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This article is dedicated to Professor Satoshi Ōmura in celebration of his 2015 Nobel Prize.

Regular Article

Glycosylation Reaction of *Thioglycosides* by Using Hypervalent Iodine(III) Reagent as an Excellent Promoter

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Thioglycosides are available donors in glycosylation due to the stability of the anomeric C–S bond under general reaction conditions of protection and deprotection, and offer orthogonality in their activation. We report now that the hypervalent iodine effectively induced glycosylation reaction of thioglycosides with various alcohols. This method features a high efficiency, completion in a short time, and proceeding under very mild conditions.

Key words glycosylation; hypervalent iodine reagent; thioglycoside

Thioglycosides are the most widely used glycosyl donors for glycoside synthesis. Since the first report in 1909, the chemistry of thioglycosides has been significantly investigated and numerous methodologies have been reported on their preparation and activation in the past three decades.[1–5] Thioglycoside donors are relatively easy to prepare, stable under various reaction conditions of protection and deprotection, and offer orthogonality in their activation.[6] An important feature of thioglycosides is their ability to serve not only as glycosyl donors, but also acceptors. This feature, as the tunable reactivity of thioglycosides, has often been used for the synthesis of various oligosaccharides.[7]

In general, the activation of thioglycosides was performed using a mercury salt, such as $HgSO_4$, $HgCl_2$, $Hg(OBz)_2$, or $Hg(NO_3)_2$.[8–11] The use of copper(II) trifluoromethanesulfonate $Cu(OTf)_2$ (Mukaiyama) or $CuBr_2$–Bu_4NBr–AgOTf (Ogawa and Ito) as an activator was further investigated.[12,13] Recently, $In(OTf)_3$ was reported to become an effective activator by ball milling under a solvent-free condition.[14] However, these reported systems for the glycosylation of thioglycosides have relied on a toxic heavy metal oxidant for product formation. On the other hand, iodonium species generated from halonium-based reagents, such as *N*-iodosuccinimide (NIS), in conjunction with a catalytic amount of a Brønsted or Lewis acid, were first reported in 1990 by van Boom and colleagues.[15] Although these methods have been effective in carrying out a range of glycosylations, most of these still have a limited scope. Generally, these methods often require low temperatures (<20°C) for generating the reactive intermediates. In recent several years, other unique methods such as thioperoxide promotor and photochemical activation using blue light emitting diode (LED) have also been successfully explored for thioglycoside based-glycosidation.[16,17]

Nowadays, the environmentally-benign hypervalent iodine oxidation has witnessed significant progress in the field of organic chemistry.[18–30] We have been engaged in the development of the oxidation of the sulfur atom utilizing hypervalent iodine reagents to form an active iodonium intermediate.[31,32] Thus, we have recently developed novel methods of hypervalent iodine-induced glycosylation of thioglycoside.[33] Besides our study, a few methods have been reported as for the activation of thioglycosides with hypervalent iodines to date[34–36]; however, activation of disarmed thioglycosides with hypervalent iodines still remains impractical and unavailable in the synthesis of biologically active oligosaccharides. Herein, we now would like to report a new organosulfur participating promoter system in which both the armed and disarmed thioglycoside donors can be activated by using the hypervalent iodine reagent (Chart 1).

Based on our previous investigation of the glycosylation,[33] we examined the glycosylation reaction of methyl 2-deoxy-2-phthalimido-3,4,6-tri-*O*-acetyl-1-*thio*-D-glucopyranoside **1a** with 1-*O*-methyl 2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside **2** using the combination of phenyliodine(III) bis(trifluoroacetate) (PIFA) with various acids. As a result, the reaction with PIFA and trifluoromethanesulfonic acid (TfOH) afforded the best yield (77%). The use of the 4-fluoro, 4-trifluoromethyl, 4-methyl and pentafluoro-substituted phenyliodine(III) reagents did not increase the yield of the coupling product **3a** (Chart 2). The use of trimethylsilyl trifluoromethanesulfonate (TMSOTf), bis[cyclohexyl]-trifluoromethanesulfonylborane, and methanesulfonic acid produced poor results. Thus, the

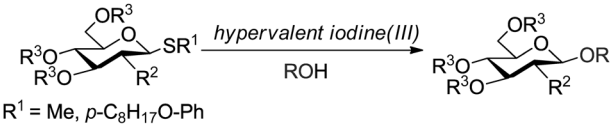

Chart 1. The Hypervalent Iodine Induced Metal-Free Glycosylation

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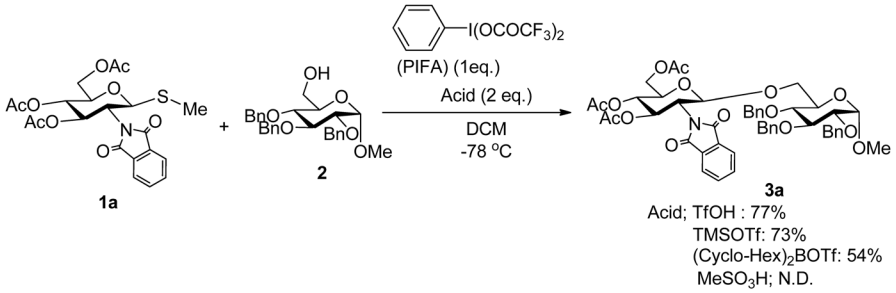


Chart 2. Glycosylation Reactions of **1a** and **2** Using PIFA with Various Acids

combination of PIFA (1.0 eq.) and TfOH (2.0 eq.) was employed as the activator of the thioglycoside donor in the glycosylation reactions. It is noted that this reaction did not proceed in the absence of TfOH. On the basis of the above finding, it could be suggested that TfOH coordinated with the carbonyl oxygen of trifluoroacetate in PIFA and assisted lowering the electron density of the iodine, of which the function played an important role to activate the thioglycosides.

