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A new glycosidation method through nitrite displacement on substituted nitrobenzenes

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Dedicated to the memory of Professor Nikolay K. Kochetkov

Abstract—Benzyl, benzoyl, and acetyl protected 1-OH and 1-SH glycoses in the glucose, glucosamine, galactose, mannose, and lactose series react with nitrobenzenes activated by one or two electron withdrawing substituents like nitro and cyano to afford the corresponding aryl glycosides in 50–100% yield. The S_NAr displacement of nitrite by 1-OH glycoses is reversible and gives predominantly the α-glycosides, whereas 1-SH glycoses do not anomerize and afford the β-glycosides. Thus, the prepared dicyanophenyl gycosides are useful building blocks for the preparation of phthalocyanine-glycoconjugates via template synthesis.
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Keywords: Glycosylation; Aryl glycosides; Nucleophilic substitution

1. Introduction

Carbohydrates habitually exist on cell surfaces as glycoproteins or glycolipid conjugates and are engaged in important functional and structural functions in various biological recognition processes like for instance, cancer metastasis, inflammatory response, innate and adaptive immunity, viral and bacterial infections, and many other receptor-mediated signalling processes.[1,2] Moreover, a large number of natural products require glycosylation in order to show proper biological performance.[3–5] However, the effect of glycosylation on the structure and function of natural products is not well understood, mostly due to the lack of efficient synthesis methods to cover the structural diversity of glycoconjugates required for answering the distinct role of glycosylation in biological systems.

Selective glycosidic bond formation in order to gain chemically well defined oligosaccharides and glycoconjugates is probably the most significant challenge of carbohydrate chemistry today. Although great achievements in the development of versatile and efficient glycosylation and building block strategies have been made during the last years, there is still need for more efficient procedures to prepare glycoconjugates.[6–9]

The basic concepts of glycosylation embrace either formation of the glycosidic bond through classical Koenigs–Knorr type reactions where the anomeric oxygen originates from the aglycon or through retention of the anomeric oxygen via anomeric O-arylation or O-alkylation reactions. The latter methodology is based on deprotonation of the anomeric hydroxyl of sugars, thus, generating an anomeric oxide. Immediate O-arylation or O-alkylation leads to the glycoside bond. This method turned out to be extremely important for the synthesis of a variety of glycosides.[10–12] Nevertheless, this methodology has limited general applicability to the synthesis of glycoconjugates.

Recently, we found a novel straightforward and efficient template synthesis of phthalocyanine-glycoconjugates from dicyanophenyl glycosides which enabled us to prepare a series of water soluble phthalocyanines suitable for photodynamic therapy (Chart 1).[13,14] For

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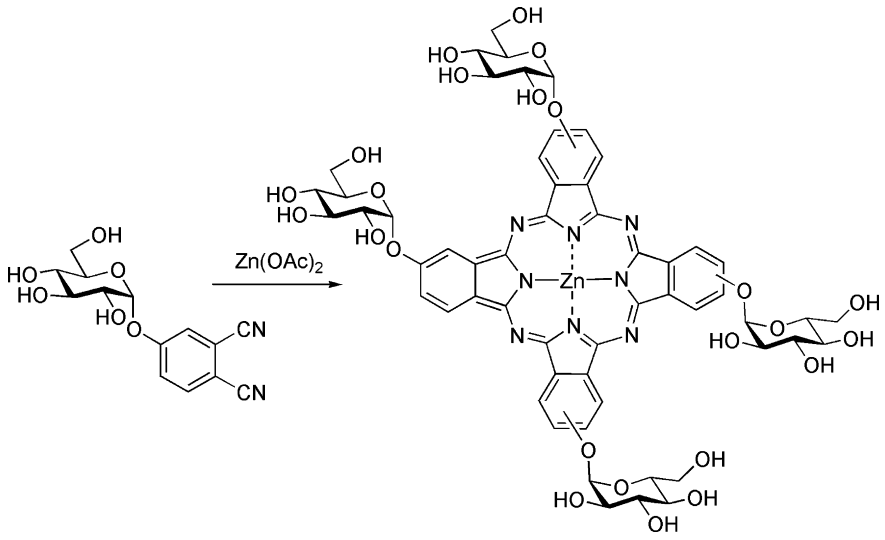


Chart 1. Synthesis of phthalocyanine-glycoconjugates from dicyanophenyl glycosides.[14]

further studies on phthalocyanine-glycoconjugates, we needed a versatile route to dicyanophenyl glycosides for which we present a novel preparation through nucleophilic nitrite displacement of nitrobenzenes by anomeric glycosyl oxides (O-arylation of sugars).

2. Results and discussion

Base promoted direct anomeric O-arylation of protected sugars has been investigated by several authors.[15–18] These methods take advantage of the excellent leaving group character of fluoride in substituted, fluorinated nitro- or dinitrobenzenes, resulting in fairly good yields of mainly β-*O*-aryl glycosides. However, similar O-arylations of glycoses by nitrite substitution on nitrobenzenes are not described in the literature yet.

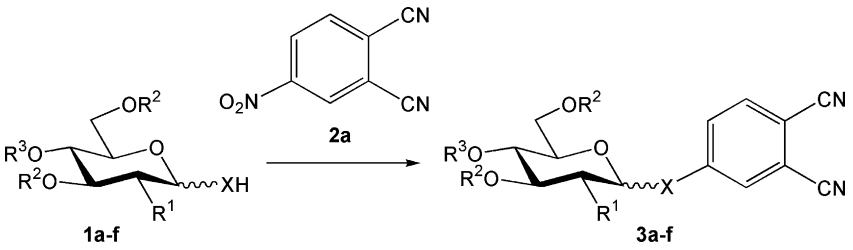
In general, nucleophilic displacement of a nitro group from an activated aromatic substrate can be effectively achieved by a variety of strong nucleophiles under dipolar aprotic conditions. For example, alcoholates,[19–21] thiolates,[19,22] and sulfinates[19] efficiently effect displacement of a nitrite group from carbonyl, nitro, cyano, sulfone, and aryl activated substrates in DMF, Me_2SO, or HMPA at room temperature.[19–23] Furthermore, nitrite is comparable to fluoride regarding its nucleofugicity in S_NAr reaction.[24]

First, we tried to prepare 3,4-dicyanophenyl glucose derivatives **3** by classical Koenigs–Knorr type glycosylation reactions of 3,4-dicyanophenol with penta-*O*-acetyl-glucose under activation with BF_3–etherate[25] and *p*-toluenesulfonic acid,[26] respectively, or by TMS–triflate activation of 2,3,4,5-tetra-*O*-benzoyl-D-glucose trichloroacemidate.[27] However, none of these methods were successful. Similarly, Mitsunobu-type conditions[28] for condensing various anomerically unprotected glycoses with 3,4-dicyanophenol also failed (experimental details not shown here).

