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ARTICLE

Halogenation and anomerization of glycopyranoside by TESH/bromine and BHQ/bromine

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Abstract

Treatment of peracetylated glycosides and β-isopropyl glycosides with halogen in the presence of TESH and BHQ has been found to result in the halogenation and the anomerization, respectively. Peracetylatedglycosides treaded with I2/TESH or Br2/TESH leading tothe formation of corresponding glycosyl halides, and b-isopropyl glycosidesreacted with Br2/BHQ resulting in the formation of a-glycosides. The anomerizationof glycosidic bond was considered to be catalyzed by in situ formation of hydrogenbromide from the mixing of Br2/BHQ.

KEYWORDS

anomerization, bromination, halogen, iodination, triethylsilane

1 | INTRODUCTION

The recent discovery on carbohydrate moiety can be important for the many biological activity and recognition events of the cellular targets, including cell–cell adhesion, bacterial attachment, and viral infection.[1–4] Synthesis of the carbohydrate moiety has been directly related to the development of new glycosylation methods. Glycosyl halide,[5] glycosyl imidates,[6] and thioglycoside[7,8] have found enormous application in the synthetic establishment of carbohydrate, especially in the synthesis of oligosaccharide. Anomeric inversion of glycosidic bond,[9,10] establishing a α-anomer from β-linkage, provided different assumption. Reported intense conditions for anomerization using protic[11,12] or Lewis acid[13–15] limited the glyosidic synthesis for oligosaccharide. Radical hydrogen-atom transfer reactions[16] of glycosyl bond developed to modify cyclodextrin[17] and to target galactofuranose residue[18] assume the application possibility about anomerization.

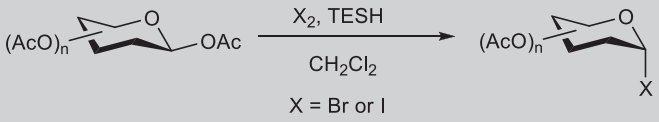
Previously, we have reported the anomerization of protected glycoside by using $BF_3{\cdot}OEt_2/CCl_4$ under photoactivated radical condition.[19] In case of this anhydrous condition, the observed and minor glycosyl chloride can be formed with in situ generation of anhydrous HCl. The synthesis of glycosyl halide has been prepared from peracetylated saccharides with HBr-AcOH,[20] AcBr-AcOH, Ac_2O-HBr-AcOH,[21,22] etc. For environmentally friendly synthesis, preparation of anhydrous hydrogen halide in situ can provide a convenient and inexpensive reagent in the preparation of glycosyl halide. Anhydrous HI can be generated by mixing solid iodine with triethylsilane[23,24] or thiolacetic acid[25] and applied in preparation of glycosyl halide. In connection with those studies, we attempted to supplement and intact the production of glycosyl halide by TESH/halogen and BHQ/Bromine. Meanwhile, dried hydrogen bromide generated in situ with those conditions was applied to study the acidic anomerization.

2 | RESULTS AND DISCUSSION

2.1 | Bromination and iodination or of saccharides

To standardize the reaction protocol, triethylsilane (1.5 equiv) and bromine (3.0 equiv) were added to a per-*O*-acetylated sugar (1.0 equiv) in dichloromethane at 0 oC.

TABLE 1 Bromination and iodination or of saccharides with Br_2/TESH or I_2/TESH



		Bromination[a]			Iodination[b]		
Entry	**Saccharide**	**Product**	**Time (hr)**	**Yield (%)**	**Product**	**Time (hr)**	**Yield (%)**
1	Glucopyranose-$(OAc)_5$ **1**	**1Br**	2	93	**1I**	2	85
2	Galactopyranose-$(OAc)_5$ **2**	**2Br**	2	95	**2I**	2	91
3	Mannopyranose-$(OAc)_5$ **3**	**3Br**	1	86	**3I**	1.5	86
4	Fucopyranose-$(OAc)_4$ **4**	**4Br**	2	87	**4I**	1.5	88
5	*N*-acetyl glucoamine-$(OAc)_4$ **5**	**5Br**	2	NR[c]	**5I**	2	NR[c]
6	Xylospyranose-$(OAc)_4$ **6**	**6Br**	2	—[d]	**6I**	1	—[d]
7	Cellobiose-$(OAc)_8$ **7**	**7Br**	2	85	**7I**	2	96
8	Maltose-$(OAc)_8$ **8**	**8Br**	2	87	**8I**	1.5	97
9	Lactose-$(OAc)_8$ **9**	**9Br**	2	88	**9I**	2	92

[a]With 1.5 equiv TESH and 3.0 equiv Br_2.
[b]With 1.5 equiv TESH and 3.0 equiv I_2, at 40°C.
[c]No reaction.
[d]Hydrolytic by-product was isolated in 62% and 65% yield for bromination and iodination, individually.

