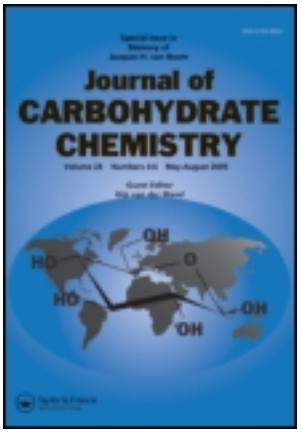

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Photoinitiated Glycosylation at 350 nm

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Photoinitiated Glycosylation at 350 nm

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A method for photochemical activation of glycosyl donors is presented. Selenoglycosides were activated by single-electron transfer using a photooxidant, *N*-methylquinolinium hexafluorophosphate, as photosensitizer and a toluene cosolvent as cosensitizer under irradiation at 350 nm. In this way we were able to synthesize glycosides including (1→6)-linked disaccharides. Benzyl ethers and benzoate esters were compatible with these conditions, allowing potentially synthetically useful transformations. The major by-products were due to hydrolysis; the reactions required the presence of oxygen and were run in air.

Keywords Glycosylation; Photochemistry; Radical ions; Oxocarbenium ions; Oxidation; Electron transfer

INTRODUCTION

The importance of oligosaccharides in biological systems is beyond question, but their roles are in many cases poorly understood.[1] Their low availability from natural sources necessitates their chemical synthesis, but general methods to achieve this remain elusive.[2] The development of new glycosylation protocols contributes to the quest for the ideal glycosylation methodology. In the vast majority of published glycosylation methods, a Lewis acid will coordinate to an anomeric substituent, transforming it into a better leaving group so that nucleophilic substitution with an alcohol nucleophile can occur. In an alternative approach that avoids the use of Lewis acids, one-electron oxidation of the anomeric substituent gives a radical cation. This then fragments into a glycosyl cation that can react analogously with an alcohol nucleophile to give a glycoside. Such one-electron chemistry has been achieved by chemical

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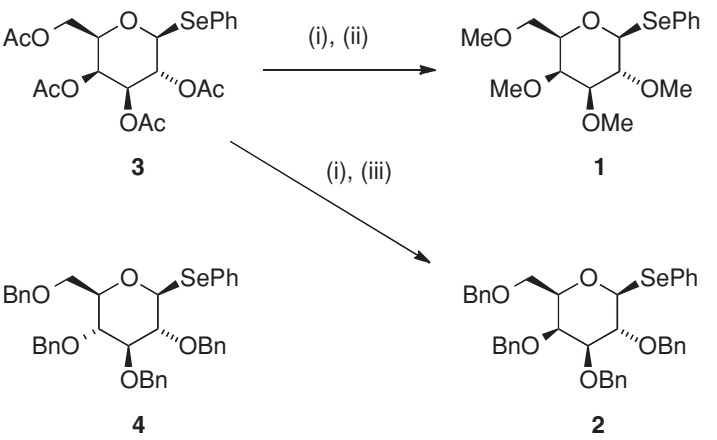
means.[3] Alternatively, electrochemical activation has been explored,[4] with the advantage that the electrode potential can be tuned exactly to match the requirements for activation of the glycoside in question.

Photochemical one-electron oxidation is potentially an attractive alternative technique; here the reaction is promoted by an external stimulus, but takes place in solution, so complications of electrochemical glycosylation due to reaction at an electrode surface or electrochemical cell design will be avoided, simplifying reaction setup. Three papers have reported on this concept: Noyori used a methyl ether–protected aryl 2-deoxyglycoside as a donor.[5] When irradiated with a high-pressure mercury lamp in the presence of photosensitizers and an alcohol, the glycoside was formed. Furuta used a methyl ether–protected selenoglycoside as a donor, with a high-pressure mercury lamp, and a 2,4,6-triphenylpyrilium salt as photosensitizer.[6] This method gave a number of glycosides in low to high yields, including a (1→6)-linked disaccharide. Photoinduced activation of methyl ether–protected thioglycosides using a 1,4-dicyanonaphthalene photocatalyst with irradiation at 350 nm gave, with methanol as cosolvent, methyl glycosides among other products.[7] Benzyl ether protection was incompatible with these glycosylation conditions, resulting in degradation, while acetate-protected donors were unreactive.

For our study of photochemical glycosylation, the results of which we report in this paper, we evaluated *N*-methyl quinolinium hexafluorophosphate (NMQ-PF_6) as photosensitizer. This salt has been used for C—Si bond cleavage,[8] or for acetal formation by oxidative C—C bond cleavage.[9,10] The corresponding tetrafluoroborate salt has also been used in photochemical oxidation reactions.[11] Using this photosensitizer, we were able to activate selenoglycosides as glycosyl donors[12] under rather mild activation conditions, irradiating



Scheme 1: (i) NaOMe, MeOH; (ii) MeI, NaH, DMF, 0°C → rt, 81% (2 steps); (iii) BnBr, NaH, DMF, 0°C → rt, 71% (2 steps).

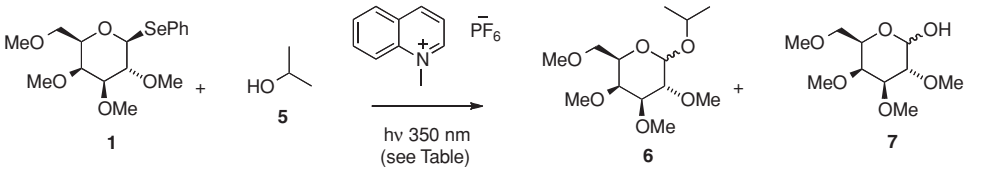
with 350-nm fluorescent tubes rather than a high-pressure mercury lamp, and to synthesize disaccharides bearing synthetically useful protecting groups.

RESULTS AND DISCUSSION

Phenyl selenogalactosides with methyl ether **1** or benzyl ether **2**[13] protection for use as glycosyl donors were synthesized from the peracetate **3** by straightforward protecting group swap (Sch. 1). The phenyl selenoglucoside **4**[12] was synthesized in the same way, as described previously.

We first studied photochemical glycosylation with a model system with a methyl ether–protected phenyl selenogalactoside **1** as glycosyl donor and isopropanol **5** as acceptor. Using a mixture of acetonitrile, dichloromethane, and toluene as solvent, 1.5 equiv. of the sensitizer NMQ-PF_6, and 2 equiv. of the acceptor alcohol **2**, in air, under light irradiation (350 nm) after 2 h 20 min, we were able to isolate the glycosides **6** (54%) and the hemiacetal **7** (40%), which presumably arose from hydrolysis (Table 1, entry 1). In control

Table 1: Optimization of the reaction conditions



Entry	Solvent	NMQ-PF_6 (equiv.)	Atmosphere	Time	Outcome
1	MeCN/CH_2Cl_2/PhMe, 2:4:1	1.5	Air	2 h 20 min	**6** (1:1.6)[a]/54%; **7**/40%[b]
2[c]	MeCN/CH_2Cl_2/PhMe, 2:4:1	1.5	Air	>48 h	No reaction
3	MeCN/CH_2Cl_2/PhMe, 2:4:1	0	Air	2 h 20 min	Very little reaction
4	MeCN/CH_2Cl_2/PhMe, 2:4:1	1.5	Argon	1 h 30 min	Very little reaction
5	MeCN/PhMe, 5:2	0.3	Air	2 h	**6** (1:1.8)[a] :**7**, 2.0:1[d]
6[e]	MeCN/PhMe, 5:2	0.3	Air	3 h	**1**:**6** (1:1.9)[a] :**7**, 2.7:1.6:1[d]
7[f]	MeCN/PhMe, 5:2	0.3	Air	3 h	**6** (1:1.8)[a] :**7**, 2.3:1[d]

