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Use of Dichlorophthaloyl (DCPhth) Group as an Amino Protecting Group in Oligosaccharide Synthesis

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Abstract: As an alternative to phthaloyl (Phth) group, 4,5-dichlorophthaloyl (DCPhth) group was investigated as an amino protecting group to prove it to be useful for the synthesis of β-glycosides of 2-acetamido-2-deoxy glucose (GlcNAc). DCPhth was introduced onto the C-2 nitrogen of glucosamine to give 2, which was further transformed into mono- and di- and trisaccharide derivatives which constitute basic structural units of asparagine linked glycoprotein oligosaccharides. DCPhth group proved to have sufficient stability under the standard conditions of protecting group manipulations (e.g. deacetylation, benzylation, benzylidenation), and Lewis acid-, silver salt- and iodonium ion-promoted glycosylation. Removal of DCPhth group was smoothly performed by using ethylenediamine in alcoholic solvent under substantially milder conditions required for deprotection of Phth.

INTRODUCTION

β-Glycosides of 2-acetamido-2-deoxy-sugars are widespread in naturally occurring glycoconjugates which include Asn-linked and Ser/Thr-linked glycoproteins, glycolipids, proteoglycans, and plant derived glycans[2]. In order to synthesize these biologically significant type of O-glycosides, phthaloyl (Phth) group has been extensively utilized as a protecting group of C-2 nitrogen[3]. This relies upon the strong 1,2-trans directing nature of 2-NPhth carrying glycosyl donor which allows stereocontrolled synthesis of β-GlcNAc and β-GalNAc containing structures in a highly predictable manner[4]. However, the utility of Phth substituent is in some cases hampered due to the harsh conditions required for its removal (i.e. prolonged heating with hydrazine hydrate or ethylenediamine). Complete deprotection of a molecule containing multiple number of Phth groups is sometimes problematic. Recently, we have reported the use of 4,5-dichlorophthaloyl (DCPhth) as a nitrogen protecting group[5]. DCPhth, which retains the 1,2-trans directing nature of Phth, can be compared favourably over parent Phth, in terms of the ease of removal. We report herein some results from our recent investigations focussing on the compatibility of DCPhth with other protecting group strategies and glycan chain elongation technologies, which may well advocate its practical utility in complex oligosaccharide synthesis.

RESULTS AND DISCUSSION

Previously reported DCPhth carrying **2**[5] was more conveniently prepared starting from acetyl protected glucosamine hydrochloride **1**[6] (**Scheme 1**). By this method, the installation of the DCPhth group could be effected very reproducibly in ~100 g scale, to give **2** as a crystalline material without recourse of chromatograhic purification. The anomeric position was then masked as a *p*-methoxyphenyl[7] (MP) glycoside **3**, under TMSOTf catalyzed conditions. Deacetylation of **3** was successfully performed under standard Zèmplen conditions with a catalytic amount of sodium methoxide, followed by acid-catalyzed benzylidenation

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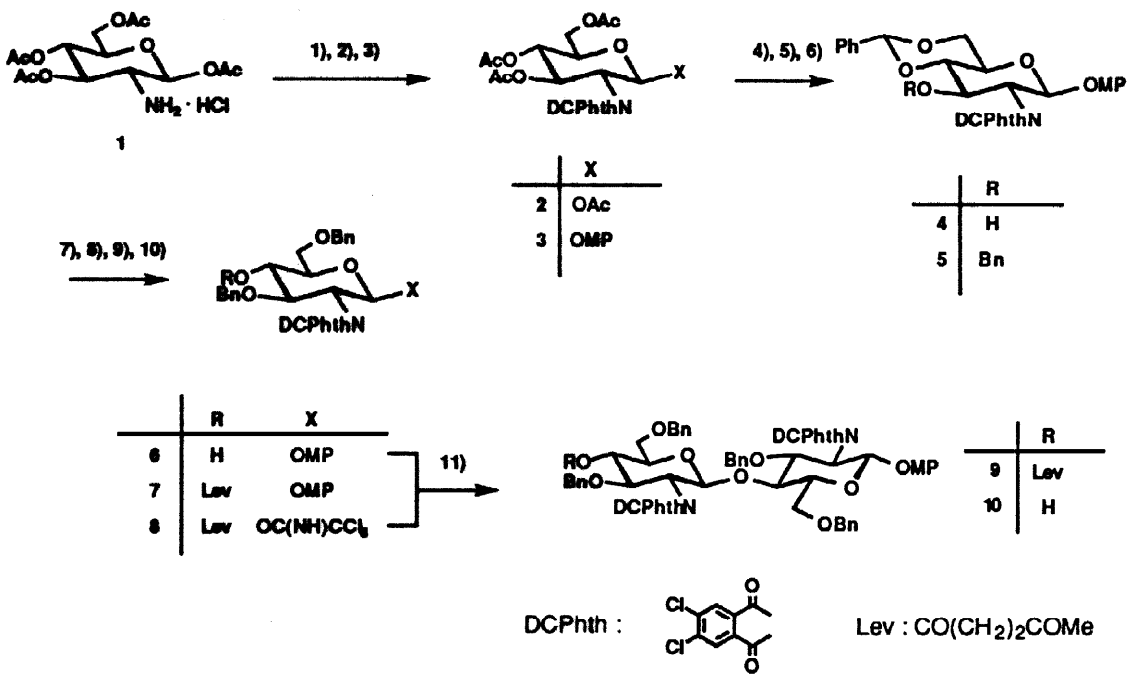
to give partially protected **4** in quite reasonable yield. Subsequent benzylation was performed under carefully controlled conditions with benzyl bromide and sodium hydride at 6°C to furnish the 3-OBn protected **5**, which was then transformed into **6** in 55 % yield from **4**. Levulinoylation under standard conditions[8] gave **7** that was then subjected to oxidative cleavage of the anomeric MP group followed by transformation into trichloroacetimidate **8**. Coupling with **6**, promoted by TMSOTf afforded fully protected chitobiose derivative **9**. Delevulinoylation of **9** was performed by brief treatment with hydrazine hydrate[8] to give **10** in nearly quantitative yield.

