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Synthesis of oligosaccharides using per-O-trimethylsilyl-glycosyl iodides as glycosyl donor

Hong Wang [b], Yanli Cui [a,*], Rong Zou [a], Zhaodong Cheng [a], Weirong Yao [b], Yangyi Mao [c], Yongmin Zhang [d]

[a] Department of Chemistry, Zhejiang University, Hangzhou 310027, PR China
[b] Carbohydrate Chemistry and Biotechnology, Jiangnan University Key Laboratory of Ministry of Education, Wuxi 214122, PR China
[c] Hangzhou Yanqing Biotechnology Co., Ltd, Hangzhou 310052, PR China
[d] Institut Parisien de Chimie Moleculaire, UMR CNRS 8232, Universite Pierre et Marie Curie-Paris 6, 75005 Paris, France

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ABSTRACT

Trimethylsilyl (TMS) protecting group has been found to be very useful for the simultaneous protection of both the glycosyl donor- and the acceptor-substrates in oligosaccharide synthesis. Thus, while the per-O-trimethylsilylated glycosyl iodides served as the glycosyl donor, those bearing selectively exposed primary hydroxyl groups were found suitable as the glycosyl acceptor for the reaction. The cheap and commercially available trialkylamine, triethylamine was found to be an effective promoter for the glycosylation. Importantly, the reaction was α-stereospecific and gave the products in 58%–78% yields.

1. Introduction

Efficient formation of glycosidic linkages is a pivotal step for the synthesis of oligosaccharides. The influencing factors for glycosylation involve leaving groups of the glycosyl donor, catalyst, promoter, solvent, protecting groups for the donor and the acceptor, etc.[1,2] Among the various classes of glycosyl halides used for glycosylation, glycosyl iodides, initially considered to be thermally unstable, were largely substituted by the more stable bromide- and chloride-analogues.[3] Then in 1972, glycosyl iodides were applied for forming *O*-glycosides.[4] Shortly thereafter, Kronzer and Schuerch[5] found that glycosyl iodides offered more advantages than glycosyl chlorides and bromides, including less reaction time and higher stereoselectivity. Stachulski[6] and co-workers stated that glycosyl iodides have remarkable stability at room temperature. Glycosyl iodides attracted more attention as glycosyl donors and have been widely utilized since then.[7–9]

As protecting group, benzyl[10–12] and acyl[11,13,14] groups are more stable than trimethylsilyl groups, but their protection and deprotection go through multistep, tedious operation or chromatography purification. In comparison, a per-*O*-trimethylsilylated carbohydrate is easy to prepare and deprotect.[15] Recently, glycosyl iodide,[16–18] especially per-*O*-trimethylsilylated glycosyl iodide,[16] was applied for preparing several biologically active glycolipids by Gervay-Hague and co-workers. Glycosyl iodides were prepared and directly used as the donor. The whole process from unprotected carbohydrate to the donor lacked purification and only needed simple post-processing when glycosyl iodides were prepared as the donor.

α-Linkage formation is more difficult than β-linkage in most situations. Inspired by α-galactosyl ceramide coupling through per-*O*-trimethylsilylated galactosyl iodide donor,[16,19] also based on our earlier results[20] wherein 6-hydroxy trimethylsilylated monosaccharide or 6′-hydroxy trimethylsilylated disaccharide was directly gained by mild ammonium acetate, we envisaged the synthesis of saccharide using per-*O*-trimethylsilylated glycosyl iodide as donor and 6-hydroxy trimethylsilylated monosaccharide or 6′-hydroxy trimethylsilylated disaccharide as acceptor. In 2002, 1,6-α-linked oligosaccharides were synthesized using glycosyl iodide, but the protecting groups for the donors and the acceptors were benzyl groups.[21] Obviously the glycosylation would be affected when the protecting groups were trimethylsilyl groups which had different electron and spatial effect with other types of protecting groups. The simultaneous application of trimethylsilyl groups in the donors and the acceptors for oligosaccharide synthesis has not yet been reported. It would be worthy to observe if α-glycosidic bond could be formed in a new structural environment and the influence of trimethylsilyl groups on the glycosylation involved.

Abbreviations: MS, molecular sieves; DCM, CH_2Cl_2.