Reaction between selenoglycoside donor **1** and isopropanol **5** (2 equiv.), carried out in Pyrex flasks. Irradiation at 350 nm.
[a]α/β ratio, measured by integration of ^{1}H NMR spectra.
[b]Isolated yields.
[c]Reaction carried out in the dark.
[d]Ratio of products from integration of crude ^{1}H NMR spectra. Generally, only the glycosides **6**, the hemiacetal **7**, and Ph_2Se_2 are visible in the crude NMR spectra (the salt NMQ-PF_6 is insoluble in $CDCl_3$).
[e]Reaction carried out with molecular sieves 4 Å powder.
[f]Reaction carried out with molecular sieves 4 Å balls.

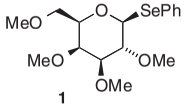
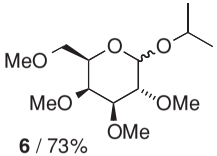
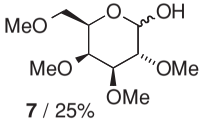
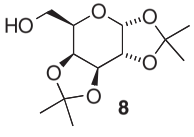
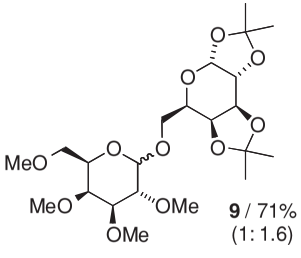
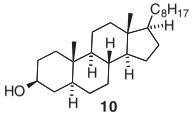
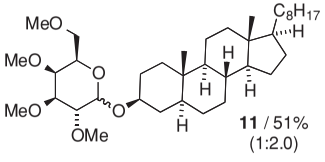
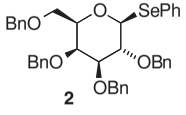
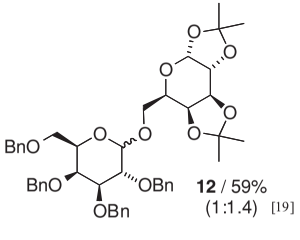
experiments, running the same reaction in the dark resulted in no reaction after 48 h (Table 1, entry 2), and running the reaction without the sensitizer NMQ-PF_6 gave mostly (>90%) starting material after 2 h 20 min, although some decomposition products and traces of hemiacetal **7** and glycosides **6** were visible in the crude ^{1}H NMR spectrum (Table 1, entry 3). This is consistent with the anticipated mechanism for the glycosylation reaction involving the photochemical activation of the sensitizer salt and subsequent activation of the selenoglycoside as a donor by single-electron transfer. The yellow by-product from the glycosylation reaction was confirmed to be diphenyl diselenide by LC-APCI mass spectrometry, which showed peaks with a mass isotope distribution consistent with $[Ph_2Se_2H]^+$ and with an identical LC trace to authentic Ph_2Se_2.

When the reaction was run under Ar rather than air, very little reaction was seen after 1 h 30 min (Table 1, entry 4), which suggests that oxygen is necessary for the reaction. This prompted us to test using a catalytic quantity of the photosensitizer. It has been shown that catalytic NMQ-PF_6 in combination with oxygen can be used as a photooxidant, where the oxygen reoxidizes the reduced NMQ radical.[10] Indeed, running the reaction under these conditions (0.3 equiv. NMQ-PF_6) resulted in complete conversion of the selenoglycoside **1** into a mixture of glycosides **6** and hemiacetal **7** after 2 h (Table 1, entry 5). Carrying out the reaction in dichloromethane and acetonitrile without toluene gave a somewhat slower reaction (5 h was needed for the disappearance of donor **1**), which is consistent with toluene's proposed role as a cosensitizer.[14] Acetonitrile is needed as cosolvent as the sensitizer NMQ-PF_6 is insoluble in toluene (and many other solvents).

The major or exclusive by-product in these glycosylation reactions was the hemiacetal **7**,[15] presumably resulting from hydrolysis. We passed the air atmosphere used in the reaction through a column of $CaCl_2$ as standard procedure, in an attempt to dry it, but in fact this had little effect on the ratio of glycosides **6** to hemiacetal **7** formed. It seems likely that one source of water is from the reduction of the molecular oxygen that is necessary for the reaction; that is, that water is produced in the reaction. When we added powdered sieves (4 Å), we saw a significantly slower reaction, presumably due to the increased light scattering and failure of the light to reach the photosensitizer (Table 1, entry 6). Ball sieves (4 Å) did not have a significantly deleterious effect on the reaction rate and did give a marginal improvement in the ratio of glycoside to hydrolysis product seen by crude ^{1}H NMR spectroscopy (Table 1, entry 7).

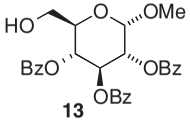
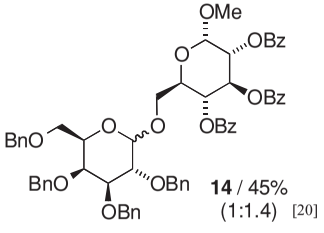
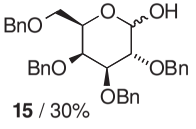
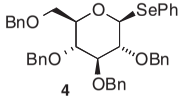
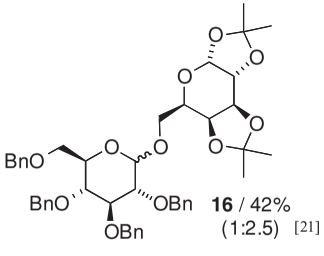
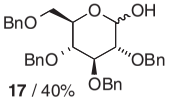
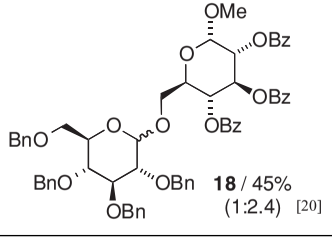
We went on to examine the scope of the reaction with other glycosyl donors and acceptors. The results are given in Table 2. Significantly, benzyl ether–protected *galacto* **2-** and *gluco* **4**-configured selenoglycosides could be used as donors without any cleavage of the benzyl ethers or other side

Table 2: Reactions carried out with 3 equiv. alcohol, 0.3 equiv. NMQ-PF_6, in MeCN-toluene 5:2 in Pyrex flasks with irradiation at 350 nm

Entry	Donor	Acceptor	Glycosides/ yield[a] (α/β)[b]	Hemiacetal/ yield[a]
1[c]	 **1**	 **5**	 **6** / 73% (1:1.6)	 **7** / 25%
2	**1**	 **8**	 **9** / 71% (1: 1.6)	**7**/26%
3[d]	**1**	 **10**	 **11** / 51% (1:2.0)	Not isolated
4	 **2**	**8**	 **12** / 59% (1:1.4) [19]	Not isolated

(Continued on next page)