Next, we turned our efforts to the nucleophilic displacement of nitrite from activated substituted benzenes **2** (Scheme 1), a method that has already been widely used for the synthesis of oxoaryl phthalonitriles.[29] Base promoted direct anomeric O- or S-arylation of several 2,4,5,6-tetra-*O*-benzyl, benzoyl, and acetyl protected hexopyranoses and 1-thio-hexopyranoses **1** to give aryl glycosides **3** was carried out either with NaH or K_2CO_3 (Table 1). NaH as the base resulted in significantly shorter reaction times, compared to K_2CO_3 as the base (approximately 1 h vs 10–12 h).

The main products in the case of **3a**–**c** were the respective α-anomers independent from the base. Similar unexpected results were also observed previously in anomeric O-arylations and were attributed to the formation of the thermodynamically favored α-anomers during reversible S_NAr reactions in polar aprotic solvents like Me_2SO or DMF in the presence of a base.[15] No such thermodynamic equilibration can take place in case of thionucleophiles **1d** and **1f**, respectively, and thus resulting in the exclusive formation of the β-linked products **3d** and **3f** (Table 1, entries 4 and 6).

For **1e** (Table 1, entry 5), the obtained product was also the β-anomer **3e**, probably due to the fact that although **1e** is an O-nucleophile, it is sterically hindered by the presence of the bulky phthalimido group at position 2 which, furthermore, strongly promotes the formation of the β-anomeric linkage. Anomeric mixtures were separated by preparative HPLC for determining the anomeric ratio and all anomers were unambiguously assigned by NMR spectroscopy, which showed the typical vicinal coupling constants between H-1 and H-2 significant for the presence of α- or β-anomers (see Section 3).



1,3a R^1 = OBn, R^2,R^3 = Bn, X = O
1,3b R^1 = OBz, R^2,R^3 = Bz, X = O
1,3c R^1 = OAc, R^2,R^3 = Ac, X = O
1,3d R^1 = OAc, R^2,R^3 = Ac, X = S
1,3e R^1 = NPhth, R^2,R^3 = Ac, X = O
1,3f R^1 = OBz, R^2 = OBz, R^3 = β-BzGal, X = S

Scheme 1. Synthesis of dicyanophenyl carbohydrate derivatives.

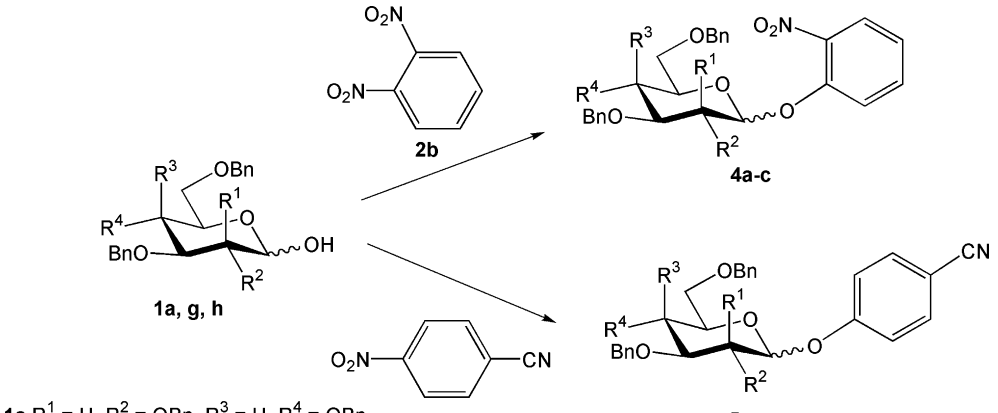
Table 1. Reactions between **1a**–**f** and 4-nitrophthalonitrile **2a**

Entry	Conditions	Product	Yield (%)	Ratio α:β
1	DMF, NaH, 1 h	**3a**	99	9:1
2	DMF, K_2CO_3, 15 h	**3b**	99	10:1
3	DMF, K_2CO_3, 15 h	**3c**	99	10:1
4	DMF, K_2CO_3, 15 h	**3d**	99	0:1
5	DMF, K_2CO_3, 15 h	**3e**	50	0:1
6	DMF, K_2CO_3, 15 h	**3f**	99	0:1

Additionally, we investigated this efficient glycosylation method for other substrates as well, namely *o*-dinitrobenzene **2b** and *p*-nitrobenzonitrile **2c** (Scheme 2). Due to the nucleophilicity of the carbohydrate moieties, we expected that the nitrite-substitution would also work well in the case of substituted phenyl compounds having only one additional electron withdrawing group. However, S_NAr reactions in DMF using K_2CO_3 or DBU as base failed completely. At room temperature, no reaction took place whereas at elevated temperatures decomposition of the starting materials occurred. Solely NaH as the base gave the desired substitution products at room temperature (Table 2).

The significantly lower anomeric selectivity for O-arylations with less activated nitrobenzenes **2b** and **2c** (Table 2, entries 1, 2, 4, and 5) can be explained in terms of a slower equilibration between the α- and β-anomer compared to the phthalodinitrile aglycon under similar reaction conditions. In case of the mannose nucleophile **1h**, only α-anomers **4c** and **5c** were found due to the steric effect in mannose.

In summary, anomeric O-arylation of partially protected glycoses by nucleophilic nitrite substitution on nitrobenzenes is a practical alternative to similar O-arylations using fluorobenzenes when the benzene moiety is activated for S_NAr reactions by at least two electron withdrawing groups. The anomeric selectivity for nucleo-



1a R^1 = H, R^2 = OBn, R^3 = H, R^4 = OBn
1g R^1 = H, R^2 = OBn, R^3 = OBn, R^4 = H
1h R^1 = OBn, R^2 = H, R^3 = H, R^4 = OBn

Scheme 2. Synthesis of nitrophenyl and cyanophenyl carbohydrate derivatives.

Table 2. Reaction of **1a**, **1g**, **1h** with **2b** and **2c** and NaH in DMF for 15 h at rt

Entry	Product	Yield (%)	Ratio α:β
1	**4a**	94	3:1
2	**4b**	92	3:1
3	**4c**	89	1:0
4	**5a**	82	3:1
5	**5b**	84	3:1
6	**5c**	84	1:0

All reactions were carried out using DMF as a solvent and NaH as a base (reaction time 15 min).

philic displacement of nitrite is comparable to the nucleophilic displacement of fluoride.

