Photocatalytic Synthesis of Glycosyl Bromides

Xiaolong Yuan, Sen Cheng, Yanbin Shi, Weihua Xue*

School of Pharmacy, Lanzhou University, Lanzhou 730000, P. R. of China
Fax +86(931)8915686; E-mail: xuewh@lzu.edu.cn

Received: 30.09.2013; Accepted after revision: 04.12.2013

Abstract: Sugar hemiacetals were smoothly transformed into the corresponding glycosyl bromides by treatment with carbon tetrabromide in *N*,*N*-dimethylformamide with tris(2,2′-bipyridyl)ruthenium(II) chloride as a catalyst under visible-light irradiation. Protecting groups commonly used in carbohydrate derivatives are unaffected by the mild conditions for bromination.

Key words: carbohydrates, halogenation, bromine, photochemistry, catalysis, ruthenium

In carbohydrate chemistry, protected glycosyl bromides are important and versatile synthons that permit the preparation of functional derivatives or intermediates, including 1,6-anhydrosaccharides,[1] azides,[2] thioglycosides,[3] glycals,[4] and thiols.[5] Moreover, aldosyl bromides, in the presence of various promoters, are sometimes used as donors for chemical O-glycosylation.[6] Therefore, the synthesis of these bromides is of great significance and considerable interest.

Continual efforts have been made to develop efficient approaches for regioselective bromination at the anomeric position. Generally, glycosyl bromides are prepared directly from their peracetyl derivatives by treatment with hydrobromic acid,[7] phosphorus tribromide,[8] or trimethylsilyl bromide.[9] Other methods involve the bromination of sugar lactols with deoxohalogenation reagents.[10] However, the harsh reaction conditions are incompatible with acid-sensitive functional groups present in the substrate. In addition, stoichiometric amounts of highly toxic reagents or heavy metal salts are required, leading to serious effects on the environment when the reactions are scaled up. Therefore, the development of an environmentally benign and mild procedure for bromination would be highly desirable and valuable. Catalytic synthesis mediated by visible light has promise in the development of practical scalable industrial processes, with considerable environmental benefits.[11] Several examples of chemical transformations at the anomeric position of sugars that are facilitated by photocatalysis have been recently reported.[12] Stephenson and co-workers described a new method for the synthesis of bromides from alcohols[13] in which, presumably, a Vilsmeier–Haack reagent or a variant thereof is generated in situ from carbon tetrabromide and *N*,*N*-dimethylformamide by irradiation in the presence of a photocatalyst. Taking our cue from this photochemical synthesis, we have developed a fairly efficacious and operationally simple protocol for preparing glycosyl bromides in the presence of the visible-light activated photocatalyst tris(2,2′-bipyridyl)ruthenium(II) chloride [$Ru(bpy)_3Cl_2$].

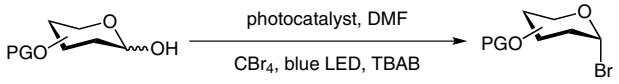
To optimize the conditions for this reaction, we chose 2,3,4,6-tetra-*O*-benzoyl-D-glucopyranose (**1b**) as a model substrate and a domestic blue light-emitting diode (LED, 13 W) as the light source, and we examined the effects of the photocatalyst loading and various quantities of carbon tetrabromide. The desired bromide **2b** was produced in 82% isolated yield (Table 1, entry 2) when a mixture of compound **1b**, tetrabutylammonium bromide (2.0 equiv), and carbon tetrabromide (2.0 equiv) in *N*,*N*-dimethylformamide containing $Ru(bpy)_3Cl_2$ (0.05 equiv) was irradiated at room temperature for 15 h. Having identified these optimal conditions, we subjected a variety of sugar hemiacetals to this visible light-promoted photocatalytic bromination protocol to establish the scope of the reaction. As shown in Table 1, the reaction proceeded smoothly in all cases to give the desired bromides in various isolated yields. Compound **1a**, protected by acid-labile acetonide groups, gave a low isolated yield (54%) because of instability of the product **2a** (entry 1). The other substrates **1b–j** were suitable substrates for our protocol and gave good to excellent yields (82–92%) of the corresponding bromides (entries 2–10).

