Synthesis, glycosylation and photolysis of photolabile 2-(2-nitrophenyl)-propyloxycarbonyl (NPPOC) protected glycopyranosides†

Hua Yi, Stéphane Maisonneuve and Juan Xie*

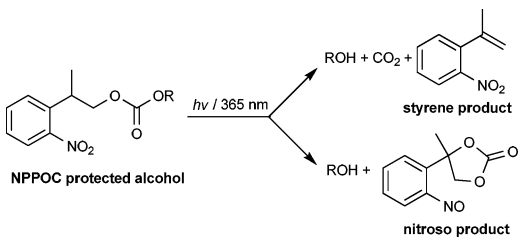
Received 28th April 2009, Accepted 29th June 2009
First published as an Advance Article on the web 22nd July 2009
DOI: 10.1039/b908404e

The photolabile NPPOC group has been successfully introduced into the 6-position of various glycopyranosides in 91–97% yield. Glycosylation of NPPOC-protected phenyl β-D-thiogluco- and galactopyranosides with appropriate acceptors afforded the corresponding disaccharides in good yield. Excellent β-stereoselectivity (β/α ≥ 10/1) can be obtained when the glycosylation was realized in CH_3CN at –40 °C. Furthermore, the 6-*O*-NPPOC thioglucoside **6** can also be readily converted into the corresponding glucopyranose or glucosyl fluoride. The photolysis of 6-*O*-NPPOC diacetone D-galactose **4** has been studied by UV–vis absorption in CH_3CN in the presence of water or DBU at 365 nm. At 100 μM concentration, photocleavage of **4** was accomplished after 5 min irradiation, with $t_{1/2}$ = 37 s (10% water), 75 s (1 equiv. DBU) or 87 s (0.05 M DBU). The formation of the nitroso byproduct can be avoided in the presence of 0.05 M DBU. All the NPPOC-protected mono- or disaccharides can be readily removed by photolysis at 365 nm in CH_3CN the presence of water or DBU in more than 87% yield.

Introduction

Carbohydrates exist in all living systems and play key roles in biological recognition processes.[1] Protection and deprotection of hydroxyl groups are indispensable for the chemical synthesis of carbohydrate. Recently, the use of photolabile protecting groups has been considerably increased in synthetic as well as biological chemistry because of their easy removal upon light irradiation[2] and their orthogonality compared to classical protecting groups. Photolabile protecting groups have been successfully used in the photolithographic synthesis of DNA chips[3] and peptide arrays[4] for genomics and proteomics. Various caged amino acids, peptides, nucleic acids as well as porphyrin have also been synthesized for *in situ* delivery of reactive compounds or for analysis of biological functions with respect to time and location.[2c,5] Light-activation of gene function in mammalian cells *via* ribozymes has also been reported.[6] The nitrobenzyl photolabile group has been used as a linker for the solid-phase synthesis of oligo- and polysaccharides,[7] however, only a few sugar derivatives protected with photoremovable groups have been reported.[8] No glycosylation reaction has ever been studied with photolabile sugars for oligosaccharides synthesis. With the emergence of glycomics research[9] and the increasing use of sugars in biomedical application,[10] there is a real need to synthesize various photolabile carbohydrates, and to study their reactivity and their photodeprotection efficiency in the glycosylation reaction. These results will certainly be very useful for the development of light-directed syntheses of oligosaccharides, glycoconjugates or carbohydrate arrays, as well as for the design and synthesis of caged glycoconjugates for various biological investigations.

The 2-(2-nitrophenyl)propoxycarbonyl (NPPOC) group has been proved to be very efficient in the photolithographic synthesis of DNA.[11] This group can be photodeprotected at 365 nm by a β-elimination reaction in the presence of water or an amine base such as piperidine, DIPEA or DBU.[11a,12] Through β-elimination cleavage, formation of the reactive nitroso byproduct, usually generated from the *o*-nitrobenzyl type of protecting group, can be suppressed (Scheme 1).[11a,12c] The NPPOC group has also been employed in peptide chemistry.[4b,13] To the best of our knowledge, this photolabile group has never been used in carbohydrate chemistry. As part of a continuing program on the synthesis of novel photolabile glycosides,[14] we decided to investigate NPPOC-protected glycosides. Herein we report our synthesis of NPPOC-protected glycopyranosides and their use as glycosyl donors in the glycosylation reaction.



Scheme 1 Principal photo cleavage products of NPPOC groups.[12e]

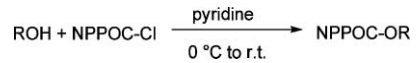
Results and discussion

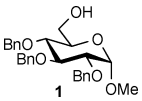
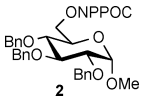
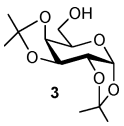
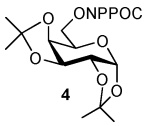
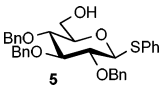
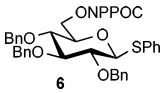
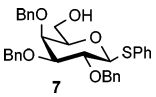
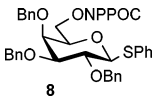
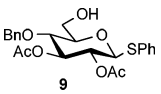
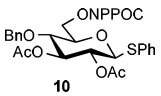
We have firstly introduced the NPPOC group on the 6-position of various glycopyranosides (Table 1). Treatment of methyl α-D-glucopyranoside **1** and diacetone α-D-galactopyranose **3** with 1.5 equiv. of NPPOC chloride[13] in pyridine led to the desired compounds **2** and **4** in very good yield. We have also prepared

PPSM, Institut d'Alembert, ENS de Cachan, CNRS UMR 8531, 61 Avenue du Pt Wilson, F-94235 Cachan, France. E-mail: joanne.xie@ens-cachan.fr; Fax: (+33) 147402454; Tel: (+33) 147405586

† Electronic supplementary information (ESI) available: ^1H and ^{13}C spectra of compounds **2**,**4**,**6**,**8**, **10**–**20**. See DOI: 10.1039/b908404e

Table 1 Synthesis of NPPOC-protected glycopyranosides



Substrate	Product	Yield[a] (%)
 1	 2	91
 3	 4	97
 5	 6	92
 7	 8	91
 9	 10	96

[a] Isolated yield after column chromatography.

phenyl β-D-thioglycosides **6**, **8** and **10**, which can be further used as glycosyl donors in the glycosylation reaction. It is to be noted that due to the presence of an asymmetric carbon in the NPPOC group,

Table 2 Photolysis of the NPPOC-protected galactopyranose **4**

Entry	Condition[a]	Concentration	Reaction time	$t_{1/2}$[b]
1	10% (*v*) H_2O	100 μM	5 min	37 s
2	1 equiv. DBU	100 μM	5 min	75 s
3	0.05 M DBU	100 μM	5 min	87 s
4	10% (*v*) H_2O	10 mM	25 min	n.d.[c]
5	1 equiv. DBU	10 mM	30 min	n.d.[c]

[a] Irradiation with a 200X Hg-Xe high pressure lamp at 365 nm in CH_3CN. [b] Calculated from the kinetics of photolysis following UV absorption. [c] n.d. = not determined.

NPPOC-protected glycosides were obtained as a mixture of two diastereomers which made their ^1H NMR spectra more complex.