Scheme 1



1) 4,5-Dichlorophthalic anhydride, $Et_3N/Cl(CH_2)_2Cl$. 50-60°C; 2) Ac_2O/Pyridine, r.t., 94%; 3) *p*-Methoxyphenol, TMSOTf/$Cl(CH_2)_2Cl$, r.t., 87%; 4) NaOMe/MeOH, 0°C; 5) $PhCH(OMe)_2$, CSA/DMF, r.t., 74% over 2 steps; 6) $PhCH_2Br$, NaH/DMF, 6°C; 7) $NaCNBH_3$, HCl-dioxane/THF, r.t., 55% over 2 steps; 8) $(Lev)_2O/CH_2Cl_2$-Pyridine, r.t., 95%; 9) CAN/Toluene-MeCN-H_2O, r.t.; 10) CCl_3CN, DBU/CH_2Cl_2, r.t., 78% over 2 steps; 11) NH_2NH_2·H_2O/AcOH-pyridine, 99%.

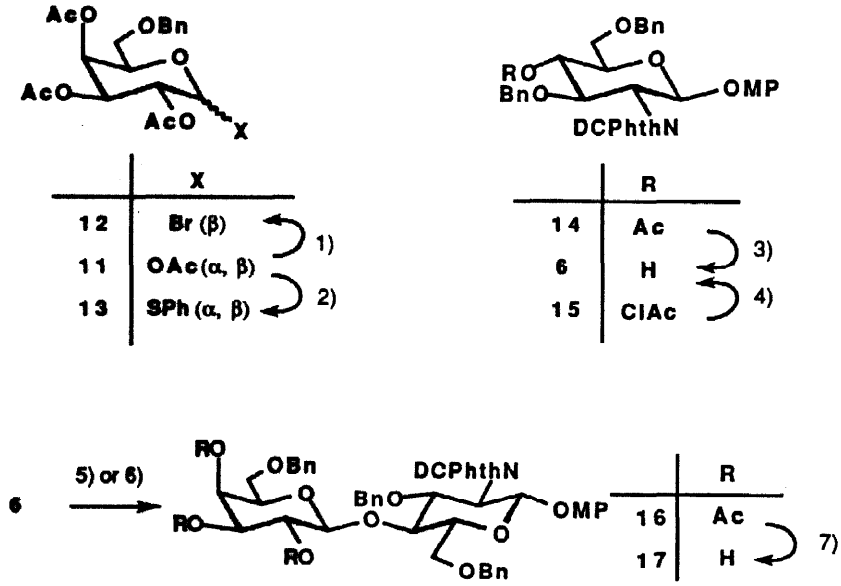
A potential problem with the use of DCPhth in oligosaccharide synthesis centers around its manifested base lability. In order that DCPhth protection can be accepted as a general tool in oligosaccharide synthesis, compatibility with standard deacylation conditions should be of particular significance. Although successful deacetylation of **3** was already described, there still remains a concern if DCPhth moiety tolerates the conditions for deprotection of acetyl groups at the advanced stage, which might require extended reaction time. Asking this question, we synthesized selectively protected lactosamine derivative **16** (Scheme 2).