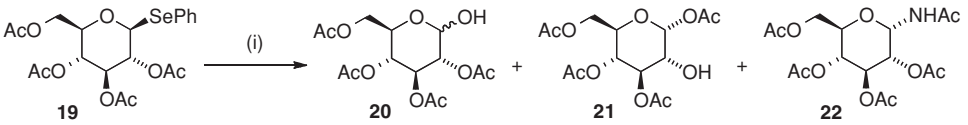
Table 2: Reactions carried out with 3 equiv. alcohol, 0.3 equiv. NMQ-PF_6, in MeCN-toluene 5:2 in Pyrex flasks with irradiation at 350 nm *(Continued)*

Entry	Donor	Acceptor	Glycosides/ yield[a] (α/β)[b]	Hemiacetal/ yield[a]
5	**2**	 **13**	 **14** / 45% (1:1.4) [20]	 **15** / 30%
6	 **4**	**8**	 **16** / 42% (1:2.5) [21]	 **17** / 40%
7	**4**	**13**	 **18** / 45% (1:2.4) [20]	**17**/47%

[a]Isolated yields.
[b]From integration of ^{1}H NMR spectra.
[c]Used 4 equiv. alcohol.
[d]Used an MeCN-toluene 1:2 solvent mixture.

reactions being observed. This represents a step forward in photochemical glycosylation as previously only methyl ethers have been used, and these can be rather difficult to deprotect, limiting the synthetic utility of any method relying on their use. Benzoate esters on the acceptor were also unaffected. We were able to synthesize (1→6)-linked disaccharides **9**, **12**, **14**, **16**, and **18** and a carbohydrate–steroid conjugate **11** uneventfully. Again, significant quantities of the hemiacetals **7**,[15] **15**,[16] and **17**[17] derived from the glycosyl donors were formed as by-products. The glycosidic α/β ratios favored the β-configured products in all cases to a greater or lesser extent, a phenomenon that may be explained by the presence of acetonitrile as cosolvent,[18] but the diastereoselectivity was only modest in all cases.

Attempted glycosylation of secondary carbohydrate alcohols with donor **2** gave worse results. Disaccharides were clearly formed, as shown by mass spectrometry, but they were not obtained pure from other by-products. Activation of an acetate-protected selenoglycoside **19** with diacetone galactose **8** as acceptor under the conditions of Table 2 gave a very slow reaction, requiring many hours for the donor **19** to be completely consumed, as would be expected from the armed–disarmed principle (and implying reversible oxidation of the selenoglycoside). Possibly surprisingly though, in this case no glycoside and only hydrolysis products **20**,[17,22] **21**,[23] and **22**[24] were formed (Sch. 2).



Scheme 2: (i) **8** (3 equiv.), NMQ-PF_6 (0.3 equiv.), MeCN–toluene 5:2, air, hν 350 nm; **20** + **21**: 70%; **22**: 16%.

Thioglycosides were also briefly examined as donors and gave inferior results. A benzyl ether–protected thioglycoside donor **23** (Fig. 1) was activated slowly and gave some disaccharide along with other by-products. A benzoate-protected thioglycoside **24** failed to react under the conditions.

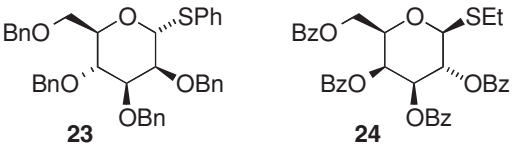


Figure 1: Thioglycosides tested as donors.

CONCLUSIONS

Benzyl ether–protected or methyl ether–protected selenophenyl glycosides can be used as donors in photochemical glycosylation reactions using *N*-methylquinolinium hexafluorophosphate as photosensitizer. The reactions use a catalytic amount of the photosensitizer and require oxygen or air for a stoichiometric oxidant. The major by-products in these reactions are the donor-derived hemiacetals.

EXPERIMENTAL

General Methods

Melting points were measured using a Büchi B-540 melting point apparatus and are uncorrected. Proton nuclear magnetic resonance (^{1}H) spectra were recorded on Bruker Avance 500 (500 MHz) or Bruker Avance 300 (300 MHz) spectrometers; multiplicities are quoted as singlet (s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), triplet (t), apparent triplet (at), quartet (q), and multiplet (m). Carbon nuclear magnetic resonance (^{13}C) spectra were recorded on Bruker Avance 500 (125 MHz) or Bruker Avance 300 (75 MHz) spectrometers. Selenium nuclear magnetic resonance (^{77}Se) spectra were recorded on a Bruker Avance 500 (95 MHz) spectrometer. ^{1}H and ^{13}C spectra and ^{13}C multiplicities were assigned using COSY, HSQC, and DEPT experiments. All chemical shifts are quoted on the δ-scale in parts per million (ppm). Residual solvent signals ($CHCl_3$, 7.26) were used as an internal reference. In disaccharides, the descriptors ^{I} and ^{II} refer to the monosaccharide residues numbered starting from the reducing terminus. In compounds that were isolated as α/β mixtures, the descriptors $_{\alpha}$ and $_{\beta}$ refer to the anomeric configuration of the newly formed glycosidic bond (in disaccharides this means the configuration of monosaccharide II). Coupling constants to selenium quoted in ^{1}H and ^{13}C NMR spectra were measured from the satellite peaks in the respective spectra. Low- and high-resolution (HRESIMS) electrospray (ESI) mass spectra were recorded using a Waters Micromass LCT premier XE instrument or using the mass spectrometry service of the ICSN. Optical rotations were measured on a Jasco P1010 polarimeter with a path length of 1 dm; concentrations are given in g/100 mL. Microanalysis was carried out by the microanalysis service of the ICSN. Thin layer chromatography (TLC) was carried out on Merck Kieselgel sheets, precoated with $60F_{254}$ silica. Plates were visualized with UV light and developed using 10% sulfuric acid. Flash column chromatography was carried out on prepacked silica columns (Chromabond, RediSep, PuriFlash, or SuperFlash). Photochemical experiments were carried out using a Rayonet photochemical reactor equipped with 350-nm tubes. Anhydrous solvents were bought and used as supplied.

N-Methylquinolinium hexafluorophosphate was prepared by methylation of quinoline with methyl iodide followed by anion exchange and recrystallization from water according to the literature procedure.[8] It was dried under vacuum over P_2O_5 before use.

General Procedure for Photochemical Glycosylation

The selenoglycoside (0.074–0.21 mmol), the alcohol (3 equiv), and NMQ-PF_6 (0.3 equiv.) were dissolved in toluene (0.2 mL) and acetonitrile (0.5 mL) in a flame-dried Pyrex flask (25 mL). Freshly activated molecular sieves (9 balls, 4 Å) were added. The reaction vessel was sealed and purged several times with air that was dried by passing through a column of $CaCl_2$. The reaction vessel was suspended in the Rayonet photoreactor and irradiated (350 nm) for the stated time. The temperature was maintained close to rt by passing a stream of air through the photoreactor around the flask. When TLC showed complete consumption of the selenoglycoside, silica gel was added, the mixture was concentrated in vacuo, and the residue purified by flash column chromatography.