* Corresponding author. Department of Chemistry, Zhejiang University, Hangzhou 310027, China. Tel.: +86 13858036095; fax: +86 57188486676.
E-mail address: cuiyl@zju.edu.cn (Y. Cui).

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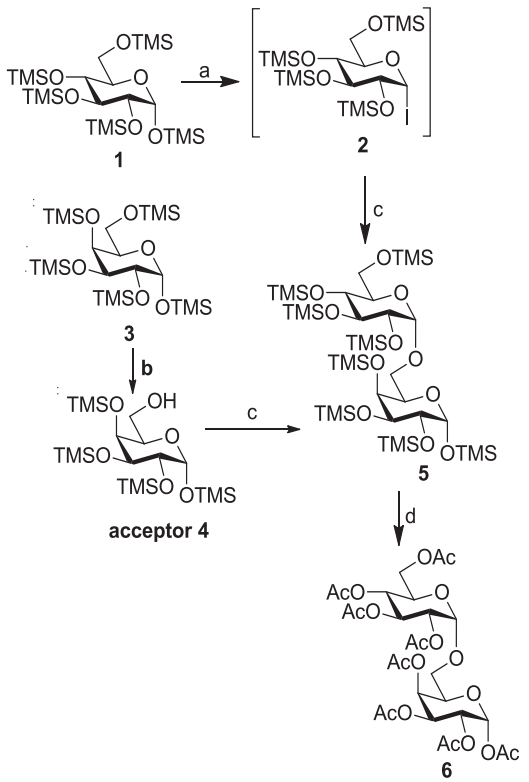


Scheme 1. Reagents: (a) **1** (0.37 mmol), TMSI (0.37 mmol), CH_2Cl_2 (3.70 mL); (b) **3** (0.14 mmol), NH_4OAc (0.28 mmol), CH_2Cl_2 (1 mL), MeOH (1 mL), 86%; (c) **2** (0.37 mmol), **4** (0.12 mmol), $^nBu_4NI$ (0.81 mmol), triethylamine (0.37 mmol), 4 Å MS (100 mg), CH_2Cl_2 (3.70 mL), 64%; (d) Ac_2O (0.37 mmol), DMAP (4.0 mg), DMF (1.5 mL), 98%.

2. Results and discussion

Firstly, per-*O*-trimethylsilylated glucose **1** was synthesized by treating glucose with a mixture of TMSCl and hexamethyldisilazane (HMDS) in pyridine overnight at 80 °C,[15] which was then converted to per-*O*-trimethylsilylated glucosyl iodide **2** by direct reaction with TMSI in CH_2Cl_2 (Scheme 1). Subsequently, active intermediate **2** was added dropwise to a mixture of alcohol **4**, $^nBu_4NI$, triethylamine and 4 Å MS in CH_2Cl_2. The resulting mixture was stirred overnight and the reaction was monitored by TLC. We noticed that the unreacted compound **2**, **4** and the by-products were difficult to analyze. So the compound **5** should be purified by flash column chromatography. At the beginning of our experiment, complete detrimethylsilylation of **5** was carried out by 40% acetic acid solution, and we found that the product was a mixture of α/β anomers, which was complicated to analyze by NMR spectrum. For concise structural analysis, the trimethylsilyl groups were changed to acetyl groups using Ac_2O/DMAP in DMF. A good yield of fully acetylated glycoside **6** was obtained.

Firstly, glycosylation was realized by DIPEA. To explore a more effective promoter for this reaction, different amino catalysts were chosen as shown in Table 1. 2,6-Di-tert-butylpyridine yielded several by-products which were difficult to separate. The yield by triethylamine was slightly higher than by DIPEA. DMAP and DBU were unsuitable for this reaction because of their low reaction-promoting activity. Under the same conditions, DBU also caused trimethylsilyl groups to fall off during the reaction. Ultimately, cheap triethylamine was proved to be most advantageous as a promoter.

In the previous application, glycosyl iodides were often excessively used. The ratio of the donor and the acceptor was worthy of investigation. Screening experiments proved that higher ratio did not produce higher yield. Therefore, a 3:1 molar ratio of the donor to the acceptor was appropriate for the reaction.