It is worth mentioning that we failed to obtain 2,3,4,6-tetra-*O*-benzyl-α-D-glycosyl bromide by chromatographic purification because the bromide is fairly labile. The procedure tolerated a number of commonly employed protecting groups, including acetals, silyl ethers, acetates, benzyl ethers, and benzoates. The crude reaction mixtures were amenable to flash column chromatography on silica gel, and the products were isolated as white amorphous solids or colorless oils. The bromides were characterized by NMR spectroscopy, which typically showed signals from anomeric protons at δ = 6–7 ppm, signifying α-anomeric configurations. No products of interglycosidic bond cleavage were detected in the cases of disaccharide substrates (entries 7–10).

In conclusion, we have developed a practical and simple protocol for the synthesis of glycosyl bromide by photocatalytic bromination. Various readily accessible sugar hemiacetals can be smoothly converted into the corresponding glycosyl bromides. The procedure is compatible with acid- or base-labile protecting groups. Readily available reagents are used, and no strong acids or hazardous reagents are required.

SYNTHESIS 2014, 46, 0331–0335
Advanced online publication: 02.01.2014
DOI: 10.1055/s-0033-1340493; Art ID: SS-20123-H0650-OP

Table 1 Photocatalytic Synthesis of Glycosyl Bromides



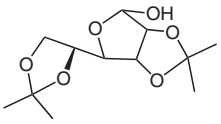
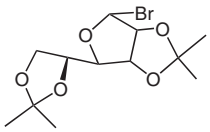
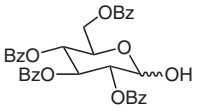
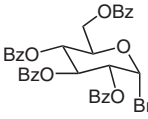
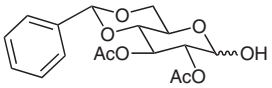
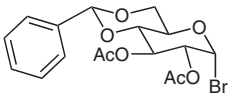
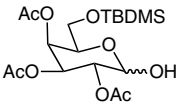
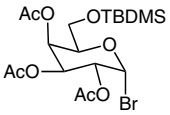
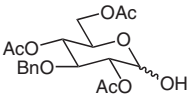
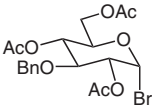
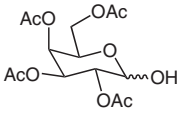
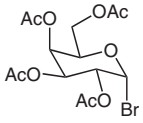
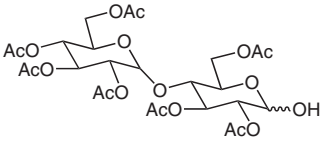
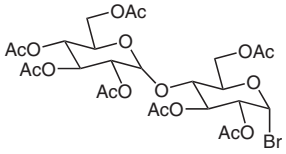
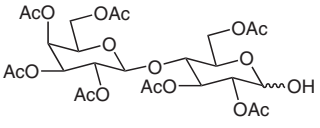
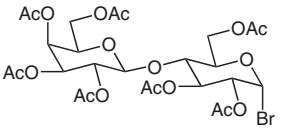
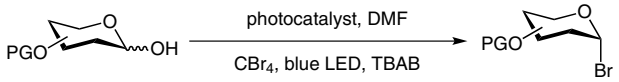
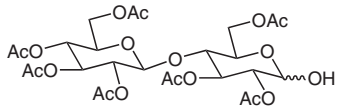
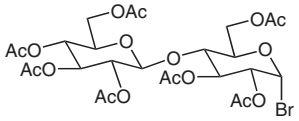
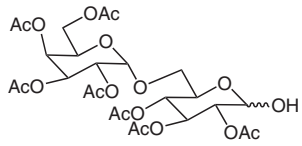
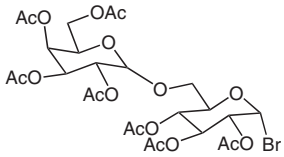
Entry	Substrate	Product	Yield[a] (%)
1	 **1a**	 **2a**	54
2	 **1b**	 **2b**	82
3	 **1c**	 **2c**	91
4	 **1d**	 **2d**	88
5	 **1e**	 **2e**	88
6	 **1f**	 **2f**	86
7	 **1g**	 **2g**	92
8	 **1h**	 **2h**	90

Table 1 Photocatalytic Synthesis of Glycosyl Bromides (continued)



Entry	Substrate	Product	Yield[a] (%)
9	 **1i**	 **2i**	93
10	 **1j**	 **2j**	87

[a] Isolated yield.