Phenyl 2,3,4,6-Tetra-*O*-methyl-1-seleno-β-D-galactopyranoside 1

Sodium (40 mg, 1.7 mmol) was added to MeOH (30 mL). Phenyl 2,3,4,6-tetra-*O*-acetyl-1-seleno-β-D-galactopyranoside **3** (6.87 g, 14.1 mmol) was added to the resulting methoxide solution, and the mixture was stirred at rt. After 45 min, TLC (EtOAc) showed the presence of a single component (R_f 0.1). AcOH (2 mL) was added, and the mixture was concentrated in vacuo.

The residue was dissolved in DMF (40 mL) and cooled to 0°C under Ar. NaH (60% in oil, 3.38 g, 85 mmol) was washed with heptane and then added to the reaction mixture. MeI (4.8 mL, 78 mmol) was added, and the mixture was stirred at rt. After 1 h, TLC (heptane–EtOAc, 1:1) showed the presence of a single component (R_f 0.2). The reaction was quenched with MeOH (*ca* 6 mL) and then concentrated in vacuo. The residue was partitioned between EtOAc (100 mL) and a mixture of water (100 mL) and brine (100 mL). The aqueous phase was re-extracted with EtOAc (3 × 100 mL), and the combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (40 g silica, heptane–EtOAc, 10:1 → 2:1) to give the tetramethyl selenogalactoside **1** (4.26 g, 81%) as a colorless oil that crystallized on standing. Recrystallization gave white crystals, m.p. 61–62°C (heptane); $[\alpha]_D^{25}$ –33.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 3.18 (1H, dd, $J_{3,4} = 2.8$ Hz, $J_{2,3} = 9.1$ Hz, H-3), 3.36, 3.52, 3.55, 3.56 (12H, 4 × s, 4 × OCH_3), 3.44–3.49 (2H, m, H-2, H-5), 3.53 (1H, m (obs), H-6), 3.59 (1H, at, $J = 8.5$ Hz, H-6′), 3.69 (1H, d, $J_{3,4} = 2.8$ Hz, H-4), 4.69 (1H, d, $J_{1,2} = 9.8$ Hz, $^2J_{H1,Se} = 12.0$ Hz, H-1), 7.24–7.65 (5H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 58.3, 59.3, 61.2, 61.4 (4 × q, 4 × OCH_3), 70.7 (t, C-6), 75.1 (d, C-4),

78.2 (d, C-5), 80.1 (d, C-2), 84.1 (d, $^1J_{C1,Se}$ = 87.1 Hz, C-1), 86.1 (d, C-3), 127.6, 129.0, 134.2 (3 × d, Ar-CH), 129.4 (s, Ar-C); ^{77}Se NMR (95 MHz, $CDCl_3$) δ_{Se} 421; *m*/*z* (ES^+) 394 ($M+NH_4^+$, 100%); HRMS calcd for $C_{16}H_{28}O_5NSe$ (MNH_4^+) 394.1127; found 394.1142. Anal calcd for $C_{16}H_{24}O_5Se$: C, 51.22; H, 6.45; found: C, 51.22; H, 6.41%.

Phenyl 2,3,4,6-Tetra-*O*-benzyl-1-seleno-β-D-galactopyranoside 2

Sodium (20 mg, 0.87 mmol) was added to MeOH (10 mL). Phenyl 2,3,4,6-tetra-*O*-acetyl-1-seleno-β-D-galactopyranoside **3** (2.10 g, 4.3 mmol) was added to the resulting methoxide solution, and the mixture was stirred at rt. After 1 h 30 min, TLC (EtOAc) showed the presence of a single component (R_f 0.1). The mixture was concentrated in vacuo.

The residue was dissolved in DMF (20 mL) and cooled to 0°C under Ar. NaH (60% in oil, 1.20 g, 30 mmol) was washed with heptane and then added to the reaction mixture. BnBr (3.15 mL, 26 mmol) was added, and the mixture was allowed to warm to rt in the ice–water bath. After 13 h, the reaction was quenched with MeOH (*ca* 6 mL) and then concentrated in vacuo. The residue was partitioned between EtOAc (100 mL) and water (100 mL). The organic phase was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (25 g silica, heptane–EtOAc, 20:1 → 2:1) to give the tetrabenzyl selenogalactoside **2** (2.07 g, 71%) as a pale yellow oil. Recrystallization gave white crystals, m.p. 89–91°C (Et_2O–heptane); $[\alpha]_D^{25}$ –9.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 3.59–3.62 (2H, m, H-3, H-5), 3.66–3.68 (2H, m, H-6, H-6′), 3.97 (1H, at, J = 9.5 Hz, H-2), 4.01 (1H, d, $J_{3,4}$ = 2.2 Hz, H-4), 4.44, 4.49 (2H, 2 × d, PhC$\underline{H}_2$), 4.60, 4.97 (2H, 2 × d, PhC$\underline{H}_2$), 4.70–4.78 (4H, m, 2 × PhC$\underline{H}_2$), 4.85 (1H, d, $J_{1,2}$ = 9.8 Hz, $^2J_{H1,Se}$ = 14.7 Hz, H-1), 7.13–7.68 (25H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 68.8 (t, C-6), 72.8, 73.7, 74.6, 75.6 (4 × t, 4 × Ph$\underline{C}H_2$), 73.9 (d, C-4), 78.0 (d, C-2), 78.5, 84.4 (2 × d, C-3, C-5), 83.8 (d, C-1), 127.5, 127.6, 127.7, 127.8, 127.9, 127.9, 128.1, 128.3, 128.4, 128.5, 128.6, 129.0 (12 × d, Ar-CH), 129.4 (s, Ar-C), 134.0 (d, Ar-CH), 138.0, 138.4, 138.4, 139.0 (4 × s, 4 × Ar-C); ^{77}Se NMR (95 MHz, $CDCl_3$) δ_{Se} 418; *m*/*z* (ES^+) 698 ($M+NH_4^+$, 100%); HRMS calcd for $C_{40}H_{44}O_5NSe$ (MNH_4^+) 698.2385; found 698.2413. Anal calcd for $C_{40}H_{40}O_5Se$: C, 70.68; H, 5.93; found: C, 70.80; H, 6.15%.

Isopropyl 2,3,4,6-Tetra-*O*-methyl-α,β-D-galactopyranoside 6

Synthesized according to the general procedure from tetramethyl *galacto* donor **1** (80 mg, 0.21 mmol) and isopropanol (60 μL, 0.81 mmol) with NMQ-PF_6 (20 mg, 0.07 mmol) in toluene (0.4 mL) and acetonitrile (1 mL). Purification by flash column chromatography (4 g silica, heptane–EtOAc, 10:1 → 2:1 → 0:1) gave the glycosides **6** (43 mg, 75%) as a colorless oil (α:β 1:1.6); ^{1}H NMR

