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Note

An α-selective, visible light photocatalytic glycosylation of alcohols with selenoglycosides

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ABSTRACT

Exceptionally mild procedures for the visible light photocatalytic activation of selenoglycoside donors in the presence of alcohol acceptors have been developed. This process is demonstrated with both 1-phenylselenyl-2,3,4,6-tetra-*O*-benzyl glucoside (**1**) and 1-phenylselenyl-2,3,4,6-tetra-*O*-benzyl galactoside (**2**). Catalysis is effected with both metal ($Ru(bpy)_3$) and organocatalysts (diphenyldiselenide). Reactions afford, in all cases, primarily the α-anomers with selectivities that vary with solvent. This represents the first example of a visible light-promoted O-glycosylation.

Chalcogenoglycosides such as thioglycosides and selenoglycosides have been used widely in the synthesis of oligosaccharides due to their stability and orthogonality to conditions bringing about the activation of other glycosyl donors.[1,2] However, it is this same stability that necessitates the often harsh conditions (e.g., toxic, heavy metal ions and highly reactive and sensitive thio- and selenophilic electrophiles) that are used to engender the activation of thioglycosides and selenoglycosides for O-glycosylation.[1,2] With the goal of developing a high-yielding, easily performed glycosylation that uses stable and inexpensive reagents and chalcogenoglycoside donors under mild conditions, we have initiated a research program aimed at the development of a visible light photoredox catalytic O-glycosylation.

Since 2008, visible light photoredox catalysis has enjoyed an increasing popularity with the contributions of MacMillan,[3] Yoon,[4] Stephenson,[5] Sanford,[6] and several others.[7] Our initial interests in developing a visible light-promoted glycosylation were turned toward visible light photoredox catalysis and the employment of polypyridyl transition metal catalysts due to mildness, ease of operation, and use of visible light that these transformations allow.

We envisioned (Scheme 1) a process where oxidative quenching of a photoexcited Ru(II) species such as that derived by the visible light irradiation of tris(2,2′-bipyridyl)ruthenium (II) ($Ru(bpy)_3$, Scheme 1)[8] would precede the 1-electron oxidation of selenoglycosides. The resulting selenoglycoside radical cations are unstable and disproportionate to the requisite glycosyl cations that intercept glycosyl acceptors en route to glycosylated products.[9a] It should be noted that processes similar to this have been demonstrated electrochemically[9] (Ru(III) is replaced by an anode), photochemically[10] (with various UV-absorbing photosensitizers), and chemically.[2b,11]

To establish a proof of concept, we pursued the conversion of selenoglycoside **1** ($E_{ox,(Ag/AgCl)} = +1.31$ V)[9c] with methanol as glycosyl acceptor (Table 1, entry 1). Structures of selenoglycoside donors, alcohol acceptors, and glycosidic products are indicated in Figure 1. Blue LED irradiation of **1** in the presence of 5 mol % $Ru(bpy)_3(PF_6)_2$,[4c] 1.1 equiv of the electron acceptor tetrabromomethane,[5h] and 1.2 equiv of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) as base and 3 equiv MeOH in CH_3CN resulted in complete consumption of **1** and a 75% yield of glycosylation product **4** (2.5:1 α/β) after 5 h of irradiation.

Subsequent experiments indicated that this method was effective for 1-octanol, cyclohexanol, and glucosyl acceptor **3** (Table 1, entries 2–4). As in the case of methanol, these experiments favored the formation of the α-anomer. Performance of this reaction in the absence of alcohol acceptor (Table 1, entry 5) results in the formation of α-glucosyl bromide **7**[12] and glycal **8**[13] (1.4:1, respectively) as determined with ^1H NMR of the crude reaction mixture. Controls indicated that this process is not viable in the absence of either light or CBr_4 when no conversion of **1** was observed (Table 1, entries 6 and 7). While these reactions characteristically reached a temperature of 40 °C under irradiation, it was found that heating these same reactions to 50 °C in the dark resulted in much slower conversion of **1**, suggesting that thermal processes are trivial (Table 1, entry 8). Despite this, the thermal conversion (Table 1, entry 8) is intriguing and suggests that an enthalpically unfavorable[8] but irreversible electron transfer from ground state $Ru(bpy)_3$ to