3. Experimental

3.1. General methods

^{1}H and ^{13}C NMR spectra were recorded with Bruker AC 300F, Avance 400 or DRX 500 spectrometers at 300, 400, or 500 MHz and 75, 100.6, or 126 MHz, respectively. Chemical shifts in $CDCl_3$ are reported in δ (ppm) relative to tetramethylsilane (TMS) as internal standard. Coupling constants J are reported in hertz. Assignment of signals was made by first order inspection of the spectra and by ^{1}H^{1}H-, ^{13}C^{1}H-COSY, HMQC, or NOESY experiments, respectively. MS spectra were recorded with Bruker Autoflex (MALDI-TOFMS) and Bruker Apex II FT-ICR (FABMS) instruments. Specific optical rotations [α] were recorded with a Perkin–Elmer polarimeter Model 341 at 589 nm (Na-D) for solns in $CHCl_3$ at 20 °C if not stated otherwise. Elemental analyses were performed with a Hekatech CHNS analysator Euro EA 300. Melting points were determined on a Büchi SMP-20 instrument. GC was performed with Varian/Chrompack CP 9000 and CP 9001 instruments using Chirasil-β-Cyclodextrin columns. TLC was performed on Macherey & Nagel Silica Gel SIL G/UV254 plates. Spots were detected by visual inspection of the plates under UV light, by charring with H_2SO_4 (5% in EtOH), with $KMnO_4$ (5% in water) and with I_2, respectively. Preparative column chromatography was performed by eluting compounds with various mixtures of solvents from glass columns of various sizes filled with Macherey & Nagel Silica Gel S (0.032–0.063 mm). Solns in organic solvents were dried with Na_2SO_4, filtered, and concentrated with a rotary evaporator. Anomeric ratios were determined by HPLC on a Sykam system using an Grom Saphir Si; 5 μm; 250 × 6 mm column. The eluents used were *n*-heptane and EtOAc. Reverse phase HPLC was performed on a Waters apparatus using a GROM SIL 120 ODS-4HE; 10 μm; 250 × 20 mm column.

3.2. 3,4-Dicyanophenyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside (3a)

NaH (280 mg, 7 mmol, 60% suspension in oil) was added at rt to a stirred soln of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose[30] **1a** (3.80 g, 7.0 mmol) and 4-nitrophthalonitrile **2a** (1.33 g, 7.7 mmol) in dry DMF (25 mL) under argon. The mixture was stirred for 2 h. At the end of this period, the reaction was poured into water (200 mL) and CH_2Cl_2 (100 mL). The aq layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with water (3 × 50 mL). After drying (Na_2SO_4), filtration, and removal of the solvent, the crude product was purified by chromatography on silica gel (10:1 toluene–acetone) to give **3a**; 4.63 g (99%; α/β = 9:1).

α-Anomer: Colorless oil; $[\alpha]_D^{20}$ +132.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.51–3.59 (m, 1H, H-6a), 3.64–3.83 (m, 5H, H-2, H-3, H-4, H-5, H-6b), 4.08–4.18 (dd, 1H, J_{3-4} 8.6, J_{3-2} 9.4 Hz, H-3), 4.38–4.65 (m, 4H, H–CH_2), 4.81–4.93 (m, 3H, H–CH_2), 5.03 (d, 1H, J 10.8 Hz, H–CH_2), 5.37 (d, 1H, J_{1-2} 3.4 Hz, H-1), 7.23–7.44 (m, 20H, H–Ar, H-2′, H-6′), 7.11–7.17 (m, 2H, H–Ar), 7.66 (d, 1H, $J_{5'-6'}$ 8.6 Hz, H-5′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 67.9 (C-6), 71.9 (C-5), 73.5, 74.0, 75.3, 75.9 (C–CH_2), 76.9 (C-2), 79.5 (C-4), 81.6 (C-3), 96.3 (C-1), 108.9 (C-4′), 115.0 (C-3′CN), 115.4 (C-4′CN), 117.5 (C-3′), 121.4 (C-2′, C-6′), 127.81, 127.87, 127.91, 127.95, 128.0, 128.2, 128.46, 128.48, 128.5, 128.6 (C-2Ar, C-3Ar, C-4Ar), 135.2 (C-5′), 137.5, 137.7, 137.8, 138.5 (C-1Ar), 159.7 (C-1′); MALDI-TOFMS: *m*/*z* 689.4 $[M+Na]^+$. Anal. Calcd for $C_{42}H_{38}N_2O_6$: C, 75.66; H, 5.74; N, 4.20; Found: C, 75.95; H, 5.76; N, 4.30.

β-Anomer (minor byproduct): ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.58–3.78 (m, 6H, H-2, H-3, H-4, H-5, H-6), 4.42–4.59 (m, 3H, H–CH_2), 3.78–4.95 (m, 5H, H–CH_2), 5.01 (d, 1H, J_{1-2} 7.8 Hz, H-1), 7.13–7.43 (m, 22H, H–Ar, H-2′, H 6′), 7.59 (d, 1H, $J_{5'-6'}$ 8.6 Hz, H-5′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 68.4 (C-6), 73.5, 75.1, 75.3 (C–CH_2), 75.5 (C-5), 75.8 (C–CH_2), 77.3 (C-2), 81.7 (C-4), 84.5 (C-3), 100.7 (C-1), 109.1 (C-4′), 115.0 (C-3′CN), 115.4 (C-4′CN), 117.4 (C-3′), 121.1 (C-2′), 121.7 (C-6′), 127.5, 127.7, 127.8, 127.9, 128.0, 128.44, 128.47, 128.5, 128.8, 128.9 (C-2Ar, C-3Ar, C-4Ar), 135.2 (C-5′), 137.7, 137.8, 138.1 (C-1Ar), 159.9 (C-1′); MALDI-TOFMS: *m*/*z* 689.4 $[M+Na]^+$.

3.3. 3,4-Dicyanophenyl 2,3,4,6-tetra-*O*-benzoyl-D-glucopyranoside (3b)

K_2CO_3 (5.60 g, 40.2 mmol) was added at rt to a stirred soln of 2,3,4,6-tetra-*O*-benzoyl-D-glucopyranose[31] **1b** (4.00 g, 6.7 mmol) and 4-nitrophthalonitrile **2a** (1.28 g, 7.4 mmol) in dry DMF (25 mL). The mixture was stirred overnight. At the end of this period, the mixture was

poured into water (200 mL) and CH_2Cl_2 (100 mL). The aq layer was extracted with CH_2Cl_2 (3 × 50 mL). The organic layer was washed with water (3 × 50 mL). After drying (Na_2SO_4), filtration, and removal of the solvent, the crude product was purified by chromatography on silica gel (10:1 toluene–acetone) to give 4.80 g (99%; α/β, 9:1) of **3b**.