The scope of the glycosylation donors **1a** and **b** with various acceptors was investigated under the optimal conditions (Table 1). The reactions of **1a** with a secondary alcohol **4** or **5** gave the corresponding glycosides **3b** and **c** in moderate yields (entries 1, 2). It was also found that cholestanol **6** could be employed as a glycosyl acceptor and gave the glycosylated product **3d** in 60% yield (entry 3). The tertiary alcohol **7** was glycosylated in 58% under the same reaction condition in spite of the steric hindrance caused by the adamantane skeleton (entry 4). In addition, a more hindered alcohol, such as the (−)-borneol **8**, was glycosylated with **1a** in a good yield (entry 5).

Encouraged by these results, we further evaluated the reaction for the synthesis of disaccharides. The glycosylations of the glycosyl donor **1a** with the benzoylated glycosyl acceptor **9** having a free hydroxyl group at the C-6 position, proceeded with a excellent yield (entry 6). The reaction of **1b** with acceptor **9** afforded the desired disaccharide **3h** in a good yield (entry 7). The glycosylations of the donor with the galactosyl acceptor **10**, having a free hydroxyl group at the C-4 position, also proceeded in a satisfactory yield (entry 8). The more stereocongested acceptor **11** was condensed with **1a** with an equal efficiency (entry 9).

On the other hand, odorless *p*-octyloxylbenzenthiol[33,37–39] was chosen as the source of the aglycon moiety of the 1-thioglycosides to avoid tedious handling of odoriferous organosulfur compounds like methanethiol or benzenethiol, generated during the conventional glycosylation reaction using methyl or phenyl 1-thioglycosides. Based on this information, *p*-octyloxyphenyl 2-deoxy-2-phthalimido-3,4,6-tri-*O*-acetyl-1-thio-*β*-D-glucopyranoside **1c** was adopted as the donor glycoside and synthesized by a method reported in the literature.[37–39] In addition, *p*-octyloxyphenyl 2-deoxy-2-phthalimido-3,4,6-tri-*O*-acetyl-1-thio-*β*-D-galactopyranoside **1d** was prepared from 2-deoxy-2-phthalimino-D-galactose tetraacetate[37] and *p*-octyloxybenzenethiol in 83% yield using the same protocol. As shown in Table 2, the reaction of the thioglycoside **1c** with alkanols smoothly proceeded and the yield was improved in comparison with the use of the glycosyl donor **1a**. Secondary alcohols **4**–**6** gave the desired products in good yields. In addition, the substrates carrying a hindered alcohol, such as the 1-adamantananol **7** (−)- and (+)-borneols **8**, **12**, (+)-fenchyl alcohol **13** and *ent*-17-nor-kauranol **14** were glycosylated with **1c** in good yields.

The synthesis of disaccharides by the described glycosylation was also performed using **1c** and 1-*O*-methyl 2,3,4-tri-*O*-benzyl-*α*-D-glucopyanoside **2** as the donor and the acceptor substrates, respectively. Since the former was "disarmed" and the latter was "armed,"[40,41] the combination seemed to be one of the most undesired ones; however, the reaction occurred to provide the desired disaccharide **3a** in 87% yield (Chart 3). Similarly, in the case of donor **1d** and acceptor **2**, the reaction smoothly proceeded and gave the disaccharides **3n** in good yield.

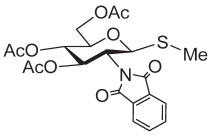
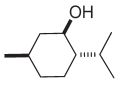
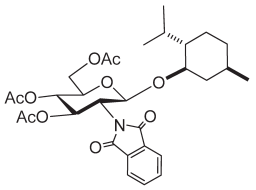
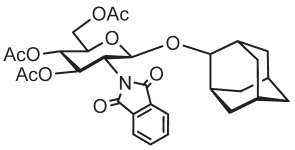
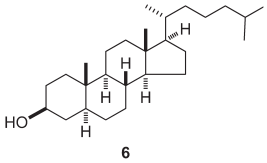
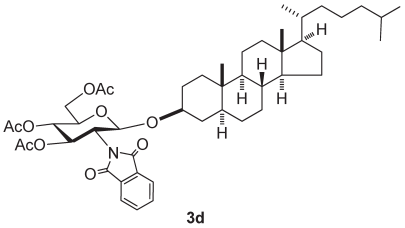
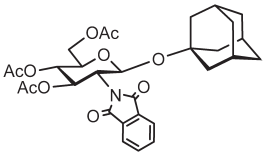
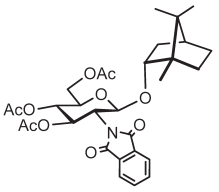
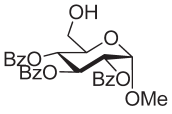
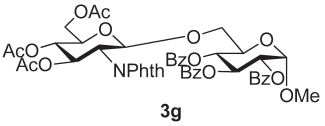
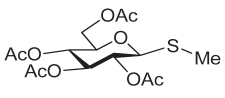
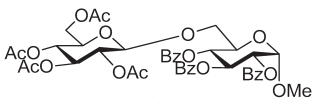
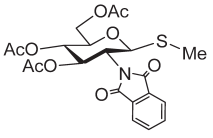
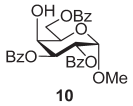
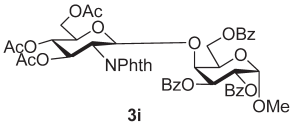
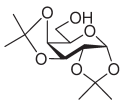
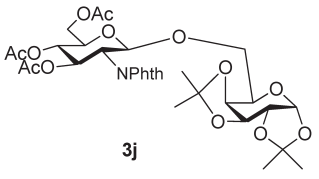
In conclusion, we found that the hypervalent iodine, PIFA, is an excellent promoter of thioglycosides in the presence of TfOH in the glycosylation reaction and the reaction afforded satisfactory results especially using the thioglycosides bearing a phthalimido group at the C-2 position. In addition, our method could allow the glycosylation of the undesirable combination of substrates, *i.e.*, the combination of the "disarmed" donor and "armed" acceptor, in excellent yields.