Disaccharide **16** was obtained, by using bromide **12** or more favourably thioglycoside **13**, as a glycosyl donor, which in turn were obtained from **11**[9]. Deacetylation of **16** was performed successfully with catalytic amounts of sodium methoxide at 0°C with no substantial destruction of the DCPhth group to give **17**. By contrast, 4-OAc **14**, which was obtained by acetylation of **6**, was somewhat more difficult to remove. The deprotection proceeded with a reasonable efficiency, only in the presence of subequimolar amount of

NaOMe[10]. For this particular position, either levulinoyl or chloroacetyl may well be a better option. For instance, installation as well as removal of chloroacetyl[11] (ClAc) group proceeded without incident as exemplified for compound **15**.

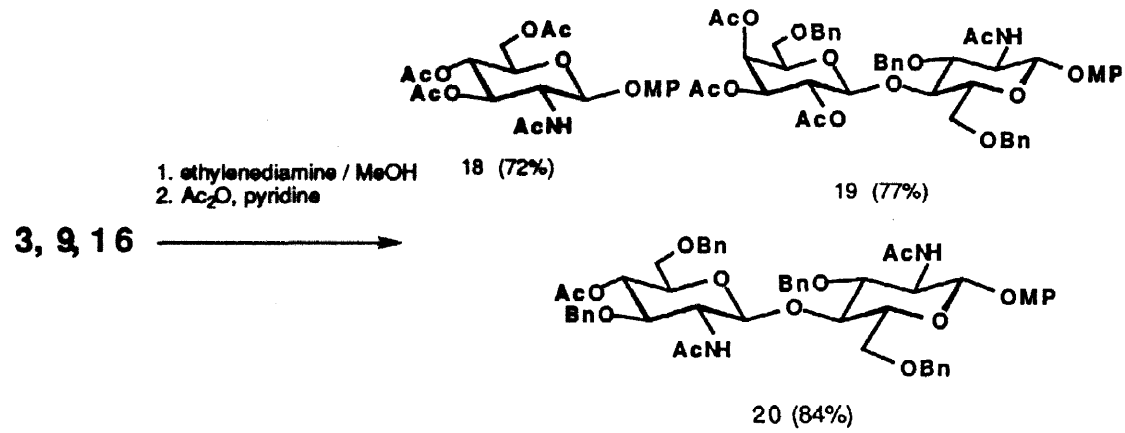
Deprotection of DCPhth group was performed using **3**, **16** and **9** as test cases (**Scheme 3**). The reactions proceeded smoothly, even at room temperature for **3** and **16**, to afford, after acetylation, corresponding acetamides **18** and **19**. Since the completion of the reaction was rather difficult to ascertained, larger excess of ethylenediamine and higher reaction temperature were applied for transformation of **9** into **20**.