α-Anomer: white solid; mp 174–174.5 °C (*n*-heptane-EtOAc); $[\alpha]_D^{20}$ +98.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 4.38–4.58 (m, 3H, H-5, H-6), 5.44–5.52 (d, 2H, J_{2-1} 3.7, J_{2-3} 10.1 Hz, H-2), 5.71–5.76 (dd, 1H, J_{4-5} 9.6, J_{4-3} 9.9 Hz, H-4), 6.14 (d, 1H, J_{1-2} 3.4 Hz, H-1), 6.27–6.39 (dd, 1H, J_{3-4} 9.9, J_{3-2} 10.1 Hz, H-3), 7.27–7.65 (m, 15H, H-2Ar, H-4Ar, H-2′, H-5′, H-6′), 7.83–7.98 (m, 8H, H-3Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 62.6 (C-6), 68.9 (C-4), 69.7 (C-5), 69.72 (C-3), 71.1 (C-2), 94.4 (C-1), 109.7 (C-4′), 114.6 (C-3′CN), 115.0 (C-4′CN), 117.7 (C-3′), 120.9 (C-2′), 121.7 (C-6′), 128.2, 128.3, 128.4, 128.54, 128.59, 128.6, 128.7, 129.1 (C-1Ar, C-3Ar), 129.5, 129.7, 129.9 (C-2Ar), 133.5, 133.7, 133.8, 133.9 (C-4Ar), 135.3 (C-5′), 158.6 (C-1′), 165.3, 165.6, 165.75, 165.76 (C–CO); FABMS: *m*/*z* 723.1 $[M+Na]^+$. Anal. Calcd for $C_{42}H_{30}N_2O_{10}$: C, 69.80; H, 4.18; N, 3.88. Found: C, 69.90; H, 4.20; N, 3.79.

β-Anomer (minor byproduct): ^{1}H NMR (250 MHz, $CDCl_3$): δ 4.39–4.57 (m, 2H, H-5, H-6a), 4.64–4.71 (dd, 1H, J_{6b-5} 2.5, J_{6b-6a} 11.8 Hz, H-6b), 5.56 (d, 1H, J_{1-2} 7.2 Hz, H-1), 5.69–5.82 (m, 2H, H-2, H-4), 5.94–6.03 (t, 1H, $J_{3-2/3-4}$ 9.1 Hz, H-3), 7.20–7.64 (m, 15H, H-2′, H-5′, H-6′, H-3Ar, H-4Ar), 8.82–8.99 (m, 8H, H-2Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 62.7 (C-6), 68.9 (C-4), 71.3 (C-2), 72.2 (C-3), 73.3 (C-5), 98.2 (C-1), 109.9 (C-4′), 114.7 (C-3′CN), 115.1 (C-4′CN), 117.6 (C-3′), 121.2 (C-2′), 121.6 (C-6′), 128.4, 128.6, 128.7 (C-3Ar), 129.1 (C-1Ar), 129.6, 129.7, 129.8, 129.9 (C-2Ar), 133.5, 133.6, 133.8 (C-4Ar), 135.1 (C-5′), 159.1 (C-1′), 164.9, 165.2, 165.6, 165.8 (C–CO); FABMS: *m*/*z* 723.1 $[M+1]^+$.

3.4. 3,4-Dicyanophenyl 2,3,4,6-tetra-*O*-acetyl-D-glucopyranoside (3c)

Treatment of 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose[31] **1c** (6.0 g, 17.0 mmol) and **2a** (3.23 g, 18.7 mmol) as described for **3b** afforded 8.06 g (100%; α/β = 10:1) of **3c**.

α-Anomer: white solid; mp 159–160 °C (*n*-heptane-EtOAc); $[\alpha]_D^{20}$ +202.0 (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.01 s, 2.02 s, 2.03 s, 2.04 s (12H, H–CH_3), 3.91–4.06 (m, 2H, H-5, H-6a), 4.15–4.24 (dd, 1H, J_{6b-5} 4.9, J_{6b-6a} 12.3 Hz, H-6b), 5.02–5.07 (dd, 1H, J_{2-1} 3.5, J_{2-3} 10.1 Hz, H-2), 5.08–5.18 (dd, 1H, J_{4-3} 9.6, J_{4-5} 10.1 Hz, H-4), 5.57–5.67 (dd, 1H, J_{3-4} 9.6, J_{3-2} 10.1 Hz, H-3), 5.81 (d, 1H, J_{1-2} 3.5 Hz, H-1), 7.38–7.45 (dd, 1H, $J_{6'-2'}$ 2.5, $J_{6'-5'}$ 8.6 Hz, H-6′), 7.53 (d, 1H, $J_{2'-6'}$ 2.5 Hz, H-2′), 7.75 (d, 1H, $J_{5'-6'}$ 2.5, 8.6 Hz, H-5′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 20.4 (C–CH_3), 61.4 (C-6), 67.8 (C-4), 69.1 (C-5), 69.4 (C-3), 69.9 (C-2), 94.6 (C-1), 109.9 (C-4′), 114.7 (C-3′CN), 115.1 (C-4′CN), 117.8 (C-3′), 121.1 (C-6′), 121.5 (C-2′), 135.4 (C-5′), 158.9 (C-1′), 169.4, 169.9, 170.0, 170.3 (C–CO); MALDI-TOFMS: *m*/*z* 497.23 $[M+Na]^+$. Anal. Calcd for $C_{22}H_{22}N_2O_{10}$: C, 55.70; H, 4.67; N 5.90. Found: C, 55.50; H, 4.63; N,5.57.

β-Anomer (minor byproduct): ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.02 s, 2.05 s, 2.09 s (12H, H–CH_3), 3.89–3.97 (m, 1H, H-5), 2.17–2.24 (m, 2H, H-6), 5.02–5.31 (m, 4H, H-1, H-2, H-3, H-4), 7.25–7.30 (dd, 1H, $J_{6'-2'}$ 2.5, $J_{6'-5'}$ 8.6 Hz, H-6′), 7.38 (d, 1H, $J_{2'-6'}$ 2.5 Hz, H-2′), 7.72 (d, 1H, $J_{5'-6'}$ 8.6 Hz, H-5′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 20.52 (C–CH_3), 61.87 (C-6), 67.90 (C-2), 70.79 (C-4), 72.25 (C-3), 72.76 (C-5), 97.98 (C-1), 110.08 (C-4′), 114.90 (C-3′CN), 115.06 (C-4′CN), 117.70 (C-3′), 121.09 (C-2′), 121.77 (C-6′), 135.21 (C-5′), 159.26 (C-1′), 169.06, 169.31, 170.03, 170.37 (C–CO); MALDI-TOFMS: *m*/*z* 497.23 $[M+Na]^+$.

