Hafnium(IV) Tetratriflate as a Glycosyl Fluoride Activation Reagent

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Supporting Information

ABSTRACT: Hafnium(IV) tetratriflate was found to be a good activator of glycosyl PO F + HOF fluoride. The protocol was operationally simple and was widely applicable to a variety of substrates in both solid-phase and solution-phase glycosylation reactions.

Velocity lycosyl fluoride is one of the most frequently used J glycosyl donors in glycosylation reactions. The relatively strong C-F bond imparts stability to such compounds; however, glycosyl fluorides can be activated under the appropriate reaction conditions. Several methodologies have been developed for achieving glycosyl fluoride activation. For example, Mukaiyama et al. reported for the first time that SnCl₂–AgClO₄ could efficiently activate glycosyl fluoride,¹ and Noyori and Nicolaou reported that TMSOTf and BF₃•OEt₂ work as effective mediators for armed glycosyl fluorides, respectively.^{2,3} Later, Suzuki reported that a combination of Cp₂HfCl₂-AgClO₄ had a high efficacy for glycosyl fluoride activation,⁴ which is now a protocol widely applied to the synthesis of complex oligosaccharides and glycoconjugates.^{5–7} However, most glycosyl fluoride activation methodologies are not operationally simple. Multiple reagents and preactivated molecular sieves are required, in addition to preactivation/ premixing of the activator prior to the addition of the glycosyl donor and acceptor. In this paper, we report an operationally simple glycosyl fluoride activation methodology.

Hafnium(IV) tetratriflate $(Hf(OTf)_4)$ is a commercially available solid that is easy to handle in air. It is known to be a good Lewis acid for a variety of reactions.⁸⁻¹⁸ It was therefore expected that it would be a good mediator for glycosyl fluoride activation.

Glycosyl fluoride $1\alpha/1\beta$ (1:4 mixture) was smoothly activated, even at -78 °C, to give disaccharides $3\alpha/3\beta$ (16:84) in 58% yield in a β -selective manner after 2 h (Table 1, entry 1). After 14 h, the yield was increased up to 70% (entry 2). At -50 °C, the reaction was completed within 1 h, and the disaccharides $3\alpha/3\beta$ (20:80) were obtained in 99% yield (entry 3). Molecular sieves 3A and 4A did not help to increase the yield (entries 6 and 7). Especially, the reaction in the presence of molecular sieves 4A was messy and the disaccharide $3\alpha/3\beta$ was not isolated in a pure form. Although activation of glycosyl fluoride using a catalytic amount of reagent has previously been reported, $^{19-21}$ the reaction did not complete, even after 10 h, if the amount of $Hf(OTf)_4$ was reduced (entry 8), with the disaccharide $3\alpha/3\beta$ being only obtained in 59% yield. Interestingly, the $\alpha:\beta$ ratio was altered, with the α -isomer obtained as the major product, although the reason was not clear. The well-known solvent effect was observed,^{2,22,23} with

the β -selectivity being increased in CH₃CN (entries 9 and 10) and the α -selectivity being increased in dioxane/toluene (entries 11 and 12).²⁴ Prolonged reaction periods completed the reaction, but did not increase the yields (entries 10 and 12), because several unidentified byproducts were formed. Both the pure α -anomer 1 α and β -anomer 1 β gave disaccharides $3\alpha/3\beta$ in a β -selective manner, with little variation in the α : β ratios (entries 13 and 14). The excess of glycosyl fluoride 1a/1b was changed to its corresponding hemiacetal and glycal as main products under the conditions for entry 1.