Experimental

General Remarks The ^{1}H-NMR and ^{13}C-NMR spectra were recorded by a JEOL JMN-400 spectrometer operating at 400 MHz in $CDCl_3$ at 25°C with tetramethylsilane as the internal standard. Data are reported as follows: chemical shift in ppm (δ), integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, brs=broad singlet, m=multiplet), coupling constant (Hz). The infrared spectra (IR) were obtained using a Hitachi 270-50 spectrometer, absorptions are reported in reciprocal centimeters. The mass spectra were obtained using a Shimadzu GCMS-QP 5000 instrument with ionization voltages of 70 eV. The high resolution mass spectra were performed by the Elemental Analysis Section of Osaka University. Column chromatography and TLC were carried out on Merck Silica gel 60 (230–400 mesh) and Merck Silica gel F254 plates (0.25 mm), respectively. The spots and bands were detected by UV irradiation (254, 365 nm).

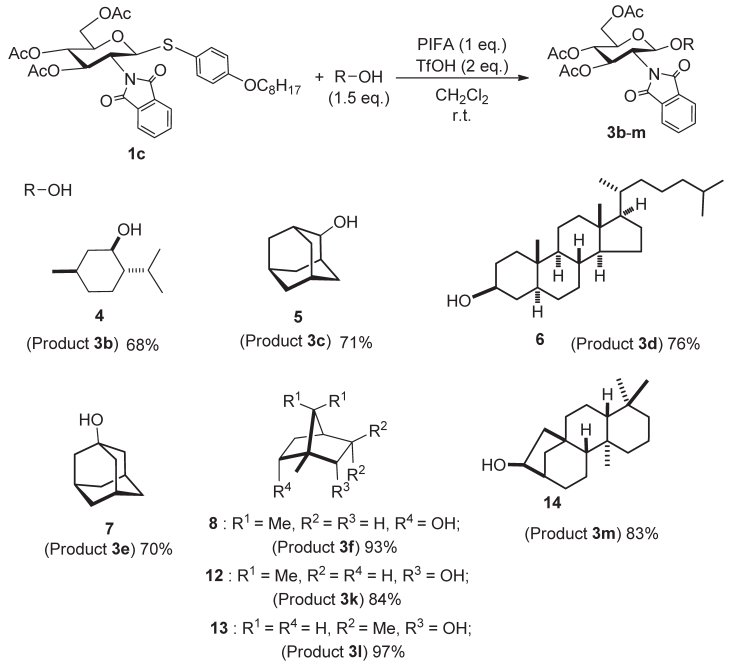
Materials $PhI(OCOCF_3)_2$ (PIFA), methyl 2-deoxy-2-phthalimido-3,4,6-tri-*O*-acetyl-1-thio-*β*-D-glucopyranoside **1a**, methyl 2,3,4,6-tetra-*O*-acetyl-1-thio-*β*-D-glucopyranoside **1b**, 1-*O*-methyl 2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside **2**, (*l*)-menthol **4**, cholestanol **6**, 2- and 1-adamanntanols **5**, **7**, (−)- and (+)-borneol **8**, **12**, and (+)-fenchyl alcohol **13** are commercially available and used as received. All other starting materials are commercially available. They were used without further purification. *p*-Octyloxyphenyl 2-deoxy-2-phthalimido-3,4,6-tri-*O*-acetyl-1-thio-*β*-D-glucopyranoside **1c**

Table 1. Reaction of Glycosyl Donors and Acceptors[a), b)]

Entry	Donor	Acceptor	Product	Yield (%)
1	 **1a**	 **4**	 **3b**	57
2	〃	 **5**	 **3c**	58
3	〃	 **6**	 **3d**	60
4	〃	 **7**	 **3e**	58
5	〃	 **8**	 **3f**	63
6	〃	 **9**	 **3g**	87
7	 **1b**	〃	 **3h**	40
8	 **1a**	 **10**	 **3i**	56
9	〃	 **11**	 **3j**	59

a) Reactions were carried out by adding PIFA (0.2 mmol) to a stirred solution of the starting glycosyl donar (0.2 mmol) and glycosyl acceptors **4**–**11** (0.3 mmol) in CH_2Cl_2 (4 mL) in the presence of TfOH (0.4 mmol) at 0°C. *b*) Yield of isolated product.

Table 2. Glycosylation Reaction of Glycosyl Donor **1c**[a), b)]



a) Reactions were carried out by adding PIFA (0.20 mmol) to a stirred solution of the starting glycosyl donar **1c** (0.20 mmol) and glycosyl acceptors **4**–**8**, **12**–**14** (0.30 mmol) in CH_2Cl_2 (4 mL) in the presence of TfOH (0.40 mmol) at 0°C. *b*) Yield of isolated product.