Table 1
The effect of diverse catalysts on the yield of compound **5**

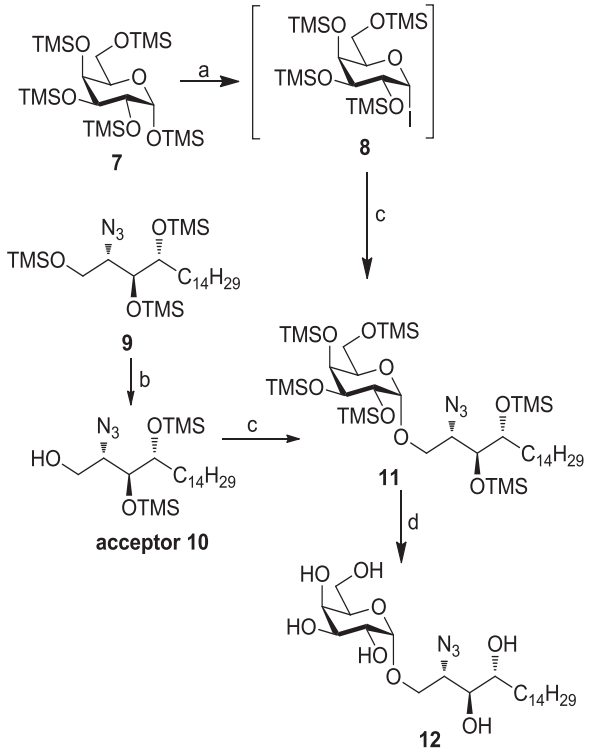
Entry	Catalyst	A:B (mol ratio)[a]	Yield (%)	α-Isomer
1	2,6-di-tert-butylpyridine	1:3	70	Single
2	Triethylamine	1:3	64	Single
3	DIPEA	1:3	60	Single
4	DMAP	1:3	15	Single
5	DBU	1:3	10	Single

[a] A:B = n (compound **4**):n (compound **1**).

Another feature of the method is the usage of catalyst NH_4OAc. After removing the 6-*O*-trimethylsilyl group, the neutral mixture was concentrated under reduced pressure and could be directly used in glycosylation without any purification because the residual per-*O*-trimethylsilylated sugar did not affect the glycosylation reaction.

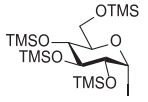
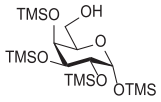
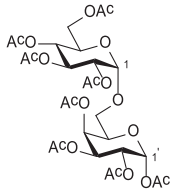
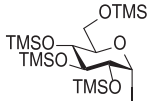
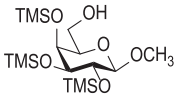
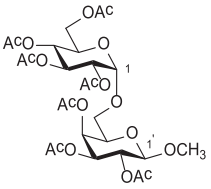
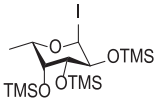
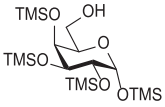
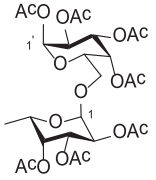
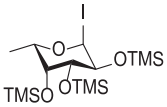
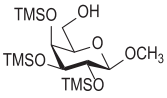
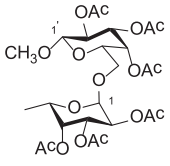
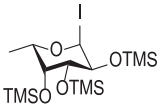
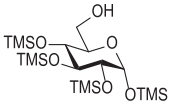
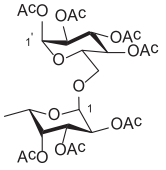
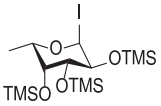
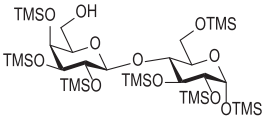
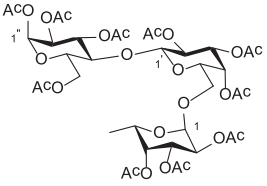
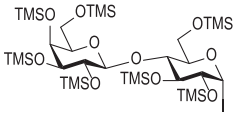
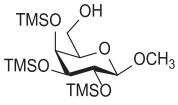
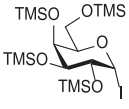
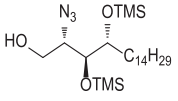
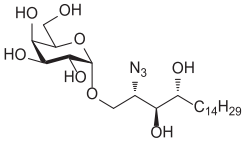
In addition, the strategy had been extended to the crucial step of α-galactosylceramide (α-GC) synthesis (Scheme 2). Previously Bz, TBDMS and other groups were used for protecting the HO-3 and the HO-4 of the phytoceramide for enhancing the glycosylation.[16,22,23] We planned to use the trimethylsilyl groups for protecting the phytoceramide hydroxyls. The primary trimethylsilyl group of per-*O*-trimethylsilylated phytoceramide was removed by NH_4OAc.[20] Other hydroxyls of the phytoceramide were protected by trimethylsilyl groups. The trimethylsilyl groups on the HO-3 and the HO-4 of compound **10** did not influence the α-glycosidic bond formation.