The scope and limitations of the methodology were subsequently investigated (Table 2). Reactive acceptor 4 reacted smoothly with donor $1\alpha/1\beta$ to give disaccharides $5\alpha/5\beta$ in a β -selective manner (entry 1). Using secondary hydroxyl group acceptor 6, the disaccharides $7\alpha/7\beta$ were obtained, and a significant solvent effect was observed (entries 2–4). In CH₃CN, the β -glycoside ratio was increased up to 80%, while dioxane-toluene gave an increase in the α -glycoside ratio up to 85%. Mannose derivative 8 gave disaccharide 9 in 64% yield (entry 6), and disarmed donor 10 could also be activated under these conditions at 4 °C (entry 7). After 2 h, disaccharide 11 was obtained in 80% yield. Unfortunately, the benzylidene group was cleaved because of the Lewis acidity of Hf(OTf)₄, and trisaccharide 14 was obtained in 37% yield based on acceptor 12 (entry 8). However, disaccharide 15 was obtained in the presence of 3 equiv of di-tert-butyl-4methylpyridine (DTBMP) (entry 9). Disaccharide 16 was also activated at -30 °C, and trisaccharide 17 and tetrasaccharide 19 were obtained in 85% and 58% yield, respectively (entries 10 and 11).

The developed methodology was applied to rapid solid-phase oligosaccharide synthesis on a polymer support. Methyl poly(ethylene glycol) (MPEG, average $M_w = 750$) was used to produce acid-stable linker²⁵ 21, which acted as a good acceptor and enabled rapid purification by a silica gel short pad because of the high polarity of MPEG, as previously reported (Scheme 1).^{26,27} After removal of the chloroacetyl temporary protecting group under basic conditions, the MPEG-glycoside was submitted to the next glycosylation reaction, where 23 was

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Table 1. Glycosylation Reaction with 1 and 2 under Various Conditions

	BnO BnO BnO 1a: 1: (1.5 e	$\begin{array}{c} \begin{array}{c} & HO \\ OBn \end{array} & \begin{array}{c} HO \\ TolO \end{array} & \begin{array}{c} OOD \\ OTol \end{array} \\ \end{array} \\ \begin{array}{c} OOD \\ OTol \end{array} \\ \begin{array}{c} OOD \\ OTol \end{array} \\ \end{array} \\ \begin{array}{c} OOD \\ OTol \end{array} \\ \begin{array}{c} OOD \\ OTol \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} OOD \\ OTol \end{array} \\ \end{array} \\ \begin{array}{c} OOD \\ OTol \end{array} \\ \end{array} \\ \end{array} \\ \end{array} $ \\ \begin{array}{c} OOD \\ OTol \end{array} \\ \\ \end{array} \\ \end{array} \\ \begin{array}{c} OOD \\ OTol \end{array} \\ \\ \end{array} \\ \\ \end{array} \\ \end{array} \\ \\ \end{array} \\ \end{array} \\ \begin{array}{c} OOD \\ OTob \\ \\ \end{array} \\ \end{array} \\ \\ \end{array} \\ \end{array} \\ \\ \end{array} \\ \\ \end{array} \\ \end{array}	Hf(OTf) ₄ (<u>1.5 equiv.</u>) BnO BnO	Ο ΟΒη ΤοΙΟ ΤοΙΟ 3α:3β	OMP Tol	
entry	donor	solvent	temp (°C)	time	yield (%)	3α:3β
1	$1\alpha/1\beta$ (1:4)	CH_2Cl_2	-78	2 h	58 ^a	16:84
2	$1\alpha/1\beta$ (1:4)	CH_2Cl_2	-78	14 h	70	12:88
3	$1\alpha/1\beta$ (1:4)	CH_2Cl_2	-50	1 h	99	20:80
4	$1\alpha/1\beta$ (1:4)	CH_2Cl_2	-20	10 min	88 ^b	31:69
5	$1\alpha/1\beta$ (1:4)	CH_2Cl_2	-20	0.5 h	91	30:70
6	$1\alpha/1\beta$ (1:4)	CH ₂ Cl ₂ , MS 3A	-20	10 min	45 ^c	39:61
7	$1\alpha/1\beta$ (1:4)	CH ₂ Cl ₂ , MS 4A	-20	10 min	mess	_
8^d	$1\alpha/1\beta$ (1:4)	CH_2Cl_2	-20	10 h	59 ^e	64:36
9	$1\alpha/1\beta$ (1:4)	CH ₃ CN	-20	10 min	51^{f}	11:89
10	$1\alpha/1\beta$ (1:4)	CH ₃ CN	-20	4 h	57	42:58
11	$1\alpha/1\beta$ (1:4)	dioxane/toluene ^g (1:1)	-20	10 min	83 ^h	51:49
12	$1\alpha/1\beta$ (1:4)	dioxane/toluene ^g (1:1)	-20	4 h	80	66:34
13	1α	CH ₂ Cl ₂	-50	1 h	82	14:86
14	1β	CH ₂ Cl ₂	-50	1 h	94	18:82