(500 MHz, $CDCl_3$) δ_H 1.17 (6H, d, $J = 6.1$ Hz, $CH(C\underline{H}_3)CH_{3\alpha,\beta}$), 1.22 (6H, d, $J = 6.1$ Hz, $CH(CH_3)C\underline{H}_{3\alpha,\beta}$), 3.38, 3.47, 3.50, 3.56 (12H, 4 × s, 4 × $OCH_{3\alpha}$), 3.38, 3.51, 3.54, 3.57 (12H, 4 × s, 4 × $OCH_{3\beta}$), 3.43–3.62 (m), 3.69 (1H, m, H-4_α), 3.90–3.95 (3H, m, 2 × H_α, H_β), 4.26 (1H, d, $J_{1,2} = 7.6$ Hz, H-1_β), 5.06 (1H, d, $J_{1,2} = 3.7$ Hz, H-1_α), 3.09 (1H, dd, $J_{3,4} = 2.9$ Hz, $J_{2,3} = 9.6$ Hz, H-3_β), 3.27 (1H, at, $J = 8.7$ Hz, H-2_β); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 21.3, 23.3 (2 × q, $CH(\underline{C}H_3)_{2\alpha}$), 22.0, 23.7 (2 × q, $CH(\underline{C}H_3)_{2\beta}$), 58.1, 58.4, 59.3, 61.4 (4 × q, 4 × $OCH_{3\alpha}$), 58.6, 60.9, 61.4 (3 × q, 4 × $OCH_{3\beta}$), 68.9, 69.2, 77.7, 80.2 (4 × d, C-2_α, C-3_α, C-5_α, $\underline{C}H(CH_3)_{2\alpha}$), 71.0 (t, C-$6_\beta$), 71.3 (t, C-$6_\alpha$), 72.0 (d, $\underline{C}H(CH_3)_{2\beta}$), 73.1 (d, C-$5_\beta$), 75.1 (d, C-$4_\beta$), 76.1 (d, C-$4_\alpha$), 80.9 (d, C-$2_\beta$), 84.0 (d, C-$3_\beta$), 94.7 (d, C-$1_\alpha$), 102.4 (d, C-$1_\beta$); *m/z* ($ES^+$) 579 ($2M+Na^+$, 35), 301 ($M+Na^+$, 100%); HRMS calcd for $C_{13}H_{26}O_6Na$ (MNa^+) 301.1627; found 301.1617.

And the hemiacetal 2,3,4,6-tetra-*O*-methyl-D-galactopyranose **7** (13 mg, 25%) as a colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ_H 3.17 (1H, dd, $J_{2,3} = 9.7$ Hz, $J_{3,4} = 3.0$ Hz, H-3_β), 3.28 (1H, dd, $J_{1,2} = 7.4$ Hz, $J_{2,3} = 9.7$ Hz, H-2_β), 3.39–3.65 (32H, m, 8 × OCH_3, H-4_β, H-5_β, H-6_β, H-$6'_\beta$, H-2_α, H-3_α, H-6_α, H-$6'_\alpha$), 3.70 (1H, d, $J_{3,4} = 1.9$ Hz, H-4_α), 4.12 (1H, at, $J = 6.5$ Hz, H-5_α) 4.55 (1H, d, $J_{1,2} = 7.2$ Hz, H-1_β), 5.39 (1H, d, $J_{1,2} = 3.5$ Hz, H-1_α); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 58.2, 59.0, 59.3, 61.4 (4 × q, 4 × $OCH_{3\alpha}$), 58.4, 61.0 (2 × q, $OCH_{3\beta}$), 69.3 (d, C-5_α), 71.2 (t, C-6_β), 71.5 (t, C-6_α), 73.5 (d, C-5_β), 75.2 (d, C-4_β), 76.1 (d, C-4_α), 78.2 (d, C-2_α), 80.2 (d, C-3_α), 82.2 (d, C-2_β), 84.1 (d, C-3_β), 91.2 (d, C-1_α), 97.7 (d, C-1_β); *m/z* (ES^+) 275 ($M+K^+$, 25), 259 ($M+Na^+$, 95), 254 ($M+NH_4^+$, 100%); HRMS calcd for $C_{10}H_{20}O_6Na$ (MNa^+) 259.1158; found 259.1151.

2,3,4,6-Tetra-*O*-methyl-α,β-D-galactopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose 9

Synthesized according to the general procedure from tetramethyl *galacto* donor **1** (60 mg, 0.16 mmol) and diacetone galactose **8** (125 mg, 0.48 mmol) with NMQ-PF_6 (14 mg, 0.05 mmol) in toluene (0.2 mL) and acetonitrile (0.5 mL). Purification by flash column chromatography (4 g silica, heptane–EtOAc, 10:1 → 2:1 → 1:10) gave the recovered nucleophile **8** (90 mg), then the glycosides **9** (54 mg, 71%) as a colorless oil (α:β 1:1.6); ^1H NMR (500 MHz, $CDCl_3$) δ_H 1.30, 1.41, 1.42, 1.47, 1.50 (24H, 5 × s, 4 × $C(CH_3)_2$), 3.10 (1H, dd, $J_{2,3} = 9.8$ Hz, $J_{3,4} = 3.2$ Hz, H-3^{II}_β), 3.30 (1H, dd, $J_{2,3} = 9.8$ Hz, $J_{1,2} = 7.8$ Hz, H-2^{II}_β), 3.37–3.71 (m), 3.79 (1H, dd, $J_{5,6} = 6.6$ Hz, $J_{6,6'} = 10.7$ Hz, H-6_α), 3.94 (1H, at, $J = 6.6$ Hz), 3.99–4.02 (2H, m), 4.05 (1H, dd, $J_{5,6} = 3.5$ Hz, $J_{6,6'} = 10.7$ Hz, H-6_β), 4.20 (1H, dd, $J_{3,4} = 7.9$ Hz, $J_{4,5} = 1.6$ Hz, H-4^I_β), 4.26–4.30 (4H, m, H-2^I_α, H-2^I_β, H-4^I_α, H-1^{II}_β), 4.55–4.59 (2H, m, H-3^I_α, H-3^I_β), 5.03 (1H, d, $J_{1,2} = 3.5$ Hz, H-1^{II}_α), 5.49–5.51 (2H, m, H-1^I_α, H-1^I_β); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 24.5, 24.6, 25.0, 25.2, 26.1, 26.1, 26.1 (7 × q, 4 × $C(\underline{C}H_3)_2$), 58.0, 58.1, 58.5, 59.2, 59.3, 60.8, 61.3, 61.4 (8 × q, 8 × OCH_3), 65.9, 67.8, 68.9, 70.7, 70.8, 70.9, 70.9, 71.6, 72.9, 74.9, 75.8, 77.7, 79.9 (13 × d, C-2^I_α, C-2^I_β, C-3^I_α, C-3^I_β, C-4^I_α, C-4^I_β,

C-5$^{I}_{\alpha}$, C-5$^{I}_{\beta}$, C-2$^{II}_{\alpha}$, C-3$^{II}_{\alpha}$, C-4$^{II}_{\alpha}$, C-4$^{II}_{\beta}$, C-5$^{II}_{\alpha}$, C-5$^{II}_{\beta}$), 66.5, 69.3, 70.8, 71.0 (4 × t, C-6$^{I}_{\alpha}$, C-6$^{I}_{\beta}$, C-6$^{II}_{\alpha}$, C-6$^{II}_{\beta}$), 80.7 (d, C-2$^{II}_{\beta}$), 83.5 (d, C-3$^{II}_{\beta}$), 96.4, 96.4, 96.8 (3 × d, C-1$^{I}_{\alpha}$, C-1$^{I}_{\beta}$, C-1$^{II}_{\alpha}$), 104.4 (d, C-1$^{II}_{\beta}$), 108.6, 108.7, 109.3, 109.4 (4 × s, 4 × $\underline{C}(CH_3)_2$); *m/z* (ES$^+$) 501 (M+Na$^+$, 27), 496 (M+NH$_4^+$, 100%); HRMS calcd for $C_{22}H_{38}O_{11}Na$ (MNa$^+$) 501.2312; found 501.2305.