An exothermic reaction started immediately, following bromotriethylsilane and hydrogen bromide were obtained at room temperature within few minutes. Reducing the quantity of TESH from 1.5 equiv to 1.0 or 0.5 equiv led a slower reaction, which was not complete even after 24 hr. After a series of experiments with monosacchardies and disacchardies (Table 1), bromination of D-sugar with mixture of triethylsilane and bromine gave complete reaction within 1–2 hr in good yield, giving only α-D-pyranosyl bromide. The presence of *N*-acetyl-glucoamine 5 (Table 1, entry 5) prevented the anomeric bromination, as the HBr forms an acid/base complex with *N*-acetyl group such that the activity of the hydrogen bromide is restricted. With TESH/Br_2 treatment (Table 1, entry 6), the conversion of xylose **6** into **6Br** was observed and examined with proton NMR experiment. However, the isolation of bromide **6Br** was prevented, and an anomeric hydrolysis was observed and the product was isolated in 62%.

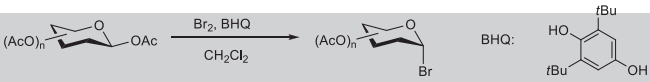
As shown in Table 1, we applied the same condition to prepare glucosyl iodide, which proceeded via the treatment with TESH/I_2 (Table 1). In contract to bromination described above, the iodination of monosaacharides and disaacharides proceeded at 40°C, and a seated tube or reflux system as reaction chamber is necessary. A computation for the titration of TESH with Br_2 and I_2 in proton NMR spectra presented that the formation of TESBr is faster than TESI (see the Figure S1 in the Supporting information), in which TESBr is observed with one equiv Br_2, and TESI is converted fully with two equiv I_2. The reactivity of iodination at the anomeric position with TESH/I_2 was suggested lower than the anomeric bromination with the TESH/Br_2 mixture. Following a standard reaction of glycosyl bromination, a series of glycosidic iodide were synthesized in a very similar manner, including the restrictions of *N*-acetyl-glucoamine **5** and xylose **6** (Table 1, entry 5–6). Glycosyl bromides **1-9Br** and iodide **1-9I** prepared from commonly available sugars gave acceptable ^1H and ^{13}C NMR spectra that matched data reported in the cited references. In most of the cases, a single α-isomer was obtained.

With anhydrous halogenation of saccharide in hand, we turned our attention to realize the reactive formation of HBr, which proceeded via the bromination of sugar formed in situ with *di-t-butyl*-1,4-benzohydroquinone (BHQ)/Br_2 mixture (Table 2). In contract to pyranosyl bromination in Table 1, the anomeric bromination with BHQ/Br_2 was monitored by TLC, and the reaction mixture was accomplished with longer reaction time in good to moderate yield. Anhydrous hydrogen bromide was generated mildly in site by the reaction of liquid bromine and BHQ. However, the presence of BHQ/Br_2 mixture prevented the anomeric iodination of sugar, as HI forms more slowly such that the activity of hydrogen iodide is restricted.

2.2 | Anomerization of saccharides

After the successful outcome of the anomeric halogenation of sugar, the application of the TESH/X_2 system for

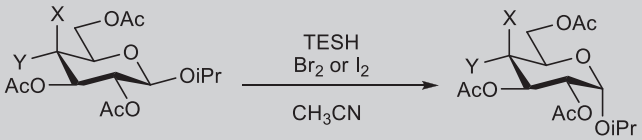
TABLE 2 Bromination of saccharides with Br2/BHQ[a]



Entry	Saccharide	Product	Time (hr)	Yield (%)
1	Glucopyranose-$(OAc)_5$ **1**	**1Br**	4	87
2	Galactopyranose-$(OAc)_5$ **2**	**2Br**	4	75
3	Mannopyranose-$(OAc)_5$ **3**	**3Br**	4	89
4	Fucopyranose-$(OAc)_4$ **4**	**4Br**	4	92
5	Cellobiose-$(OAc)_8$ **7**	**7Br**	8	68
6	Maltose-$(OAc)_8$ **8**	**8Br**	8	70
7	Lactose-$(OAc)_8$ **9**	**9Br**	8	75

[a]With 1.5 equiv BHQ and 3.0 equiv Br_2.