^a32% of 2 was recovered. ^b12% of 2 was recovered. ^c18% of 2 was recovered. ^d30% of 2 was recovered. 0.4 equiv of Hf(OTf)₄ was used. ^e40% of 2 was recovered. ${}^{f}12\%$ of **2** was recovered. g Dioxane/toluene 3:1 solvent system reported in ref 23 was frozen at low temperature. The ratio of toluene was increased. ${}^{h}17\%$ of **2** was recovered.

Table 2. Scope and Limitations of the Glycosylation Reaction Mediated by Hf(OTf)₄

Hf(OTf) ₄ PO (1.5 equiv.) CH-CL PO (-1.5 equiv.)												
		1α/1 _β	B, 8 , 10 , 13 , 16	2, 4, 6, 12, 18	²⁰¹² 5α/5β, 14,	7α/7β, 9, 11, I5, 17, 19						
entry	donor	acceptor	sol	vent	temp (°C)	time	product	yield (%)	α:β			
1	$1\alpha/1\beta$ (1:4)	4	CH_2Cl_2		-50	1 h	$5\alpha/5\beta$	94	16:84			
2	$1\alpha/1\beta$ (1:4)	6	CH_2Cl_2		-50	1 h	$7\alpha/7\beta$	75	44:56			
3	$1\alpha/1\beta$ (1:4)	6	CH_2Cl_2		-20	0.5 h	$7\alpha/7\beta$	80	45:55			
4	$1\alpha/1\beta$ (1:4)	6	CH ₃ CN		-20	0.5 h	$7\alpha/7\beta$	94	20:80			
5	$1\alpha/1\beta$ (1:4)	6	dioxane/tolue	ene (1:1)	-20	0.5 h	$7 \alpha / 7 \beta$	80	85:15			
6	8	6	CH_2Cl_2		-50	1 h	9	64	64:0			
7	10	4	CH_2Cl_2		4	2 h	11	80	80:0			
8	13	12	CH_2Cl_2		-50	0.5 h	14	37	0:37			
9	13	12	CH ₂ Cl ₂ , DTH	3MP (3 equiv)	-30	1 h	15	65	0:65			
10	16	2	CH_2Cl_2		-30	0.5 h	17	85	0:85			
11	16	18	CH_2Cl_2		-30	0.5 h	19	58	0:58			
BnO BnO BnO 10	HO OBn BnO δι:1β Δ		$a_{n}^{m} O = B_{nO}^{m} B_{nO}^{m} B_{nO}^{m} B_{nO}^{m} B_{nO}^{m} O Me$	nO BnO nO BnO BnO BnO OMe BnO	0 0 0 0 0 0 0 0 0 0 0 0 0 0	BnO BnO OMe 8	OAc Bno OA Bno CC	BnO BnO BnO BnO BnO OMe				
AcO AcO AcO Bnt B	Ac 0 0 0 0 0 0 0 0 0 0 0 0 0	12	BnO BnO AcO F	BnO BnO BnO BnO BnO OAc BnO OAc Ac		BnO Ph nO O BnO OAc	0 N ₃ OMP					
Aco Co	Bn O BnO NPhth NPhth	AcO BnO NPhth	NPhthTolO	OTOL HOLL	OBn O AcO NPhth NPhth	MP Aco	Bn OBn O OC NPhth NPh	DOBN 0000 0000 0000 0000 0000 0000	OBn O NPhth			