3.5. 3,4-Dicyanophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (3d)

Treatment of 2,3,4,6-tetra-*O*-acetyl-1-thio-D-glucopyranose[32] **1d** (4.00 g, 11.0 mmol) and **2a** (3.23 g, 18.7 mmol) as described for **3b** afforded **3d** (5.48 g; 100%); white powder; mp 164–165 °C (*n*-heptane–EtOAc); $[\alpha]_D^{20}$ −51.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.98 s, 2.02 s, 2.06 s, 2.12 s (12H, H–CH_3), 3.78–3.86 (m, 1H, H-5), 4.18–4.23 (m, 2H, H-6), 4.82 (d, 1H, J_{1-2} 10 Hz, H-1), 4.92–5.08 (m, 2H, H-2, H-4), 5.20–5.30 (dd, 1H, J_{3-4} 9.1, J_{3-4} 9.3 Hz, H-3), 7.67–7.71 (dd, 1H, $J_{5'-2'}$ 1, $J_{5'-6'}$ 8.4 Hz, H-5′), 7.71–7.76 (dd, 1H, $J_{6'-2'}$ 2, $J_{6'-5'}$ 8.4 Hz, H-6′), 7.86–7.88 (dd, 1H, $J_{2'-5'}$ 1, $J_{2'-6'}$ 2 Hz, H-2′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 20.5, 20.7, 20.8 (C–CH_3), 61.9 (C-6), 67.8 (C-4), 69.4 (C-2), 73.4 (C-3), 76.4 (C-5), 83.9 (C-1), 114.3 (C-4′), 114.9 (C-3′CN), 115.0 (C-4′CN), 116.5 (C-3′), 133.3 (C-5′), 134.9 (C-2′), 135.0 (C-6′), 140.88 (C-1′), 169.1, 169.3, 169.9, 170.5 (C–CO); MALDI-TOFMS: *m*/*z* 513.24 $[M+Na]^+$. Anal. Calcd for $C_{22}H_{22}N_2O_9S$: C, 53.87; H, 4.52; N, 5.71; S, 6.54. Found: C, 53.86; H, 4.73; N, 5.33; S, 6.24.

3.6. 3,4-Dicyanophenyl 3,4,6-tri-*O*-acetyl-2-desoxy-2-phthalimido-β-D-glucopyranoside (3e)

Treatment of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranose[31] **1e** (6.5 g, 15.0 mmol) and **2a** (3.23 g, 18.7 mmol) as described for **3b** afforded **3e** (4.25 g; 50%); white powder; mp 102–103 °C (*n*-heptane–EtOAc); $[\alpha]_D^{20}$ +74.9 (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.87 s, 2.05 s, 2.12 s (H–CH_3), 4.03–4.15 (m, 1H, H-5), 2.16–4.31 (m, 2H, H-6), 4.56–4.65 (dd, 1H, J_{2-1} 8.8,

J_{2-3} 10.6 Hz, H-2), 5.15–5.25 (dd, 1H, J_{4-3} 9.1, J_{4-5} 10.1 Hz, H-4), 5.78–5.88 (dd, 1H, J_{3-4} 9.1, J_{3-2} 10.6 Hz, H-3), 6.11 (d, 1H, J_{1-2} 8.8 Hz, H-1), 4.18–4.24 (dd, 1H, $J_{6'-2'}$ 2, $J_{6'-5'}$ 8.8 Hz, H-6′), 7.33 (d, 1H, $J_{2'-6'}$ 2 Hz, H-2′), 7.65 (d, 1H, $J_{5'-6'}$ 8.8 Hz, H-5′), 7.72–7.79 (m, 2H, H-3Ar, H-4Ar), 7.80–7.88 (m, 2H, H-2Ar, H-6Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 20.3, 20.6, 20.7 (C–CH_3), 54.1 (C-2), 61.9 (C-6), 68.4 (C-4), 70.3 (C-3), 72.8 (C-5), 95.3 (C-1), 110.0 (C-4′), 114.9 (C-3′CN), 115.1 (C-4′CN), 117.6 (C-3′), 121.4 (C-2′), 121.7 (C-6′), 123.9 (C-2Ar, C-5Ar), 131.1 (C-1Ar, C-6Ar), 134.7 (C-3Ar, C-4Ar), 135.1 (C-5′), 159.1 (C-1′), 169.37, 170.02, 170.43 (C–CO); MALDI-TOFMS: *m/z* 584.32 $[M+Na]^+$. Anal. Calcd for $C_{28}H_{23}N_3O_{10}$: C, 59.89; H, 4.13; N, 7.48. Found: C, 59.95; H, 4.18; N, 7.28.

3.7. 2,3,6,2′,3′,4′,6′-Hepta-*O*-benzoyl-1-thio-β-lactose (1f)

A soln of lactose (6.50 g, 19 mmol) in pyridine (60 mL) was heated at 80 °C for 30 min, and on cooling, benzoyl chloride (30 mL, 258 mmol) was added dropwise. The reaction mixture was heated for another 2 h at 80 °C and cooled to rt. Water (10 mL) was added and after 10 min, the mixture was poured into ice water (500 mL). The aq phase was extracted with CH_2Cl_2 (3×100 mL). The combined organic phases were washed with 2 M HCl (3×50 mL), satd aq $NaHCO_3$ soln (1×50 mL) and water (1×50 mL), dried (Na_2SO_4), filtrated, and concentrated. The intermediate octa-*O*-benzoyl-lactose was used without further purification for the next step. A soln of crude 1,2,3,6,2′,3′,4′,6′-octa-*O*-benzoyl-lactose (19 mmol) in CH_2Cl_2 (50 mL) was treated with 33% HBr in AcOH (20 mL) at rt for 2 h. The soln was cooled in an ice-bath, diluted with CH_2Cl_2 (100 mL), washed sequentially with ice-cold water (50 mL), ice-cold, satd soln of $NaHCO_3$ (2×50 mL) and ice-cold water (50 mL), dried (Na_2SO_4), filtrated, and then concentrated. The intermediate hepta-*O*-benzoyl-lactosyl bromide was used without further purification for the next step. A soln of 2,3,6,2′,3′,4′,6′-hepta-*O*-benzoyl-α-lactosyl bromide and thiourea (1.90 g, 25 mmol) in anhyd acetone (200 mL) was boiled under reflux for 7 h, cooled, and the acetone was evaporated under diminished pressure. The residue was stirred with CH_2Cl_2 (100 mL) and an aq soln of $K_2S_2O_7$ (5.60 g in 100 mL water) at reflux overnight. After cooling, the organic layer was separated and washed with water (25 mL). After drying (Na_2SO_4), filtration, and removal of the solvent, the crude product was purified by chromatography on silica gel (10:1 toluene–acetone) to give **1f** (12.47 g; 60%); white solid; mp 129–130 °C (*n*-heptane–EtOAc); $[\alpha]_D^{20}$ −69.8 (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.68–3.76 (m, 2H, H-6′), 3.80–3.91 (m, 2H, H-5, H-5′), 4.20–4.30 (dd, 1H, J_{4-3} 9.4, J_{4-5} 9.8 Hz, H-4), 4.47–4.60 (m, 2H, H-6), 4.68–4.77 (dd, 1H, J_{1-2} 9.6, $J_{1\text{-SH}}$ 9.8 Hz, H-1), 4.86 (d, 1H, J_{1-2} 7.9 Hz, H-1′), 5.31–5.45 (m, 2H, H-2, H-3′), 5.65–5.81 (m, 3H, H-3, H-2′, H-4′), 7.09–7.60 (m, 21H, H-3Ar, H-4Ar), 7.84–8.02 (m, 14H, H-2Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 61.0 (C-6′), 62.5 (C-6), 67.5 (C-4′), 69.9 (C-2′), 71.4 (C-5′), 71.8 (C-3′), 73.7 (C-3), 74.1 (C-2), 75.7 (C-4), 77.5 (C-5), 78.9 (C-1), 100.9 (C-1′), 128.2, 128.4, 128.51, 128.55, 128.6 (C-3Ar), 129.5, 129.64, 129.67, 129.7, 129.9, 129.9 (C-1Ar, C-2Ar), 133.2, 133.4, 133.5 (C-4Ar), 164.8, 165.2, 165.3, 165.5, 165.9 (C–CO); MALDI-TOFMS: *m/z* 1109.65 $[M+Na]^+$. Anal. Calcd for $C_{61}H_{50}O_{17}S$: C, 67.39; H, 4.64; S, 2.95. Found: C, 67.41; H, 4.68; S, 2.80.