TABLE 3 Anomerization of saccharides with Br_2/TESH or I_2/TESH



10β X = H, Y = OAc
11β X = OAc, Y = H

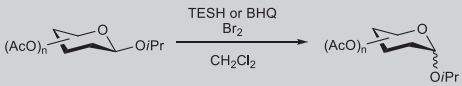
10α X = H, Y = OAc
10α X = OAc, Y = H

Entry	Hexose	TESH (equiv)	Br_2 (equiv)	I_2 (equiv)	Time (hr)	Yield (%)	α/β[a]
1	**10β**	1.2	1.2	—	1	94	4.4/1
2	**10β**	1.2	1.2	—	3	97	4.6/1
3	**10β**	1.2	1.2	—	24	66	4.4/1
4	**10β**	0.6	0.6	—	3	100	3.4/1
5	**10β**	0.6	0.6	—	6	74	5.4/1
6	**10β**	0.6	0.6	—	24	80	5.2/1
7	**10β**	1.2	—	1.2	3	85	4.1/1
8	**10β**	1.2	—	1.2	6	88	5.5/1
9	**10β**	1.2	—	1.2	24	74	5.5/1
10	**11β**	1.2	1.2	—	2	89	3.4/1
11	**11β**	1.2	1.2	—	6	84	3.7/1
12	**11β**	1.2	1.2	—	24	66	4.0/1
13	**11β**	1.2	—	1.2	2	88	4.0/1
14	**11β**	1.2	—	1.2	6	83	4.0/1
15	**11β**	1.2	—	1.2	24	63	4.2/1

[a]NMR result, see Supporting Information Figure S2.

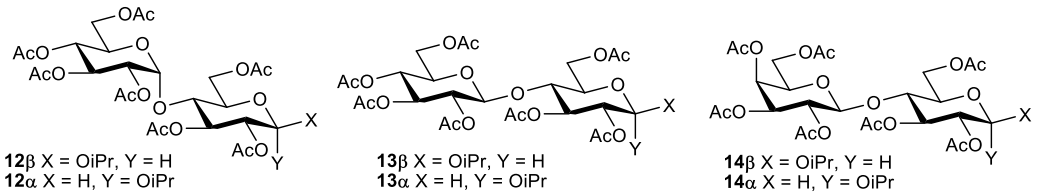
the anomerization of monosaccharide and disaccharide was also examined. Thus β-*O*-isopropyl monosaccharides **10–11β** and disaccharides **12–14β** were prepared in single isomer, and the 1,2-trans-glycoside were obtained, which is due to the neighboring group participation of the acetyl group at C-2, followed by the attack of isopropanol. To optimize the anomerization condition, TESH (1.2 equiv) and Br_2 (1.2 equiv) were added to a solution of saccharides **10–14β**. The results are presented in Table 3. As shown in entries 1–3, β-glucose **10β** provides the corresponding α/β anomers in the same ratio of 4.4/1 in 1 hr and 24 hr with 94% and 66% yields, respectively. The isolated yield was lower after longer reaction, during which *O*-isopyopyl pyranose underwent anomeric hydrolysis. Decreasing the quantity of TESH and Br_2 from 1.2 to 0.6 equiv led to an α/β ratio of 3.4/1 after 3 hr, while