In order to explore the application range, a series of trimethylsilylated glycosyl iodide and per-*O*- trimethylsilylated sugar alcohol were subjected to glycosylation and the results are presented in Table 2. Glucosyl iodide and fucosyl iodide had similar reactivity leading to almost identical yields. Surprisingly, practical



Scheme 2. Reagents: (a) **7** (0.37 mmol), TMSI (0.37 mmol), CH_2Cl_2 (3.70 mL); (b) **9** (0.15 mmol), NH_4OAc (0.30 mmol), CH_2Cl_2 (1 mL), MeOH (1 mL), 82%; (c) **8** (0.37 mmol), **10** (0.12 mmol), $^nBu_4NI$ (0.81 mmol), triethylamine (0.37 mmol), 4 Å MS (100 mg), CH_2Cl_2 (3.70 mL),.79%; (d) 40% acetic acid solution (5 mL), 98%.

Table 2
Formation of α-glycosidic bond

Entry	Donor	Acceptor	Product	Time (h)	Yield[a] (%)
1	 **2**[8]	 **4**[20]	 **6**	12	63%
2	 **2**	 **14**	 **15**	12	66%
3	 **13**[9]	 **4**	 **16**	12	70%
4	 **13**	 **14**	 **17**	12	74%
5	 **13**	 **18**[20]	 **19**	12	60%
6	 **13**	 **20**[20]	 **21**	12	58%
7	 **22**[8]	 **14**	—	12	0
8	 **8**[8]	 **10**[20]	 **12**	12	77%

[a] Yields based on the acceptors.

glycosyl coupling did not happen in any substrates. When the donor was per-*O*-trimethylsilylated lactosyl iodide, the reaction did not proceed while using 6-monohydroxy trimethylsilylated monosaccharide **14** as the acceptor (Table 2, entry 7), which implied that the monosaccharide donor iodide had sufficient activity to attack the acceptor. Other new disaccharides, trisaccharide and α-galactosylceramide (α-GC) were obtained by the above accessible procedures. The outcomes were confirmed by NMR, formed

α-glycosidic bond, which was inferred from the chemical shifts and coupling constants of the anomeric proton signals. The other anomeric bonds connected to the acetyl group on compound **6**, **16**, **19**, and **21** were confirmed as α-glycosidic bonds.

3. Conclusion

In summary, we report a novel and efficient pathway for the synthesis of oligosaccharides with exclusive α-stereoselectivity. The trimethylsilyl groups as protecting groups for the acceptor did not affect the α-glycosidic bond formation with the trimethylsilylated monosaccharide iodide as the donor. Given the mild conditions and the easy operation of trimethylsilyl groups, this method is labor-saving, eco-friendly and economic. It provides rapid access to biologically relevant carbohydrates.

4. Experimental methods

4.1. General

All reagents were obtained from commercial sources (some from Adamas-beta, PRC) and used without further purification. Solvents were dried using standard methods. Reactions were monitored by TLC using a silica gel 60 F 254 precoated plate (Merk, Darmstadt, Germany), and detection was performed by charring with sulfuric acid. Flash column chromatography was performed on silica gel 60 (100–400 mesh, Qingdao Marine Chemical Ltd., Qingdao, PRC). NMR spectra were recorded at ambient temperature (400 MHz for 1H NMR and 101 MHz for 13C NMR) on a Bruker DRX 400 (Karlsruhe, Germany). Mass spectral data were determined by LTQ FT Ultra (Thermo Fisher Scientific, USA).

