1H), 4.19 (dd, *J*=11.9, 6.2 Hz, 1H), 4.31 (dd, *J*=12.4, 4.5 Hz, 1H), 4.44 (dd, *J*=11.7, 2.5 Hz, 1H), 4.69 (d, *J*=8.0 Hz, 1H), 4.82 (dd, *J*=6.1, 3.3 Hz, 1H), 4.98 (dd, *J*=9.4, 8.0 Hz, 1H), 5.09 (dd, *J*=10.0, 9.4 Hz, 1H), 5.19 (dd, *J*=9.6, 9.4 Hz, 1H), 5.42 (m, 1H), 6.41 (d, *J*=6.1 Hz, 1H).

3,6,2',3',4',6'-Hexa-*O*-acetyl-*α*-*D*-lactal (22) Colorless syrup, $[\alpha]_D^{25}$ −9 (*c* 0.5, $CHCl_3$) [lit.[14a] $[\alpha]_D^{23}$ −16 (*c* 1.4, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ: 1.98 (s, 3H), 2.05 (s, 3H), 2.06 (s, 3H), 2.09 (s, 3H), 2.12 (s, 3H), 2.16 (s, 3H), 3.91 (dd, *J*=7.1, 6.4 Hz, 1H), 4.00 (dd, *J*=7.4, 5.5 Hz, 1H), 4.09 (dd, *J*=11.2, 7.2 Hz, 1H), 4.14—4.17 (m, 2H), 4.20 (dd, *J*=11.8, 6.1 Hz, 1H), 4.44 (dd, *J*=11.7, 2.5 Hz, 1H), 4.66 (d, *J*=8.0 Hz, 1H), 4.84 (dd, *J*=6.1, 3.3 Hz, 1H), 5.01 (dd, *J*=10.6, 3.5 Hz, 1H), 5.19 (dd, *J*=10.4, 8.0 Hz, 1H), 5.37 (d, *J*=2.6 Hz, 1H), 5.41 (dd, *J*=4.1, 3.9 Hz, 1H), 6.41 (d, *J*=6.1 Hz, 1H).

3,4,6-Tri-*O*-acetyl-*D*-glucal (23) White power, m.p. 50—51 ℃ (lit.[14c] m.p. 50—52 ℃); $[\alpha]_D^{25}$ −22 (*c* 4.1, $CHCl_3$) [lit.[14c] $[\alpha]_D^{25}$ −22 (*c* 2.1, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ: 2.05 (s, 3H), 2.08 (s, 3H), 2.10 (s, 3H), 4.20 (dd, *J*=12.4, 3.1 Hz, 1H), 4.26 (m, 1H), 4.40 (dd, *J*=12.2, 5.8 Hz, 1H), 4.85 (dd, *J*=9.5, 3.3 Hz, 1H), 5.22 (dd, *J*=7.5, 6.0 Hz, 1H), 5.35 (dd, *J*=4.2, 3.7 Hz, 1H), 6.47 (d, *J*=6.2 Hz, 1H).

3,4,6-Tri-*O*-acetyl-*D*-galactal (24) Colorless syrup, $[\alpha]_D^{25}$ −9 (*c* 0.1, EtOAc) [lit.[14a] $[\alpha]_D^{25}$ −17 (*c* 1.1, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ: 2.03 (s, 3H), 2.09 (s, 3H), 2.13 (s, 3H), 4.22 (dd, *J*=11.6, 5.2 Hz, 1H), 4.28 (dd, *J*=11.6, 7.2 Hz, 1H), 4.32—4.33 (m, 1H), 4.72—4.74 (m, 1H), 5.43 (dd, *J*=3.8, 1.1 Hz, 1H), 5.56 (d, *J*=1.0 Hz, 1H), 6.46 (d, *J*=5.2 Hz, 1H).