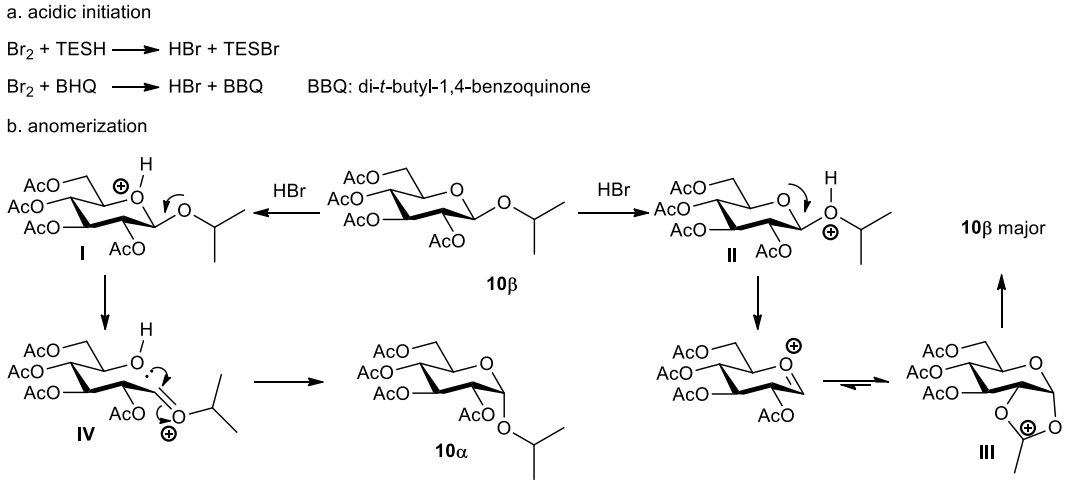
TABLE 4 Anomerization of saccharides with TESH/Br_2 and BHQ/Br_2



		TESH/Br_2[a]			BHQ/Br_2[b]		
Entry	Saccharide	Time (hr)	Yield (%)	α/β[c]	Time (hr)	Yield (%)	α/β[c]
1	**10β**	0.5	93	8.6/1	0.5	95	7.6/1
2	**10β**	1	91	9.5/1	1	97	8.5/1
3	**10β**	6	92	9.2/1	6	93	8.2/1
4	**11β**	0.5	94	6.0/1	0.5	97	6.8/1
5	**11β**	1	96	5.2/1	1	96	7.3/1
6	**11β**	6	93	5.6/1	6	91	7.1/1
7	**12β**	2	97	3.1/1	2	95	7.5/1
8	**12β**	4	98	7.2/1	4	94	7.4/1
9	**13β**	2	99	3.2/1	2	99	4.6/1
10	**13β**	4	98	4.9/1	4	98	4.5/1
11	**14β**	2	98	4.3/1	2	99	5.3/1
12	**14β**	4	97	4.0/1	4	97	5.1/1

[a]With 1.2 equiv TESH and 1.2 equiv Br_2.
[b]With 1.2 equiv BHQ and 1.2 equiv Br_2.
[c]NMR result, see Supporting Information Figure S3 and S4.





SCHEME 1 Postulated acidic TESH/Br_2 or BHQ/Br_2 mediated anomerization of isopropyl glycosides

following a longer reaction time of 6 and 24 hr, the α/β ratios were 4.7/1 and 5.2/1, respectively (entries 4–6). With I_2 (Table 3, entry 7–9) treatment, the anomerization of β-anomer **10β** into ratios of 4.1/1 and 5.5/1 after 3 and 24 hr, respectively. The same conditions were applied to galactosyl derivative **11β** (entries 10–15). The resulting α/β ratios were 4.0 for TESH/Br_2 and 4.2 for TESH/I_2 treatment in 24 hr, and the acidic inversion of reactant in acetonitrile **11β** showed lower yield (~65%).

To further reduce the involuted hydrolytic by-product, dried CH_2Cl_2 was selected as solvent to replace CH_3CN. The results are presented in Table 4. Results in the formation of the corresponding anomers were isolated in good to excellent isolated yields. As shown in entries 1–6 of the table with TESH/Br_2, β-glucoside **10β** and β-galactoside **11β** provided the corresponding α/β anomers in ratios of 9.5/1 and 5.2/1 in 1 hr and within isolated yields 92% and 96% in 6 hr (entry 3 and 6). The hydrolytic reaction is restricted in dried dichloromethane. For the disaccharide **12β**, **13β**, and **14β** (entries 9–14), the α/β ratios of obtained with anomerization were 7.2/1, 4.5/1, and 4.0/1 in 4 hr, respectively. Significant α/β anomerization for the internal glycosidic bond of the available disaccharides was not observed. We applied the BHQ/Br_2 condition to pyranosyl saccharides **10β–14β**. The presented results are similar to that treated with acidic TESH/Br_2. This result indicated that hydrogen bromide generated from BHQ/Br_2 catalyzed the anomerization in a similar reaction pathway as HBr from TESH/Br_2.