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Note

OTol

17

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Scheme 1. Glycosylation Reaction on a Polymer Support Using Glycosyl Fluoride, Mediated by $Hf(OTf)_4$



quantitatively yielded. The acceptor immobilized on TentaGel 24^{28} also served as a good substrate for the glycosylation reaction with glycosyl fluoride 8 using the same methodology. Disaccharide 25 was obtained after cleavage from the TentaGel under basic conditions in 78% yield from 24 (Scheme 2), and the corresponding acceptor was not obtained.





In conclusion, $Hf(OTf)_4$ was shown to be a good activator for glycosyl fluoride. The reagent was observed to be stable, and the procedure was simple. This methodology is widely applicable to solid-phase and polymer-supported oligosaccharide synthesis, as well as solution-phase synthesis.

EXPERIMENTAL SECTION

General Experimental Methods. All commercial reagents were used without further purification. Analytical TLC was performed on silica gel 60 F254 plates and visualized by UV fluorescence quenching and 12 Molybdo(VI) phosphoric acid acid/phosphoric acid staining. Flash column chromatography was performed on silica gel 60N (spherical, neutral, 40–100 μ m). Yields refer to chromatographically and spectroscopically pure compounds. ¹H and ¹³C NMR spectra were recorded at ambient temperature (23–24 °C) in CDCl₃ using a 400 MHz spectrometer. Chemical shifts are reported in ppm relative to internal TMS (δ = 0.00 ppm) for ¹H and CDCl₃ (δ = 77.00 ppm) for ¹³C NMR spectra. HRMS was measured by Quadrupole-TOF mass spectrometry. Novasyn TentaGel was purchased from Novabiochem.

General Procedure. Hf(OTf)₄ was added to a solution of donor (1.5 equiv) and acceptor (1.0 equiv) in CH_2Cl_2 (acceptor concentration, 0.1 M) at the stated temperature. After the starting material was consumed or after adequate periods, the reaction was quenched with sat. NaHCO₃, and the aqueous layer was extracted several times with EtOAc. The combined layers were washed with brine and dried over Na₂SO₄. After concentration, the crude product

was purified by preparative TLC. The products 3a,²² 3b,²² 5a,²⁹ 5b,²⁹ 7a,³⁰ 7b,³⁰ 9,³¹ 11,³² 16,³³ 18,³⁴ and 20²⁶ were reported. *p*-Methoxyphenyl 3,6-Di-O-(2-O-acetyl-3,4,6-O-tribenzyl-β-

p-Methoxyphenyl 3,6-Di-O-(2-O-acetyl-3,4,6-O-tribenzyl-βp-glucopyranoside)-2-azido-2-deoxy-β-D-glucopyranoside. ¹H NMR δ 7.28–7.12 (m, 30H), 6.97 (d, J = 8.8 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 4.99 (t, J = 8.0 Hz, 1H), 4.98 (t, J = 8.0 Hz, 1H), 4.76– 4.60 (m, 6H), 4.53–4.38 (m, 8H), 4.20 (d, J = 11.2 Hz, 1H), 3.70– 3.40 (m, 17H), 3.34 (t, J = 8.8 Hz, 1H), 3.13 (t, J = 8.8 Hz, 1H), 1.99 (s, 3H), 1.77 (s, 3H); ¹³C NMR δ 169.5, 169.4, 155.5, 151.2, 138.2, 138.0, 137.9, 137.4, 128.5, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 118.0, 114.8, 102.0, 101.4, 101.1, 85.8, 83.1, 82.7, 78.0, 77.8, 75.7, 75.3, 75.1, 75.1, 75.0, 74.5, 73.5, 73.4, 73.0, 72.8, 69.1, 68.7, 68.7, 64.5, 55.6, 20.8, 20.6; [α] 13.3 (c 1.0, CHCl₃); HRMS (MALDI-Q-TOF) m/z: [M + Na]⁺ Calcd for C₇₁H₇₇N₃O₁₈Na 1282.5094; Found 1282.5103.