3,4-Di-*O*-acetyl-*D*-arabinal (25) Colorless syrup, $[\alpha]_D^{25}$ +200 (*c* 0.9, CH_2Cl_2) [lit.[14c] $[\alpha]_D^{25}$ +262 (*c* 0.9, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 2.07 (s, 3H), 2.08 (s, 3H), 3.98 (dd, *J*=10.6, 9.6 Hz, 1H), 3.97—4.04 (m, 1H), 4.85 (dd, *J*=5.8, 5.2 Hz, 1H), 5.18—5.20 (m, 1H), 5.44 (dd, *J*=4.8, 4.2 Hz, 1H), 6.50 (d, *J*=6.0 Hz, 1H). HR-ESIMS calcd for $C_9H_{12}NaO_5$ [M + Na] 223.0577, found 223.0564.

3,4-Di-*O*-acetyl-*D*-xylal (26) Colorless syrup, $[\alpha]_D^{25}$ −301 (*c* 1.9, $CHCl_3$) [lit.[14c] $[\alpha]_D^{25}$ −303 (*c* 2.3, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ: 2.07 (s, 3H), 2.10 (s, 3H), 3.98 (dd, *J*=12.3, 1.4 Hz, 1H), 4.18—4.20 (m, 1H), 4.95—4.97 (m, 2H), 5.00 (s, 1H), 6.60 (d, *J*=6.3 Hz, 1H).

3,4-Di-*O*-acetyl-*L*-rhamnal (27) Colorless syrup, $[\alpha]_D^{25}$ +65 (*c* 1.1, CH_2Cl_2) [lit.[14d] $[\alpha]_D^{25}$ +55 (*c* 1.0, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ: 1.31 (d, *J*=6.6 Hz, 3H), 2.04 (s, 3H), 2.08 (s, 3H), 4.09—4.13 (m, 1H), 4.78 (dd, *J*=6.2, 3.1 Hz, 1H), 5.03 (dd, *J*=8.2, 6.2 Hz, 1H), 5.34—5.35 (m, 1H), 6.43 (d, *J*=6.0 Hz, 1H).

3,4-Di-*O*-acetyl-6-*O*-mesyl-*D*-glucal (28) Colorless syrup, $[\alpha]_D^{25}$ −4 (*c* 0.3, $CHCl_3$) [lit.[15a] $[\alpha]_D^{25}$ +15 (*c* 1.6, EtOH)]; ^{1}H NMR ($CDCl_3$) δ: 2.06 (s, 3H), 2.10 (s, 3H), 3.07 (s, 3H), 4.33—4.37 (m, 2H), 4.47 (dd, *J*=11.6, 6.2 Hz, 1H), 4.89 (dd, *J*=6.2, 3.5 Hz, 1H), 5.21 (dd, *J*=7.4, 5.6 Hz, 1H), 5.34—5.36 (m, 1H), 6.48 (d, *J*=6.2 Hz, 1H).

3,4-Di-*O*-acetyl-6-*O*-tosyl-*D*-glucal (29) White power, m.p. 106—107 ℃ (lit.[15b] 106—107 ℃); $[\alpha]_D^{25}$ +16 (*c* 1.5, $CHCl_3$) [lit.[15b] $[\alpha]_D^{25}$ +14 (*c* 1.0, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ: 2.03 (s, 3H), 2.04 (s, 3H), 2.46 (s, 3H), 4.19—4.27 (m, 3H), 4.82 (dd, *J*=6.2, 3.5 Hz, 1H), 5.13 (dd, *J*=3.7, 3.7 Hz, 1H), 5.27 (dd, *J*=6.2, 5.5 Hz, 1H), 6.35 (d, *J*=6.0 Hz, 1H), 7.35 (d, *J*=7.9 Hz, 2H), 7.80 (d, *J*=8.4 Hz, 2H).