And then the hemiacetal **7** (13 mg, 25%) as a colorless oil.

Cholestan-3β-yl 2,3,4,6-Tetra-*O*-methyl-α,β-D-galactopyranoside 11

Synthesized according to the general procedure from tetramethyl *galacto* donor **1** (60 mg, 0.16 mmol) and cholestanol **10** (186 mg, 0.48 mmol) with NMQ-PF_6 (14 mg, 0.05 mmol) in toluene (2 mL) and acetonitrile (1 mL). Purification by flash column chromatography (4 g silica, heptane–EtOAc, 10:1 → 2:1 → 0:1) gave the recovered alcohol **10** (142 mg) as a white solid, then the glycosides **11** (49 mg, 51%) as a white solid (α:β 1:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.59–1.56 (92H, m, steroid-H), 3.09 (1H, dd, $J_{2,3}$ = 9.8 Hz, $J_{3,4}$ = 2.8 Hz, H-3$_\beta$), 3.28 (1H, dd, $J_{1,2}$ = 7.6 Hz, $J_{2,3}$ = 9.8 Hz, H-2$_\beta$), 3.39–3.62 (34H, m, 2 × steroid-OCH, 8 × OCH_3, H-4$_\beta$, H-5$_\beta$, H-6$_\beta$, H-6′$_\beta$, H-2$_\alpha$, H-3$_\alpha$, H-6$_\alpha$, H-6′$_\alpha$), 3.69 (1H, d, $J_{3,4}$ = 1.6 Hz, H-4$_\alpha$), 3.95 (1H, at, J = 6.6 Hz, H-5$_\alpha$), 4.31 (1H, d, $J_{1,2}$ = 7.6 Hz, H-1$_\beta$), 5.10 (1H, d, $J_{1,2}$ = 3.5 Hz, H-1$_\alpha$); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 12.2, 12.4, 12.5, 18.8, 22.7, 23.0, 28.2, 35.7, 35.9, 45.0, 45.3, 54.5, 54.6, 56.5, 56.6, 56.7 (16 × d, q, steroid-CH and steroid-CH_3), 21.4, 24.0, 24.4, 27.6, 28.4, 28.9, 29.0, 29.7, 32.2, 32.3, 34.7, 36.0, 36.3, 37.0, 37.2, 39.7, 40.2, 40.2 (18 × t, steroid-CH_2), 58.0, 58.3, 58.6, 59.3, 59.3, 60.9, 61.3, 61.4 (8 × q, 8 × OCH_3), 68.9 (d, C-5$_\alpha$), 71.0 (t, C-6$_\beta$), 71.3 (t, C-6$_\alpha$), 73.0, 75.1, 78.9 (3 × d, C-4$_\beta$, C-5$_\beta$, steroid-OCH_β), 76.1, 76.5, 77.7, 80.2 (4 × d, C-2$_\alpha$, C-3$_\alpha$, C-4$_\alpha$, steroid-OCH_α), 80.9 (d, C-2$_\beta$), 84.0 (d, C-3$_\beta$), 94.8 (d, C-1$_\alpha$), 102.3 (d, C-1$_\beta$); *m/z* (ES$^+$) 629 (M+Na$^+$, 21), 624 (M+NH$_4^+$, 100%); HRMS calcd for $C_{37}H_{66}O_6Na$ (MNa$^+$) 629.4757; found 629.4748.

2,3,4,6-Tetra-*O*-benzyl-α,β-D-galactopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose 12[19]

Synthesized according to the general procedure from tetrabenzyl *galacto* donor **2** (109 mg, 0.16 mmol) and diacetone galactose **8** (125 mg, 0.48 mmol) with NMQ-PF_6 (14 mg, 0.044 mmol) in toluene (0.2 mL) and acetonitrile (0.5 mL). Purification by flash column chromatography (4 g silica, heptane–EtOAc, 10:1 → 5:1) gave the glycosides **12** (74 mg, 59%) as a colorless oil (α:β 1:1.4); ^{1}H NMR (300 MHz, $CDCl_3$) 1.32, 1.33, 1.34, 1.45, 1.46, 1.51, 1.54 (24H, 7 × s, 4 × $C(CH_3)_2$), 3.52–3.63 (6H, m, 2 × H-6, 2 × H-6′), 3.72 (1H, dd, $J_{6,6'}$ = 10.7 Hz, $J_{5,6}$ = 7.3 Hz, H-6), 3.76 (1H, dd, $J_{6,6'}$ = 10.4 Hz, $J_{5,6}$ = 7.3 Hz, H-6), 3.81 (1H, dd, $J_{6,6'}$ = 10.4 Hz, $J_{5,6'}$ = 6.3 Hz, H-6′), 3.85 (1H, dd,

J = 7.9 Hz, J = 9.8 Hz), 3.90 (1H, d, J = 2.2 Hz), 3.98 (1H, dd, J = 10.1 Hz, J = 2.8 Hz), 4.02 (1H, d, J = 1.6 Hz), 4.04–4.11 (4H, m), 4.15 (1H, dd, $J_{5,6'}$ = 3.5 Hz, $J_{6,6'}$ = 10.7 Hz, H-6′), 4.23 (1H, dd, J = 1.9 Hz, J = 7.9 Hz), 4.31–4.35 (3H, m, H-2^{I}_{α}, H-2^{I}_{β}), 4.41–4.51 (5H, m, H-1^{II}_{β}, 2 × PhC$\underline{H}_2$), 4.58–4.64 (4H, m, 2 × PhC$\underline{H}$H′), 4.72–4.87 (7H, m, 3 × PhC$\underline{H}_2$, PhC$\underline{H}$H′), 4.93–4.97 (2H, m, 2 × PhCH$\underline{H}$′), 5.03 (1H, d, $J_{1,2}$ = 3.8 Hz, H-1^{II}_{α}), 5.07 (1H, d, J = 11.0 Hz, PhCH$\underline{H}$′), 5.53 (1H, d, $J_{1,2}$ = 5.0 Hz, H-1^{I}_{α}), 5.58 (1H, d, $J_{1,2}$ = 4.7 Hz, H-1^{I}_{β}), 7.26–7.48 (40H, m, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 24.6, 24.7, 25.1, 25.2, 26.1, 26.2, 26.3 (7 × q, 4 × C($\underline{C}H_3$)$_2$), 66.0, 67.5, 69.3, 70.6, 70.8, 70.8, 70.9, 71.0, 71.6, 73.4, 73.7, 75.1, 76.6, 79.1, 79.2, 82.0 (16 × d, C-2^{I}_{α}, C-3^{I}_{α}, C-4^{I}_{α}, C-5^{I}_{α}, C-2^{II}_{α}, C-3^{II}_{α}, C-4^{II}_{α}, C-5^{II}_{α}, C-2^{I}_{β}, C-3^{I}_{β}, C-4^{I}_{β}, C-5^{II}_{β}, C-2^{II}_{β}, C-3^{II}_{β}, C-4^{II}_{β}, C-5^{II}_{β}), 66.5, 68.8, 68.8, 69.7 (4 × t, C-6^{I}_{α}, C-6^{II}_{α}, C-6^{I}_{β}, C-6^{II}_{β}), 72.8, 73.2, 73.3, 73.5, 73.6, 74.6, 74.9, 74.9 (8 × t, 8 × Ph$\underline{C}H_2$), 96.4, 96.5 (2 × d, C-1^{I}_{α}, C-1^{I}_{β}), 97.7 (d, C-1^{II}_{α}), 104.8 (d, C-1^{II}_{β}), 108.6, 108.7, 109.3, 109.4 (4 × s, 4 × $\underline{C}(CH_3)_2$), 127.4, 127.5, 127.5, 127.6, 127.6, 127.6, 127.8, 127.8, 127.9, 127.9, 128.0, 128.2, 128.2, 128.3, 128.3, 128.3, 128.4, 128.5, 128.5, 128.7 (20 × d, Ar-CH), 138.1, 138.2, 138.8, 138.8, 138.9, 138.9, 139.1, 139.2 (8 × s, Ar-C); m/z (ES^+) 800 ($M+NH_4^+$, 100%); HRMS calcd for $C_{46}H_{58}O_{11}N$ (MNH_4^+) 800.4010; found 800.4015.