p-Methoxyphenyl (2-O-Acetyl-3,4,6-tri-O-benzyl-β-D-glucopyranoside)-(1→3)-4,6-O-benzylidene-2-deoxy-2-azido-β-D-glucopyranoside. ¹H NMR δ 7.37-7.02 (m, 20H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 8.0 Hz, 2H), 5.45 (s, 1H), 5.04 (t, *J* = 8.8 Hz, 1H), 4.81-4.41 (m, 7H), 4.36 (d, *J* = 12.4 Hz, 1H), 4.31 (dd, *J* = 11.2, 5.2 Hz, 1H), 3.80-3.58 (m, 8H), 3.77 (s, 3H), 3.52-3.42 (m, 3H), 3.29 (m, 1H), 1.98 (s, 3H); ¹³C NMR δ 170.6, 155.9, 150.8, 138.2, 138.2, 137.9, 137.0, 129.1, 128.4, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 126.1, 118.6, 114.7, 102.2, 101.6, 100.0, 82.9, 70.4, 78.7, 77.8, 75.2, 75.0, 74.9, 73.5, 73.4, 68.5, 68.4, 66.5, 66.1, 55.7, 30.2, 20.9; [α] 7.0 (*c* 0.64, CHCl₃); HRMS (MALDI Q-TOF) *m*/*z*: [M + Na]⁺ Calcd for C₄₉H₅₁N₃O₁₂Na 896.3365; Found 896.3377.

p-Methoxyphenyl (4-O-Acetyl-3,6-di-O-benzyl-2-deoxy-2phthalimido- β -glucopyranoside)-(1 \rightarrow 4)-(3,6-O-dibenzyl-2deoxy-2-phthalimido- β -glucopyranoside)-(1 \rightarrow 3)-2,3,4-tri-O-(4methylbenzoyl)- β -D-glucoside. ¹H NMR δ 7.73 (d, J = 8.4 Hz, 2H), 7.50 (s, 4H), 7.32 (d, J = 8.4 Hz, 2H), 7.80–760 (br, 8H), 7.31– 6.89 (m, 21H), 6.85 (m, 3H), 6.69 (s, 4H), 5.69 (t, J = 9.2 Hz, 1H), 5.47 (t, J = 8.4 Hz, 1H), 5.27 (d, J = 8.4 Hz, 1H), 5.19 (t, J = 9.6 Hz, 1H), 5.12 (t, J = 9.2 Hz, 1H), 5.02 (d, J = 7.6 Hz, 1H), 4.94 (d, J = 7.6 Hz, 1H), 4.78 (d, J = 12.4 Hz, 1H), 4.56 (d, J = 12.0 Hz, 1H), 4.50-4.03 (m, 11H), 3.94 (m, 1H), 3.79-3.76 (m, 1H), 3.76 (s 3H), 3.60-3.30 (m, 5H), 3.18 (m, 1H), 2.31 (s, 3H), 2.29 (s, 3H), 2.25 (s, 3H), 1.88 (s, 3H); 13 C NMR δ 169.6, 165.6, 155.4, 151.3, 144.1, 143.9, 138.4, 138.3, 138.2, 137.7, 133.3, 131.6, 129.8, 129.0, 129.0, 128.3, 128.1, 127.8, 127.6, 127.4, 127.3, 127.2, 126.9, 126.5, 126.1, 125.9, 123.1, 118.2, 114.6, 100.6, 98.2, 96.9, 75.8, 74.5, 74.4, 73.8, 73.5, 73.3, 72.7, 72.6, 71.5, 69.5, 69.4, 56.2, 55.7, 55.5, 21.6, 20.9; $[\alpha]$ 22.3 (c 1.45, CHCl₃); HRMS (MALDI Q-TOF) m/z: [M + Na]⁺ Calcd for C₉₅H₈₈N₂O₂₃Na 1647.5670; Found 1647.5673.