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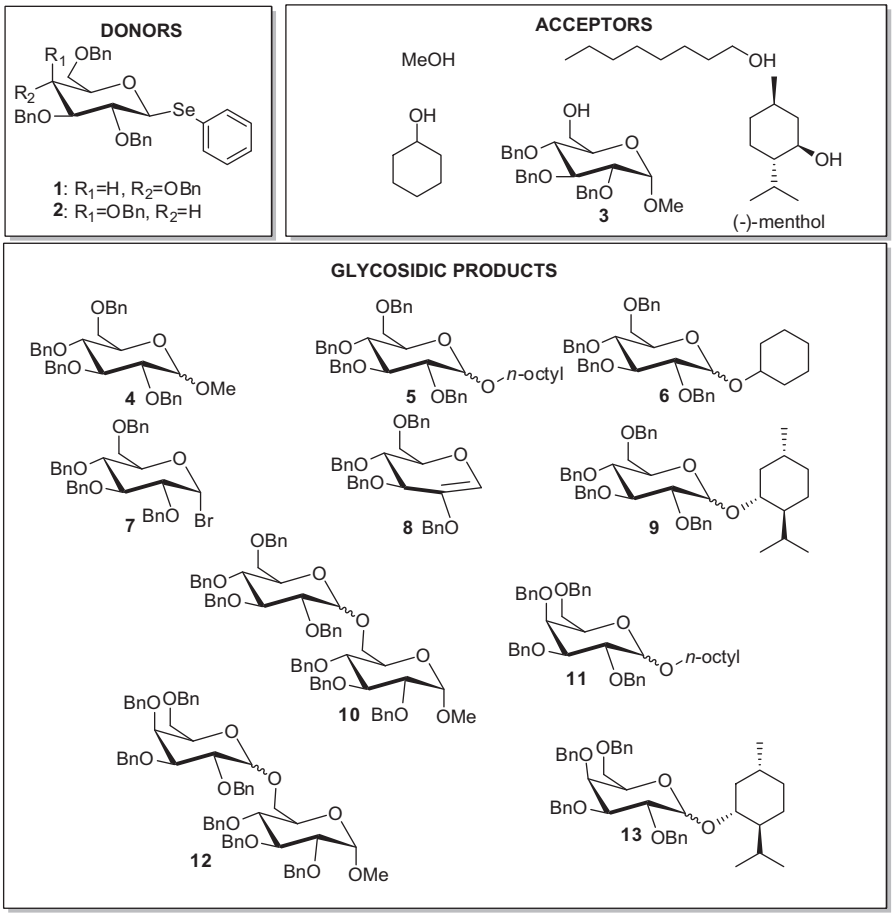
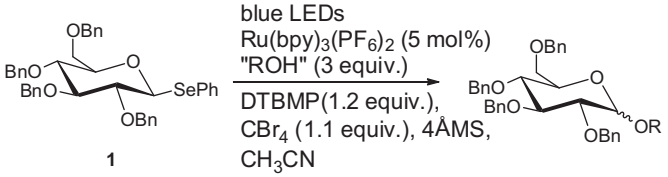


Figure 1. Glycosyl donors, acceptors, and glycosidic products.