A postulated mechanism is illustrated in Scheme 1. Hydrogen bromide initially generated from mixture of Br_2 with TESH or BHQ reacts with pyranosyl oxygen and exocyclic oxygen to yield the possible oxonium cation **I** and **II**, respectively. Owing to neighboring group participation of 2-*O*-acetoxyl group and the formation of transition structure **III**, such that it can accept an *O*-isopropyl group from the Si-face to predominately produce β-anomer. In contract, glycoside **10β** reacts with HBr to give the protonated intermediate **I**. Unlike in the case of oxonium cation **II** where the protonated derivative is derived front the reaction at exocyclic oxygen, the protonation at the pyranosyl *O*-5 to give the reactive intermediate **I**. Upon a subsequent endocyclic ring-opening generates **IV** in the open-chain form. Due to thermodynamic anomeric effect, the ring closure takes place in favor of the more stable axial orientation of the α-anomer moiety.

3 | CONCLUSIONS

In summary, triehtylsilane/bromine and triehtylsilane/iodine systems have been demonstrated to be highly effective for preparation of bromo- and iodo-linked glycoside as well as anomeric bromination with BHQ/Br2. Furthermore, those activated conditions were also examined with anomerization of 1-isopropyl monosaccharides and disaccharide and interpreted mechanistically. Further investigation on this will include subjecting the above conditions with photo-activated anomerization for the internal glycosidic bond of oligosaccharide.

4 | EXPERIMENTAL

General experiment: Acetonitrile and dichloromethane were dried and distilled from CaH_2. Flash column chromatography was carried out with silica gel 60 (230–400 mesh, E. Merck). TLC was performed on precoated glass plates of silica gel 60 F254 (0.25 mm, E. Merck); detection was executed by spraying with cerium ammonium sulfate and subsequent heating on a hot plate. TESH, BHQ, glucose penta-acetylated 1, and glactose penta-acetylate 2 were purchased from Sigma-Aldrich. Acetylatedoligosaccharide 3–9 were prepared from relative saccharide by per-*O*-acetylation with Ac_2O/pyridine.[25] ^1H and ^{13}C NMR spectra were recorded with 300 MHz instruments. Proton chemical shifts are in ppm from $CHCl_3$ lock signal at 7.26 ppm, and carbon chemical shifts are in ppm from $CHCl_3$ lock signal at 77 ppm. Mass spectra were obtained in the EI or FAB mode.

4.1 | 1-Bromo-tetra-*O*-acetate-α-D-monosaccharides (1Br–4Br) and 1-Bromo-hepta-*O*-acetate-α-D-disaccharides (7Br–9Br)

To a solid of per-OAc saccharide (0.26 mmol) in dichloromethane (1 ml), the mixture was added bromine (40 μl, 0.78 mmol) and triethylsilane (63 μl, 0.39 mmol) at 0°C for the reaction time listed in Table 1. The reaction progress was monitored with TLC (EA/Hex = 1/2) until the per-OAc saccharide disappeared. The reaction was diluted with ethyl acetate (60 ml), and extracted with water, 10% $Na_2S_2O_3$, 10% $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, concentrated under reducing pressure, and dried in vaco. The crude mixture was purified by flash column chromatography (EA/Hex = 1/2) to afford the product.

To a solid of per-OAc saccharide (0.26 mmol) in dichloro-methane (1 ml), the mixture was added bromine (40 μl, 0.78 mmol) and di-tert-butylhydroquinone (87 mg, 0.39 mmol) at 0°C for the reaction time listed in Table 2. The reaction progress was monitored with TLC (EA/Hex = 1/2) until the per-OAc saccharide disappeared.

The reaction was diluted with ethyl acetate (60 ml), and extracted with water, 10% $Na_2S_2O_3$, 10% $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, concentrated under reducing pressure, and dried in vaco. The crude mixture was purified by flash column chromatography (EA/Hex = 1/2) to afford the product.