Then a mixture of the hemiacetal **15** and unreacted alcohol **8** (127 mg).

Methyl 2,3,4,6-Tetra-*O*-benzyl-α,β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside 14[20]

Synthesized according to the general procedure from tetrabenzyl *galacto* donor **2** (50 mg, 0.074 mmol) and *gluco* acceptor **13** (112 mg, 0.22 mmol) with NMQ-PF_6 (7 mg, 0.022 mmol) in toluene (0.2 mL) and acetonitrile (0.5 mL). Purification by flash column chromatography (4 g silica, heptane–EtOAc, 6:1 → 2:1) gave the glycosides **14** (34 mg, 45%) as a colorless oil (α:β 1:1.4); ^{1}H NMR (500 MHz, $CDCl_3$) 3.35, 3.36 (6H, 2 × s, $OCH_{3\alpha}$, $OCH_{3\beta}$), 3.42–4.40 (18H, m, H-5^{I}_{α}, H-6^{I}_{α}, H-$6'^{I}_{\alpha}$, H-2^{II}_{α}, H-3^{II}_{α}, H-4^{II}_{α}, H-5^{II}_{α}, H-5^{I}_{β}, H-6^{I}_{β}, H-$6'^{I}_{\beta}$, H-2^{II}_{β}, H-3^{II}_{β}, H-4^{II}_{β}, H-5^{II}_{β}, H-6^{II}_{α}, H-$6'^{II}_{\alpha}$, H-6^{II}_{β}, H-$6'^{II}_{\beta}$), 4.44 (1H, d, $J_{1,2}$ = 7.6 Hz, H-1^{II}_{β}), 4.55–5.03 (17H, m, H-1^{II}_{α}, 8 × PhC$\underline{H}_2$), 5.16 (1H, d, $J_{1,2}$ = 3.7 Hz, H-1^{I}_{α}), 5.19 (1H, d, $J_{1,2}$ = 3.4 Hz, H-1^{I}_{β}), 5.21–5.27 (2H, m, H-2^{I}_{α}, H-2^{I}_{β}), 5.41 (1H, at, J = 9.9 Hz, H-4^{I}_{β}), 5.53 (1H, at, J = 9.9 Hz, H-4^{I}_{α}), 6.11–6.18 (2H, m, H-3^{I}_{α}, H-3^{I}_{β}), 7.20–8.00 (70H, m, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 55.6 (q, 2 × OCH_3), 66.7, 68.8, 68.8, 69.1 (4 × t, C-6^{I}_{α}, C-6^{II}_{α}, C-6^{I}_{β}, C-6^{II}_{β}), 68.6, 69.1, 69.4, 69.7, 70.1, 70.6, 70.8, 72.3, 73.5, 73.6, 75.2, 76.6, 78.7, 79.8, 82.2 (15 × d, C-2^{I}_{α}, C-3^{I}_{α}, C-4^{I}_{α}, C-5^{I}_{α}, C-2^{II}_{α}, C-3^{II}_{α}, C-4^{II}_{α}, C-5^{II}_{α}, C-2^{I}_{β}, C-3^{I}_{β}, C-4^{I}_{β}, C-5^{II}_{β}, C-2^{II}_{β}, C-3^{II}_{β}, C-4^{II}_{β}, C-5^{II}_{β}), 73.0, 73.2, 73.3, 73.3, 73.6, 74.6, 74.9, 75.3 (8 × t, 8 × Ph$\underline{C}H_2$), 96.8, 96.9 (2 × d, C-1^{I}_{α}, C-1^{I}_{β}), 98.0 (d, C-1^{II}_{α}), 104.4 (d, C-1^{II}_{β}), 127.6, 127.6, 127.7, 127.7, 127.7, 127.7, 127.8, 127.9, 128.0, 128.0,

128.3, 128.3, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.5 (20 × d, Ar-CH), 129.0, 129.2, 129.3, 129.3, 129.4, 129.5 (6 × s, 6 × Bz-C), 129.8, 129.8, 130.0, 130.0, 130.1, 133.2, 133.4, 133.5, 133.5 (9 × d, Ar-CH), 138.0, 138.3, 138.7, 138.8, 138.9, 139.0 (6 × d, Bn-C), 165.5, 165.7, 165.9, 165.9, 166.0 (5 × s, C = O); m/z (ES^+) 1051 ($M+Na^+$, 15), 1046 ($M+NH_4^+$, 100%); HRMS calcd for $C_{62}H_{60}O_{14}Na$ (MNa^+) 1051.3881; found 1051.3920.

And then the hemiacetal **15** (12 mg, 30%) as a colorless oil, and then the recovered alcohol **13** (93 mg) as a white solid.

2,3,4,6-Tetra-*O*-benzyl-α,β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose 16[21]