Table 1
Visible light-promoted, ru(bpy)$_3$-catalyzed glucosylation

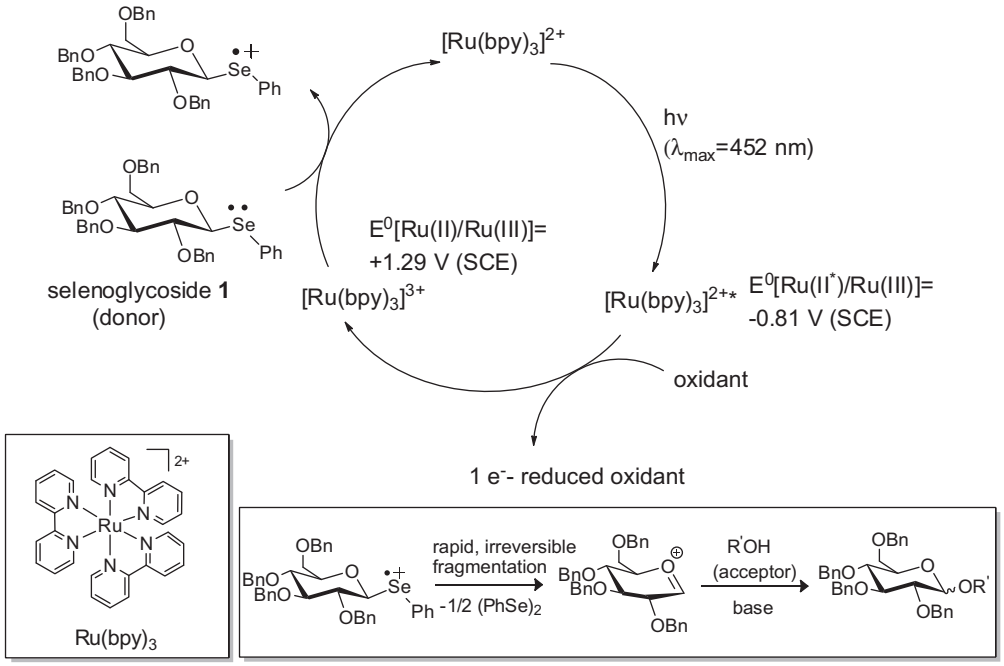


Entry	'ROH' (3 equiv)	Irradiation time	Product, yield (%)	Anomeric ratio (α/β)
1	MeOH	5 h	**4**, 75	2.5:1
2	1-Octanol	3 h	**5**, 81	4:1
3	Cyclohexanol	5 h	**6**, 53	8.5:1
4	**3**	13 h	**10**, 43	2:1
5	None	5 h	**7** and **8** (1.4:1, not isolated)	n/a
6[a]	1-Octanol	24 h	**5**, 0	n/a
7[b]	1-Octanol	24 h	**5**, 0	n/a
8[c]	1-Octanol	2.5 days	**5**, 76	2.5:1
9[d]	1-Octanol	18 h	**5**, 30	4:1
10[e]	1-Octanol	5 h	**5**, 59	4:1

All experiments were performed in 5 mL Pyrex reactor vials with blue LED irradiation from the side (see Section 1 for details). We employed 0.147 mmol donor **1** with 3 equiv alcohol acceptor, and 1.1 equiv CBr_4 with 1.2 equiv DTBMP in 2 mL CH_3CN. Powdered 4 Å MS (400 mg) was employed with acceptors other than MeOH. Reaction mixtures characteristically reached a temperature of 40 °C. Anomeric ratios were determined with ^{1}H NMR analysis of purified product mixtures.

[a] Performed in the absence of light.
[b] Performed in the absence of CBr_4.
[c] Performed at 50 °C in the absence of light.
[d] Performed in the absence of $Ru(bpy)_3(PF_6)_2$.
[e] Performed in the absence of $Ru(bpy)_3(PF_6)_2$ with 10 mol % diphenyldiselenide.

CBr_4 (resulting in fragmentation to bromide anion and tribromomethyl radical) to generate the necessary Ru^{3+} species may be operative. Thermal, single electron transfer-mediated glycosylations are not without precedent and have been demonstrated with thioglycosides[11] and selenoglycosides[2b] using the radical cationic oxidant *tris*-(4-bromophenyl)-ammoniumyl hexachloroantimonate

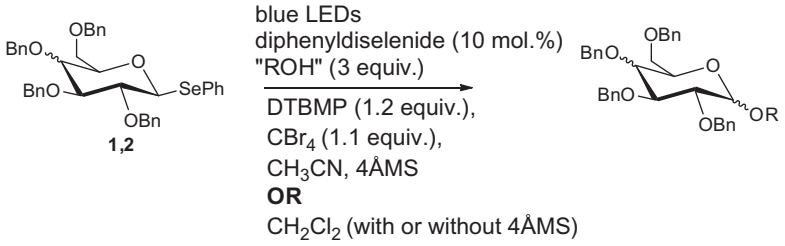


Scheme 1. Original concept for photocatalytic glycosylation.

(BAHA). Further, we found that removal of $Ru(bpy)_3$ resulted in the complete consumption of **1** and formation of a 30% yield of glycosylated product **5** (Table 1, entry 9) with an increased irradiation time. In addition, 10 mol % of diphenyldiselenide, a byproduct of both the $Ru(bpy)_3$-catalyzed and uncatalyzed reactions, nearly restored the reactivity afforded with $Ru(bpy)_3$ when **1** was consumed under the same conditions employed for previous experiments in 5 h (Table 1, entry 10).

Because of the low cost of diphenyldiselenide relative to $Ru(bpy)_3(PF_6)_2$ (~$4/g and $111/g, respectively), solubility in a wider range of solvents and unprecedented reactivity as a visible light photocatalyst, we sought the development of the diphenyldiselenide-catalyzed reaction as an inexpensive and perhaps more versatile alternative to the $Ru(bpy)_3$-catalyzed reaction. To explore the scope of this 'organocatalytic' glycosylation, we performed a number of preparative experiments (Table 2) with 10 mol %