7Br[21]: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.520 (d, J = 3.9 Hz, 1H), 5.549 (t, J = 9.66, 1H), 5.172 (t, J = 9.27, 1H), 5.093 (t, J = 9.44, 1H), 4.954 (t, J = 8.50, 1H), 4.775 (dd, J = 9.96, 4.05, 1H), 4.547–4.499 (m, 2H), 4.385 (dd, J = 12.48, 4.44, 1H), 4.212–4.132 (m, 2H), 4.064 (dd, J = 12.45, 2.19, 1H), 3.859 (t, J = 9.72, 1H), 3.690 (ddd, J = 9.63, 4.38, 2.25, 1H), 2.125 (s, 3H), 2.078 (s, 3H), 2.032 (s, 3H), 1.998 (s, 3H), 1.974 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.64 (C), 170.41 (C), 170.26 (C), 170.13 (C), 169.45 (C), 169.13 (C), 100.71 (CH), 86.57 (CH), 77.62 (CH), 77.19 (CH), 76.77 (CH), 75.37 (CH), 73.16 (CH), 73.09 (CH), 72.20 (CH), 71.75 (CH), 70.92 (CH), 69.58 (CH), 67.92 (CH), 61.76 (CH_2), 61.09 (CH_2), 20.96 (CH_3), 20.83 (CH_3), 20.73 (CH_3), 20.69 (CH_3).

8Br[21]: 1H NMR (300 MHz, $CDCl_3$) 6.508 (d, J = 3.9 Hz, 1H), 5.644 (t, J = 9.45 Hz, 1H), 5.428 (d, J = 3.9 Hz, 1H), 5.377 (d, J = 10.5 Hz, 1H), 5.111 (t, J = 9.9 Hz, 1H), 4.891 (dd, J = 10.5, 3.9 Hz, 1H), 4.734 (dd, J = 9.9, 3.9 Hz, 1H), 4.540–4.506 (m, 1H), 4.283–4.220 (m, 3H), 4.129–4.036 (m, 2H), 3.970–3.917 (m, 2H), 2.149 (s, 3H), 2.101 (s, 3H), 2.081 (s, 3H), 2.070 (s, 3H), 2.040 (s, 3H), 2.031 (s, 3H), 2.010 (s, 3H); 13C NMR (75 MHz, CDCl3) 170.85 (C), 170.68 (C), 170.46 (C), 170.03 (C), 169.69 (C), 169.61 (C), 95.93 (CH), 86.20 (CH), 72.69 (CH), 72.49 (CH), 71.72 (CH), 71.17 (CH), 70.17 (CH), 69.40 (CH), 68.79 (CH), 68.06 (CH), 62.00 (CH_2), 61.49 (CH_2), 21.02 (CH_3), 20.93 (CH_3), 20.83 (CH_3), 20.79 (CH_3), 20.75 (CH_3).

9Br[21]: 1H NMR (300 MHz, $CDCl_3$) 6.532 (d, J = 3.9 Hz, 1H), 5.588 (t, J = 9.6 Hz, 1H), 5.365 (dd, J = 3.3, 0.9 Hz, 1H), 5.160 (dd, J = 10.5, 7.95 Hz, 1H), 4.982 (dd, J = 10.5, 3.6 Hz, 1H), 4.784 (dd, J = 9.9, 4.2 Hz, 1H), 4.521–4.486 (m, 2H), 4.215–4.047 (m, 4H), 3.909–3.828 (m, 2H), 2.164 (s, 3H), 2.136 (s, 3H), 2.095 (s, 3H), 2.070 (s, 3H), 2.064 (s, 3H), 2.057 (s, 3H), 1.969 (s, 3H); 13C NMR (75 MHz, $CDCl_3$) δ 170.52(C), 170.35 (C), 170.32 (C), 170.25 (C), 170.15 (C), 169.41 (C), 169.14 (C), 100.96 (CH), 86.55 (CH), 75.12 (CH), 73.14 (CH), 71.16 (CH), 71.01 (CH), 70.95 (CH), 69.76 (CH), 69.19 (CH), 66.77 (CH), 61.21 (CH_2), 61.04 (CH_2), 20.96 (CH_3), 20.82 (CH_3), 20.66 (CH_3).