Photodeprotection of NPPOC-protected compounds can be realized in aqueous MeOH or CH_3CN,[12] or in a CH_3CN solution of piperidine or DBU (0.05 M).[11a] We have studied the photolysis of the NPPOC galactose **4** under different conditions and followed the reaction by TLC and UV–vis absorption (Table 2 and Fig. 1 and 2). In the aqueous CH_3CN at 100 μM concentration (entry 1, Table 2), the photolysis is completed after 5 min irradiation. The half time was estimated to be 37 s (Fig. 2a) which is in accordance with the value reported by A. Hasan *et al.* in a solution of MeOH/H_2O (1:1, $t_{1/2} = 40$ s).[12a] The cleavage rate is dependent on the reaction concentration, with shorter reaction times in a more diluted medium since at higher concentration (10 mM, entry 4), 25 min irradiation was necessary to accomplish the photodeprotection. The absorption spectra showed the presence of nitroso byproduct at 290 and 317 nm (Fig. 1a and 2a).[12c] We have also realized the reaction in the presence of DBU. With 1 equiv. of DBU (entry 2), the reaction was finished after 5 min, with a half time of 75 s (Fig. 2b) which is a little bit longer than in the presence

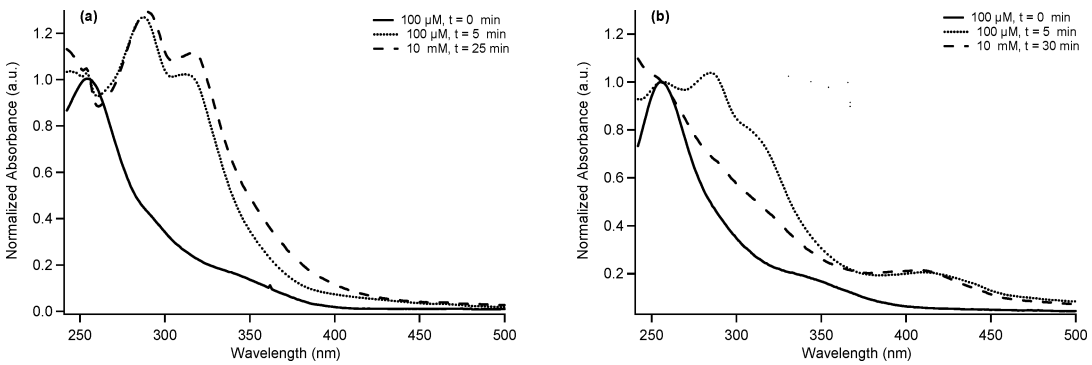


Fig. 1 Normalized UV–vis spectra of **4** before and after photolysis at 365 nm in CH_3CN/H_2O 9:1 (*v*/*v*) (a) or in CH_3CN containing 1 equiv. of DBU (b) at 100 μM or 10 mM concentrations.

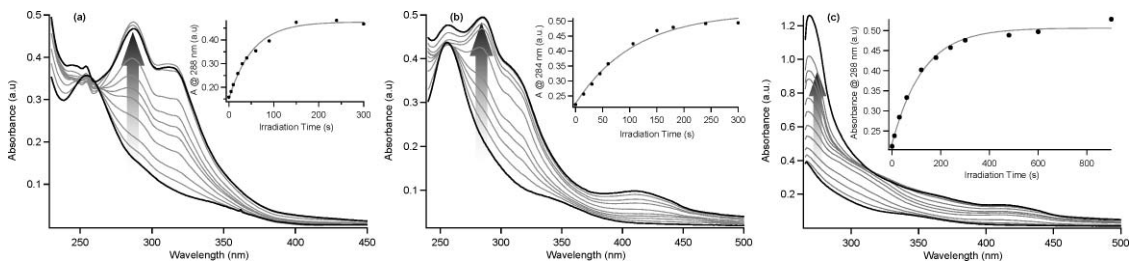
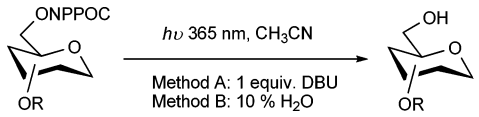


Fig. 2 UV–vis traces of photolysis of **4** at 100 μM concentration in CH_3CN/H_2O 9:1 (*v*/*v*) (a), in CH_3CN containing 1 equiv. of DBU (b), or 0.05 M DBU (c). Inset: titration curve of the absorbance at 288 or 284 nm as a function of irradiation time.

Table 3 Deprotection of NPPOC-protected glycopyranosides



Entry	Substrate	Product	Method A[a]	Method B[a]
1	**2**	**1**	95%	91%
2	**4**	**3**	95%	96%
3	**6**	**5**	93%	95%
4	**8**	**7**	97%	98%
5	**10**	**9**	95%	95%

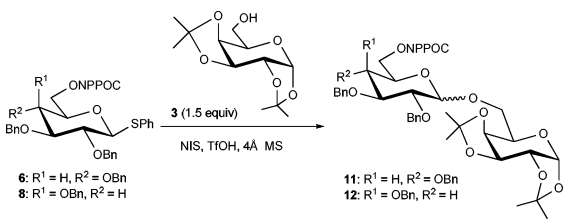
[a] Isolated yield after column chromatography.

of water. Nitroso byproduct was also present in this case (Fig. 1b). Nevertheless, formation of nitroso byproduct can be suppressed when the reaction was conducted in the presence of 0.05 M DBU (Fig. 2c), condition optimized by M. Beier and J. D. Hoheisel.[11a] The half time of the reaction was estimated to be 87 s. At 10 mM concentration in the presence of 1 equiv. of DBU (entry 5), no nitroso byproduct was observed at the end of the reaction (30 min) (Fig. 1b).

We then realized the photodeprotection of the NPPOC-protected glycosides (~0.05 M solution) in CH_3CN in the presence of DBU (1 equiv.) (Method A) or 10% water (Method B) for 1 to 2 h irradiation at 365 nm (Table 3). The result showed that whatever the reaction conditions, the deprotected glycosides were obtained in excellent yield after purification.

In the second step, we turned our attention to the glycosylation reaction with NPPOC-protected β-D-thioglycosides **6** and **8** (Table 4). Glycosylation of **6** with **3** using NIS in the presence of TfOH in CH_2Cl_2 at −78 °C afforded the desired disaccharide **11** as a mixture of α/β (1:1.7) isomers in 89% yield (entry 1). In order to increase the β-selectivity, the reaction was then realized in CH_3CN (entries 2 and 3).[15] The best β-selectivity (α:β = 1:10) was obtained at −40 °C. The β-anomeric configuration was confirmed on the basis of its coupling constant ($J_{1',2'} = 7.8$ Hz, H-1′) for the anomeric proton at 4.46 ppm in the ^{1}H NMR spectrum and the chemical

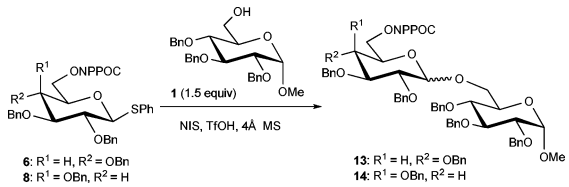
Table 4 Effects of solvents and temperature on the glycosylation of glycosyl donors **6** and **8** with alcohol **3**



Entry	Donor	Solvent	T (°C)	Yield[a]	α : β[b]
1	**6**	CH_2Cl_2	−78	89%	1:1.7
2	**6**	CH_3CN	−15	90%	1:8
3	**6**	CH_3CN	−40	87%	1:10
4	**8**	CH_2Cl_2	−78	97%	1:2.3
5	**8**	CH_3CN	−15	91%	1:8
6	**8**	CH_3CN	−40	89%	1:20

[a] Isolated yield after column chromatography. [b] The ratio was determined by ^{1}H NMR.