p-Methoxyphenyl (3,4-Di-O-acetyl-6-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside)-(1→4)-(3-O-acetyl-6-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside) (1→4)-(3-O-acetyl-6-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside) (1→4)-3-O-acetyl-6-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside. ¹H NMR δ 7.76-7.72 (m, 16H), 7.18-7.6.82 (m, 20H), 6.72 (d, J = 9.2 Hz, 2H), 6.60 (d, J = 9.2 Hz, 2H), 5.63 (d, J = 8.0 Hz, 1H), 5.61 (t, J = 10.0 Hz, 1H), 5.41 (t, J = 9.2 Hz, 1H), 5.20 (t.d, J = 8.0 Hz, 1H), 5.07 (t, J = 9.2 Hz, 1H), 4.93 (d, J = 7.6 Hz, 1H),

4.79 (d, J = 12.4 Hz, 1H), 4.54 (t, J = 12.8 Hz, 1H), 4.48–3.92 (m, 30H), 3.62 (s, 3H), 3.49 (m, 3H), 3.38–3.36 (m, 5H), 3.13 (m, 2H), 2.94 (d, J = 9.6 Hz, 1H), 2.69 (d, J = 9.6 Hz, 1H), 1.72 (s, 3H), 1.54 (s, 3H), 1.52 (s, 3H); ¹³C NMR δ 170.3, 170.2, 169.6, 167.3, 155.4, 150.6, 138.5, 138.2, 137.7, 134.2, 131.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 127.1, 126.9, 126.8, 123.5, 123.3, 118.8, 114.3, 97.3, 96.5, 96.3, 76.7, 76.4, 75.2, 74.4, 73.9, 73.7, 73.3, 72.7, 72.5, 72.4, 72.1, 72.1, 70.9, 70.7, 69.3, 67.6, 67.5, 56.2, 56.0, 55.5, 55.2, 54.8, 20.9, 20.5, 20.3; $[\alpha]$ 10.4 (c 0.95, CHCl₃); HRMS (MALDI Q-TOF) *m*/*z*: [M + Na]⁺ Calcd for [C₁₁₁H₁₀₂N₄O₂₉ + Na]⁺ 1977.6522. Found 1977.6520.

Poly(ethylene glycol) Bound 4-Hydroxy-3-nitro-benzyloxy-3,6-O-benzyl-4-O-chloroacetyl-2-azido-2-phthalimide-β-D-glucopyranoside. To a solution of glycosyl fluoride 20 (211 mg, 0.705 mmol) and MPEG bound linker 21 (211 mg, 0.235 mmol) in CH₂Cl₂ (5 mL), Hf(OTf)₄ (546 mg, 0.705 mmol) was added at -30 °C. After 1 h, the reaction was quenched with sat. NaHCO₃, and the aqueous layer was extracted with CHCl₃. The combined layers were extracted with CHCl₃ and then washed with brine. After drying the extract over Na₂SO₄, the solvent was removed *in vacuo*. The residue was passed through a short silica gel pad (AcOEt only–MeOH/AcOEt 1:1) to give compound 22 (340 mg, quant.). Representative peaks of ¹H NMR δ 5.18 (d, *J* = 8.0 Hz, 1H), 4.76–4.50 (m, 8H), 4.45 (d, *J* = 12.4 Hz, 1H), 4.27–4.12 (m, 5H).