4.2. O-(2,3,4,6-Tetra-O-acetyl-α-D-glucopyranosyl)-(1→6)-1,2,3,4-tetra-O-acetyl-α-D-galactopyranose (6)

TMSI (50 μL, 0.37 mmol) was added to a solution of **1** (0.20 g, 0.37 mmol) in CH_2Cl_2 (3.70 mL) at 0 °C. The reaction mixture was stirred under an argon atmosphere for 15 min. In a separate flask, a mixture of activated 4 Å molecular sieves (100 mg), $^nBu_4NI$ (0.30 g, 0.81 mmol), triethylamine (51 μL, 0.37 mmol), and alcohol **4** (34.8 mg, 0.12 mmol) in CH_2Cl_2 (3.70 mL) was prepared and stirred under argon for 20 min. The solution of glycosyl iodide was then added dropwise over 20 min to this mixture, and the resulting mixture was stirred overnight. After removal of the solvent under reduced pressure, the mixture was purified by flash column chromatography (petroleum ether/ethyl acetate = 15:1) to afford glycoside **5**. Then DMAP (4.0 mg) and Ac_2O (35 μL, 0.37 mmol) were added to a solution of glycoside **5** in DMF (1.50 mL) and stirred overnight providing the fully acetylated glycoside, and then concentrated under reduced pressure. The resulting solid was purified by flash column chromatography (petroleum ether/ethyl acetate = 2:1) to afford glycoside **6** (single α-anomer) as a white solid (51.2 mg, 63%). R_f = 0.55 (petroleum ether/ethyl acetate = 1:1). $[\alpha]_D^{20} = +22.6$ (c = 0.5, DCM). ^{1}H NMR($CDCl_3$, 400 MHz) δ 6.36 (d, 1H, J = 3.2 Hz, H–1′ α), 5.53 (s, 1H), 5.43 (t, 1H), 5.33 (d, 2H), 5.04 (t, 1H), 4.90 (d, 1H, J = 4.0 Hz, anomeric proton), 4.86 (dd, 1H), 4.33 (t, 1H), 4.25 (dd, 1H), 4.11 (dd, 1H), 4.03–3.99 (m, 1H), 3.73–3.69 (m, 1H), 3.45–3.41 (m, 1H), 2.21 (s, 3H), 2.15 (s, 3H), 2.10 (s, 3H),2.08 (s, 3H), 2.04 (s, 6H), 2.01 (s, 3H), 2.00 (s, 3H); ^{13}C NMR($CDCl_3$, 101 MHz) δ 170.66, 170.41, 170.14, 170.06, 170.00, 169.94, 169.61, 169.08, 96.13 (C–1, anomeric carbon), 89.63 (C–1′ α anomer), 70.23, 69.95, 69.26, 68.32, 67.58, 67.58, 67.53, 66.47, 65.67, 61.70, 20.95, 20.73, 20.68, 20.63, 20.62, 20.57, 20.55, 20.55. HRMS (ESI) calcd for $C_{28}H_{38}O_{19}$ $[M + Na]^+$ 701.1899,found 701.1898.

4.3. α-D-Galactopyranosyl-(1→1)-(2S,3R,4R)-2-azido-octadecane-1,3,4-triol (12)

TMSI (50 μL, 0.37 mmol) was added to a solution of **7** (0.2 g, 0.37 mmol) in CH_2Cl_2 (3.7 mL) at 0 °C. The reaction mixture was stirred under an argon atmosphere for 15 min. In a separate flask, a mixture of activated 4 Å molecular sieves (100 mg), $^nBu_4NI$ (0.30 g, 0.81 mmol), triethylamine (51 μL, 0.37 mmol), and alcohol **10** (58.5 mg, 0.12 mmol) in CH_2Cl_2 (3.70 mL) was prepared and stirred under argon for 20 min. The solution of glycosyl iodide was then added dropwise over 20 min to this mixture, and the resulting mixture was stirred overnight. After removal of the solvent under reduced pressure, the mixture was purified by flash column chromatography (petroleum ether/ethyl acetate = 17:3) to afford glycoside **11**. Then treating the glycoside **11** with 40% acetic acid solution 5 mL overnight provided the fully deprotected glycoside **12** (single α-anomer) as a white solid (46.7 mg, 77%). $[\alpha]_D^{20} = -7.6$ (c = 1.2 in $CHCl_3$:MeOH(1:1)). ^{1}H NMR (DMSO–*d*6, 400 MHz,) δ 4.70 (d, 1H, J = 4.0 Hz, anomeric proton), 3.94 (d, 1H, J = 8.0 Hz), 3.71 (s, 1H), 3.66–3.58 (m, 3H), 3.54–3.50 (m, 1H), 3.47–3.41 (m, 1H), 3.35 (s, 4H), 1.59 (s, 1H), 1.45 (s, 1H), 1.24 (s, 24H), 0.85 (t, 3H, J = 4.0 Hz); ^{13}C NMR (DMSO–*d*6, 101 MHz) δ 99.89 (C–1, anomeric carbon), 74.77, 71.42, 70.66, 69.41, 68.69, 68.13, 66.87, 62.44, 60.42, 33.09, 31.27, 29.23, 29.11, 29.04, 28.99, 28.69, 25.04, 22.07, 13.93. HRMS (ESI) calcd for $C_{24}H_{47}N_3O_8$ $[M + Na]^+$ 528.3255, found 528.3254.