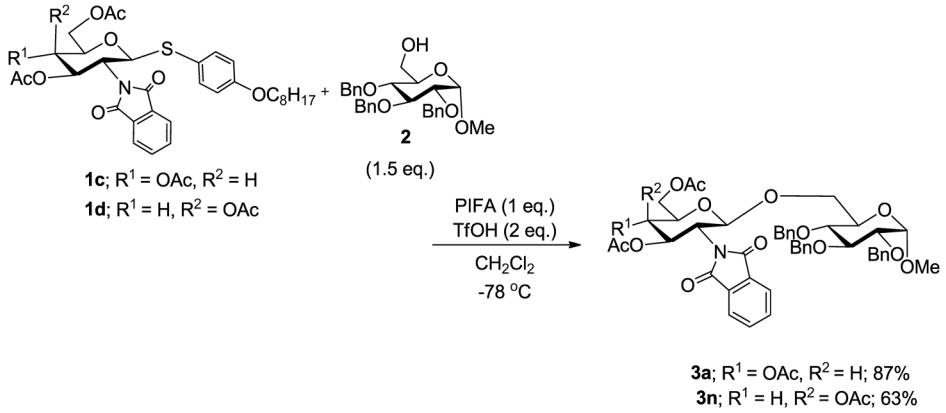


Chart 3. Synthesis of Disaccharides **3a** and **n** Using Thioglycoside Activation with PIFA

was synthesized by the method in the literature,[31] *i.e.*, $BF_3 \cdot Et_2O$ (268 mL, 2.12 mmol) was added to a solution of 2-deoxy-2-phthalimido-1,3,4,6-tetra-*O*-acetyl-D-glucopyranose (676 mg, 1.41 mmol), and *p*-octyloxybenzenethiol (506 mg, 2.12 mmol) in dichloromethane (5 mL) at 0°C and the mixture was stirred for 20 h at room temperature (r.t.). After the reaction, the reaction mixture was poured into ice water and extracted with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride, dried over magnesium sulfate, and evaporated. The residue was purified by silica gel column chromatography (*n*-hexane–ethyl acetate=2 : 1) to afford *p*-octyloxyphenyl 2-deoxy-2-phthalimido-3,4,6-tri-*O*-acetyl-1-thio-*β*-D-glucopyranoside **1c** (829 mg, 89%) as a colorless syrup.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.89 (3H, t, J=7.0 Hz), 1.78 (2H, quint, J=7.0 Hz), 1.83, 2.01, 2.10 (3H, each s), 3.86 (1H, dq, J=10.0, 2.4 Hz), 3.93 (2H, t, J=6.6 Hz), 4.20 (1H, dd, J=12.3, 2.4 Hz), 4.26 (1H, dd, J=12.3, 5.0 Hz), 4.28 (1H, t, J=10.0 Hz), 5.09 (1H, t, J=10.0 Hz), 5.56 (1H, d, J=10.0 Hz), 5.76 (1H, t, J=10.0 Hz), 6.78, 7.33 (2H, each d, J=8.8 Hz), 7.76 (2H, dd, J=5.3, 3.0 Hz), 7.88 (2H, dd, J=5.3, 3.0 Hz) ppm; ^{13}C-NMR (100 MHz, C_5D_5N) δ: 13.6, 19.5, 19.7, 20.0, 22.2, 25.8, 28.7, 28.76, 28.85, 31.3, 53.8, 61.9, 67.6, 68.6, 71.6, 75.9, 83.2, 114.9 (2C), 120.5, 122.3 (2C), 130.9, 131.3, 134.2, 134.3, 135.8 (2C), 159.7, 166.9, 167.8, 169.0, 169.7, 169.8 ppm; IR: 2930, 2856, 1778, 1747, 1719, 1593, 1495, 1470 cm^{-1}; high resolution (HR)-MS: Calcd for $C_{34}H_{41}NNaO_{10}S$ $[M+Na]^+$: 678.2349. Found: 678.2343.

p-Octyloxyphenyl 2-deoxy-2-phthalimido-3,4,6-tri-*O*-acetyl-1-thio-*β*-D-galactopyranoside **1d** was also prepared from 2-deoxy-2-phthalimino-D-galactose tetraacetate and *p*-octyloxybenzenethiol with good yield (83%) in the same way as the synthesis of **1c**, *i.e.*, **1d** was obtained by the reaction of 2-deoxy-2-phthalimino-D-galactose tetraacetate with *p*-octyloxybenzenethiol in the presence of $BF_3 \cdot Et_2O$ in CH_2Cl_2.

p-Octyloxyphenyl 2-Deoxy-2-phthalimido-3,4,6-tri-*O*-acetyl-1-thio-*β*-D-galactopyranoside (**1d**)

^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 0.85–0.86 (3H, m), 1.26–1.29 (8H, m), 1.41 (2H, m), 1.74 (2H, q, *J*=6.8 Hz), 1.81 (3H, s), 2.02 (3H, s), 2.14 (3H, s), 3.89 (2H, t, *J*=6.4 Hz), 4.03–4.05 (1H, m), 4.09–4.14 (1H, m), 4.18–4.20 (1H, m), 4.56 (1H, t, *J*=10.8 Hz), 5.45 (1H, s), 5.54 (1H, d, *J*=9.3 Hz), 5.77 (1H, d, *J*=10.8 Hz), 6.75–6.77 (2H, m), 7.31–7.34 (2H, m), 7.75–7.76 (2H, m), 7.86 (2H, brs) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 14.1, 20.5, 20.7, 22.6, 26.0, 29.1, 29.2, 29.3, 31.8, 50.1, 61.6, 66.8, 68.0, 68.9, 74.4, 77.2, 84.6, 114.8 (2C), 121.3, 123.6, 123.7, 131.3, 131.5, 134.3, 134.4, 135.8 (2C), 159.8, 167.3, 168.0, 169.8, 170.3, 170.4 ppm; IR (KBr): 3052, 2930, 2857, 2253, 1748, 1716, 1594, 1569, 1494, 1470, 1384, 1245, 1174, 1118, 1088, 1045, 912, 831, 741, 672 cm^{-1}; HR-FAB-MS: Calcd for $C_{34}H_{41}NNaO_{10}S$ $[M+Na]^+$ 678.2349. Found 678.2343.