1-Iodo-tetra-*O*-acetate-α-D-monosaccharides (1I–4I) and 1-Iodo-hepta-*O*-acetate-α-D-disaccharides (7I–9I): To a solid of per-OAc saccharide (0.26 mmol), iodine (198 mg, 0.78 mmol) in seat tubein, the mixture was added dichloromethane (1 ml) and triethylsilane (63 μl, 0.39 mmol) at 0°C and stirred at 60°C for the reaction time listed in Table 1. The reaction progress was monitored with TLC (EA/Hex = 1/2) until the per-OAc saccharide disappeared. The reaction was diluted with ethyl acetate (60 ml), and extracted with water, 10% $Na_2S_2O_3$, 10% $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, concentrated under reducing pressure, and dried in vaco. The crude mixture was purified by flash column chromatography (EA/Hex = 1/2) to afford the product.

To a solid of isopropyl-tetra-OAc-β-saccharide (0.26 mmol) in Pyrex tube, the mixture was added dichloromethane (1 ml) and bromine (15 μl, 0.31 mmol) and di-tert-butylhydroquinone (69 mg, 0.31 mmol) at 0°C for the reaction time listed in Table 4. The reaction progress was monitored with TLC (EA/Hex = 1/2). The reaction was diluted with ethyl acetate (60 ml), and extracted with water, 10% $Na_2S_2O_3$, 10% $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, concentrated under reducing pressure, and dried in vaco. The crude mixture was checked and examined with NMR and purified by flash column chromatography (EA/Hex = 1/2) to afford the product.

10α: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.472 (t, J = 9.8 Hz,1H), 5.181 (d, J = 3.8 Hz, 1H), 5.037 (t, J = 9.8 Hz, 1H), 4.797 (dd, J = 10.3, 3.8 Hz, 1H), 4.251 (dd, J = 11.9, 4.4 Hz, 1H), 4.127–4.050 (m, 2H), 3.895–3.813 (m, 1H), 2.085 (s, 3H), 2.054 (s, 3H), 2.029 (s, 3H), 2.012 (s, 3H), 1.235 (d, J = 6.1 Hz, 3H), 1.116 (d, J = 6.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.69 (C), 170.21 (C), 170.16 (C), 169.66 (C), 94.13 (CH), 71.39 (CH),70.94 (CH), 70.14 (CH), 68.65 (CH), 67.06 (CH), 61.94 (CH_2), 23.06 (CH_3), 21.54 (CH_3), 20.70 (CH_3), 20.64 (CH_3). HRMS (ESI, M + Na^+) calcd for $C_{17}H_{26}O_{10}Na$: 413.1424, found 413.1426.

11α: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.443 (dd, J = 3.4, 1.0 Hz, 1H), 5.334 (dd, J = 10.9, 3.4 Hz, 1H), 5.213 (d, J = 3.8 Hz, 1H), 5.054 (dd, J = 10.9, 3.8 Hz, 1H), 4.304 (t, J = 6.6 Hz, 1H), 4.092–4.068 (m, 2H), 3.915–3.791 (m, 1H), 2.136 (s, 3H), 2.065 (s, 3H), 2.036 (s, 3H), 1.983 (s, 3H), 1.229 (d, J = 6.2 Hz, 3H), 1.113 (d, J = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.38 (C), 170.22 (C), 170.00 (C), 94.67 (CH), 71.24 (CH), 68.25 (CH), 68.12 (CH), 67.59 (CH), 66.05 (CH), 61.79 (CH_2), 23.00 (CH_3), 21.59 (CH_3), 20.69 (CH_3), 20.60 (CH_3). HRMS (ESI, M + Na^+) calcd for $C_{17}H_{26}O_{10}Na$: 413.1424, found 413.1428.