4.4. Methyl 2,3,4-tri-O-trimethylsilyl-β-D-galactopyranoside (14)

Compound **14** was afforded according to the method described in previous literature[20] as a white solid (33.5 mg, 85%). R_f = 0.52 (petroleum ether/ethyl acetate = 8:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11 (d, *J* = 8.0 Hz, 1H), 3.86 (dd, 1H), 3.77 (d, *J* = 3.2 Hz, 1H), 3.66–3.62 (m, 2H), 3.52 (s, 3H), 3.50–3.47 (m, 1H), 3.42 (dd, 1H), 0.16 (s, 9H), 0.15 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 104.63, 74.67, 74.49, 71.89, 71.59, 62.40, 56.83, 0.23, 0.17, 0.00. HRMS (DART) calcd for $C_{16}H_{38}O_6Si_3$ $[M + H]^+$ 411.2048, found 411.2048.

4.5. O-(2,3,4,6-Tetra-O-acetyl-α-D-glucopyranosyl)-(1→6)-1-O-methyl-2,3,4-tri-O-acetyl-β-D-glycosides (15)

The procedure was the same as that for compound **6**. Compound **15** was afforded from glycosyl iodide **2** and alcohol **14** as a white solid (51.6 mg, 66%): R_f = 0.60 (petroleum ether/ethyl acetate = 1:1). $[\alpha]_D^{20} = +20.1$ (c = 0.5, DCM). ^{1}H NMR($CDCl_3$, 400 MHz) δ 5.46 (d, 1H, J = 8.0 Hz), 5.42 (d, 1H, J = 4.0 Hz), 5.19 (dd, 1H), 5.07 (d, 1H, J = 8.0 Hz), 5.03–5.00 (m, 1H), 4.94 (d, 1H, J = 4.0 Hz, anomeric proton), 4.88 (dd, 1H), 4.42 (d, 1H, J = 8.0 Hz, H–1′ β), 4.25 (dd, 1H), 4.15–4.11 (m, 2H), 4.09–4.04 (m, 1H), 3.90 (t, 1H), 3.80 (dd, 1H), 3.52 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.01 (d, 6H), 1.97 (s, 3H); ^{13}C NMR($CDCl_3$, 101 MHz) δ170.64, 170.36, 170.18, 170.16, 170.11, 169.58, 169.54, 102.17 (C–1′ β anomer), 96.00 (C–1, anomeric carbon), 71.50, 71.06, 70.26, 70.00, 68.82, 68.37, 67.52, 67.39, 65.83, 61.67, 57.05, 20.83, 20.72, 20.69, 20.63, 20.59. HRMS (ESI) calcd for $C_{27}H_{38}O_{18}$ $[M + Na]^+$ 673.1950, found 673.1941.

4.6. O-(2,3,4-Tri-O-acetyl-α-L-fucopyranosyl)-(1→6)-1,2,3,4-tetra-O-acetyl-α-D-galactopyranose (16)

The procedure was the same as that for compound **6**. Compound **16** was afforded from the glycosyl iodide **13** and alcohol **4** as a white solid (52.1 mg, 70%): R_f = 0.63 (petroleum ether/ethyl acetate = 1:1). $[\alpha]_D^{20} = -62.1$ (c = 0.5, DCM). ^{1}H NMR($CDCl_3$, 400 MHz) δ 6.38 (d, 1H, J = 3.2 Hz, H–1′ α), 5.52 (s, 1H), 5.36–5.38 (m, 2H), 5.31–5.27 (m, 2H), 5.10–5.08 (m, 1H), 5.06 (d, 1H, J = 2.8 Hz, anomeric proton), 4.28 (t, 1H), 4.06–4.02 (m, 1H), 3.66 (dd, 1H), 3.57–3.52 (m, 1H), 2.18 (s, 3H), 2.17 (s, 3H), 2.16 (s, 3H), 2.08 (s, 3H), 2.03 (s, 3H),