General Procedure To a stirred solution of 2-deoxy-2-phthalimido-3,4,6-tri-*O*-acetyl-1-*thio*-D-glucopyranoside **1a** and 1-*O*-methyl 2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside **2** (1 equiv) in the presence of MS 4A in CH_2Cl_2 (0.2 M), TfOH (2 equiv) was added at −78°C. Then, PIFA (1 equiv) was subsequently added to the reaction mixture with stirring and stirred for an additional 3 h under the same conditions, while the reaction was monitored by TLC. A saturated aqueous solution of sodium hydrogen carbonate was added to the mixture when the reaction completed. The aqueous phase was extracted with CH_2Cl_2. The extract was dried over anhydrous Na_2SO_4 and then evaporated to dryness. The crude residue was purified by column chromatography on silica gel (eluent: *n*-hexane–CH_2Cl_2) to give the pure glycosylation product **3a** in 77% yield.

Methyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranosyl-*β*(1→6)-2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside (**3a**)

White solid, mp 150–151°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 1.78 (3H, s), 1.96 (3H, s), 2.02 (3H, s), 3.10 (3H, s), 3.16 (1H, t, *J*=9.2 Hz), 3.31 (1H, dd, *J*=10.0, 3.6 Hz), 3.57–3.60 (2H, m), 3,75–3.82 (2H, m), 4.01–4.12 (3H, m), 4.23–4.35 (4H, m), 4.50 (1H, d, *J*=12.0 Hz), 4.58 (1H, d, *J*=11.2 Hz), 4.65 (1H, d, *J*=11.6 Hz), 4.78 (1H, d, *J*=11.8 Hz), 5.11 (1H, t, *J*=11.2 Hz), 5.36 (1H, d, *J*=8.4 Hz), 5.72 (1H, dd, *J*=11.4, 8.8 Hz), 6.94–6.96 (2H, m), 7.14–7,24 (15H, m), 7.48 (2H, brs) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 20.4, 20.6, 20.8, 54.4, 55.0, 62.0, 68.7, 68.9, 69.1, 70.7, 71.9, 73.4, 74.7, 75.7, 77.5, 79.6, 81.8, 97.8, 98.3, 123.5, 127.5, 127.6, 127.7, 127.9, 127.93, 128.1, 128.3 (2C), 128.4, 131.1, 134.1, 137.7, 138.1, 138.6, 169.4, 170.2, 170.8 ppm; IR (KBr): 2930, 1752, 1719, 1455, 1386, 1366, 1234, 1071, 1043, 913, 745, 700, 647 cm^{-1}; HR-FAB-MS: Calcd for $C_{48}H_{51}NNaO_{15}$ $[M+Na]^+$ 904.3156. Found 904.3151.

(−)-Menthyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranoside (**3b**)

White solid, mp 130–131°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 0.68 (6H, d, *J*=3.4 Hz), 0.78 (3H, d, *J*=7.3 Hz), 0.85–1.22 (4H, m), 1.50–1.70 (5H, m), 1.84 (3H, s), 2.01 (3H, s), 2.06 (3H, s), 3.37 (1H, td, *J*=10.8, 4.0 Hz), 3.80–3.85 (1H, m), 4.12–4.29 (3H, m), 5.11 (1H, t, *J*=9.2 Hz), 5.37 (1H, d, *J*=8.4 Hz), 5.79 (dd, 1H, *J*=10.7, 8.8 Hz), 7.70–7.74 (2H, m), 7.83–7.85 (2H, m) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 15.4, 20.5, 20.66, 20.7, 20.8, 22.0, 22.9, 25.0, 31.2, 34.0, 40.3, 47.3, 54.9, 62.5, 69.5, 70.9, 71.4, 78.4, 95.7, 123.5 (2C), 134.2 (2C), 169.6, 170.2, 170.7 ppm; IR (KBr): 2954, 2923, 2870, 1751, 1719, 1387, 1260, 1231, 1102, 1079, 1035, 806, 748, 721 cm^{-1}; HR-FAB-MS: Calcd for $C_{30}H_{39}NNaO_{10}$ $[M+Na]^+$ 596.2472. Found 596.2466.