3,4-Di-*O*-acetyl-6-*O*-mesyl-*D*-galactal (30) Colorless syrup, $[\alpha]_D^{25}$ −5 (*c* 0.4, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ: 2.06 (s, 3H), 2.10 (s, 3H), 3.07 (s, 3H), 4.33—4.37 (m, 2H), 4.48 (dd, *J*=6.0, 2.9 Hz, 1H), 4.89 (dd, *J*=6.0, 3.3

Hz, 1H), 5.21 (dd, J=7.2, 5.5 Hz, 1H), 5.35 (dd, J=4.3, 3.5 Hz, 1H), 6.48 (d, J=6.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ: 20.8, 20.9, 37.8, 65.6, 66.9, 67.0, 73.6, 99.4, 145.3, 169.8, 170.3. HR-ESIMS calcd for $C_{11}H_{16}Na_1O_8S_1$ [M+Na] 331.0458, found 331.0474.

3,4-Di-*O*-acetyl-6-*O*-tosyl-*D*-galactal (31) Colorless syrup, $[\alpha]_D^{25}$ +3 (*c* 1.8, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ: 2.01 (s, 3H), 2.05 (s, 3H), 2.46 (s, 3H), 4.14 (dd, J=10.5, 4.4 Hz, 1H), 4.28 (dd, J=10.6, 7.7 Hz, 1H), 4.31—4.32 (m, 1H), 4.72 (dd, J=6.1, 3.1 Hz, 1H), 5.37 (s, 1H), 5.48 (s, 1H), 6.35 (d, J=6.1 Hz, 1H), 7.36 (d, J=8.2 Hz, 2H), 7.79 (d, J=8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 20.5, 20.7, 21.7, 63.5, 63.8, 66.7, 72.4, 98.9, 128.0, 129.9, 132.6, 145.2, 169.8, 170.1. HR-ESIMS calcd for $C_{17}H_{20}Na_1O_8S_1$ [M+Na] 407.0771, found 407.0779.

3,4-Di-*O*-acetyl-6-azide-*D*-glucal (32) Colorless syrup, $[\alpha]_D^{25}$ −46 (*c* 0.1, CH_2Cl_2) [lit.[15c] $[\alpha]_D^{25}$ −6 (*c* 1.9, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ: 2.06 (s, 3H), 2.10 (s, 3H), 3.56 (dd, J=11.0, 6.5 Hz, 1H), 3.61 (dd, J=11.2, 5.0 Hz, 1H), 4.29 (dd, J=11.8, 6.0 Hz, 1H), 4.87 (dd, J=6.0, 3.5 Hz, 1H), 5.28—5.31 (m, 2H), 6.50 (d, J=6.1 Hz, 1H).

3,4,6-Tri-*O*-benzyol-*D*-glucal (33)[14b] Colorless syrup, $[\alpha]_D^{25}$ −59 (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 4.68—4.71 (m, 3H), 5.12 (dd, J=6.2, 3.6 Hz, 1H), 5.72 (dd, J=4.4, 4.0 Hz, 1H), 5.80 (dd, J=5.6, 5.3 Hz, 1H), 6.60 (dd, J=6.1, 0.8 Hz, 1H), 7.39—7.44 (m, 6H), 7.52—7.57 (m, 3H), 7.99—8.05 (m, 6H).

3,4,6-Tri-*O*-benzyol-*D*-galactal (34)[9] Colorless syrup, $[\alpha]_D^{25}$ −43 (*c* 0.43, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 4.57 (dd, J=11.8, 4.8 Hz, 1H), 4.70—4.71 (m, 1H), 4.80 (dd, J=11.8, 7.7 Hz, 1H), 4.99 (dd, J=6.1, 1.7 Hz, 1H), 5.92—5.94 (m, 2H), 6.62 (d, J=6.2 Hz, 1H), 7.33 (dd, J=7.9, 7.7 Hz, 2H), 7.42 (dd, J=7.7, 7.7 Hz, 4H), 7.50 (dd, J=7.5, 7.3 Hz, 1H), 7.54—7.58 (m, 2H), 7.89 (d, J=7.3 Hz, 2H,), 8.00—8.07 (m, 4H).