2.01 (s, 3H), 1.98 (s, 3H), 1.12 (d, 3H, J = 8.0 Hz); ^{13}C NMR($CDCl_3$, 101 MHz) δ 170.68, 170.58, 170.08, 170.00, 169.92, 169.42, 169.03, 96.59 (C–1, anomeric carbon), 89.74 (C–1′ α anomer), 70.96, 69.58, 67.96, 67.89, 67.75, 67.47, 66.53, 66.15, 64.77, 20.98, 20.71, 20.65, 20.57, 19.78, 15.87. HRMS (ESI) calcd for $C_{26}H_{36}O_{17}$ $[M+Na]^+$ 643.1844, found 643.1844.

4.7. O-(2,3,4-Tri-O-acetyl-α-L-fucopyranosyl)-(1→6)-1-O-methyl-2,3,4-tri-O-acetyl-β-D-glycosides (17)

The procedure was the same as that for compound **6**. Compound **17** was afforded from the glycosyl iodide **13** and alcohol **14** as a white solid (52.6 mg, 74%). R_f = 0.65 (petroleum ether/ethyl acetate = 1:1). $[\alpha]_D^{20} = -58.1$ (c = 0.5, DCM). ^{1}H NMR($CDCl_3$, 400 MHz) δ 5.40 (d, 1H, J = 3.6 Hz), 5.33–5.27 (m, 2H), 5.20 (dd, 1H), 5.11 (d, 1H, J = 2.8 Hz), 5.09 (d, 1H, J = 2.8 Hz, anomeric proton), 5.02 (dd, 1H), 4.40 (d, 1H, J = 8.0 Hz, H–1′ β), 4.06 (dd, 1H), 3.87 (t, 1H), 3.72–3.61 (m, 2H), 3.52 (s, 3H), 2.16 (d, 6H, J = 1.2 Hz), 2.07 (d, 6H, J = 2.4 Hz), 1.98 (s, 6H), 1.12 (d, 3H, J = 8.0 Hz); ^{13}C NMR($CDCl_3$, 101 MHz) δ 170.58, 170.52, 170.25, 170.13, 169.99, 169.56, 102.02 (C–1′ β anomer), 96.52 (C–1, anomeric carbon), 71.74, 71.02, 70.97, 68.84, 68.00, 67.78, 67.65, 66.19, 64.73, 56.88, 20.83, 20.76, 20.71, 20.66, 20.60, 19.77, 15.90. HRMS (ESI) calcd for $C_{25}H_{36}O_{16}$ $[M+Na]^+$ 615.1895, found 615.1893.

4.8. O-(2,3,4-Tri-O-acetyl-α-L-fucopyranosyl)-(1→6)-1,2,3,4-tetra-O-acetyl-α-D-glucopyranoside (19)

The procedure was the same as that for compound **6**. Compound **19** was afforded from the glycosyl iodide **13** and alcohol **18** as a white solid (44.7 mg, 60%). R_f = 0.63 (petroleum ether/ethyl acetate = 1:1). $[\alpha]_D^{20} = +18.6$ (c = 0.5, DCM). ^{1}H NMR($CDCl_3$, 400 MHz) δ 6.34 (d, 1H, J = 3.2 Hz, H–1′ α), 5.46 (t, 1H), 5.35–5.32 (m, 2H), 5.22 (t, 1H), 5.15–5.09 (m, 2H), 4.98 (d, 1H, J = 2.8 Hz, anomeric proton), 4.14 (dd, 1H), 4.04–4.00 (m, 1H), 3.79–3.75 (m, 1H), 3.42 (dd, 1H), 2.18 (s, 3H), 2.16 (s, 3H), 2.11 (s, 3H), 2.02 (m, 9H), 1.99 (s, 3H), 1.13 (d, 3H, J = 8.0 Hz); ^{13}C NMR($CDCl_3$, 101 MHz) δ 170.86, 170.61, 170.37, 170.03, 169.60, 169.16, 168.83, 96.72 (C–1, anomeric carbon), 89.16 (C–1′ α anomer), 71.03, 70.63, 70.12, 69.14, 68.11, 68.00, 67.86, 65.66, 64.49, 20.92, 20.76, 20.73, 20.70, 20.68, 20.61, 20.48, 15.89. HRMS (ESI) calcd for $C_{26}H_{36}O_{17}$ $[M+Na]^+$ 643.1844, found 643.1843.