2-Adamantyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranoside (**3c**)

White solid, mp 187–190°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 1.22–1.35 (4H, m), 1.46–1.76 (10H, m), 1.81 (3H, s), 2.00 (3H, s), 2.09 (3H, s), 3.74 (1H, brs), 3.84 (1H, dq, *J*=7.8, 2.4 Hz), 4.12 (1H, dd, *J*=12.0, 2.4 Hz), 4.31–4.39 (2H, m), 5.16 (1H, t, *J*=9.3 Hz), 5.40 (1H, d, *J*=8.2 Hz), 5.82 (1H, dd, *J*=10.7, 9.2 Hz), 7.70–7.72 (2H, m), 7.82–7.84 (2H, m) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 20.5, 20.7, 20.8, 26.9, 27.0, 30.9, 31.2, 31.3, 33.2, 36.1, 36.5, 37.2, 54.8, 62.1, 69.2, 70.7, 71.6, 81.4, 96.3, 123.5 (2C), 131.3 (2C), 134.3 (2C), 169.5, 170.3, 170.8 ppm; IR (KBr): 2911, 2852, 1761, 1716, 1387, 1226, 1043, 903, 817, 791, 746, 722, 684 cm^{-1}; HR-FAB-MS: Calcd for $C_{30}H_{35}NNaO_{10}$ $[M+Na]^+$ 592.2159. Found 592.2153.

Cholestan-3*β*-yl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranoside (**3d**)

White solid, mp 167–170°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 0.57 (3H, s), 0.62 (3H, s), 0.81–1.83 (40H, m), 1.88 (3H, s), 2.00 (3H, s), 2.08 (3H, s), 3.47–3.52 (1H, m), 3.80–3.86 (1H, m), 3.99–4.14 (1H, m), 4.24–4.32 (2H, m), 5.13 (1H, t, *J*=9.2 Hz), 5.43 (1H, d, *J*=8.8 Hz), 5.75 (1H, t, *J*=9.2 Hz), 7.71–7.73 (2H, m), 7.83–7.85 (2H, m) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 11.9, 12.2, 18.6, 20.5, 20.6, 20.8, 21.1, 22.5, 22.8, 23.8, 24.1, 28.0, 28.2, 28.6, 29.1, 32.0, 34.3, 35.36, 35.4, 35.7, 36.1, 36.9, 39.5, 39.9, 42.5, 44.5, 54.2, 54.9, 56.2, 56.4, 62.2, 69.1, 70.9, 71.6, 79.5, 96.9, 123.6 (2C), 131.4 (2C), 134.2 (2C), 169.5, 170.2, 170.8 ppm; IR (KBr): 2927, 2867, 1748, 1716, 1387, 1229, 1074, 1040, 833, 803, 749, 721, 678 cm^{-1}; HR-FAB-MS: Calcd for $C_{47}H_{67}NNaO_{10}$ $[M+Na]^+$ 828.4663. Found 828.4568.

1-Adamantyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranoside (**3e**)

White solid, mp 185–189°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 1.22–1.25 (4H, m), 1.45–1.57 (7H, m), 1.67–1.70 (4H, m), 1.83 (3H, s), 2.00 (3H, s), 2.06 (3H, s), 3.83–3.88 (1H, m), 4.08–4.12 (1H, m), 4.25–4.31 (2H, m), 5.09 (1H, t, *J*=9.6 Hz), 5.54 (1H, d, *J*=8.0 Hz), 5.82 (1H, dd, *J*=10.7, 9.2 Hz), 7.71–7.74 (2H, m), 7.83–7.85 (2H, m) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 20.5, 20.7, 20.8, 29.7, 30.5 (2C), 35.9 (2C), 42.1 (2C), 55.0, 62.5, 69.4, 70.8, 71.3, 75.8, 91.6, 123.6 (2C), 131.4 (2C), 134.2 (2C), 169.6, 170.2, 170.7 ppm; IR (KBr): 2911, 2854, 1749, 1718, 1386, 1275, 1262, 1226, 1068, 1031, 971, 789, 750, 724 cm^{-1}; HR-FAB-MS: Calcd for $C_{30}H_{35}NNaO_{10}$ $[M+Na]^+$ 592.2159. Found 592.2153.

(−)-Bornyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranoside (**3f**)

White solid, mp 130–134°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 0.45–0.58 (2H, m), 0.72 (3H, s), 0.74 (3H, s), 0.79 (3H, s), 0.96–1.02 (1H, m), 1.22–1.41 (3H, m), 1.58–1.64 (1H, m), 2.82 (3H, s), 2.00 (3H, s), 2.08 (3H, s), 3.79–3.83 (1H, m), 3.89–3.93 (1H, m), 4.13 (1H, dd, *J*=12.0, 2.4 Hz), 4.28–4.33 (2H, m), 5.15 (1H, t, *J*=9.6 Hz), 5.25 (1H, d, *J*=8.0 Hz), 5.82 (1H, dd, *J*=10.8, 8.8 Hz), 7.70–7.73 (2H, m), 7.83–7.85 (2H, m) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 13.2, 18.8, 19.6, 20.5, 20.7, 20.8, 26.3, 27.9, 35.8, 44.6, 47.7, 49.1, 54.9, 62.2, 69.4, 70.6, 71.6, 83.6, 96.9, 123.5 (2C), 131.3 (2C), 134.3 (2C), 169.5, 170.2, 170.8 ppm; IR (KBr): 2955, 2874, 1749, 1718, 1386, 1368, 1226, 1076, 1033, 752, 722, 675 cm^{-1}; HR-FAB-MS: Calcd for $C_{30}H_{37}NNaO_{10}$ $[M+Na]^+$ 594.2315. Found 594.2310.