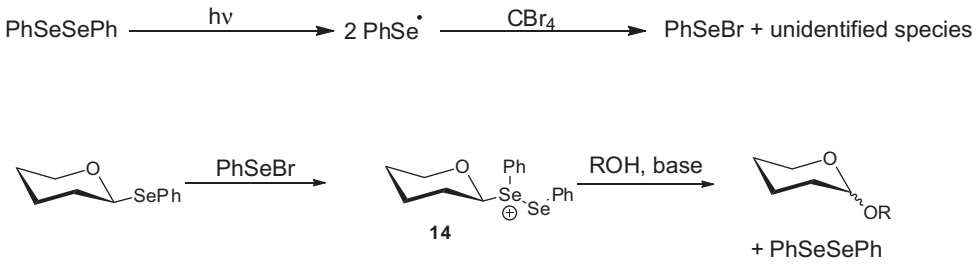
Table 2
Visible light-promoted, diphenyldiselenide-catalyzed glucosylation/galactosylation



Entry	Donor	'ROH' (3 equiv)	Solvent	Irradiation time	Product, yield (%)	Anomeric ratio (α/β)
1	**1**	Cyclohexanol	CH_3CN, 4 ÅMS	5 h	**6**, 65	1.5:1
2	**1**	(−)-Menthol	CH_3CN, 4 ÅMS	10 h	**9**, 57	4:1
3	**1**	**3**	CH_3CN, 4 ÅMS	8 h	**10**, 33	2:1
4	**2**	1-Octanol	CH_3CN, 4 ÅMS	6.5 h	**11**, 65	2:1
5	**2**	**3**	CH_3CN, 4 ÅMS	10.5 h	**12**, 50	3:1
6[a]	**1**	1-Octanol	CH_3CN, 4 ÅMS	3 days	**5**, 0	n/a
7	**1**	1-Octanol	CH_2Cl_2, 4 ÅMS	36 h	**5**, 53	20:1
8	**1**	1-Octanol	CH_2Cl_2	12 h	**5**, 72	8:1
9	**1**	Cyclohexanol	CH_2Cl_2	12 h	**6**, 71	6:1
10	**1**	(−)-Menthol	CH_2Cl_2	50 h	**9**, 66	10:1
11	**1**	**3**	CH_2Cl_2	76 h	**10**, 20	4:1
12	**2**	1-Octanol	CH_2Cl_2	21 h	**11**, 71	4:1
13	**2**	(−)-Menthol	CH_2Cl_2	39 h	**13**, 55	8:1
14	**2**	**3**	CH_2Cl_2	70 h	**12**, 49	5.5:1

All experiments (unless otherwise stated) were performed in 5 mL Pyrex reactor vials with blue LED irradiation from the side. We employed 0.147 mmol donors **1** and **2** with 3 equiv of acceptor in the presence of 1.1 equiv CBr_4 and 1.2 equiv DTBMP in 2 mL of the indicated solvent. Powdered 4 Å MS (400 mg) was used in all cases with CH_3CN as solvent and in one case with CH_2Cl_2 as solvent. Anomeric ratios were determined by ^1H NMR analysis of purified product mixtures.

[a] Performed in the absence of light at a temperature of 50 °C.



Scheme 2. Proposed mechanism.

diphenyldiselenide, 1.1 equiv of CBr_4, and 1.2 equiv of DTBMP on the scale reported for previous preparative experiments (0.147 mmol donor). The use of 3 equiv of cyclohexanol, (−)-menthol, and glucosyl acceptor **3** with donor **1** resulted in low to moderate yields of glycosidic products and a preponderance of α-anomers in all cases (Table 2, entries 1–3). We further demonstrated the efficacy of this method when galactoside **2** (Fig. 1) underwent conversion in the presence of both 1-octanol and **3** to generate a preponderance of the α-anomers of **11** and **12** (Table 2, entries 4 and 5). Finally, while irradiation with blue LEDs resulted in the warming of reaction mixtures to a temperature of 39–40 °C, we also observed that warming at a temperature of 50 °C in the dark did not result in any detected consumption of starting material **1** over the course of 3 days, demonstrating that the diphenyldiselenide-catalyzed process is light-dependent and not the result of adventitious heating (Table 2, entry 6). This effect is likely the result of inefficient Se–Se bond homolysis (vide infra) in the dark at 50 °C.

Hypothesizing that CH_3CN might facilitate ionization pathways that we believed to be a cause for the low stereoselectivity, we conducted a number of experiments in CH_2Cl_2. In all cases with donors **1** and **2**, we observed increased selectivity for the α-anomeric products. Reaction of glucosyl donor **1** with 1-octanol in CH_2Cl_2 in the presence of 4 Å molecular sieves resulted in a 53% yield of **5** (Table 2, entry 7) whereas reaction of glucosyl donor **1** with 1-octanol, cyclohexanol, (−)-menthol, and acceptor **3** in the absence of 4 Å molecular sieves resulted in 72%, 71%, 66%, and 20% yields of glucosides (respectively, Table 2, entries 8–11). Galactosyl donor **2** underwent reaction with 1-octanol, (−)-menthol, and acceptor **3** to generate 71%, 55%, and 49% yields of products (Table 2, entries 12–14). All of these reactions showed higher selectivity for α-anomer but an increased irradiation time to bring about consumption of **1** and **2** relative to reactions in CH_3CN.