3,4-Di-*O*-benzyol-*D*-arabinal (35)[9] Colorless syrup, $[\alpha]_D^{25}$ +226 (*c* 2.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 4.22—4.28 (m, 2H), 5.07 (dd, J=5.6, 5.3 Hz, 1H), 5.44 (m, 1H), 5.81 (s, 1H), 6.62 (d, J=5.9 Hz, 1H), 7.34 (d, J=7.7 Hz, 1H), 7.36 (d, J=7.6 Hz, 1H), 7.41 (d, J=7.7 Hz, 1H), 7.42 (d, J=7.6 Hz, 1H), 7.50—7.56 (m, 2H), 7.93 (d, J=7.3 Hz, 1H), 8.02 (d, J=7.4 Hz, 1H).

3,4-Di-*O*-benzyol-*L*-rhamnal (36) Colorless syrup, $[\alpha]_D^{25}$ +209 (*c* 0.6, $CHCl_3$) [lit.[15d] $[\alpha]_D^{22}$ +229 (*c* 0.6, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ: 1.45 (d, J=6.5 Hz, 3H), 4.36 (m, 1H), 5.00 (dd, J=5.9, 2.9 Hz, 1H), 5.51 (dd, J=7.1, 6.7 Hz, 1H), 5.71 (m, 1H), 6.53 (d, J=6.1 Hz, 1H), 7.40—7.44 (m, 4H), 7.52—7.57 (m, 2H), 8.01 (dd, J=19.1, 7.9 Hz, 4H)

3,4-Di-*O*-benzyl-*L*-rhamnal (37) Colorless syrup, $[\alpha]_D^{25}$ +37 (*c* 0.9, CH_2Cl_2) [lit.[15e] $[\alpha]_D^{25}$ +64 (*c* 1.0, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ: 1.40 (d, J=6.5 Hz, 3H), 3.51 (dd, J=9.0, 7.3 Hz, 1H), 3.95—3.99 (m, 1H), 4.23—4.24 (m, 1H), 4.59 (d, J=11.7 Hz, 1H), 4.68 (d, J=11.8 Hz, 1H), 4.73 (d, J=11.3 Hz, 1H), 4.8—4.91 (m, 2H), 6.38 (d, J=6.1 Hz, 1H), 7.29—7.38 (m, 10H).

Results and discussion

Initially, acetobromo-α-*D*-maltose (**1**) was chosen to survey the sonochemical effects and catalytic effects of β-CD on the synthesis of *D*-maltal (**2**) at room temperature (Scheme 2). This reaction was carried out in an ultrasound cleaning bath (40 kHz, 600 W) equipped with an automatic thermally regulated heating/cooling circulation system.

Compound **1** was treated in phosphate buffer, PEG600-H_2O or β-CD-H_2O under ultrasound irradiation and high-speed magnetic stirring (Table 1, Entries 1—3). A low yield of **2** was obtained in phosphate buffer, and a high yield was obatined in water and β-CD. The reaction time was also significantly shortened under ultrasound irradiation. The yield obtained by ultrasound irradiation with high-speed magnetic stirring increased by more than 7% (Table 1, Entry 3). Hence, the sensitivity of **1** toward acid hydrolysis and nucleophilic substitution led to the low yield and the appearance of by-products in phosphate buffer. In addition, water mixed with β-CD was more efficient than PEG600-H_2O. The 1,4-glycosidic bond of **1** and **2** cannot be cleaved by hydrolysis in β-CD-H_2O, thus, this method can offer a general route for the preparation of glycals substituted with both acid- and base-labile functionalities.

Afterward, the effects of zinc and β-CD were tested. When the reaction was carried out using 1.0 mmol substrate in β-CD-H_2O (Table 1, Entries 1—11), 1.5 equiv. of zinc and 0.2 mmol of β-CD produced a 95% yield (Table 1, Entry 11).