4.9. Trimethylsilyl 1,2,3,6,2′,3′,4′-hepta-O-trimethylsilyl-α-D-lactoside (20)

Compound **20** was afforded according to the method described in previous literature[20] as a white solid (76 mg, 52.7%). R_f = 0.38 (petroleum ether/ethyl acetate = 8:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (d, *J* = 3.1 Hz, 1H), 4.28 (t, *J* = 8.7 Hz, 1H), 4.00 (dd, 1H), 3.83 (dd, 1H), 3.73 (q, *J* = 8.6 Hz, 2H), 3.70–3.56 (m, 4H), 3.50 (dd, 1H), 3.44–3.29 (m, 3H), 0.13 (s, 9H), 0.12 (s, 27H), 0.08 (s, 18H), 0.07 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 102.47, 94.19, 75.82, 75.65, 74.90, 74.01, 72.43, 72.24, 71.85, 71.15, 62.53, 60.73, 0.91, 0.83, 0.69, 0.51, 0.47, 0.29, 0.02. HRMS (DART) calcd for $C_{33}H_{78}O_{11}Si_7$ $[M+H]^+$ 847.4001, found 847.4002.

4.10. O-(2,3,4-Tri-O-acetyl-α-L-fucopyranosyl)-(1→6)-2,3,4-tri-O-acetyl-β-D-galactopyranosyl-(1→4)-1,2,3,6-tetra-O-acetyl-α-D-glucopyranoside (21)

The procedure was the same as that for compound **6**. Compound **21** was afforded from the glycosyl iodide **13** and alcohol **20** as a white solid (63.2 mg, 58%). R_f = 0.50 (petroleum ether/ethyl acetate = 1:1). $[\alpha]_D^{20} = +42.4$ (c = 0.5, DCM). ^{1}H NMR($CDCl_3$, 400 MHz) δ 6.26 (d, 1H, J = 3.6 Hz, H–1″ α), 5.46 (t, 1H), 5.38 (d, 1H, J = 3.2 Hz), 5.30–5.26 (m, 2H), 5.16–5.10 (m, 1H), 5.11 (s, 1H, J = 3.2 Hz, anomeric proton), 5.09–5.06 (m, 1H), 5.04–4.95 (m, 2H), 4.48 (d, 1H, J = 8.0 Hz, H–1′ β), 4.45 (d, 1H, J = 2.0 Hz), 4.13–4.08 (m, 1H), 4.05–3.98 (m, 2H), 3.85–3.78 (m, 2H), 3.64–3.59 (m, 2H), 2.18–2.16 (m, 9H), 2.13 (s, 3H), 2.10 (s, 3H), 2.06 (s, 6H), 2.01 (m, 3H), 1.98 (s, 3H), 1.96 (s, 3H), 1.13 (d, 3H, J = 8.0 Hz); ^{13}C NMR($CDCl_3$, 101 MHz) δ 170.62, 170.51, 170.33, 170.03, 169.98, 169.90, 169.87, 169.58, 169.20, 168.95, 101.28 (C–1′ β anomer), 96.31 (C–1, anomeric carbon), 89.03 (C–1″ α anomer), 75.73, 71.60, 71.06, 70.87, 70.75, 69.69, 69.33, 69.19, 68.07, 67.59, 67.07, 65.00, 64.96, 61.51, 20.97, 20.87, 20.85, 20.79, 20.69, 20.65, 20.51, 19.78, 15.95. HRMS (ESI) calcd for $C_{38}H_{52}O_{25}$ $[M+Na]^+$ 931.2689, found 931.2692.

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Supplementary material

General information and analytical data for compound 6, 12, 14-17, 19-21 to this article can be found online at doi:10.1016/j.carres.2016.03.019.

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