Irradiation of both CH_3CN and CH_2Cl_2 solutions of CBr_4 and diphenyldiselenide in the absence of **1** and **2** results in the formation of phenylselenyl bromide (PhSeBr) as observed with ^{77}Se NMR (Section 1). We propose a mechanism where visible light-promoted homolysis of the Se–Se bond[14] of diphenyldiselenide (Scheme 2) results in the formation of phenylselenyl radicals that react with CBr_4 to generate PhSeBr. The fate of CBr_4 in these reactions is not clear at this time. The reaction of PhSeBr with the Se atom in donors **1** and **2** results in the formation of onium species **14**.[15] Whether the intermediates **14** proceed directly to glycosylated products or via glycosyl bromides or oxocarbenium ions (or some combination of these pathways) to glycosylated products will be the subject of ongoing mechanistic investigation.

We have demonstrated that visible light promotion with $Ru(bpy)_3$ and diphenyldiselenide catalysis provides an effective means for O-glycosylation with phenylselenoglycosides and various alcohol acceptors. This method employs inexpensive reagents and exceptionally mild conditions using commercially available and non-hazardous light sources. Glycosylation of both simple and complex 1° and 2° alcohol acceptors with glucosyl and galactosyl donors **1** and **2** has been demonstrated. Our method is selective for the α-anomer with benzyl-protected glucosyl and galactosyl donors. We have observed that choice of solvent can have a marked effect on stereoselectivity. Further studies of the scope and mechanism of both the $Ru(bpy)_3$ and diphenyldiselenide-catalyzed glycosylations and related visible light-promoted, selenium-mediated transformations are currently underway in our laboratory.

1. Experimental

1.1. General methods

Tris(bipyridyl)ruthenium(II) bis(hexafluorophosphate) ($Ru(bpy)_3(PF6)_2$),[4c] 1-phenylselenyl-2,3,4,6-tetra-*O*-benzyl glucopyranoside,[2e] and 1-phenylselenyl-2,3,4,6-tetra-*O*-benzyl galactopyranoside[10a] were prepared as previously described. Flash column chromatography was performed using 60 Å silica gel. ^1H NMR and ^{13}C NMR spectroscopy were performed on a Bruker AV-400, DPX 400, or DPX 250 spectrometer. Mass spectra were obtained using an Agilent 6210 electrospray time-of-flight mass spectrometer. Optical rotation measurements were obtained using a JASCO P-2000 polarimeter. Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. TLC analysis was conducted on aluminum sheets (Merck, silica gel 60, F254). Compounds were visualized by UV absorption (254 nm) and staining with anisaldehyde. Pyrex micro reaction vessels (5 mL, Supelco) were used in the glycosylation reactions. All glassware was flame-dried under vacuum and backfilled with dry nitrogen prior to use. Deuterated solvents were obtained from Cambridge Isotope Labs. All solvents were purified according to the method of Grubbs.[16]

1.2. General procedure for the visible light-mediated glycosylation

1.2.1. $Ru(bpy)_3(PF_6)_2$-catalyzed reactions

A flame dried 5 mL Pyrex reactor vial was charged with the glycosyl donor (1 equiv, 0.147 mmol), $Ru(bpy)_3(PF_6)_2$ (5 mol %, 7.4 μmol), CBr_4 (1.1 equiv, 0.161 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, 1.2 equiv, 0.176 mmol), the glycosyl acceptor (3 equiv, 0.441 mmol), 400 mg of freshly activated 4 Å molecular sieves, and 2 mL of dry acetonitrile under nitrogen atmosphere. The reactor vial was placed 1–2 cm away from the light source (blue LEDs, 2 strips, Sapphire Blue LED Flex Strips from Creative Lighting Solutions, were wrapped around a 250 mL beaker, Fig. S1) and irradiated from the side. Reaction progress was monitored by TLC. After consumption of the glycosyl donor, the reaction mixture was filtered through a silica gel pad to remove molecular sieves and the crude products were concentrated and then purified by gradient silica gel chromatography.