3.8. 3,4-Dicyanophenyl 2,3,6,2′,3′,4′,6′-hepta-*O*-benzyl-1-thio-β-lactoside (3f)

Treatment of 2,3,6,2′,3′,4′,6′-hepta-*O*-benzoyl-1-thio-β-lactose **1f** (10.0 g, 9.2 mmol) and **2a** (1.61 g, 9.3 mmol) as described for **3b** afforded **3f** (11.0 g; 100%); white solid; mp 134–135 °C (*n*-heptane–EtOAc); $[\alpha]_D^{20}$ +20.6 (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.64–3.84 (m, 2H, H-6′), 3.92–4.03 (m, 2H, H-5, H-5′), 4.12–4.21 (dd, 1H, J_{4-3} 9.4, J_{4-5} 9.6 Hz, H-4), 4.45–4.54 (dd, 1H, J_{6a-5} 4.9, J_{6a-6b} 12.3 Hz, H-6a), 4.63–4.71 (dd, 1H, J_{6b-5} 1.7, J_{6b-6a} 12.3 Hz, H-6b), 4.90 (d, 1H, $J_{1'-2'}$ 7.9 Hz, H-1′), 4.99 (d, 1H, J_{1-2} 9.9 Hz, H-1), 4.34–4.45 (m, 2H, H-2, H-3′), 4.67–4.76 (m, 2H, H-2′, H-4′), 4.80–4.89 (t, 1H, $J_{H2/H5}$ 9.4 Hz, H-3), 7.09–7.60 (m, 24H, H-3Ar, H-4Ar, H-2″, H-5″, H-6″), 7.84–8.02 (m, 14H, H-2Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 60.9 (C-6′), 62.1 (C-6), 67.5 (C-4′), 69.9 (C-2′), 70.0 (C-2), 71.5 (C-5′), 71.7 (C-3′), 73.5 (C-3), 75.8 (C-4), 77.6 (C-5), 83.9 (C-1), 101.1 (C-1′), 114.2 (C-4″), 114.6 (C-3″CN), 114.9 (C-4″CN), 116.2 (C-3″), 128.3, 128.4, 128.5, 128.6, 128.7 (C-3Ar), 128.8, 129.2, 129.4 (C-1Ar), 128.5, 129.6, 129.7, 129.92, 129.98 (C-2Ar), 133.2, 133.3, 133.4, 133.5, 133.6, 133.7, 133.8 (C-5″, C-4Ar), 135.3 (C-6″), 135.4 (C-2″), 140.4 (C-1″), 164.8, 165.1, 165.19, 165.22, 165.4, 165.6 (C–CO); MALDI-TOFMS: *m/z* 1235.92 $[M+Na]^+$. Anal. Calcd for $C_{69}H_{52}N_2O_{17}S$: C, 68.31; H, 4.32; N, 2.31; S, 2.64. Found: C, 68.02; H, 4.29; N, 2.23; S, 2.56.

3.9. 2-Nitrophenyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside (4a)

Treatment of **1a** (1.0 g, 1.85 mmol), NaH (88 mg) and **2b** (0.34 g, 2.2 mmol) as described for **3a** afforded **4a** (1.22 g; 94%; α/β 3:1).

α-Anomer: $[\alpha]_D^{20}$ +120.1 (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.52–3.58 (dd, 1H, J_{6a-5} 2, J_{6a-6b} 11 Hz, H-6a), 3.67–3.78 (m, 3H, H-2, H-4, H-6b), 3.89–3.95 (m, 1H, H-5), 4.17–4.27 (dd, 1H, J_{3-2} 9.1, J_{3-4} 9.3 Hz, H-3), 4.4 (d, 1H, *J* 12 Hz, H–CH_2), 4.47–4.64 (m, 3H, H–CH_2), 4.77–4.91 (m, 3H, H–CH_2),

5.00 (d, 1H, *J* 11 Hz, H–CH_2), 5.46 (d, 1H, J_{1-2} 3.5 Hz, H-1), 7.02–7.11 (ddd, 1H, $J_{4'-6'}$ 1.2, $J_{4'-5'}$ 7.4, $J_{4'-3'}$ 8.4 Hz, H-4′), 7.13–7.37 (m, 21H, H-6′, H-2Ar, H-3Ar, H-4Ar), 7.38–7.45 (ddd, 1H, $J_{5'-3'}$ 1.7, $J_{5'-4'}$ 7.4, $J_{5'-6'}$ 9.1 Hz, H-5′), 7.80–7.84 (dd, 1H, $J_{3'-5'}$ 1.7, $J_{3'-4'}$ 8.4 Hz, H-3′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 68.2 (C-6), 71.9 (C-5), 73.4, 73.5, 74.9, 75.9 (C–CH_2), 77.1 (C-4), 79.8 (C-2), 81.5 (C-3), 96.9 (C-1), 117.1 (C-6′), 121.8 (C-4′), 125.4 (C-3′), 127.6, 127.7, 127.8, 128.9, 128.1, 128.3, 128.4, 128.5 (C-2Ar, C-3Ar, C-4Ar), 133.8 (C-5′), 137.7, 138.2, 138.3, 138.7 (C-1Ar), 140.8 (C-2′), 149.9 (C-1′); MALDI-TOFMS: *m*/*z* 684.6 $[M+Na]^+$. Anal. Calcd for $C_{40}H_{39}NO_8$: C, 72.60; H, 5.94; N, 2.12. Found: C, 72.98; H, 5.84; N, 2.09.