Table 5 Glycosylation of glycosyl donors **6** and **8** with alcohol **1**



Entry	Donor	Solvent	T (°C)	Yield[a]	α : β[b]
1	**6**	CH_2Cl_2	−78	92	1:1.5
2	**6**	CH_3CN	−40	87	1:20
3	**8**	CH_2Cl_2	−78	91	1:10
4	**8**	CH_3CN	−40	90	1:20

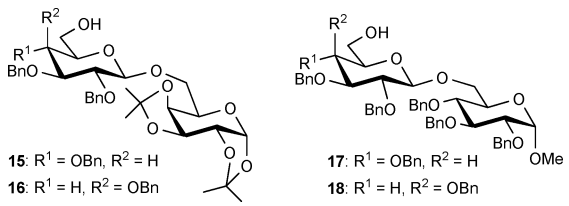
[a] Isolated yield after column chromatography. [b] The ratio was determined by ^{1}H NMR.

shift in the ^{13}C NMR spectrum at 104.5 ppm (C-1′). In a similar way, glycosylation of the NPPOC-protected β-D-thiogalactoside **8** with **3** in CH_2Cl_2 led successfully to the disaccharide **12** in 97% yield with a 1:2.3 α:β ratio (entry 4). In this case, the α/β anomers can be separated by column chromatography. As for the *gluco* derivative **11**, the β-anomer **12** had the anomeric proton around 4.40 ppm with $J_{1',2'} = 7.8$ Hz in the ^{1}H NMR spectrum and the anomeric carbon at 104.8 ppm (C-1′) in the ^{13}C NMR spectrum. For the α-anomer, the anomeric proton appeared at 4.91 ppm with $J_{1',2'} = 2.3$ Hz in the ^{1}H NMR spectrum and the anomeric carbon at 97.7 ppm (C-1′) in the ^{13}C NMR spectrum. Better β-selectivity was obtained in CH_3CN (entries 5 and 6).

We have also used methyl α-D-glucopyranoside **1** as a glycosyl acceptor for the glycosylation reaction (Table 5). Reaction of **6** with **1** in CH_2Cl_2 afforded the disaccharide **13** with similar yield and stereoselectivity (α:β = 1:1.5) as obtained with the glycosyl acceptor **3** (entry 1). Glycosylation in CH_3CN improved the β-selectivity (α:β = 1:20, entry 2). For the galactosyl donor **8**, the disaccharide **14** was obtained with a very good β-selectivity whatever the reaction conditions (entry 3 and 4).

After the successful glycosylation reaction, we tried the photolysis of the NPPOC-protected disaccharides (~0.05 M solution) (Table 6). Once again, the photodeprotection can be easily realized in the presence of water or DBU, leading to the corresponding

Table 6 Deprotection of NPPOC-protected disaccharides

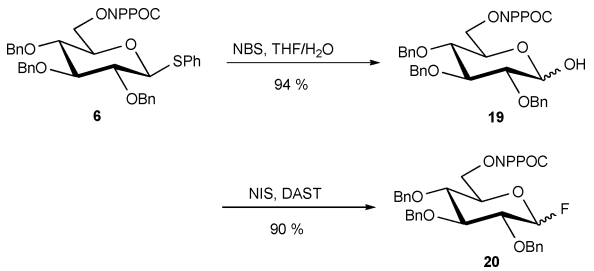


Substrate	Product	Method A[a,c]	Method B[b,c]
11	**15**	89%	91%
12	**16**	87%	92%
13	**17**	90%	93%
14	**18**	88%	90%

[a] Irradiation at 365 nm in the presence of 50 μL DBU in 2 mL of CH_3CN. [b] Irradiation at 365 nm in aqueous CH_3CN (CH_3CN/H_2O: 9:1). [c] Isolated yield after column chromatography.

disaccharides **15**, **16**,[16] **17**[17] and **18**[18] in good yield. These compounds can be further employed as glycosyl acceptors for the synthesis of complex oligosaccharides.

It's well known that thioglycosides can be easily hydrolysed or transformed into other glycosyl donors. Treatment of NPPOC-protected glucopyranoside **6** with NBS in a mixture of THF/H_2O led to the corresponding glucopyranose **19** in 94% yield (Scheme 2). This compound can be further transformed into other glycosyl donors like trichloroacetimidate. By treatment with NIS and DAST, compound **6** can also be converted into the glucosyl fluoride **20** as a mixture of α/β anomers.



Scheme 2 Transformation of NPPOC-protected glucopyranoside **6**.

Conclusions

In summary, we have synthesized for the first time the 6-*O*-NPPOC protected glycopyranosides in very good yield. The NPPOC-protected thioglycosides have been successfully used as glycosyl donors for photolabile disaccharide synthesis with very good β-selectivity in CH_3CN. The 6-*O*-NPPOC thioglucoside **6** can also be readily converted into the corresponding glucopyranose or glucosyl fluoride, which could extend the application of NPPOC-protected sugars. Finally, we have demonstrated that NPPOC-protected carbohydrates can be easily photodeprotected under neutral or basic conditions. At 100 μM concentration, the NPPOC group was removed in less than five minutes. These results showed that the NPPOC group should be useful as a photolabile protecting group in carbohydrate chemistry, especially in automated oligosaccharide synthesis as well as for caged sugar derivatives.

Experimental section

General techniques

^1H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer. Column chromatography was performed on Silica Gel 60 (230–400 mesh). Analytical thin-layer chromatography was performed on aluminium percolated plates of Silica Gel 60F-254 with detection by UV and by spraying with 6 N H_2SO_4 and heating for about 2 min at 300 °C. IR spectra were recorded on a Thermo Nicolet Nexus FT-IR spectrometer. ESI-HRMS mass spectra were recorded on a Thermo LTQ-Orbitrap spectrometer at the Service of Mass Spectrometry of University Pierre and Marie Curie. The UV light was supplied by a 200 W Hg-Xe high pressure lamp (Hamamatsu LC6). The light is passed successively through a 365 nm interference filter, only light of a wavelength of 365 nm was used. The output from the light guide is about 150 mW/cm^2 at the optimal distance (about 1.0 cm away from its end). UV/vis absorption spectra were recorded on a Uvikon-940 KONTRON spectrophotometer. The kinetics of the photolysis of **4** was realized in CH_3CN at 100 μM concentration by irradiation at 365 nm. The order 1 kinetics reactions are fitted with the model eqn (1). A_n is the measured absorbance, A_{max} is the finished reaction absorbance. t_0: time zero, t_n: time of irradiation. The half-time ($t_{\frac{1}{2}}$) was calculated according to eqn (2):

$$A_n = A_{max}.(1 - \exp(-(t_n + t_0)\,\tau^{-1})) \quad (1)$$

$$t_{\frac{1}{2}} = \tau \ln 2 \quad (2)$$

General procedure for the synthesis of NPPOC-protected glycopyranosides

To a solution of glycopyranoside (1 mmol) in anhydrous pyridine (10 mL) at 0 °C, was added dropwise a solution of 2-(2-nitrophenyl) propyloxycarbonyl chloride (1.5 mmol in 2.5 mL CH_2Cl_2). The mixture was stirred for 2 h at 0 °C and then gradually raised to rt. After evaporation, the residue was diluted in EtOAc, washed with HCl (0.5 N, 2 × 5 mL), saturated $NaHCO_3$ (3 × 10 mL) and brine (3 × 10 mL). The organic layer was dried over $MgSO_4$ and concentrated under vacuum to give a crude product which was purified by column chromatography to give the desired NPPOC-protected product.

General procedure for the glycosylation of NPPOC protected thioglycosides

A mixture of NPPOC protected thioglycoside (1.0 mmol), glycosyl acceptor (1.5 mmol), NIS (2.0 mmol), and powdered 4 Å molecular sieves (1 g) in CH_2Cl_2 (20 mL) or CH_3CN (20 mL) was stirred for 20 min at −78 °C (or −40 °C) before the addition of TfOH (0.015 mmol). The mixture was stirred at −78 °C (or −40 °C) for 2 h and then gradually raised to rt. After the completion of the reaction, Na_2SO_3 (2 g), $NaHCO_3$ (2 g), and a few drops of water were added into the reaction mixture, and the mixture was stirred for 5 min, then diluted with CH_2Cl_2 (25 mL), filtered through Celite, washed with saturated $NaHCO_3$ (3 × 10 mL) and brine (3 × 10 mL), dried over $MgSO_4$, and concentrated in vacuum to give a crude product which was purified by chromatography.