Glassware was dried in an oven at 150 °C and cooled under a dry atmosphere before use. Unless otherwise indicated, reactions were performed open to the air. All reagents and solvents were commercial products and were used as received, unless otherwise noted. DMF was distilled over CaH_2 before use. Conversion was monitored by TLC on precoated plates of silica gel HF_{254} (0.5 mm; Yantai, China). Compounds were visualized by UV radiation at 254 nm or by dipping the plates into 20% H_2SO_4 in EtOH with subsequent rapid heating. Flash column chromatography was performed on silica gel (300–400 mesh). ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz on Varian Mercury 400 spectrometers. Chemical shifts are reported in ppm relative to TMS or the appropriate solvent as internal standard. Optical rotations were measured with a JASCO DIP-370 digital polarimeter with a sodium lamp (λ = 589 nm) at 20 °C. High-resolution mass spectra were recorded on a Bruker APEX II mass spectrometer using electrospray ionization. IR spectra were recorded on a Nicolet Nexus 670 Fourier-transform spectrophotometer by using thin films on NaCl plates for oils or KBr discs for solids.

Glycosyl Bromides 2a–j; General Procedure

A dry 25 mL Schlenk tube was charged with substrate **1a–j** (1 mmol), CBr_4 (2.0 equiv), $Ru(bipy)_3Cl_2$ (0.05 equiv), and TBAB (2.0 equiv) in anhydrous DMF (5 mL). The tube was sealed with a rubber septum and the solution was degassed by three freeze–pump–thaw cycles under argon. The tube was placed approximately 5 cm from the irradiation source (blue LEDs, 13 W), and the mixture was stirred and irradiated for 10–15 h until the starting alcohol was completely consumed (TLC). Et_2O (25 mL) and H_2O (25 mL) were added, the layers were separated, and the aqueous layer was extracted with Et_2O (2 × 25 mL). The organic layers were combined, washed with sat. aq $Na_2S_2O_3$, dried ($NaSO_4$), and concentrated in vacuo. The residue was purified by chromatography (silica gel).

2,3:5,6-Di-*O*-isopropylidene-α-D-mannofuranosyl Bromide (2a)

Colorless oil; yield: 174 mg (54%; unstable); $[\alpha]_D^{20}$ +82.6 (*c* 0.5, $CHCl_3$); R_f = 0.78 (PE–EtOAc, 4:1).

IR (thin film): 3467, 3074, 1238, 1126, 921, 848 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.39 (s, 1 H), 5.16 (d, *J* = 6.4 Hz, 1 H), 4.89 (dd, *J* = 4.0, 5.2 Hz, 1 H), 4.47 (dd, *J* = 6.4, 11.2 Hz, 1 H), 4.20–4.12 (m, 1 H), 4.10–4.08 (m, 1 H), 4.02–3.98 (m, 1 H), 1.47 (s, 3 H), 1.46 (s, 3 H), 1.39 (s, 3 H), 1.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 113.2, 109.6, 92.8, 90.0, 83.3, 78.3, 72.0, 66.7, 26.9, 25.8, 25.1, 24.6.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{12}H_{19}BrNaO_5$: 345.0314; found: 345.0311.

2,3,4,6-Tetra-*O*-benzoyl-α-D-glucopyranosyl Bromide (2b)[14]

White solid; yield: 540 mg (82%); mp 128 °C; $[\alpha]_D^{20}$ +108.6 (*c* 2.0, $CHCl_3$); R_f = 0.66 (PE–EtOAc, 3:1).

IR (KBr): 3487, 3062, 3029, 3007, 1721, 1250 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.09–7.87 (m, 8 H), 7.24–7.58 (m, 12 H), 6.88 (d, *J* = 4.0 Hz, 1 H), 6.29 (t, *J* = 10.0 Hz, 1 H), 5.86 (t, *J* = 10.0 Hz, 1 H), 5.35 (dd, *J* = 4.0, 9.6 Hz, 1 H), 4.77–4.67 (m, 2 H), 4.52 (dd, *J* = 4.4, 12.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9, 165.5, 165.2, 165.0, 133.7, 133.6, 133.2, 130.0, 129.8, 129.7, 129.6, 129.4, 128.7, 128.4, 128.3, 86.8, 72.6, 71.4, 70.5, 67.9, 61.8.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{34}H_{27}BrNaO_9$: 681.0736; found: 681.0734.