β-Anomer (minor byproduct): ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.55–3.87 (m, 6H, H-2, H-3, H-4, H-5, H-6), 4.45–4.58 (m, 3H, H–CH_2), 4.77–4.85 (m, 3H, H–CH_2), 4.97 (d, 1H, *J* 11 Hz, H–CH_2), 5.04 (d, 1H, *J* 11 Hz, H–CH_2), 5.11 (d, 1H, J_{1-2} 7 Hz, H-1), 7.15–7.50 (m, 23H, H-4′, H-5′, H-6′, H-2 Ar, H-3 Ar, H-4Ar), 7.83 (d, 1H, $J_{3'-4'}$ 7.9 Hz, H-3′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 68.9 (C-6), 73.5 (C-5), 75.1, 75.2, 75.5, 75.8 (C–CH_2), 77.5 (C-2), 81.6 (C-4), 84.6 (C-3), 100.9 (C-1), 117.1 (C-6′), 122.0 (C-4′), 125.4 (C-3′), 127.7, 127.8, 127.9, 128.0, 128.3, 128.4, 128.5 (C-2Ar, C-3 Ar, C-4 Ar), 133.9, 137.8, 137.9, 138.4 (C-1Ar), 140.5 (C-2′), 150.1 (C-1′); MALDI-TOFMS: *m*/*z* 684.6 $[M+Na]^+$.

3.10. 2-Nitrophenyl 2,3,4,6-tetra-*O*-benzyl-D-galacto-pyranoside (4b)

Treatment of **1g** (0.5 g, 0.92 mmol), NaH (44 mg) and **2b** (0.17 g, 1.1 mmol) as described for **3a** afforded **4b** (0.55 g; 92%; α/β 3:1).

α-Anomer: $[\alpha]_D^{20}$ +129 (*c* 0.75, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.42–3.54 (m, 2H, H-6), 3.99 (br s, 1H, H-4), 4.07–4.15 (dd, 1H, J_{5-6a} 6.4, J_{5-6b} 6.9 Hz, H-5), 4.17–4.25 (m, 2H, H-2, H-3), 4.27–4.39 (m, 2H, H–CH_2), 4.30 (d, 1H, *J* 11.6 Hz, H–CH_2), 4.37 (d, 1H, *J* 11.8 Hz, H–CH_2), 4.56 (d, 1H, *J* 11.3 Hz, H–CH_2), 4.63 (d, 1H, *J* 12.3 Hz, H–CH_2), 4.78 (d, 1H, *J* 11.6 Hz, H–CH_2), 4.82–4.92 (m, 2H, H–CH_2), 4.96 (d, 1H, *J* 11.3 Hz, H–CH_2), 5.56 (d, 1H, J_{1-2} 2.2 Hz, H-1), 7.00–7.07 (ddd, 1H, $J_{4'-6'}$ 0.9, $J_{4'-5'}$ 7.2, $J_{4'-3'}$ 8.1 Hz, H-4′), 7.12–7.43 (m, 22H, H-2Ar, H-3Ar, H-4Ar), 7.78–7.84 (dd, 1H, $J_{3'-5'}$ 1.7, $J_{3'-4'}$ 8.1 Hz, H-3′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 68.6 (C-6), 71.2 (C-5), 73.2, 73.5, 73.6, 74.9 (C–CH_2), 75.2 (C-4), 76.1 (C-2), 78.6 (C-3), 97.2 (C-1), 117.0 (C-6′), 121.5 (C-4′), 125.4 (C-3′), 127.55, 127.58, 127.61, 127.63, 127.73, 127.74, 128.21, 128.26, 128.29, 128.31, 128.39 (C-2Ar, C-3Ar, C-4Ar), 133.8 (C-5′), 137.8, 138.51, 138.54, 138.6 (C-1Ar), 140.7 (C-2′), 150.1 (C-1′); MALDI-TOFMS: *m*/*z* 684.0 $[M+Na]^+$. Anal. Calcd for $C_{40}H_{39}NO_8$: C, 72.60; H, 5.94; N, 2.12. Found: C, 73.05; H, 5.97; N, 2.10.

β-Anomer (minor byproduct): ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.53–3.70 (m, 2H, H-6), 3.76–3.78 (m, 1H, H-5), 4.10–4.15 (dd, 1H, J_{3-4} 3.9, J_{3-2} 7.6 Hz, H-3), 4.29–4.61 (m, 9H, H-2, H-2, H–CH_2), 4.69 (d, 1H, *J* 11.8 Hz, H–CH_2), 5.66 (1H, J_{1-2} 1.2 Hz, H-1), 7.04–7.11 (ddd, 1H, $J_{4'-6'}$ 1 Hz, $J_{4'-5'}$ 7.1, $J_{4'-3'}$ 8.1 Hz, H-4′), 7.12–7.43 (m, 22H, H-2Ar, H-3Ar, H-4Ar), 7.78–7.82 (dd, 1H, $J_{3'-5'}$ 1.7, $J_{3'-4'}$ 8.1 Hz, H-3′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 70.5 (C-6), 72.2, 72.5, 73.4, 75.5 (×2) (C–CH_2) (C-5), 82.1 (C-4), 82.3 (C-3), 88.5 (C-2), 106.4 (C-1), 119.4 (C-6′), 122.2 (C-4′), 125.5 (C-3′), 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.33, 128.37, 128.36, 128.39, 128.4 (C-2Ar, C-3Ar, C-4Ar), 133.7 (C-5′), 137.3, 137.6, 138.1, 138.2 (C-1Ar), 141.3 (C-2′), 149.8 (C-1′); MALDI-TOFMS: *m*/*z* 684.0 $[M+Na]^+$.