1.2.2. PhSeSePh catalyzed reactions

A flame dried 5 mL Pyrex reactor vial was charged with the glycosyl donor (1 equiv, 0.147 mmol), PhSeSePh (0.1 equiv, 0.014 mmol), CBr_4 (1.1 equiv, 0.161 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) (1.2 equiv, 0.176 mmol), the glycosyl acceptor (3 equiv, 0.441 mmol), 400 mg of freshly activated 4 Å molecular sieves (with acetonitrile as solvent and in one case with CH_2Cl_2 as solvent), and 2 mL of dry solvent (acetonitrile or CH_2Cl_2) under nitrogen atmosphere. The reactor vial was placed 1–2 cm away from the blue LEDs (2 strips, vide supra for details, were wrapped around a 250 mL beaker, Fig. S1) and irradiated from the side. Reaction progress was monitored by TLC. After consumption of the glycosyl donor, the reaction mixture was filtered through a silica gel pad to remove molecular sieves and the crude products were concentrated and then purified by silica gel chromatography.

1.3. Determination of anomeric ratios

In all cases, the major product (α-anomer) was purified by silica gel chromatography or preparative TLC. The anomeric ratio (α/β) was determined based on the integration of key resonances identified with the assistance of published NMR data (references provided for each compound, vide infra) in the ^{1}H NMR of the purified anomeric mixtures.

1.4. Formation of PhSeBr from PhSeSePh and CBr_4 under irradiation

To a reaction vial containing 30.8 mg (0.0987 mmol) diphenyl diselenide and 349.5 mg (1.054 mmol) CBr_4 was added 3.0 mL solvent of choice (CH_2Cl_2 or CH_3CN) at once. The capped reaction vial was placed in a beaker surrounded by blue LEDs (setup similar to Fig. S1) and was allowed to stir under N_2. At the indicated time intervals, an aliquot of the reaction mixture was concentrated and redissolved in $CDCl_3$. The ^{77}Se NMR spectrum of these aliquots indicated the presence of diphenyl diselenide at δ 464 and formation of phenylselenyl bromide at δ 867.

1.5. Methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (4)[17]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.37 (3H, s), 3.56 (1H, dd, J = 9.6, 3.6 Hz), 3.62 (2H, m), 3.68–3.77 (2H, m), 3.98 (1H, t, J = 9.3 Hz),4.44–4.50 (2H, m), 4.57–4.69 (3H, m), 4.76–4.85 (3H, m), 4.97 (1H, d, J = 10.9 Hz), 7.13 (2H, m), 7.23–7.38 (18H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 68.5, 70.1, 73.4, 73.5, 75.0, 75.7, 77.2, 77.7, 82.1, 98.2, 127.6, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4, 128.5, 137.9, 138.2, 138.3, 138.8; HRMS m/z Calcd for $C_{35}H_{38}KO_6$ $(M+K)^+$ 593.2300, found 593.2316; $[\alpha]_D^{25}$ +43.1 (c 0.24, CH_2Cl_2).

1.6. *n*-Octyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (5)[18]

^{1}H NMR (250 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 6.8 Hz), 1.19–1.40 (10H, m), 1.53–1.67 (2H, m), 3.40 (1H, dt, J = 9.9, 6.7 Hz), 3.55 (1H, dd, J = 9.7, 3.5 Hz), 3.55–3.68 (3H, m), 3.72 (1H, m), 3.78 (1H, m), 3.99 (1H, t, J = 9.2 Hz), 4.47 (2H, d, J = 11.5 Hz), 4.61 (1H, d, J = 12.2 Hz), 4.64 (1H, d, J = 12.2 Hz), 4.76 (2H, m), 4.81 (1H, d, J = 10.8 Hz), 4.83 (1H, d, J = 10.8 Hz), 4.99 (1H, d, J = 10.8 Hz), 7.06–7.18 (2H, m), 7.20–7.44 (18H, m); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 14.2, 22.8, 26.3, 29.4, 29.5, 29.5, 32.0, 68.4, 68.7, 70.4, 73.2, 73.6, 75.2, 75.8, 78.0, 80.3, 82.3, 97.0, 127.6, 127.8, 127.9, 128.0, 128.0, 128.1, 128.5, 128.5, 138.1, 138.4, 138.5, 139.1; HRMS m/z Calcd for $C_{42}H_{52}NaO_6$ $(M+Na)^+$ 675.3656, found 675.3658; $[\alpha]_D^{25}$ +38.6 (c 0.46, DCM).