General procedure for the photolysis of NPPOC-protected saccharides

A solution of NPPOC-protected saccharide (0.1 mmol) in CH_3CN (2.0 mL) in the presence of DBU (Method A) or H_2O (10% v) (Method B) in a 1 cm path-length quartz cell was irradiated by 365 nm UV-light. The reaction was monitored by UV/vis absorption spectra or TLC. After the completion of the reaction, the reaction mixture was evaporated to dryness and the residue purified by column chromatography to give the desired photodeprotected product.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-2-(2-nitrophenyl)propyloxycarbonyl-α-D-glucopyranoside 2. Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **1** (0.47 g, 1.0 mmol) was treated with NPPOCCl according to the general procedure. Purification by column chromatography (EtOAc:cyclohexane, 1:9–1:4) gave 0.61 g (91%)

of compound **2** as an oil. $R_f = 0.57$ (EtOAc:cyclohexane, 3:7). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 and 1.34 (2d, $J = 6.8$ Hz, 3H, CH_3), 3.32 (s, 3H, OMe), 3.41–3.52 (m, 2H, 2 × CH), 3.65–3.72 (m, 1H, CH), 3.76 (td, $J = 3.0$, 9.8 Hz, 1H), 3.96 (t, $J = 9.6$ Hz, 1H), 4.23–4.26 (m, 2H, CH_2), 4.50 (dd, $J = 10.1$ and 11.0 Hz, 1H), 4.55 (d, $J = 3.7$ Hz, 1H), 4.63 (d, $J = 12.4$ Hz, 1H), 4.77 (d, $J = 11.9$ Hz, 1H), 4.79 (d, $J = 10.6$ Hz, 1H), 4.83 (dd, $J = 5.0$, 11.0 Hz, 1H), 4.97 (d, $J = 10.6$ Hz, 1H), 7.23–7.31 (m, 16H), 7.42–7.54 (m, 2H, 2 × CH), 7.73 (d, $J = 9.2$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$):δ 17.9, 33.3, 33.4, 55.4, 66.5, 68.6, 68.6, 71.6, 73.5, 75.2, 75.8, 77.3, 77.4, 79.9, 82.1, 98.1, 124.5, 127.6, 127.7, 127.9, 128.0, 128.1, 128.2, 128.4, 128.5, 128.56, 128.58, 132.8, 136.9, 138.0, 138.2, 138.8, 150.28, 150.32. ESI HRMS (m/z): calcd for $C_{38}H_{41}NNaO_{10}$: 694.2628, found: 694.2623.

1,2:3,4-Di-*O*-isopropylidene-6-*O*-2-(2-nitrophenyl)propyloxycarbonyl-α-D-galactopyranose 4. 1,2:3,4-Diisopropylidene-α-D-galactopyranose **3** (0.52 g, 2 mmol) was treated with NPPOCCl according to the general procedure. Purification by column chromatography (EtOAc:cyclohexane, 1:9–1:4) gave 0.9 g (97%) of compound **4** as an oil. $R_f = 0.50$ (EtOAc:cyclohexane, 3:7). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23–1.42 (m, 15H, 5 × CH_3), 3.61–3.62 (m, 1H), 3.95–3.97 (m, 1H), 4.15–4.23 (m, 6H), 4.51–4.53 (m, 1H), 5.42–5.43 (m, 1H), 7.26–7.30 (m, 1H), 7.38–7.41 (m, 1H), 7.47–7.50 (m, 1H), 7.65–7.68 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.6, 17.8, 24.4, 25.85, 25.92, 33.24, 33.29, 65.6, 66.5, 70.3, 70.5, 70.7, 71.4, 96.1, 108.7, 109.5, 124.2, 127.5, 128.3, 132.7, 136.8, 150.1, 154.8. ESI HRMS (m/z): calcd for $C_{22}H_{29}NNaO_{10}$: 490.1689, found: 490.1681.

Phenyl 2,3,4-tri-*O*-benzyl-6-*O*-2-(2-nitrophenyl)propyloxycarbonyl-1-thio-β-D-glucopyranoside 6. Phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranoside **5** (0.38 g, 0.71 mmol) was treated with NPPOCCl according to the general procedure. Purification by column chromatography (EtOAc : cyclohexane, 1:9–1:4) gave 0.49 g (92%) of compound **6** as an oil. $R_f = 0.27$ (EtOAc:cyclohexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (d, $J = 6.9$ Hz, 3H, CH_3), 3.46–3.53 (m, 3H), 3.68–3.76 (m, 2H), 4.21–4.25 (m, 1H), 4.30(d, $J = 6.4$ Hz, 2H, CH_2), 4.37 (d, $J = 11.4$ Hz, 1H), 4.54 and 4.55 (2d, $J = 11.0$ Hz, 1H), 4.63 and 4.64 (2d, $J = 9.6$ Hz, 1H), 4.72 (d, $J = 10.1$ Hz, 1H), 4.82–4.92 (m, 4H), 7.22–7.39 (m, 19H), 7.45–7.54 (m, 4H), 7.74–7.78 (m, 1H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 18.0, 33.4, 66.8, 71.6, 75.2, 75.6, 76.0, 77.4, 80.9, 86.8, 87.7, 124.5, 127.7, 127.9, 128.07, 128.18, 128.36, 128.43, 128.48, 128.59, 128.63, 128.67, 129.1, 132.0, 132.2, 132.9, 133.7, 137.0, 137.7, 138.0, 138.4, 150.3, 155.0. ESI HRMS (m/z): calcd for $C_{43}H_{43}NNaO_9S$: 772.2556, found: 772.2551.

Phenyl 2,3,4-tri-*O*-benzyl-6-*O*-2-(2-nitrophenyl)propyloxycarbonyl-1-thio-β-D-galactopyranoside 8. Phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranoside **7** (0.54 g, 1 mmol) was treated with NPPOCCl according to the general procedure. Purification by column chromatography (EtOAc : cyclohexane, 1:9–1:4) gave 0.68 g (91%) of compound **8** as an oil. $R_f = 0.28$ (EtOAc:cyclohexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 and 1.45 (2d, $J = 6.9$ Hz, 3H, CH_3), 3.59–3.73 (m, 3H), 3.89–3.92 (m, 2H), 4.08–4.20 (m, 1H), 4.23–2.29 (m, 3H), 4.56–4.62 (m, 2H), 4.71–4.77 (m, 4H), 4.98 and 4.99 (2d, $J = 11.4$ Hz, 1H), 7.20–7.50 (m, 22H), 7.56–7.61 (m, 2H), 7.76–7.78 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8, 17.9, 33.3, 66.3, 66.6, 71.6, 71.7, 71.8, 73.0, 73.2, 73.3, 74.5, 75.6, 75.7, 75.8, 77.2, 84.1, 87.8, 124.3, 124.4, 127.3, 127.66, 127.70, 127.8, 128.1, 128.3, 128.4, 128.6, 128.9, 131.7, 131.8, 132.80, 132.84, 134.0, 136.9, 138.2, 138.3, 138.4, 150.3, 154.7, 154.9. ESI HRMS (m/z): calcd for $C_{43}H_{43}NNaO_9S$: 772.2556, found: 772.2551.