Methyl (3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranosyl)-*β*-(1→6)-2,3,4-tri-*O*-benzoyl-*α*-D-glucopyranoside (**3g**)[42]

^{1}H-NMR (400 MHz, $CHCl_3$) *δ*: 1.84 (3H, s), 2.00 (3H, s), 2.03 (3H, s), 3.05 (3H, s), 3.59 (1H, dd, *J*=7.3, 3.4 Hz), 3.86 (1H, d, *J*=7.5 Hz), 4.05 (1H, d, *J*=10.5 Hz), 4.10–4.13 (m, 2H), 4.31 (dd, 1H, *J*=12.5, 4.5 Hz), 4.36 (t, 1H, *J*=10.0, 9.0, Hz), 4.70 (1H, d, *J*=3.4 Hz), 5.05 (1H, dd, *J*=3.9, 2.4 Hz), 5.14 (1H, t, *J*=9.3 Hz), 5.25 (1H, t, *J*=9.8 Hz), 5.40 (1H, d, *J*=8.8 Hz), 5.80 (1H, t, *J*=9.8 Hz), 5.99 (1H, t, *J*=9.8 Hz), 7.19–7.49 (7H, m), 7.71–7.90 (12H, m) ppm.

Methyl (2,3,4,6-Tetra-*O*-acetyl-D-glucopyranosyl)-*β*-(1→6)-2,3,4-tri-*O*-benzoyl-*α*-D-glucopyranoside (**3h**)[43]

^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 1.99 (9H, s), 2.07 (3H, s), 3.43 (3H, s), 3.66–3.70 (2H, m), 4.01–4.06 (2H, m), 4.19–4.25 (2H, m), 4.56 (1H, d, *J*=8.3 Hz), 5.00–5.07 (2H, m), 5.17–5.22 (3H, m), 5.39 (1H, t, *J*=9.8 Hz), 6.10 (1H, t, *J*=9.8 Hz), 7.24–7.52 (9H, m), 7.81–7.83 (2H, m), 7.90–7.95 (4H, m) ppm.

Methyl 4-*O*-[3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranosyl]-*β*-(1→6)-2,3,6-tri-*O*-benzoyl-*α*-D-galactopyranoside (**3i**)

White solid, mp 87–89°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 1.81 (3H, s), 1.94 (3H, s), 2.04 (3H, s), 3.33 (3H, s), 3.61–3.65 (1H, m), 3.95–3.99 (1H, m), 4.07–4.12 (1H, m), 4.30 (1H, t, *J*=6.4 Hz), 4.37–4.49 (2H, m), 4.58–4.62 (1H, m), 4.70–4.71 (1H, m), 4.96 (1H, d, *J*=3.4 Hz), 5.10 (1H, t, *J*=9.3 Hz), 5.21–5.25 (1H, m), 5.46–5.50 (2H, m), 5.77 (1H, dd, *J*=8.8, 2.0 Hz) 7.34–7.33 (6H, m), 7.42 (3H, t, *J*=7.3 Hz), 7.50–7.56 (2H, m), 7.70–7.74 (6H, m), 8.03 (2H, d, *J*=6.8 Hz) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 20.3, 20.4, 20.5, 54.7, 55.2, 61.4, 63.9, 67.9, 68.0, 68.7, 70.1, 71.5, 73.3, 77.4, 97.4 (2C), 123.7 (2C), 128.1 (2C), 128. 3 (4C), 129.0, 129.1, 129.5 (5C), 129.9 (3C), 131.3, 133.0 (2C), 133.2, 133.8 (2C), 165.0, 165.9, 166.7, 169.3, 169.9, 170.7 ppm; IR (KBr): 3055, 2987, 2685, 2358, 2306, 1718, 1387, 1259, 1044, 896, 765 cm^{-1}; MS (MALDI-TOF): *m/z* (%): Calcd for $C_{48}H_{45}NNaO_{18}$: 946.25; $[M+Na]^+$; Found: 946.17 (100), 947.15 (50), 948.15 (26).

2-Deoxy-2-phthalimido-3,4,6-tri-*O*-acetyl-D-glucopyranosyl-*β*-(1→6)-1,2 : 3,4-di-*O*-isopropylidene-*α*-D-galactopyranoside (**3j**)[44]

White solid, mp 207–210°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 0.98 (6H, s), 1.19 (3H, s), 1.35 (3H, s), 1.82 (3H, s), 1.98 (3H, s), 2.07 (3H, s), 3.64–3.66 (2H, m), 3.83–3.96 (3H, m), 4.04–4.14 (2H, m), 4.25–4.37 (3H, m), 5.06 (1H, d, *J*=5.4 Hz), 5.14 (1H, dd, *J*=10.0, 9.5 Hz), 5.40 (1H, d, *J*=8.3 Hz), 5.80 (1H, dd, *J*=10.7, 9.1 Hz), 7.66–7.68 (2H, m), 7.78–7.79 (2H, m) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 20.4, 20.6, 20.7, 24.1, 24.6, 25.3, 25.8, 54.5, 62.0, 67.4, 69.0, 70.1, 70.5, 70.6, 70.8, 71.5, 76.7, 77.0, 77.3, 95.9, 99.3, 107.9, 109.3, 123.4, 133.7, 169.5, 170.1, 170.7 ppm.