Poly(ethylene glycol) Bound 4-Hydroxy-3-nitro-benzyloxy-(3,4,6-tri-O-benzyl-2-O-acetyl-β-D-glucopuranosy)3,6-O-benzyl-2-azido-2-phthalimide- β -D-glucopyranoside. To a solution of compound 22 (150 mg, 0.10 mmol) in MeOH (1 mL), 1 drop of NaOMe (28% MeOH solution) was added by Pasteur pipet, in the presence of phenolphthalein. The progress of the reaction was monitored using a *p*-nitrobenzyl pyridine color test.²⁶ The mixture was then neutralized by Amberlyst 15E and filtered, and the resin was washed with MeOH. After concentration, the crude product was passed though a short silica gel pad (AcOEt only-MeOH/AcOEt 1:1) to give the acceptor (141 mg, quant.). The PEG-bound acceptor was dried in vacuo overnight and then dissolved in CH2Cl2 (2 mL). Glycosyl fluoride 13 (141 mg, 0.285 mmol) and Hf(OTf)₄ (221 mg, 0.285 mmol) were added at -30 °C. After 1 h, the reaction was guenched with sat. NaHCO₂, and the aqueous layer was extracted with CHCl₃. The combined layers were extracted with CHCl₃ and then washed with brine. After drying the extract over Na₂SO₄, the solvent was removed in vacuo. The residue was passed through a short silica gel pad (AcOEt only-MeOH/AcOEt 1:1) to give compound 23 (177 mg, quant.). Representative peaks of ¹H NMR δ 5.10 (d, J = 6.4 Hz, 1H), 5.00 (t, I = 8.4 Hz, 1H), 1.98 (s, 3H).

1-Methoxycarbonylbutyl-(3,4,6-tri-O-benzyl-α-D-mannopyranoside)(1→6)-2,3,4-tri-O-benzyl-β-D-glycopyranoside. To a suspension of acceptor-immobilized TentaGel 24 (0.30 mmol/g as OH, 313 mg, 0.09 mmol; 0.23 mmol/g as 24, the content rate was determined after cleavage from resin), glycosyl fluoride 13 (133 mg, 0.32 mmol) and Hf(OTf)₄ (250 mg, 0.32 mmol) were added at -30 °C. The mixture was gently stirred for 3 h, then neutralized by Et₃N, and filtered. The resin was washed with CH₂Cl₂, MeOH, and H₂O. After the resin was dried *in vacuo* overnight, it was suspended in MeOH (2 mL) and THF (2 mL). A NaOMe solution (0.50 mL) was added, and the mixture was stirred at 60 °C overnight. AcOH (0.1 mL) was then added, and the resin was filtered and washed with THF. After concentration, disaccharide 25 (46 mg, 50% based on 0.30 mmol/g as OH; 78% from 24) was obtained.

¹H NMR δ 7.30–7.16 (m, 30H), 4.89–4.78 (m, 5H), 4.46 (d, J = 11.2 Hz, 1H), 4.28 (d, J = 8.0 Hz, 1H), 4.01 (s, 1H), 3.83–4.49 (m, 11H), 3.58 (s, 3H), 3.41 (t, J = 9.2 Hz, 1H), 3.35–3.31 (m, 2H), 2.35 (t, J = 7.2 Hz, 2H), 1.88–1.84 (m, 2H); ¹³C NMR δ 173.8, 138.4, 138.3, 137.9, 137.7, 128.6, 128.5, 128.4, 128.4, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 103.4, 99.5, 84.7, 79.6, 77.7, 75.7, 75.1, 75.0, 74.9, 74.2, 74.0, 71.9, 71.5, 68.8, 68.1, 65.8, 62.0, 51.6, 30.7, 25.1; [α] 30.9 (c 1.0, CHCl₃); HRMS (MALD Q-TOF) m/z: [M + Na]⁺ Calcd for [C₅₉H₆₆O₁₃ + Na]⁺ 1005.4396, Found 1005.4390.

ASSOCIATED CONTENT

Supporting Information

Spectroscopic and analytical data for new compounds. This material is available free of charge via the Internet at http:// pubs.acs.org.

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Notes

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