Phenyl 2,3-*O*-acetyl-4-*O*-benzyl-6-*O*-2-(2-nitrophenyl)propyloxycarbonyl-1-thio-β-D-glucopyranoside 10. Phenyl 2,3-*O*-acetyl-4-*O*-benzyl-1-thio-β-D-glucopyranoside **9** (90 mg, 0.20 mmol) was treated with NPPOCCl according to the general procedure. Purification by column chromatography (EtOAc : cyclohexane, 1:9–1:4) gave 126 mg (96%) of compound **10** as an oil. $R_f = 0.30$ (EtOAc:cyclohexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (d, $J = 6.8$ Hz, 1.5H, 0.5 × CH_3), 1.40 (d, $J = 7.3$ Hz, 1.5H, 0.5 × CH_3), 1.93 and 1.94 (2 s, 3H, Ac), 2.07 (s, 3H, Ac), 3.61–3.66 (m, 2H, H-4,5), 3.33–3.81 (m, 1H, CH-Ar), 4.21–4.24 (m, 1H, H-6), 4.28–4.36 (m, 2H), 4.42 (dd, $J = 4.6$, 11.4 Hz, 1H), 4.51–4.58 (m, 2H), 4.67 (d, $J = 8.9$ Hz, 1H, H-1), 4.87 and 4.88 (2t, $J = 10.1$ Hz, H-2), 5.22–5.27 (m, 1H, H-3), 7.21–7.41 (m, 9H, Ar), 7.45–7.50 (m, 3H, Ar), 7.55–7.60 (m, 1H, Ar), 7.76–7.80 (m, 1H, Ar). ^{13}C NMR (400 MHz, $CDCl_3$) δ 18.0, 18.1, 21.0, 33.46, 33.53, 66.3, 66.4, 70.6, 71.9, 75.0, 75.6, 76.2, 77.1, 77.5, 85.9, 124.6, 127.9, 128.2, 128.3, 128.36, 128.43, 128.5, 128.8, 129.1, 132.2, 133.0, 133.1, 137.0, 137.3, 137.4, 150.4, 154.9, 169.8, 170.2. ESI HRMS (m/z): calcd for $C_{33}H_{35}NNaO_{11}S$: 676.1828, found: 676.1823.

2,3,4-Tri-*O*-benzyl-6-*O*-2-(2-nitrophenyl)propyloxycarbonyl-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose 11. Compound **6** (66 mg, 0.088 mmol) was treated with alcohol **3** (35 mg, 0.13 mmol) in CH_3CN according to the general procedure. Purification by chromatography (EtOAc:cyclohexane, 1:4–1:2) gave 69 mg (87%) of **11** (β/α = 10:1) as an oil. $R_f = 0.62$ (EtOAc:cyclohexane, 3:7). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31–1.49 (m, 15H, 5 × CH_3), 3.40–3.50 (m, 2H), 3.61–3.78 (m, 3H), 4.06–4.14 (m, 2H), 4.23–4.38 (m, 5H), 4.46 (d, $J = 7.8$ Hz, 1H), 4.50 (dd, $J = 5.0$, 11.0 Hz, 1H), 4.59 (dd, $J = 2.8$, 8.3 Hz, 1H), 4.72 (d, $J = 11.0$ Hz, 1H), 4.77 (d, $J = 11.0$ Hz, 1H), 4.83 (d, $J = 10.6$ Hz, 1H), 4.98 (d, $J = 11.0$ Hz, 1H), 5.06 (d, $J = 11.0$ Hz, 1H), 5.57 (d, $J = 2.3$ Hz, 1H), 7.22–7.42 (m, 16H), 7.47–7.49 (m, 1H), 7.53–7.58 (m, 1H), 7.76 (d, $J = 8.2$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 24.5, 25.0, 25.1, 26.0, 26.1, 33.3, 60.5, 62.4, 66.6, 66.7, 67.4, 70.2, 70.5, 70.8, 71.4, 71.5, 72.8, 74.4, 75.2, 75.8, 77.2, 81.4, 84.4, 96.4, 96.4, 104.5, 108.6, 108.7, 109.5, 124.5, 127.6, 127.7, 127.9, 128.0, 128.2, 128.3, 128.4, 128.5, 128.6, 128.8, 132.8, 136.9, 137.8, 138.6, 150.2, 150.2, 154.9. ESI HRMS (m/z): calcd for $C_{49}H_{57}NNaO_{15}$: 922.3626, found: 922.3620.

2,3,4-Tri-*O*-benzyl-6-*O*-2-(2-nitrophenyl)propyloxycarbonyl-β-D-galactopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose 12. Compound **8** (108 mg, 0.14 mmol) was treated with alcohol **3** (65 mg, 0.25 mmol) in CH_3CN according to the general procedure. Purification by chromatography (EtOAc:cyclohexane, 1:4–1:2) gave 117 mg (91%) of **12** (β/α = 8:1) as an oil. Reaction in CH_2Cl_2 followed by purification allowed us to isolate a small quantity of α-anomer as the minor product. Data for α-Anomer: $R_f = 0.26$ (EtOAc:cyclohexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28–1.42 (m, 15H, 5 × CH_3), 3.61–3.67 (m, 2H), 3.85–4.01 (m, 6H), 4.06–4.11 (m, 1H), 4.20–4.24 (m, 4H), 4.47–4.55 (m, 2H), 4.67 (s, 2H), 4.69 (d, $J = 11.5$ Hz, 1H), 4.79