Synthesized according to the general procedure from tetrabenzyl *gluco* donor **4** (50 mg, 0.074 mmol) and diacetone galactose **8** (57 mg, 0.22 mmol) with NMQ-PF_6 (7 mg, 0.022 mmol) in toluene (0.2 mL) and acetonitrile (0.5 mL). Purification by flash column chromatography (4 g silica, heptane–EtOAc, 10:1 → 6:1) gave the glycosides **16** (24 mg, 42%) as a colorless oil (α:β 1:2.5); ^{1}H NMR (300 MHz, $CDCl_3$) 1.32, 1.46, 1.51, 1.54 (24H, 4 × s, 4 × $C(CH_3)_2$), 3.42–3.68 (m), 4.00 (1H, at, J = 9.2 Hz, H_β), 4.03–4.12 (2H, m, H_α, H_β), 4.17 (1H, dd, J = 3.8 Hz, J = 10.6 Hz, H_β) 4.25 (1H, dd, J = 1.9 Hz, J = 7.9 Hz, H_β), 4.31–4.34 (2H, m, H-2^I_α, H-2^I_β), 4.36 (1H, dd, J = 1.9 Hz, J = 7.9 Hz, H_α), 4.45–5.08 (m, H-1^{II}_α, H-1^{II}_β), 4.36 (1H, dd, J = 1.9 Hz, J = 7.9 Hz, H_α), 4.45–5.08 (m, H-1^{II}_α, H-1^{II}_β, 8 × PhC$\underline{H}_2$), 5.53 (d, $J_{1,2}$ = 5.1 Hz, H-1^I_α), 5.57 (d, $J_{1,2}$ = 4.9 Hz, H-1^I_β), 7.13–7.44 (40H, m, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 24.6, 25.2, 26.2, 26.2 (4 × q, 2 × C($\underline{C}H_3$)$_{2\beta}$), 24.8, 25.1, 26.2, 26.3 (4 × q, 2 × C($\underline{C}H_3$)$_{2\alpha}$), 65.8, 70.4, 70.8, 70.8, 71.0, 77.7, 80.0, 82.1 (8 × d, C-2^I_α, C-3^I_α, C-4^I_α, C-5^I_α, C-2^{II}_α, C-3^{II}_α, C-4^{II}_α, C-5^{II}_α), 66.4, 68.5 (2 × t, C-6^I_α, C-6^{II}_α), 67.5, 70.6, 70.9, 71.6, 74.9, 77.9, 81.8, 84.7 (8 × d, C-2^I_β, C-3^I_β, C-4^I_β, C-5^I_β, C-2^{II}_β, C-3^{II}_β, C-4^{II}_β, C-5^{II}_β), 68.9, 69.8 (2 × t, C-6^I_β, C-6^{II}_β), 72.5, 73.6, 75.1, 75.8 (4 × d, 4 × Ph$\underline{C}H_{2\alpha}$), 73.6, 74.5, 75.1, 75.8 (4 × d, 4 × Ph$\underline{C}H_{2\beta}$), 96.4 (d, C-1^I_α), 96.5 (d, C-1^I_β), 97.2 (d, C-1^{II}_α), 104.5 (d, C-1^{II}_β), 108.7, 109.3, 109.5 (4 × s, 4 × $\underline{C}(CH_3)_2$), 127.6, 127.7, 127.7, 127.8, 128.0, 128.0, 128.0, 128.1, 128.1, 128.3, 128.5, 128.8 (12 × d, Ar-CH), 138.3, 138.3, 138.5, 138.9, 139.1 (5 × s, Ar-C); m/z (ES^+) 800 ($M+NH_4^+$, 100%); HRMS calcd for $C_{46}H_{58}O_{11}N$ (MNH_4^+) 800.4010; found 800.3994.

And then the hemiacetal **17** (16 mg, 40%), and then the recovered alcohol **8** (46 mg).

Methyl 2,3,4,6-Tetra-*O*-benzyl-α,β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside 18[20]

Synthesized according to the general procedure from tetrabenzyl *gluco* donor **4** (50 mg, 0.074 mmol) and *gluco* acceptor **13** (112 mg, 0.22 mmol) with

NMQ-PF_6 (7 mg, 0.022 mmol) in toluene (0.2 mL) and acetonitrile (0.5 mL). Purification by flash column chromatography (4 g silica, heptane–EtOAc, 10:1 → 6:1) gave the glycosides **18** (34 mg, 45%) as a colorless oil (α:β 1:2.4); ^{1}H NMR (500 MHz, $CDCl_3$) 3.38 (3H, s, $OCH_{3\beta}$), 3.42–3.68 (14H, m, 2 × $H^{II}{}_\alpha$, 4 × $H^{II}{}_\beta$, 3 × H-6_α, 2 × H-6_β, $OCH_{3\alpha}$), 3.80–3.88 (3H, m, $H^{II}{}_\alpha$, H-6_α, H-6_β), 3.97 (1H, at, J = 9.1 Hz, $H^{II}{}_\alpha$), 4.12 (1H, d, J = 10.7 Hz, H-$6'_\beta$), 4.33 (1H, m, H-$5^I{}_\alpha$), 4.37–4.93 (11H, m, H-$1^{II}{}_\alpha$, H-$1^{II}{}_\beta$, H-$5^I{}_\beta$, 7 × PhC$\underline{H}_2$, PhC$\underline{H}H'_\beta$), 5.06 (1H, d, J = 10.7 Hz, PhCH$\underline{H}'_\beta$), 5.21–5.27 (4H, m, H-$1^I{}_\alpha$, H-$1^I{}_\beta$, H-$2^I{}_\alpha$, H-$2^I{}_\beta$), 5.48 (1H, at, J = 9.8 Hz, H-$4^I{}_\beta$), 5.53 (1H, at, J = 10.1 Hz, H-$4^I{}_\alpha$), 6.14 (1H, at, J = 9.5 Hz, H-$3^I{}_\alpha$), 6.18 (1H, at, J = 9.8 Hz, H-$3^I{}_\beta$), 7.13–7.99 (70H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 55.7, 55.7 (2 × q, 2 × OCH_3), 66.8, 68.5 (2 × t, C-$6^I{}_\alpha$, C-$6^{II}{}_\alpha$), 68.7 (d, C-$5^I{}_\alpha$), 68.8, 69.0 (2 × t, C-$6^I{}_\beta$, C-$6^{II}{}_\beta$), 69.2 (d, C-$5^I{}_\beta$), 69.8, 70.4, 70.8, 72.4, 77.7, 80.0, 81.9 (7 × d, C-$2^I{}_\alpha$, C-$3^I{}_\alpha$, C-$4^I{}_\alpha$, C-$2^{II}{}_\alpha$, C-$3^{II}{}_\alpha$, C-$4^{II}{}_\alpha$, C-$5^{II}{}_\alpha$), 70.1, 70.7, 72.3, 75.1, 77.8, 82.5, 84.7 (7 × d, C-$2^I{}_\beta$, C-$3^I{}_\beta$, C-$4^I{}_\beta$, C-$2^{II}{}_\beta$, C-$3^{II}{}_\beta$, C-$4^{II}{}_\beta$, C-$5^{II}{}_\beta$), 73.3, 73.6, 74.9, 75.6 (4 × t, 4 × Ph$\underline{C}H_{2\alpha}$), 73.6, 74.9, 75.1, 75.8 (4 × t, 4 × Ph$\underline{C}H_{2\beta}$), 96.9, 96.9 (2 × d, C-$1^I{}_\alpha$, C-$1^I{}_\beta$), 97.4 (d, C-$1^{II}{}_\alpha$), 104.2 (d, C-$1^{II}{}_\beta$), 127.6, 127.6, 127.7, 127.8, 127.8, 127.9, 127.9, 128.0, 128.0, 128.1, 128.1, 128.3, 128.4, 128.5, 128.5, 128.5, 128.5 (17 × d, Ar-CH), 129.1, 129.2, 129.2, 129.3, 129.4, 129.4 (6 × s, Bz-C), 129.8, 130.0, 130.1, 133.2, 133.5, 133.5 (6 × d, Bz-CH), 138.1, 138.3, 138.3, 138.6, 138.7, 138.8, 139.0 (7 × d, Bn-C), 165.4, 165.6, 165.9, 166.0 (4 × s, C = O); m/z (ES^+) 1046 ($M+NH_4^+$, 100%); HRMS calcd for $C_{62}H_{64}O_{14}N$ (MNH_4^+) 1046.4321; found 1046.4310.

Then the hemiacetal **17** (19 mg, 47%) as a white solid.

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