2,3-Di-*O*-acetyl-4,6-*O*-benzylidene-α-D-Glucopyranosyl Bromide (2c)

White solid; yield: 377 mg (91%); mp 125 °C; $[\alpha]_D^{20}$ +108 (*c* 0.1, $CHCl_3$); R_f = 0.42 (PE–EtOAc, 4:1).

IR (KBr): 3057, 1749, 1637, 1572, 1263, 1137, 720 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.45 (m, 5 H), 6.60 (d, *J* = 3.6 Hz, 1 H), 5.67 (t, *J* = 6.0 Hz, 1 H), 5.52 (s, 1 H), 4.85 (dd, *J* = 4.0, 9.6 Hz, 1 H), 4.37–4.33 (m, 1 H), 4.28–4.22 (m, 1 H), 3.85–3.73 (m, 2 H), 2.12 (s, 3 H), 2.08 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0, 136.5, 129.2, 128.2, 126.1, 101.6, 86.9, 78.1, 71.3, 68.8, 68.6, 67.8, 67.0, 20.8.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{19}NaBrO_7$: 437.0212; found: 437.0213.

2,3,4-Tri-*O*-acetyl-6-*O*-[*tert*-butyl(dimethyl)silyl]-α-D-mannopyranosyl Bromide (2d)

Colorless oil; yield: 424 mg (88%); $[\alpha]_D^{20}$ +77.6 (*c* 0.2, $CHCl_3$); R_f = 0.52 (PE–EtOAc, 3:1).

IR (thin film): 2998, 1756, 1268, 1108, 830 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.33 (d, *J* = 3.6 Hz, 1 H), 5.70 (dd, *J* = 3.2, 10.0 Hz, 1 H), 5.45 (m, 1 H), 5.37 (t, *J* = 9.6 Hz, 1 H), 4.36–

4.32 (m, 1 H), 4.24–4.21 (m, 1 H), 4.15–4.12 (m, 1 H), 2.07 (s, 3 H), 1.98 (s, 3 H), 1.94 (s, 3 H), 0.85 (s, 9 H), 0.02 (s, 3 H), 0.00 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.3, 170.2, 169.7, 91.9, 71.2, 70.3, 69.1, 66.6, 62.6, 25.8, 20.8, 20.7, 18.4, –5.4, –5.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{31}BrNaO_8Si$: 505.0869; found: 505.0865.

2,4,6-Tri-*O*-acetyl-3-*O*-benzyl-α-D-glucopyranosyl Bromide (2e)
Colorless oil; yield: 403 mg (88%); $[\alpha]_D^{20}$ +132 (*c* 0.5, $CHCl_3$); R_f = 0.46 (PE– EtOAc, 3:1).

IR (thin film): 3379, 2907, 2859, 1728, 892 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.25 (m, 5 H), 6.64 (d, *J* = 3.6 Hz, 1 H), 5.18 (t, *J* = 10.0 Hz, 1 H), 4.78–4.73 (m, 2 H), 4.63 (m, 1 H), 4.26 (dd, *J* = 4.4, 12.8 Hz, 1 H), 4.19–4.16 (m, 1 H), 4.10–4.04 (m, 2 H), 2.08 (s, 6 H), 1.96 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 169.6, 169.1, 137.7, 128.3, 127.8, 127.5, 87.9, 75.0, 72.9, 72.5, 68.0, 61.1, 20.1, 20.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{23}BrO_8Na$: 481.0474; found: 481.0477.

2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl Bromide (2f)[15]
White solid; yield: 353 mg (86%); mp 86 °C; $[\alpha]_D^{20}$ +216 (*c* 1.0, $CHCl_3$); R_f = 0.70 (PE– EtOAc, 1:1).

IR (thin film): 3422, 1745, 1378, 1249, 1053, 901 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.71 (d, *J* = 4.0 Hz, 1 H), 5.52–5.46 (m, 1 H), 5.40 (dd, *J* = 3.2, 10.8 Hz, 1 H), 5.05 (dd, *J* = 4.0, 10.8 Hz, 1 H), 4.51–4.48 (m, 1 H), 4.19 (dd, *J* = 6.4, 11.8 Hz, 1 H), 4.11 (dd, *J* = 6.4, 11.2 Hz, 1 H), 2.16 (s, 3 H), 2.12 (s, 3 H), 2.07 (s, 3 H), 2.01 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.1, 169.8, 169.7, 169.5, 88.0, 70.9, 67.8, 67.6, 66.8, 60.6, 20.5, 20.4, 20.3, 20.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{19}BrNaO_9$: 433.0110; found: 433.0112.