(d, J = 11.5 Hz, 1H), 4.87 and 4.89 (2d, J = 11.0 Hz, 1H), 4.91 and 4.92 (2d, J = 2.3 Hz, 1H), 5.42 and 5.43 (2d, J = 2.3 Hz, 1H), 7.19–7.34 (m, 16H), 7.37–7.41 (m, 1H), 7.46–7.52 (m, 1H), 7.68–7.72 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 24.7, 25.0, 26.1, 26.2, 33.3, 33.4, 65.9, 66.4, 66.6, 66.7, 70.7, 70.8, 71.6, 72.9, 73.4, 74.5, 74.6, 74.8, 76.3, 77.4, 78.9, 96.4, 97.7, 108.6, 109.3, 124.5, 127.5, 127.6, 127.7, 127.8, 127.9, 128.4, 128.5, 132.9, 137.0, 138.4, 138.7, 138.9, 150.3, 154.8. Data for β-Anomer: R_f = 0.25 (EtOAc:cyclohexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (s, 6H, 3 × CH_3), 1.36 (2d, J = 7.8 Hz, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 3.48–3.58 (m, 1H), 3.64–3.76 (m, 1H), 3.80–3.83 (m, 1H), 4.06–4.14 (m, 2H), 4.16–4.32 (m, 3H), 4.40 and 4.41 (2d, J = 7.8 Hz, 1H), 4.57 (td, J = 2.3, 7.8 Hz, 1H), 4.60 (t, J = 11.9 Hz, 1H), 4.74 and 4.75 (2d, J = 11.9 Hz, 1H), 4.83 (d, J = 11.9 Hz, 1H), 4.94 (dd, J = 6.0, 11.4 Hz, 1H), 5.05 (d, J = 11.0 Hz, 1H), 5.56 (d, J = 1.0 Hz, 1H), 7.24–7.38 (m, 15H), 7.44–7.47 (m, 2H), 7.53–7.58 (m, 1H), 7.75 (d, J = 8.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ17.9, 24.6, 26.08, 26.11, 33.3, 66.3, 66.6, 67.5, 69.9, 70.6, 70.8, 71.5, 71.68, 71.74, 71.8, 71.9, 73.1, 73.2, 73.4, 74.5, 74.8, 77.4, 79.0, 81.8, 96.4, 104.7, 104.8, 108.7, 109.4, 109.4, 124.4, 127.5, 127.5, 127.6, 127.67, 127.72, 127.8, 128.2, 128.3, 128.4, 128.6, 128.7, 132.8, 136.86, 136.89, 138.3, 138.59, 138.61, 139.0, 150.3, 154.6, 154.7. ESI HRMS (m/z): calcd for $C_{49}H_{57}NNaO_{15}$ (M + Na^+) 922.3626, found 922.3620.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-2-(2-nitrophenyl)propyloxycarbonyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside 13. Compound **6** (154 mg, 0.2 mmol) was treated with alcohol **1** (116 mg, 0.25 mmol) in CH_3CN according to the general procedure. Purification by chromatography (EtOAc:cyclohexane, 1:4–1:2) gave 198 mg (87%) of the desired product **13** (β/α = 20:1) as an oil. R_f = 0.13 (EtOAc:cyclohexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 and 1.33 (2d, J = 6.9 Hz, 3H, CH_3), 3.31 (s, 3H, CH_3), 3.42–3.52 (m, 6H), 3.59–3.72 (m, 3H), 3.77–3.79 (m, 1H), 3.98 (t, J = 9.6 Hz, 1H), 3.99–4.14 (m, 1H), 4.18 (dd, J = 4.6, 11.4 Hz, 1H), 4.25–4.27 (m, 2H), 4.31 and 4.32 (2d, J = 7.8 Hz, 1H), 4.36 (d, J = 11.4 Hz, 1H), 4.47 (d, J = 11.0 Hz, 1H), 4.51 (d, J = 11.0 Hz, 1H), 4.59 (d, J = 3.2 Hz, 1H), 4.65 (d, J = 12.8 Hz, 1H), 4.71 (d, J = 12.8 Hz, 1H), 4.76–4.84 (m, 4H), 4.92 (d, J = 11.0 Hz, 1H), 4.95 (d, J = 10.6 Hz, 2H), 7.15–7.34 (m, 31H), 7.42–7.45 (m, 1H), 7.49–7.55 (m, 1H), 7.71–7.75 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ17.9, 33.4, 55.3, 66.7, 68.6, 69.8, 71.6, 71.7, 73.0, 73.5, 75.1, 75.2, 75.8, 79.9, 82.0, 82.1, 84.8, 98.2, 103.7, 124.5, 127.68, 127.74, 127.8, 127.97, 128.04, 128.1, 128.16, 128.19, 128.3, 128.49, 128.5, 128.6, 132.8, 136.9, 137.8, 138.2, 138.3, 138.4, 138.9, 150.3, 154.9. ESI HRMS (m/z): calcd for $C_{65}H_{69}NNaO_{15}$: 1126.4565, found: 1126.4559.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-2-(2-nitrophenyl)propyloxycarbonyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside 14. Compound **8** (168 mg, 0.22 mmol) was treated with alcohol **1** (123 mg, 0.26 mmol) in CH_3CN according to the general procedure. Purification by chromatography (EtOAc:cyclohexane, 1:4–1:2) gave 0.22 g (90%) of the desired product **14** (β/α = 20:1) as an oil. R_f = 0.42 (EtOAc:cyclohexane, 3:7). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 and 1.34 (2d, J = 6.9 Hz, 3H, CH_3), 3.31 (s, 3H, CH_3), 3.46–3.53 (m, 4H), 3.58–3.64 (m, 1H), 3.70–3.76 (m, 1H), 3.80–3.89 (m, 4H), 3.97 (t, J = 9.0 Hz, 1H), 4.10–4.16 (m, 2H), 4.19–4.31 (m, 3H), 4.50 (2d, J = 11.0 Hz, 1H), 4.55–4.60 (m, 2H), 4.63 (d, J = 11.4 Hz, 1H), 4.67–4.72 (m, 2H), 4.76–4.80 (m, 4H), 4.93–4.98 (m, 3H), 7.19–7.34 (m, 31H), 7.41–7.43 (m, 1H), 7.50–7.54 (m, 1H), 7.70–7.74 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8, 17.9, 33.2, 33.3, 55.3, 66.2, 66.6, 68.58, 68.64, 70.0, 71.77, 71.82, 71.9, 72.0, 73.2, 73.3, 73.4, 74.6, 75.0, 75.3, 75.8, 77.4, 78.1, 79.9, 82.19, 82.24, 98.0, 104.1, 104.2, 124.4, 127.5, 127.6, 127.7, 128.0, 128.1, 128.2, 128.3, 128.4, 128.51, 128.54, 132.8, 132.9, 136.9, 138.3, 138.4, 138.5, 138.7, 139.0, 150.4, 154.7, 154.7. ESI HRMS (m/z): calcd for $C_{65}H_{69}NNaO_{15}$: 1126.4565, found: 1126.4559.

2,3,4-Tri-*O*-benzyl-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose 15. Photolysis of compound **11** (β/α = 8:1) (40 mg, 0.04 mmol) according to the general procedure gave, after purification by chromatography (EtOAc:cyclohexane, 1:4–3:7) 27 mg (89%) of **15** (β/α = 8:1) as an oil. Data for β-anomer: R_f = 0.18 (EtOAc:cyclohexane, 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32, 1.34, 1.52, 1.54 (4 s, 12H, 4 × CH_3), 2.21 (s, 1H, OH), 3.36 (ddd, J = 2.7, 5.0, 9.6 Hz, 1H), 3.42 (dd, J = 8.2, 9.2 Hz, 1H), 3.50 (dd, J = 8.7, 9.6 Hz, 1H), 3.63–3.68 (m, 1H), 3.66 (t, J = 9.2 Hz, 1H), 3.77 (dd, J = 6.4, 10.1 Hz, 1H), 3.83–3.3.86 (m, 1H), 4.02–4.06 (m, 1H), 4.09 (dd, J = 5.0, 10.1 Hz, 1H), 4.28 (dd, J = 4.6, 7.8 Hz, 1H), 4.33 (dd, J = 2.8, 5.0 Hz, 1H), 4.50 (d, J = 7.8 Hz, 1H), 4.61 (d, J = 10.6 Hz, 2H), 4.71 (d, J = 11.0 Hz, 1H), 4.79 (d, J = 11.0 Hz, 1H), 4.84 (d, J = 11.0 Hz, 1H), 4.95 (d, J = 11.0 Hz, 1H), 5.01 (d, J = 11.4 Hz, 1H), 5.57 (d, J = 5.0 Hz, 1H), 7.24–7.31 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 25.1, 26.1, 26.2, 62.3, 67.2, 69.5, 70.6, 70.9, 71.3, 74.6, 75.1, 75.2, 75.8, 77.4, 77.8, 81.9, 84.5, 96.5, 104.3, 108.8, 109.6, 127.7, 128.0, 128.1, 128.4, 128.5, 128.6, 138.1, 138.6, 138.7. ESI HRMS (m/z): calcd for $C_{39}H_{48}NaO_{11}$: 715.3094, found: 715.3089.

2,3,4-Tri-*O*-benzyl-β-D-galactopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose 16. Photolysis of compound **12** (β/α = 8:1) (32 mg, 0.035 mmol) according to the general procedure gave, after purification by chromatography (EtOAc:cyclohexane, 1:4–3:7) 21 mg (87%) of **16** (β/α = 8:1) as an oil. R_f = 0.12 (EtOAc:cyclohexane, 1:4). ν_{max}/cm^{-1} 3411, 2923, 1641, 1453, 1381, 1254, 1210, 1167, 1069, 1028, 1006, 898, 734, 698.^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 2.21 (s, 1H, OH), 3.35–3.39 (m, 1H), 3.42 (dd, J = 8.2, 9.2 Hz, 1H), 3.51 (t, J = 8.7 Hz, 1H), 3.64–3.68 (m, 1H), 3.66 (t, J = 9.2 Hz, 1H), 3.83–3.86 (m, 1H), 4.04 (td, J = 1.4, 6.4 Hz, 1H), 4.27 (dd, J = 1.8, 7.8 Hz, 1H), 4.33 (dd, J = 2.8, 5.0 Hz, 1H), 4.50 (d, J = 7.8 Hz, 1H), 4.59–4.62 (m, 2H), 4.71 (d, J = 11.0 Hz, 1H), 4.79 (d, J = 11.0 Hz, 1H), 4.84 (d, J = 11.0 Hz, 1H), 4.95 (d, J = 11.0 Hz, 1H), 5.01 (d, J = 11.4 Hz, 1H), 5.56 (d, J = 5.0 Hz, 1H), 7.26–7.31 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 25.2, 26.1, 26.2, 62.2, 67.4, 69.5, 70.7, 70.9, 71.4, 73.2, 73.6, 74.3, 74.8, 75.0, 79.4, 82.2, 96.6, 104.8, 108.8, 109.5, 127.6, 127.8, 128.1, 128.3, 128.6, 128.7, 128.8, 138.3, 138.6, 139.1.