3.11. 2-Nitrophenyl 2,3,4,6-tetra-*O*-benzyl-α-D-manno-pyranoside (4c)

Treatment of **1h** (0.5 g, 0.92 mmol), NaH (44 mg) and **2b** (0.17 g, 1.1 mmol) as described for **3a** afforded **4c** (0.53 g; 89%); $[\alpha]_D^{20}$ +59.7 (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.66–3.71 (dd, 1H, J_{6a-5} 2.2, J_{6a-5} 10.8 Hz, H-6a), 3.73–3.80 (dd, 1H, J_{6b-5} 4.9, J_{6b-5} 11.1 Hz, H-6b), 3.89–4.13 (m, 4H, H-2, H-3, H-4, H-5), 4.46 (d, 1H, *J* 11.8 Hz, H–CH_2), 4.52 (d, 1H, *J* 11.1 Hz, H–CH_2), 4.60 (d, 1H, *J* 11.8 Hz, H–CH_2), 3.67–4.75 (m, 3H, H–CH_2), 4.81 (d, 1H, *J* 12.1 Hz, H–CH_2), 4.89 (d, 1H, *J* 11.1 Hz, H–CH_2), 5.57 (d, 1H, J_{1-2} 2.0 Hz, H-1), 7.04–7.12 (ddd, 1H, $J_{4'-6'}$ 1.7, $J_{4'-5'}$ 6.7, $J_{4'-3'}$ 8.1 Hz, H-4′), 7.16–7.45 (m, 22H, H-2Ar, H-3Ar, H-4Ar), 7.78–7.83 (dd, 1H, $J_{3'-5'}$ 1.4, $J_{3'-4'}$ 8.1 Hz, H-3′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 69.1 (C-6), 72.7, 73.2 (C–CH_2), 73.3 (C-5, C–CH_2), 74.4 (C-4), 74.8 (C-2), 75.0 (C–CH_2), 79.6 (C-3), 98.3 (C-1), 118.7 (C-6′), 122.3 (C-4′), 125.4 (C-3′), 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 128.4, 128.5 (C-2Ar, C-3Ar, C-4Ar), 134.1 (C-5′), 138.1, 138.2 (×2), 138.4 (C-1Ar), 140.7 (C-2′), 149.7 (C-1′); MALDI-TOFMS: *m*/*z* 684.0 $[M+Na]^+$. Anal. Calcd for $C_{40}H_{39}NO_8$: C, 72.60; H, 5.94; N, 2.12. Found: C, 73.02; H, 5.96; N, 2.11.

3.12. 4-Cyanophenyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside (5a)

Treatment of **1a** (0.5 g, 0.92 mmol), NaH (44 mg) and **2c** (0.17 g, 1.1 mmol) as described for **3a** afforded **5a** (0.48 g; 82%) as an inseparable anomeric mixture; α/β 3:1 (determined by NMR). Representative ^{13}C NMR signals for α and β isomers.

α-Anomer: ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 68.1 (C-6), 71.3 (C-5), 77.1 (C-4), 79.6 (C-2), 81.8 (C-3), 95.4 (C-1), 105.6 (C-4′), 117.2 (C-2′, C-6′), 133.9 (C-3′, C-5′), 159.9 (C-1′).

β-Anomer: ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 68.7 (C-6), 75.3 (C-5), 77.5 (C-2), 81.8 (C-4), 84.6 (C-3), 100.7 (C-1), 105.9 (C-4′), 117.2 (C-2′, C-6′), 133.9 (C-3′, C-5′), 160.3 (C-1′); MALDI-TOFMS: *m*/*z* 663.9 $[M+Na]^+$.

3.13. 4-Cyanophenyl 2,3,4,6-tetra-*O*-benzyl-D-galactopyranoside (5b)

Treatment of **1g** (0.5 g, 0.92 mmol), NaH (44 mg) and **2c** (0.17 g, 1.1 mmol) as described for **3a** afforded **5a** (0.49 g; 84%) as an inseparable anomeric mixture; α/β 3:1 (determined by NMR). Representative ^{13}C NMR signals for α and β isomers.

α-Anomer: ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 68.6 (C-6), 70.6 (C-5), 74.7 (C-4), 76.0 (C-2), 78.7 (C-3), 96.4 (C-1), 105.5 (C-4′), 117.4 (C-2′, C-6′), 133.8 (C-3′, C-5′), 160.3 (C-1′).

β-Anomer: ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 70.3 (C-6), 75.9 (C-5), 82.3 (C-4), 82.4 (C-3), 88.5 (C-2), 104.3 (C-1), 105.5 (C-4′), 117.4 (C-2′, C-6′), 133.8 (C-3′, C-5′), 160.3 (C-1′); MALDI-TOFMS: *m*/*z* 663.9 $[M+Na]^+$.

3.14. 4-Cyanophenyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside (5c)

Treatment of **1h** (0.5 g, 0.92 mmol), NaH (44 mg) and **2c** (0.17 g, 1.1 mmol) as described for **3a** afforded **5c** (0.49 g; 84%); slightly yellow oil; $[\alpha]_D^{20}$ +80.8 (*c* 0.75, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.59–3.66 (dd, 1H, J_{6a-5} 3.9, J_{6a-5} 12.5 Hz, H-6a), 3.70–3.80 (m, 2H, H-5, H-6b), 3.91–3.95 (t, 1H, $J_{2-1/2-3}$ 3.9 Hz, H-2) 4.01–4.13 (m, 2H, H-3, H-4), 4.43 (d, 1H, *J* 11.8 Hz, H–CH_2), 4.51 (d, 1H, *J* 10.5 Hz, H–CH_2), 4.59 (d, 1H, *J* 11.8 Hz, H–CH_2), 3.67–4.90 (m, 5H, H–CH_2), 5.58 (d, 1H, J_{1-2} 2.0 Hz, H-1), 7.05 (d, 2H, $J_{2'-3'/6'-5'}$ 8.9 Hz, H-2′, H-6′), 7.13–7.40 (m, 20H, H-2Ar, H-3Ar, H-4Ar), 7.52 (d, 2H, $J_{3'-4'/5'-6'}$ 8.9 Hz, H-3′, H-5′); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 68.8 (C-6), 72.6 (C–CH_2), 72.9 (C-5), 73.1, 73.3 (C–CH_2), 74.4 (C-4), 74.5 (C-2), 75.1 (C–CH_2), 79.6 (C-3), 96.5 (C-1), 105.6 (C-4′), 117.1 (C-2′, C-6′), 127.5, 127.6, 127.71, 127.75, 127.83, 127.87, 127.9, 128.3, 128.4, 128.5 (C-2Ar, C-3Ar, C-4Ar), 133.9 (C-3′, C-5′), 137.9, 138.1, 138.2 (×2) (C-1Ar), 159.3 (C-1′); MALDI-TOFMS: *m*/*z* 663.9 $[M+Na]^+$. Anal. Calcd for $C_{41}H_{39}NO_6$: C, 76.73; H, 6.13; N, 2.18. Found: C, 76.81; H, 6.14; N, 2.18.

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