2,3,6,2′,3′,4′,6′-Hepta-*O*-acetyl-α-D-maltosyl bromide (2g)[16]
White solid; yield: 642 mg (92%); mp 83 °C; $[\alpha]_D^{20}$ +107 (*c* 1.0, $CHCl_3$); R_f = 0.32 (PE–EtOAc, 1:1).

IR (KBr): 3426, 2971, 1749, 1376, 1230 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.53 (d, *J* = 4.0 Hz, 1 H), 5.61 (dd, *J* = 8.8, 9.6 Hz, 1 H), 5.41 (d, *J* = 3.6 Hz, 1 H), 5.54–5.51 (m, 1 H), 5.35 (t, *J* = 10.0 Hz, 1 H), 5.08 (dd, *J* = 9.6, 10.0 Hz, 1 H), 4.87 (dd, *J* = 3.6, 10.0 Hz, 1 H), 4.72 (dd, *J* = 10.0, 12.5 Hz, 1 H), 4.29–4.24 (m, 3 H), 4.14–4.03 (m, 3 H), 2.15 (s, 3 H), 2.10 (s, 3 H), 2.08 (s, 3 H), 2.05 (s, 3 H), 2.04 (s, 3 H), 2.03 (s, 3 H), 2.01 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.3, 170.1, 169.9, 169.4, 169.2, 169.0, 95.4, 85.9, 72.2, 72.0, 71.3, 70.6, 69.7, 68.8, 68.3, 67.5, 61.5, 61.0, 20.7, 20.5, 20.4, 20.3, 20.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{35}BrNaO_{17}$: 721.0955; found: 721.0957.

2,3,6,2′,3′,4′,6′-Hepta-*O*-acetyl-α-D-lactosyl Bromide (2h)[17]
White solid; yield: 649 mg (93%); mp 140 °C; $[\alpha]_D^{20}$ +112 (*c* 1.0, $CHCl_3$); R_f = 0.30 (PE–EtOAc, 1:1).

IR (KBr): 3432, 2935, 1751, 1641, 1371, 1223, 1048 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.53 (d, *J* = 4.0 Hz, 1 H), 5.55 (t, *J* = 9.6 Hz, 1 H), 5.35 (dd, *J* = 9.6, 10.0 Hz, 1 H), 4.97 (dd, *J* = 3.6, 10.4 Hz, 1 H), 4.76 (dd, *J* = 4.0, 10.0 Hz, 1 H), 4.53–4.49 (m, 2 H), 4.22–4.03 (m, 4 H), 3.92–3.85 (m, 2 H), 2.17 (s, 3 H), 2.14 (s, 3 H), 2.10 (s, 3 H), 2.07 (s, 3 H), 2.06 (s, 3 H), 2.05 (s, 3 H), 1.97 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.2, 170.0, 169.8, 100.6, 86.3, 74.8, 72.8, 70.6, 69.5, 68.9, 66.5, 60.9, 60.8, 20.6, 20.5, 20.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{35}BrNaO_{17}$: 721.0955; found: 721.0957.

2,3,6,2′,3′,4′,6′-Hepta-*O*-acetyl-α-D-cellobiosyl Bromide (2i)[18]
White solid; yield: 628 mg (90%); mp 186 °C; $[\alpha]_D^{20}$ +96 (*c* 1.0, $CHCl_3$); R_f = 0.33 (PE–EtOAc, 1:1).

IR (KBr): 3469, 1745, 1434, 1372, 1229, 1047, 908 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.53 (d, *J* = 4.0 Hz, 1 H), 5.53 (dd, *J* = 9.6, 10.0 Hz, 1 H), 5.13 (dd, *J* = 9.2, 10.0 Hz, 1 H), 5.08 (dd, *J* = 9.6, 10.0 Hz, 1 H), 4.94 (dd, *J* = 8.8, 10.0 Hz, 1 H), 4.77 (dd, *J* = 4.0, 10.0 Hz, 1 H), 4.56–4.52 (m, 2 H), 4.38 (dd, *J* = 4.4, 12.0 Hz, 1 H), 4.21–4.15 (m, 2 H), 4.04 (dd, *J* = 2.0, 12.0 Hz, 1 H), 3.84 (t, *J* = 9.6 Hz, 1 H), 3.68 (ddd, *J* = 2.0, 4.0, 9.6 Hz, 1 H), 2.15 (s, 6 H), 2.10 (s, 3 H), 2.05 (s, 3 H), 2.02 (s, 6 H), 1.99 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 170.2, 170.0, 169.9, 169.2, 168.9, 100.5, 86.4, 75.1, 72.9, 72.8, 72.6, 71.9, 71.5, 70.7, 69.3, 67.7, 61.5, 60.8, 20.7, 20.6, 20.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{35}BrNaO_{17}$: 721.0955; found: 721.0955.