1.7. Cyclohexyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (6)[19]

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12–1.57 (6H, m), 1.67–1.94 (4H, m), 3.55 (2H, m), 3.63 (2H, m), 3.73 (1H, dd, J = 10.6, 3.7 Hz), 3.88 (1H, dd, J = 10.0, 3.0 Hz), 4.00 (1H, t, J = 9.3 Hz), 4.47, (2H, m), 4.61 (1H, d, J = 12.2 Hz), 4.65 (1H, d, J = 12.0 Hz), 4.73 (1H, d, J = 12.0 Hz), 4.82 (2H, m), 4.95 (1H, d, J = 2.8 Hz), 4.99 (1H, d, J = 10.8 Hz), 7.09–7.18 (2H, m), 7.22–7.40 (18, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.2, 24.4, 25.6, 31.4, 33.3, 68.6. 70.1, 73.0, 73.4, 75.1, 75.3, 75.6, 77.9, 80.0, 82.1, 94.7, 127.6, 127.8, 127.8, 127.9, 128.0, 128.1, 128.1, 128.2, 128.5, 128.5, 138.0, 138.3, 138.3, 139.0; HRMS m/z Calcd for $C_{40}H_{46}NaO_6$ $(M+Na)^+$ 645.3187, found 645.3179; $[\alpha]_D^{25}$ +52.7 (c 0.63, DCM).

1.8. Menthyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (9)[19]

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.70 (3H, d, J = 6.9 Hz), 0.75–1.12 (9H, m), 1.20–1.40 (2H, m), 1.56–1.65 (2H, m), 2.13 (1H, d, J = 12.0 Hz), 2.37–2.46 (1H, m), 3.35 (1H, dt, J = 10.6, 4.3 Hz), 3.54 (1H, dd, J = 9.8, 3.6 Hz), 3.58–3.69 (2H, m), 3.75 (1H, dd, J = 10.5, 3.8 Hz), 3.92–3.98 (1H, m), 4.01 (1H, t, J = 9.3 Hz), 4.46 (1H, d, J = 10.8 Hz), 4.47 (1H, d, J = 12.0 Hz), 4.61–4.73 (3H, m), 4.82 (1H, d, J = 10.8 Hz), 4.83 (1H, d, J = 10.8 Hz), 4.97 (1H, d, J = 11.0 Hz), 5.02 (1H, d, J = 3.6 Hz), 7.09–7.17 (2H, m), 7.21–7.37 (18H, m) ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 21.1, 22.3, 23.1, 24.6, 31.7, 34.3, 43.0, 48.8, 68.7, 70.3, 73.2, 73.4, 75.0, 75.5, 78.1, 80.6, 81.0, 82.0, 98.6, 127.6, 127.6, 127.7, 128.0, 128.3, 128.4, 138.0, 138.3, 138.4, 138.9; HRMS m/z Calcd for $C_{44}H_{54}NaO_6$ $(M+Na)^+$ 701.3813, found 701.3821; $[\alpha]_D^{25}$ +92.5 (c 0.25, CH_2Cl_2).

1.9. Methyl-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (10)[20]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.32 (3H, s), 3.40 (1H, dd, J = 9.6, 3.6 Hz), 3.50 (2H, m), 3.58 (1H, t, J = 9.0 Hz), 3.69–3.82 (3H, m), 3.87–3.99 (4H, m), 4.02 (1H, dd, J = 9.3, 3.5 Hz), 4.36 (1H, d, J = 11.8 Hz), 4.43 (1H, d, J = 11.9 Hz), 4.51–4.60 (4H, m), 4.65–4.75 (4H, m), 4.75–4.82 (2H, m), 4.84 (1H, d, J = 11.0 Hz), 4.93 (1H, d, J = 11.5 Hz), 4.95 (1H, d, J = 10.9 Hz), 4.99 (1H, d, J = 3.6 Hz), 7.18–7.36 (35H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.0, 66.4, 68.9, 69.4, 70.3, 72.5, 72.8, 73.3, 74.7, 75.0, 75.1, 75.7, 76.5, 77.2, 78.0, 78.3, 80.2, 82.1, 97.9, 97.9, 127.3, 127.4, 127.5, 127.6, 127.6, 127.7, 127.8, 127.9, 128.0, 128.2, 128.2, 128.2, 128.3, 128.3, 128.4, 128.4, 138.1, 138.2, 138.4, 138.7, 138.8, 138.9, 138.9; HRMS m/z Calcd for $C_{62}H_{66}NaO_{11}$ $(M+Na)^+$ 1009.4497, found 1009.4490; $[\alpha]_D^{25}$ +87.2 (c 0.55, CH_2Cl_2).