Since **2** was readily obtained from **1** using 1.5 equiv. of Zn and β-CD in water, the syntheses of all the glycals shown in Scheme 1 and Table 2 were explored under same conditions. In the beginning, acetylated maltal, cellobial, and lactal could be obtained in excellent yield (Table 2, Entries 1—3), and the 1,4-glycosidic bond could not be hydrolyzed. Based on this result, the acetylated bromoglycosides were treated with Zn and β-CD in water, in order to obtain an excellent yield of the glycals **23**—**27** (Table 2, Entries 4—9). Furthermore, the generality of the synthesis of the benzyolated glycals, 6-*O*-mesyl, 6-*O*-tosyl, 6-azide glycals, and benzylated glycals under the same conditions was investigated. The results show that benzyolated glycals **33**—**37**, 6-*O*-mesyl **28**, **31**, 6-*O*-tosyl **29**, **30**, 6-azide glycals **32**, and benzylated rhamnal **37** were also obtained in excellent yields (Table 2, Entries 10—19). Compared with previous method, the yields of peracetylated and benzoylated rhamnal, 6-azido glycals, and benzylated rhamnal in β-CD and water under ultrasound irradiation were improved. Moreover, ultrasound irradiation improved the yield of glycals and markedly shortened the reaction time in water and β-CD (Table 2, Entries 1—4, 7—9, 14, 18, and 19). In all cases, the glycals (**2**, **21**—**37**) were obtained in 85%—96% isolated yields (Table 2, Entries 1—19).

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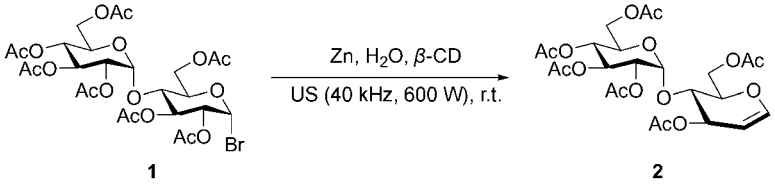
Scheme 2 Synthesis of maltal (**2**) from acetylated maltosyl bromide (**1**)



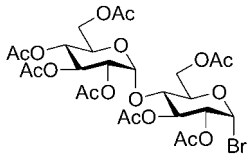
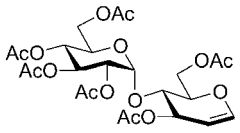
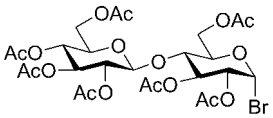
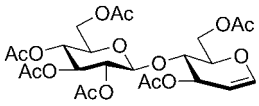
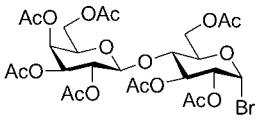
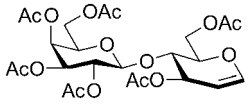
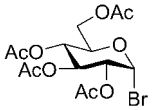
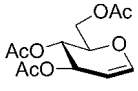
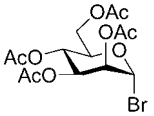
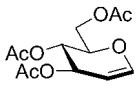
1 **2**

Table 1 Optimization of reaction conditions for the synthesis of **2**[a]