2,3,6,2′,3′,4′,6′-Hepta-*O*-acetyl-α-D-melibiosyl Bromide (2j)
White solid; yield: 607 mg (87%); mp 133 °C; $[\alpha]_D^{20}$ +105.3 (*c* 0.5, $CHCl_3$); R_f = 0.35 (PE–EtOAc, 1:1).

IR (KBr): 3411, 2896, 1737, 1427, 1364, 1219, 1169, 1038 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.60 (d, *J* = 4.0 Hz, 1 H), 5.56 (t, *J* = 9.6 Hz, 1 H), 5.47 (m, 1 H), 5.35 (m, 1 H), 5.32 (dd, *J* = 5.2, 11.2 Hz, 1 H), 5.20–5.17 (m, 1 H), 5.10 (dd, *J* = 10.0, 11.2 Hz, 1 H), 4.80 (dd, *J* = 4.0, 9.6 Hz, 1 H), 4.20 (m, 1 H), 4.16–4.08 (m, 1 H), 4.07–4.05 (m, 2 H), 3.79–3.75 (m, 1 H), 3.65–3.62 (m, 1 H), 2.14 (s, 3 H), 2.13 (s, 3 H), 2.11 (s, 3 H), 2.07 (s, 3 H), 2.05 (s, 3 H), 2.04 (s, 3 H), 1.99 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 170.2, 169.7, 169.2, 96.1, 86.4, 72.8, 70.5, 70.1, 67.9, 66.3, 65.3, 61.5, 20.7, 20.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{35}Br\,O_{17}Na$: 721.0955; found: 721.0954.

Acknowledgment

This work was financially supported by the Fundamental Research Funds for Lanzhou University (lzujbky-2013-74).

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

References

(1) (a) Fujimaki, I.; Ichikawa, Y.; Kuzuhara, H. *Carbohydr. Res.* **1982**, *101*, 148. (b) Boons, G.-J.; Isles, S.; Setälä, P. *Synlett* **1995**, 755.
(2) Tropper, F. D.; Andersson, F. O.; Braun, S.; Roy, R. *Synthesis* **1992**, 618.
(3) (a) Tropper, F. D.; Andersson, F. O.; Grand-Maître, C.; Roy, R. *Synthesis* **1991**, 734. (b) Tsvetkov, Y. E.; Byramova, N. É.; Backinowsky, L. V. *Carbohydr. Res.* **1983**, *115*, 254.
(4) (a) Roth, W.; Pigman, W. *Methods Carbohydr. Chem.* **1963**, *2*, 405. (b) Spencer, R. P.; Cavallaro, C. L.; Schwartz, J. *J. Org. Chem.* **1999**, *64*, 3987. (c) Cavallaro, C. L.; Schwartz, J. *J. Org. Chem.* **1995**, *60*, 7055. (d) Hansen, T.; Daasbjerg, K.; Skrydstrup, T. *Tetrahedron Lett.* **2000**, *41*, 8645. (e) Forbes, C. L.; Franck, R. W. *J. Org. Chem.* **1999**, *64*, 1424. (f) Zhao, J.; Wei, S.; Ma, X.; Shao, H. *Carbohydr. Res.* **2010**, *345*, 168.
(5) (a) Matta, K. L.; Girotra, R. N.; Barlow, J. J. *Carbohydr. Res.* **1975**, *43*, 101. (b) Fulton, D. A.; Stoddart, J. F. *J. Org.*

Chem. **2001**, *66*, 8309. (c) Ibatullin, F. M.; Shabalin, K. A.; Jänis, J. V.; Shavva, A. G. *Tetrahedron Lett.* **2003**, *44*, 7961. (d) Xue, W.; Cheng, X.; Fan, J.; Diao, H.; Wang, C.; Dong, L.; Luo, Y.; Chen, J.; Zhang, J. *Tetrahedron Lett.* **2007**, *48*, 6092. (e) Pei, Z.; Dong, H.; Caraballo, R.; Ramström, O. *Eur. J. Org. Chem.* **2007**, 4927.