1.10. *n*-Octyl 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranoside (11)[21]

~4:1 (α/β) mixture, ^{1}H NMR (α-anomer, 400 MHz, $CDCl_3$) δ 0.88 (3H, m), 1.26 (10H, m), 1.62 (2H, m), 3.43 (1H, dt, J = 9.9, 6.6 Hz), 3.48–3.66 (3H, m), 3.91–3.98 (3H, m), 4.03 (1H, dd, J = 9.3, 3.6 Hz), 4.33–4.96 (9H, m), 7.20–7.40 (20H, m); ^{13}C NMR (α-anomer, 100 MHz, $CDCl_3$) δ 14.1, 22.6, 26.2, 29.2, 29.4, 31.8, 68.2, 69.0, 69.2, 73.2, 73.4, 74.7, 75.1, 76.6, 79.1, 97.4, 127.4, 127.5, 127.6, 127.7, 127.7, 127.8, 127.9, 128.1, 128.1, 128.2, 128.2, 128.3, 128.3, 128.4, 138.0, 138.5, 138.7, 138.9; HRMS m/z Calcd for $C_{42}H_{52}NaO_6$ $(M+Na)^+$ 675.3656, found 675.3660; $[\alpha]_D^{25}$ +33.5 (c 1.65, CH_2Cl_2)

1.11. Methyl-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-galactopyranoside (12)[22]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.29 (3H, s), 3.41 (1H, dd, J = 9.6, 3.6 Hz), 3.46–3.55 (2H, m), 3.58 (1H, t, J = 9.1 Hz), 3.63 (1H, m),

3.70–3.82 (3H, m), 3.88–4.00 (3H, m), 4.03 (1H, dd, J = 9.5, 3.5 Hz), 4.36 (1H, d, J = 11.8 Hz), 4.43 (1H, d, J = 11.8 Hz), 4.52–4.61 (4H, m), 4.67–4.75 (4H, m), 4.77–4.82 (2H, m), 4.85 (1H, d, J = 11.0 Hz), 4.93 (1H, d, J = 11.2 Hz), 4.95 (1H, d, J = 11.2 Hz), 4.99 (1H, d, J = 3.6 Hz), 7.15–7.45 (35H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.0, 66.4, 68.9, 69.7, 70.5, 72.5, 72.8, 73.3, 73.5, 74.7, 75.0, 75.1, 75.7, 76.5, 78.0, 78.2, 80.2, 82.1, 97.9, 97.9, 127.5, 127.6, 127.7, 127.8, 127.8, 127.8, 127.9, 128.1, 128.3, 128.4, 128.4, 128.5, 128.5, 138.0, 138.2, 138.4, 138.7, 138.8, 138.9; HRMS m/z Calcd for $C_{62}H_{66}NaO_{11}$ $(M+Na)^+$ 1009.4497, found 1009.4490; $[\alpha]_D^{25}$ +71.19 (c 0.83, DCM).

1.12. Menthyl 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranoside (13)[20]

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.69 (3H, δ, J = 6.9 Hz), 0.81 (3H, d, J = 6.9 Hz), 0.82 (3H, d, J = 6.0 Hz), 0.75–0.97 (2H, m), 1.02 (1H, q, J = 12.0 Hz), 1.20–1.40 (2H, m), 1.53–1.63 (2H, m), 2.08 (1H, d, J = 12.0 Hz), 2.41 (1H, m), 3.33 (1H, td, J = 10.8, 4.5 Hz), 3.54 (2H, m), 3.96 (1H, dd, J = 10.1, 2.8 Hz), 3.99 (1H, m), 4.02 (1H, dd, J = 10.1, 3.7 Hz), 4.10 (1H, t, J = 9.3 Hz), 4.42 (1H, d, J = 11.9 Hz), 4.48 (1H, d, J = 11.9 Hz), 4.57 (1H, d, J = 11.5 Hz), 4.67 (1H, d, J = 11.7 Hz), 4.74 (1H, d, J = 11.8 Hz), 4.80 (1H, d, J = 11.5 Hz), 4.81 (1H, d, J = 12.0 Hz), 4.95 (1H, d, J = 11.5 Hz), 5.02 (1H, d, J = 3.7 Hz), 7.23–7.39 (20H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.0, 21.1, 22.3, 22.9, 24.5, 31.8, 34.3, 42.9, 48.9, 59.2, 69.3, 72.2, 73.4, 73.6, 74.7, 75.1, 79.3, 80.2, 99.3, 127.4, 127.5, 127.6, 127.7, 128.1, 128.3, 128.3, 138.1, 138.8, 138.9; HRMS m/z Calcd for $C_{44}H_{54}NaO_6$ $(M+Na)^+$ 701.3813, found 701.3832; $[\alpha]_D^{25}$ +58.3 (c 0.15, CH_2Cl_2).

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2013.01.004.

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