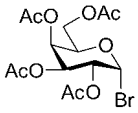
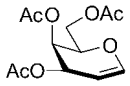
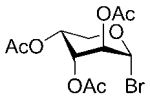
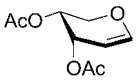
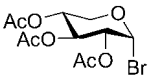
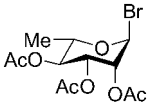
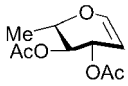
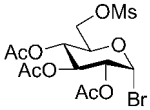
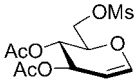
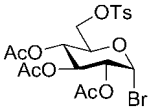
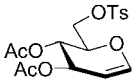
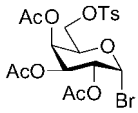
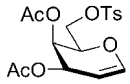
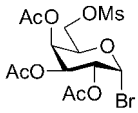
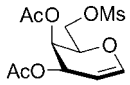
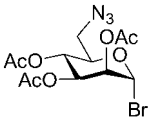
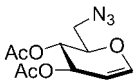
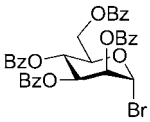
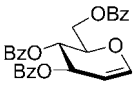
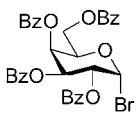
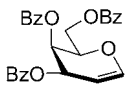
Entry	Solvent	Zn/mmol	β-CD/mmol	Time (stir.[b])/h	Isolated yield (stir.[b])/%
1	NaH_2PO_4-H_2O	6	0	2 (6)	26 (20)
3	PEG600-H_2O	2	0	3 (8)	83 (81)
4	H_2O	2	2	1.5 (4)	89 (82)
5	H_2O	2	1	1.5	92
6	H_2O	2	0.5	1.5	90
7	H_2O	2	0.2	1.5	95
8	H_2O	2	0.1	1.5	91
9	H_2O	2	0.05	1.5	85
10	H_2O	2	0	1.5	59
11	H_2O	1.5	0.2	1.5	95
12	H_2O	1	0.2	1.5	76

[a] Acetylated maltosyl bromide (1 mmol), H_2O (20 mL) under ultrasound irradiation at room temperature. [b] Using magnetic stirrer under silent conditions.

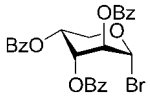
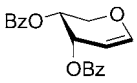
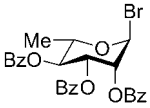
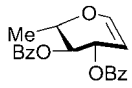
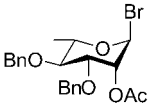
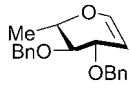
Table 2 Synthesis of various substituted glycals from pyranosyl bromides[a]

Entry	Substrate	Product	Time (stir.[b])/h	Isolated yield (stir.[b])/%
1	 **1**	 **2**	1.5 (4)	92 (89)
2	 **3**	 **21**	2 (5)	90 (83)
3	 **4**	 **22**	1.5 (4)	91 (85)
4	 **5**	 **23**	0.5 (0.5)	96 (93)
5	 **6**	 **23**	0.5	92

Continued

Entry	Substrate	Product	Time (stir.[b])/h	Isolated yield (stir.[b])/%
6	 **7**	 **24**	0.5	93
7	 **8**	 **25**	0.5 (0.5)	95 (90)
8	 **9**	 **26**	0.5 (1)	85 (70)
9	 **10**	 **27**	0.5 (1)	91 (80)
10	 **11**	 **28**	1	95
11	 **12**	 **29**	1	90
12	 **13**	 **30**	1	92
13	 **14**	 **31**	1	94
14	 **15**	 **32**	1 (1.5)	89 (78)
15	 **16**	 **33**	1	95
16	 **17**	 **34**	1	92

Continued

Entry	Substrate	Product	Time (stir.[b])/h	Isolated yield (stir.[b])/%
17	 **18**	 **35**	1	93
18	 **19**	 **36**	1 (3)	89 (83)
19	 **20**	 **37**	0.5 (1)	86 (75)

[a] Glycosyl bromide (1.0 mmol), zinc (1.5 mmol), β-CD (0.2 mmol), and water (20 mL) under ultrasound irradiation at room temperature. [b] Using magnetic stirrer under silent conditions.

Conclusions

In summary, combining β-CD and ultrasound to activate zinc dust *in situ* is an efficient development of the Fischer-Zach glycal synthesis. The present method involves nontoxic species, neutral conditions and simple operations. It is a low-cost procedure with a high yield. All of these make it an attractive strategy for the synthesis of glycals, especially for peracetylated and benzoylated rhamnal, 6-azido glycals, and benzylated pyranoid glycals, as their glycosyl bromide precursors are sensitive to acidic or basic medium.

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