(6) (a) Koenigs, W.; Knorr, E. *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 957. (b) Lipták, A.; Nánási, P.; Neszmélyi, A.; Wagner, H. *Tetrahedron* **1980**, *36*, 1261. (c) Presser, A.; Kunert, O.; Pötschger, I. *Monatsh. Chem.* **2006**, *137*, 365. (d) Beale, T. M.; Taylor, M. S. *Org. Lett.* **2013**, *15*, 1358.

(7) (a) Ditmar, R. *Monatsh. Chem.* **1902**, *23*, 865. (b) Fischer, E.; Fischer, H. *Ber. Dtsch. Chem. Ges.* **1910**, *43*, 2521. (c) Fischer, E. *Ber. Dtsch. Chem. Ges.* **1911**, *44*, 1898. (d) Koto, S.; Morishima, N.; Irisawa, T.; Hashimoto, Y.; Yamazaki, M.; Zen, S. *Nippon Kakgaku Kaishi* **1982**, 1651. (e) Koto, S.; Morishima, N.; Shichi, S.; Haigoh, H.; Hirooka, M.; Okamoto, M.; Higuchi, T.; Shimizu, K.; Hashimoto, Y.; Iriawa, T.; Kawasaki, H.; Takahashi, Y.; Yamazaki, M.; Mori, Y.; Kudo, K.; Ikegaki, T.; Suzuki, S.; Zen, S. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 3257. (f) Kartha, C. P. R.; Jennings, H. J. *J. Carbohydr. Chem.* **1990**, *9*, 777. (g) Larsen, K.; Olsen, C. E.; Motawia, M. S. *Carbohydr. Res.* **2003**, *338*, 199.

(8) (a) Montero, J.-L.; Winum, J.-Y.; Leydet, A.; Kamal, M.; Pavia, A. A.; Roque, J.-P. *Carbohydr. Res.* **1997**, *297*, 175. (b) Schmidt, R. R.; Rilcker, E. *Tetrahedron Lett.* **1980**, *21*, 1421.

(9) Gillard, J. W.; Israel, M. *Tetrahedron Lett.* **1981**, *22*, 513.

(10) (a) Hanessian, S.; Ponpipom, M. M. *Lavallee P.* **1972**, *24*, 45. (b) Pinto, B. M.; Reimer, K. B.; Morissette, D. G.; Bundle, D. R. *J. Org. Chem.* **1989**, *54*, 2650. (c) Iversen, T.; Bundle, D. R. *Carbohydr. Res.* **1982**, *103*, 29.

(11) Yoon, T. P.; Ischay, M. A.; Du, J. *Nat. Chem.* **2010**, *2*, 527.

(12) (a) Andrews, R. S.; Becker, J. J.; Gagné, M. R. *Angew. Chem. Int. Ed.* **2010**, *49*, 7272. (b) Wever, W. J.; Cinelli, M. A.; Bowers, A. A. *Org. Lett.* **2013**, *15*, 30. (c) Spell, M.; Wang, X.; Wahba, A. E.; Conner, E.; Ragains, J. *Carbohydr. Res.* **2013**, *369*, 42.

(13) Dai, C.; Narayananam, J. M. R.; Stephenson, C. R. J. *Nat. Chem.* **2011**, *3*, 140.

(14) Bhowmik, S.; Maitra, U. *Chem. Commun.* **2012**, *48*, 4624.

(15) Richards, S.-J.; Jones, M. W.; Hunaban, M.; Haddleton, D. M.; Gibson, M. I. *Angew. Chem. Int. Ed.* **2012**, *51*, 7812.

(16) Braitsch, M.; Kählig, H.; Kontaxis, G.; Fischer, M.; Kawada, T.; Konrat, R.; Schmid, W. *Beilstein J. Org. Chem.* **2012**, *8*, 448.

(17) Zhang, Z.; Magnusson, G. *Carbohydr. Res.* **1996**, *295*, 41.

(18) Zheng, X.; Morgan, J.; Pandey, S. K.; Chen, Y.; Tracy, E.; Baumann, H.; Missert, J. R.; Batt, C.; Jackson, J.; Bellnier, D. A.; Henderson, B. W.; Pandey, R. K. *J. Med. Chem.* **2009**, *52*, 4306.