Methyl 2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside 17. Photolysis of compound **13** (38 mg, 0.04 mmol) according to the general procedure gave, after purification by chromatography (EtOAc:cyclohexane, 1:4–3:7) 28 mg (90%) of **17** as an oil. R_f = 0.17 (EtOAc:cyclohexane, 1:4). ν_{max}/cm^{-1} 3659, 2972, 2901, 1453, 1357, 1140, 1067, 1028, 737, 695. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.98 (s, 1H, OH), 3.32 (s, 3H),

3.22–3.34 (m, 1H), 3.45 (dd, J = 7.8, 9.2 Hz, 1H), 3.49–3.57 (m, 3H), 3.64 (t, J = 9.2 Hz, 2H), 3.68 (dd, J = 4.1, 10.5 Hz, 1H), 3.75–3.84 (m, 2H), 3.97 (t, J = 9.6 Hz, 1H), 4.08 (dd, J = 1.4, 11.0 Hz, 1H), 4.36 (d, J = 7.8 Hz, 1H), 4.48 (d, J = 11.5 Hz, 1H), 4.60–4.64 (m, 3H), 4.66 (d, J = 12.4 Hz, 1H), 4.70 (d, J = 11.0 Hz, 1H), 4.73–4.97 (m, 7H), 7.24–7.31 (m, 30H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 62.1, 68.8, 69.9, 73.5, 75.0, 75.1, 75.2, 75.9, 77.7, 77.9, 79.8, 82.1, 84.7, 98.3, 103.9, 127.1, 127.8, 127.9, 128.0, 128.08, 128.13, 128.2, 128.3, 128.5, 128.60, 128.64, 138.1, 138.2, 138.3, 138.4, 139.5, 138.9.

Methyl 2,3,4-tri-*O*-benzyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside 18. Photolysis of compound **14** (31 mg, 0.028 mmol) according to the general procedure gave, after purification by chromatography (EtOAc:cyclohexane, 1:4–3:7) 22 mg (88%) of **18** as an oil. R_f = 0.13 (EtOAc:cyclohexane, 1:4). ν_{max}/cm^{-1} 3519, 3064, 3031, 2923, 1496, 1453, 1357, 1212, 1086, 1060, 1028, 911, 736, 696, 679. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.31 (s, 3H, CH_3), 3.45–3.52 (m, 4H), 3.64 (dd, J = 4.5, 11.0 Hz, 1H), 3.73–3.77 (m, 1H), 3.80–3.83 (m, 1H), 3.85 (dd, J = 7.8, 9.6 Hz, 1H), 3.98 (t, J = 9.2 Hz, 1H), 4.10 (dd, J = 1.8, 11.0 Hz, 1H), 4.30 (d, J = 7.8 Hz, 1H), 4.51 (d, J = 11.4 Hz, 1H), 4.58 (d, J = 3.7 Hz, 1H), 4.61 (d, J = 11.9 Hz, 1H), 4.64 (d, J = 11.9 Hz, 1H), 4.71–4.79 (m, 8H), 4.91–4.97 (m, 3H), 7.19–7.34 (m, 30H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 62.2, 68.9, 70.2, 73.2, 73.4, 73.5, 74.3, 74.8, 75.0, 75.3, 75.8, 78.2, 79.5, 80.0, 82.2, 82.5, 98.1, 104.4, 126.8, 127.67, 127.72, 127.76, 127.8, 128.0, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 138.3, 138.4, 138.5, 138.6, 138.8, 139.0.

2,3,4-Tri-*O*-benzyl-6-*O*-2-(2-nitrophenyl)propyloxycarbonyl-α-D-glucopyranose 19. To a solution of compound **6** (0.15 g, 0.20 mmol) in THF/H_2O (10/1, 5 ml), was added NBS (0.80 g, 1.0 mmol) at 0 °C. The reaction mixture was stirred 2 h at rt. After completion of the reaction, Na_2SO_3 (1 g), $NaHCO_3$ (1 g), and a few drops of water were added. The mixture was stirred for 20 min, diluted with EtOAc (50 mL), washed with saturated $NaHCO_3$ (3 × 10 mL) and brine (3 × 10 mL), dried over $MgSO_4$, and concentrated in vacuum to give a crude product which was purified by chromatography (EtOAc:cyclohexane, 1:4–1:2) to give 0.124 g (94%) of **19** as a mixture of α and β anomers about 3:2. R_f = 0.09 (EtOAc:cyclohexane, 1:4).^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 and 1.34 (2d, J = 6.8 Hz, 3H, CH_3), 3.29–3.31 (m, 0.6H), 3.37–3.60 (m, 2.2H), 3.63–3.86 (m, 2H), 3.99 (t, J = 9.2 Hz, 0.6H), 4.07–4.40 (m, 4.8H), 4.50–4.58 (m, 1H), 4.67–4.77 (m, 2H), 4.82–4.86 (m, 2H), 4.93–4.98 (m, 1.2H), 5.18 (m, 0.6H), 7.23–7.31 (m, 16H), 7.42–7.54 (m, 2H, 2 × CH), 7.73 (d, J = 9.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.9, 33.3, 66.6, 66.7, 68.9, 71.7, 71.8, 72.9, 73.0, 73.4, 74.8, 75.2, 75.8, 77.3, 77.4, 80.0, 81.7, 83.0, 83.10, 84.6, 91.2, 97.5, 124.4, 127.6, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 128.56, 128.59, 128.63, 132.8, 132.9, 137.5, 137.8, 137.9, 138.0, 138.4, 138.5, 138.6, 150.3, 154.9, 155.0. ESI HRMS (m/z): calcd for $C_{37}H_{39}NNaO_{10}$: 680.2472, found: 680.2466.

2,3,4-Tri-*O*-benzyl-6-*O*-2-(2-nitrophenyl)propyloxycarbonyl-D-glucopyranosyl fluoride 20. A mixture of compound **6** (78 mg, 0.1 mmol), NIS (49 mg, 0.2 mmol), and powdered 4 Å molecular sieves (0.1 g) in CH_2Cl_2 (5 mL) was stirred for 10 min at −78 °C before the addition of DAST (35 μL, 0.27 mmol). The mixture was stirred at −78 °C for 2 h and then gradually raised to rt. The reaction was monitored by TLC. After completion of the reaction, Na_2SO_3 (250 mg), $NaHCO_3$ (250 mg), and a few drops of water were added. The mixture was stirred for 5 min, then diluted with CH_2Cl_2 (50 mL), filtered through Celite, washed with saturated $NaHCO_3$ (2 × 10 mL) and brine (2 × 10 mL), dried over $MgSO_4$, and concentrated in vacuum. Purification by chromatography (EtOAc: cyclohexane, 1:9–1:4) gave 61 mg (90%) of **20** as a mixture of α and β anomers about 1:1. Rf = 0.2 (EtOAc:cyclohexane, 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 and 1.37 (2d, J = 6.8 Hz, 3H, CH3), 3.49–3.75 (m, 3.7H), 3.94–4.01 (m, 1.3H), 4.20–4.41 (m, 4H), 4.49–4.58 (m, 1H), 4.68–4.72 (m, 1H), 4.77 (d, J = 11.0 Hz, 1H), 4.81–4.91 (m, 2H), 4.97 (d, J = 11.0 Hz, 1H), 5.26 (dd, J = 6.9, 52.7 Hz, 0.5H, H-1β), 5.26 (dd, J = 6.9, 52.7 Hz, 0.5H, H-1β), 5.49 and 5.51 (2dd, J = 2.3, 52.7 Hz, 0.5H, H-1α), 7.23–7.35 (m, 16H), 7.42–7.46 (m, 1H), 7.60–7.66 (m, 1H), 7.75 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.0, 33.3, 65.8, 66.2, 71.2, 71.8, 72.9, 73.7, 74.5, 75.1, 75.3, 75.4, 75.9, 76.1, 76.2, 76.4, 79.2, 79.5, 81.2, 81.4, 83.4, 83.5, 104.2, 106.5, 108.5, 110.7, 124.5, 127.7, 127.9, 128.0, 128.1, 128.2, 128.25, 128.3, 128.4, 128.6, 128.63, 128.7, 132.8, 136.9, 137.6, 137.7, 138.2, 138.4, 150.3, 154.8. ESI HRMS (m/z): calcd for $C_{37}H_{38}FNNaO_9$: 682.2428, found: 682.2428.