12α: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.513 (dd, J = 10.1, 8.9 Hz, 1H), 5.415–5.351 (m, 2H), 5.100–5.034 (m, 1H), 4.870 (dd, J = 10.6, 3.9 Hz, 1H), 4.672 (dd, J = 10.1, 3.9 Hz, 1H), 4.433 (dd, J = 12.1, 2.6 Hz, 1H), 4.241–4.203 (set, 1H), 4.122–4.023 (m, 2H), 3.993–3.913 (m, 2H), 3.859 (set, J = 6.2 Hz, 1H), 2.136 (s, 3H), 2.101 (s, 3H), 2.074 (s, 3H), 2.025 (s, 3H), 2.020 (s, 3H), 2.004 (s, 6H), 1.278 (d, J = 6.2 Hz, 3H), 1.130 (d, J = 6.2 Hz, 3H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.69 (C), 170.55 (C), 170.35 (C), 169.96 (C), 169.84 (C), 169.46 (C), 95.58 (CH), 94.06 (CH), 72.95 (CH), 72.69 (CH), 71.58 (CH), 69.98 (CH), 69.40(CH), 68.43 (CH), 68.01 (CH), 67.45 (CH), 62.87 (CH_2), 61.44 (CH_2), 23.12 (CH_3), 21.62 (CH_3), 20.98 (CH_3), 20.81 (CH_3), 20.67 (CH_3), 20.60 (CH_3). HRMS (ESI, M + Na^+) calcd for $C_{29}H_{42}O_{18}Na$: 701.2269, found 701.2270.

13α: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.420 (t, J = 9.8 Hz, 1H), 5.155–5.023 (m, 3H), 4.910 (t, J = 8.2 Hz, 1H), 4.699 (dd, J = 10.2, 3.9 Hz, 1H), 4.489 (d, J = 8.2 Hz, 1H), 4.439 (dd, J = 12.0, 1.9 Hz, 1H), 4.358 (dd, J = 12.5, 4.6 Hz, 1H), 4.100 (dd, J = 12.0, 4.6 Hz, 1H), 4.045–3.961 (m, 2H), 3.841–3.738 (m, 1H), 3.699–3.614 (m, 2H), 2.100 (s, 3H), 2.068 (s, 3H), 2.021 (s, 6H), 2.001 (s, 3H), 1.988 (s, 3H), 1.963 (s, 3H), 1.203 (d, J = 6.2 Hz, 3H), 1.087 (d, J = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.48 (C), 170.40 (C), 170.31 (C), 170.23 (C), 169.56 (C), 169.25 (C), 169.07 (C), 100.79 (CH), 94.15 (CH), 73.03 (CH), 71.86 (CH), 71.66 (CH), 71.50 (CH), 71.17 (CH), 69.63 (CH), 68.06 (CH), 67.73 (CH), 61.91 (CH_2), 61.52 (CH_2), 23.07 (CH_3), 21.58 (CH_3), 20.79 (CH_3), 20.62 (CH_3), 20.54 (CH_3), 20.49 (CH_3). HRMS (ESI, M + Na^+) calcd for $C_{29}H_{42}O_{18}Na$: 701.2269, found 701.2267.

14α: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.462 (t, J = 9.7 Hz, 1H), 5.345 (dd, J = 3.4, 0.8 Hz, 1H), 5.148–5.081 (m, 2H), 4.951 (dd, J = 10.3, 3.4 Hz, 1H), 4.716 (dd, J = 10.3, 3.8 Hz, 1H), 4.479 (d, J = 7.4 Hz, 1H), 4.431 (dd, J = 11.9, 1.9 Hz, 1H), 4.159–4.045 (m, 3H), 4.025–3.985 (m, 1H), 3.888–3.678 (m, 3H), 2.156 (s, 3H), 2.114 (s, 3H), 2.058 (s, 3H), 2.054 (s, 3H), 2.046 (s, 6H), 1.963 (s, 3H), 1.224 (d, J = 6.2 Hz, 3H), 1.109 (d, J = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.47 (C), 170.42 (C), 170.35 (C), 170.19 (C), 170.11 (C), 169.53 (C), 169.12 (C), 101.15 (CH), 94.21 (CH), 71.54 (CH), 71.32 (CH), 71.13 (CH), 70.62 (CH), 69.99 (CH), 69.19 (CH), 68.06 (CH), 66.62 (CH), 62.07 (CH_2), 60.79 (CH_2), 23.11 (CH_3), 21.63 (CH_3), 20.93 (CH_3), 20.83 (CH_3), 20.65 (CH_3), 20.50 (CH_3). HRMS (ESI, M + Na^+) calcd for $C_{29}H_{42}O_{18}Na$: 701.2269, found 701.2267.

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