(+)-Bornyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranoside (**3k**)

White solid, mp 114–116°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 0.33 (3H, s), 0.68 (3H, s), 0.73 (3H, s), 0.96–0.99 (2H, m), 1.16–1.26 (4H, m), 1.52–1.61 (1H, m), 1.85 (3H, s), 2.00 (3H, s), 2.08 (3H, s), 3.62–3.68 (1H, m), 3.80–3.84 (1H, m), 4.06–4.13 (1H, m), 4.28–4.35 (2H, m), 5.13 (1H, t, *J*=10.0 Hz), 5.27 (1H, d, *J*=8.4 Hz), 5.80 (1H, dd, *J*=10.8, 8.8 Hz), 7.70–7.73 (2H, m), 7.82–7.84 (2H, m) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 13.1, 14.2, 18.7, 19.4, 20.5, 20.7, 20.8, 26.4, 27.8, 37.0, 44.9, 47.2, 49.0, 54.8, 62.2, 69.3, 70.7, 71.6, 87.8, 99.8, 123.5 (2C), 131.4 (2C), 134.3 (2C), 169.5, 170.2, 170.7 ppm; IR (KBr): 2949, 1779, 1749, 1718, 1388, 1368, 1229, 1079, 1047, 1035, 780, 747, 719 cm^{-1}; HR-FAB-MS: Calcd for $C_{30}H_{37}NNaO_{10}$ $[M+Na]^+$ 594.2315. Found 594.2310.

(+)-Fenchyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranoside (**3l**)

White solid, mp 117–119°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 0.59 (3H, s), 0.80 (3H, s), 0.94 (3H, s), 1.22–1.32 (4H, m), 1.58 (3H, s), 1.85 (3H, s), 2.02 (3H, s), 2.06 (3H, s), 3.00 (1H, d, *J*=1.6 Hz), 3.81–3.85 (1H, m), 4.19 (2H, d, *J*=4.0 Hz), 4.33 (1H, dd, *J*=10.8, 8.0 Hz), 5.07–5.16 (2H, m), 5.83 (1H, dd, *J*=10.8, 9.2 Hz), 7.70–7.73 (2H, m), 7.82–7.84 (2H, m) ppm: ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 19.1, 20.5, 20.68, 20.7, 21.5, 25.4, 25.9, 29.5, 39.1, 40.9, 48.0, 48.6, 54.8, 62.6, 69.5, 70.6, 71.4, 94.6, 99.5, 123.5 (2C), 134.3 (2C), 131.0 (2C), 169.6, 170.2, 170.7 ppm; IR (KBr): 2949, 2874, 1749, 1718, 1387, 1367, 1275, 1258, 1228, 1110, 1081, 1051, 971, 749, 721 cm^{-1}; HR-FAB-MS: Calcd for $C_{30}H_{37}NNaO_{10}$ $[M+Na]^+$ 594.2315. Found 594.2310.

Ent-17-nor-kauran-16*α*-yl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranoside (**3m**)

White solid, mp 209–211°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 0.57–0.69 (3H, m), 0.71 (3H, s), 0.78 (3H, s), 0.83 (3H, s), 1.04–1.81 (18H, m), 1.84 (3H, s), 2.00 (3H, s), 2.09 (3H, s), 3.82 (1H, dq, *J*=7.8, 2.4 Hz), 4.08–4.20 (2H, m), 4.29–4.34 (2H, m), 5.13 (1H, d, *J*=9.6 Hz), 5.25 (1H, t, *J*=8.8 Hz), 5.86 (1H, dd, *J*=10.8, 9.2 Hz), 7.70–7.73 (2H, m), 7.82–7.84 (2H, m) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): *δ*: 17.5, 18.0, 19.9, 20.5, 20.6, 20.8, 21.0, 21.5, 25.6, 33.2, 33.5, 37.4, 37.9, 39.1, 40.1, 41.6, 42.0, 43.2, 48.0, 54.9, 56.1, 56.7, 62.2, 69.4, 70.6, 71.6, 79.4, 97.7, 123.5 (2C), 131.4 (2C), 134.3 (2C), 169.5, 170.2, 170.7 ppm; IR (KBr): 2930, 2857, 1752, 1719, 1467, 1386, 1227, 1170, 1082, 1032, 764, 748, 722 cm^{-1}; HR-FAB-MS: Calcd for $C_{39}H_{51}NNaO_{10}$ $[M+Na]^+$ 716.3411. Found 716.3405.

Methyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-D-galactopyranosyl-*β*-(1→6)-2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside (**3n**)

White solid, mp 58–67°C; ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 1.77 (3H, s), 1.98 (3H, s), 2.10 (3H, s), 3.10 (3H, s), 3.16 (1H, t, *J*=9.2 Hz), 3.31 (1H, dd, *J*=9.6, 3.6 Hz), 3.55–3.60 (2H, m), 3.77 (1H, t, *J*=9.2 Hz), 4.00–4.15 (5H, m), 4.30–4.33 (2H, m), 4.50–4.66 (4H, m), 4.78 (1H, d, *J*=11.8 Hz), 5.28 (1H, d, *J*=8.4 Hz), 5.40 (1H, d, *J*=3.4 Hz), 5.73 (1H, dd, *J*=11.2, 3.2 Hz), 6.96–6.98 (2H, m), 7.14–7.24 (15H, m), 7.45 (2H, br s) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 20.5, 20.7, 20.72, 51.2, 54.9, 61.3, 66.6, 68.0, 68.7, 69.1, 70.8, 73.3, 74.7, 75.6, 77.6, 79.7, 81.8, 97.8, 98.7, 123.4 (2C), 127.6, 127.7, 127.86, 127.9 (3C), 128.0 (3C), 128.2 (3C), 128.4 (3C), 131.0 (2C), 134.1 (2C), 137.7, 138.1, 138.6, 169.8, 170.3, 170.4 ppm; IR (KBr): 3029, 2926, 1752, 1717, 1454, 1389, 1368, 1235, 1131, 1070, 1052, 950, 798, 750, 724 cm^{-1}; HR-FAB-MS: Calcd for $C_{48}H_{51}NNaO_{15}$ $[M+Na]^+$ 904.3156. Found 904.3151.

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