Notes and references

1 (*a*) A. Varki, *Glycobiology*, 1993, **3**, 97–130; (*b*) R. A. Dwek, *Chem. Rev.*, 1996, **96**, 683–720; (*c*) C.-H. Wong, *Acc. Chem. Res.*, 1999, **32**, 376–385.

2 (*a*) V. N. R. Pillai, *Synthesis*, 1980, 1–26; (*b*) C. G. Bochet, *J. Chem. Soc., Perkin Trans.*, 2002, **1**, 125–142; (*c*) C. G. Bochet, *Synlett*, 2004, 2268–2274; (*d*) G. Mayer and A. Heckel, *Angew. Chem., Int. Ed.*, 2006, **45**, 4900–4921.

3 (*a*) S. P. A. Fodor, J. L. Read, M. C. Pirrung, L. Stryer, A. T. Liu and D. Solas, *Science*, 1991, **251**, 767–773; (*b*) S. P. A. Fodor, R. P. Rava, X. C. Huang, A. C. Pease, C. P. Holmes and C. L. Adams, *Nature*, 1993, **364**, 555–556; (*c*) A. C. Pease, D. Solas, E. J. Sullivan, M. T. Cronin, C. P. Holmes and S. P. A. Fodor, *Proc. Natl. Acad. Sci. U. S. A.*, 1994, **91**, 5022–5026.

4 (*a*) S. Li, N. Marthandan, D. Bowerman, H. R. Garner and T. Kodadek, *Chem. Commun.*, 2005, 581–583; (*b*) K. R. Bhushan, *Org. Biomol. Chem.*, 2006, **4**, 1857–1859.

5 (*a*) S. Sando, H. Masu, C. Farutani and Y. Aoyama, *Org. Biomol. Chem.*, 2008, **6**, 2666–2668; (*b*) K. Usui, M. Aso, M. Fukuda and H. Suemune, *J. Org. Chem.*, 2008, **73**, 241–248; (*c*) W. Lin, D. Peng, B. Wang, L. Long, C. Guo and J. Yuan, *Eur. J. Org. Chem.*, 2008, 793–796; (*d*) E. A. Lemke, D. Summerer, B. H. Geierstanger, S. M. Brittain and P. G. Schultz, *Nature Chem. Biol.*, 2007, **3**, 769–772; (*e*) S. K. Nandy, R. S. Agnes and D. S. Lawrence, *Org. Lett.*, 2007, **9**, 2249–2252.

6 D. D. Young, R. Aaron Garner, J. A. Yoder and A. Deiters, *Chem. Commun.*, 2009, 568–570.

7 (*a*) K. C. Nicolaou, N. Winssinger, J. Pastor and F. DeRoose, *J. Am. Chem. Soc.*, 1997, **119**, 449–450; (*b*) R. Rodebaugh, S. Joshi, B. Fraser-Reid and H. M. Geysen, *J. Org. Chem.*, 1997, **62**, 5660–5661; (*c*) R. Rodebaugh, B. Fraser-Reid and H. M. Geysen, *Tetrahedron Lett.*, 1997, **38**, 7653–7656; (*d*) K. C. Nicolaou, N. Watanabe, J. Li, J. Pastor and N. Winssinger, *Angew. Chem., Int. Ed.*, 1998, **37**, 1559–1561.

8 (*a*) U. Zehavi, B. Amit and A. Patchornik, *J. Org. Chem.*, 1972, **37**, 2281–2285; (*b*) U. Zehavi and A. Patchornik, *J. Org. Chem.*, 1972, **37**, 2285–2288; (*c*) U. Zehavi, *Adv. Carbohydr. Chem. Biochem.*, 1988, **46**, 179–204; (*d*) K. C. Nicolaou, C. W. Hummel, M. Nakada, K. Shibayama, E. N. Pitsinos, E. H. Saimoto, Y. Mizuno, K.-U. Baldenius and A. L. Smith, *J. Am. Chem. Soc.*, 1993, **115**, 7625–7635; (*e*) J. E. T. Corrie, *J. Chem. Soc., Perkin Trans.*, 1993, **1**, 2161–2166; (*f*) S. Watanabe, T. Sueyoshi, M. Ichihara, C. Uehara and M. Iwamura, *Org. Lett.*, 2001, **3**, 255–257; (*g*) K. Mannerstedt and O. Hindsgaul, *Carbohydr. Res.*, 2008, **343**, 875–881.

9 P. H. Seeberger and D. B. Werz, *Nature*, 2007, **446**, 1046–1051.

10 (*a*) W. Meutermans, G. T. Le and B. Becker, *ChemMedChem*, 2006, **1**, 1164–1194; (*b*) M. Gottschaldt and U. S. Schubert, *Chem.–Eur. J.*, 2009, **15**, 1548–1557.

11 (*a*) M. Beier and J. D. Hoheisel, *Nucleic Acids Res.*, 2000, **28, e11**, i–vi; (*b*) M. C. Pirrung, L. Wang and M. P. Montague-Smith, *Org. Lett.*, 2001, **3**, 1105–1108.
12 (*a*) A. Hasan, K.-P. Stengele, H. Giegrich, P. Cornwell, K. Isham, R. Sachleben, W. Pfleiderer and R. Foote, *Tetrahedron*, 1997, **53**, 4247–4264; (*b*) H. Giegrich, S. Eisele-Buhler, C. Hermann, E. Kvasyuk, R. Charubala and W. Pfleiderer, *Nucleosides Nucleotides*, 1998, **17**, 1987–1996; (*c*) S. Walbert, W. Pfleiderer and U. E. Steiner, *Helv. Chim. Acta*, 2001, **84**, 1601–1611; (*d*) S. Bühler, H. Lagoja, H. Giegrich, K.-P. Stengele and W. Pfleiderer, *Helv. Chim. Acta*, 2004, **87**, 620–659; (*e*) D. Wöll, S. Laimgruber, M. Galetskaya, J. Smirnova, W. Pfleiderer, B. Heinz, P. Gilch and U. E. Steiner, *Chem.–Eur. J.*, 2008, **14**, 6490–6497.
13 K. R. Bhushan, C. DeLisi and R. A. Laursen, *Tetrahedron. Lett.*, 2003, **44**, 8585–8588.
14 C.-J. Zhu, H. Yi, G.-R. Chen and J. Xie, *Tetrahedron.*, 2008, **64**, 10687–10693.
15 (*a*) W. Schmidt and E. Steckhan, *Chem. Ber.*, 1980, **117**, 1679–1694; (*b*) A. J. Patcliffe and B. Fraser-Reid, *J. Chem. Soc., Perkin Trans.*, 1990, **1**, 747–750.
16 Q. Pan, Y. Du, F. Kong, J. Pan and M. Lü, *J. Carbohydr. Chem.*, 2001, **20**, 297–306.
17 R. R. Schmidt, U. Moering and M. Reichrath, *Tetrahedron. Lett.*, 1980, **21**, 3565–3568.
18 S. Manabe, A. Ueki and Y. Ito, *Tetrahedron. Lett.*, 2008, **49**, 5159–5161.