Scheme 2



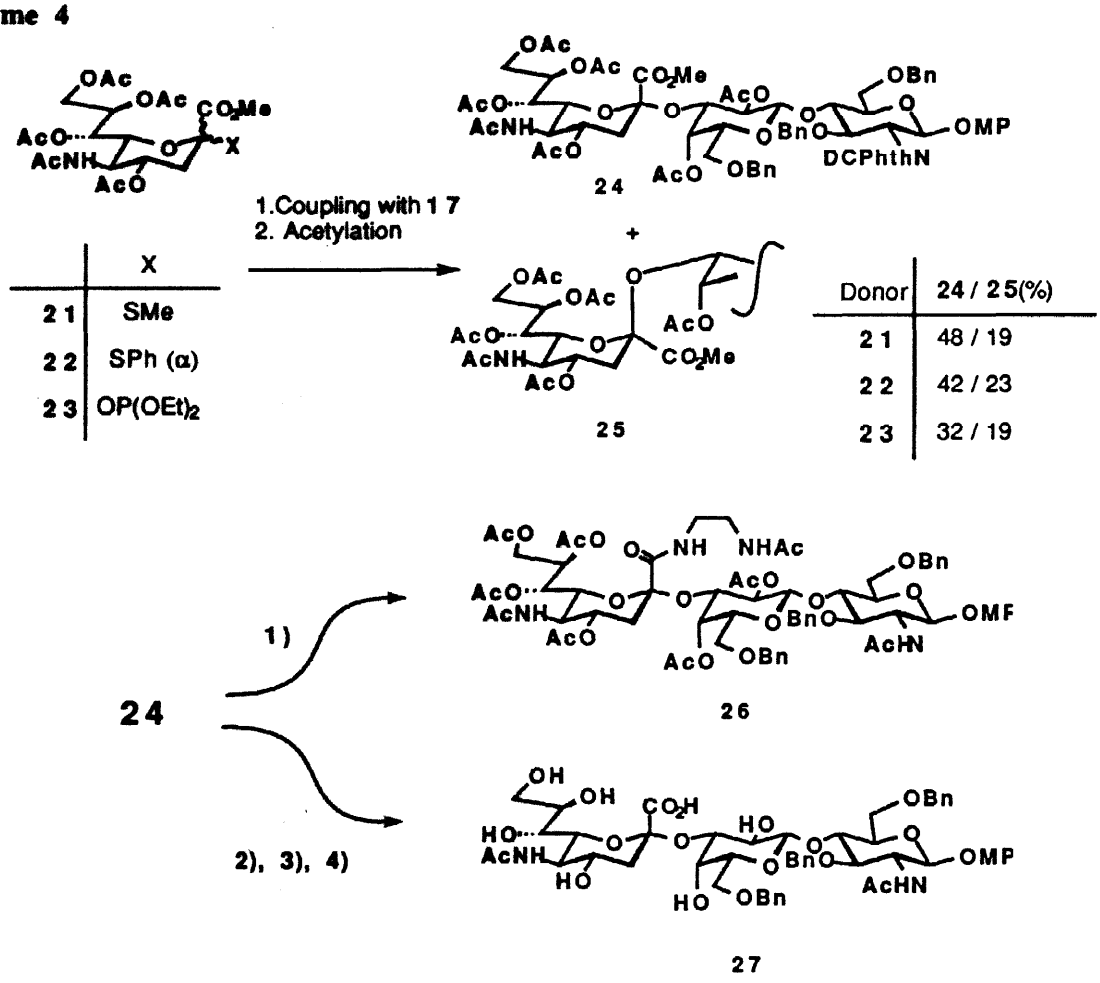
1) HBr-AcOH/CH_2Cl_2, r.t, 58%; 2) PhSH, BF_3·OEt_2/CH_2Cl_2, r.t., 52% (β:α=50:1);
3) NaOMe/MeOH, r.t., 58%; 4) Thiourea/CH_2Cl_2-MeOH, r.t., 83%; 5) **12**, $AgOSO_2CF_3$/CH_2Cl_2, -40°C, 67%; 6) **13**, NIS, CF_3SO_3H/CH_2Cl_2, 0°C, 82%; 7) NaOMe/MeOH, 0°C, 74%.

Scheme 3



Compatibility of DCPhth with operations required for sialic acid containing glycan formation is also of critical significance, considering the application into wider range of complex type glycans. Preparation of sialyl lactosamine component in a DCPhth protected form was performed as depicted in **Scheme 4**.Sialylations were performed in acetonitrile-containing systems, and as sialic acid donors, methylthioglycoside **21**[12], phenylthioglycoside **22**[13] and phosphite **23**[14] were compared in terms of their efficiency. In order to avoid the risk of purifying out the minor isomer(s), so that the accurate estimation of the stereoselectivity can be made, reaction mixtures were first purified by size exclusion column chromatography to remove low molecular weight materials derived from reagents and sialyl donors. Subsequent acetylation and chromatographic purification afforded **24** and **25**. On contrary to high α-selectivity previously reported by other authors in related systems[12a,13a,14b], stereoselectivity was only marginal (α/β=1.7 to 2.5) in these particular combinations. Since reactions were performed in substantial scales (0.5-1.0 g acceptor **17**) and both products were rigorously confirmed to be stereoisomeric[15], assessments of stereoselectivity should be with high degree of accuracy. By any means, the methyl thioglycoside **21** proved to be the most effective donor for our purpose to furnish the trisaccharide **24** in 47% yield.

Scheme 4



1) $H_2N(CH_2)_2NH_2$/MeOH, r.t., 71%; 2) LiI/Pyridine, reflux; 3) $H_2N(CH_2)_2NH_2$/MeOH, 50°C; 4) Ac_2O/MeOH, r.t., 46% over 3 steps.

Attempted removal of DCPhth from **24** by using ethylenediamine resulted in the concomitant formation sialic acid amide **26**. In order to avoid such a complexity, methyl ester was first cleaved by LiI and then derivatized into **27**.

In summary, DCPhth-carrying mono- and disaccharide components can be manipulated selectively in various manners.Oligosaccharide fragments **10** and **24**, which have DCPhth masked amino groups constitute basic structures of complex-type glycoprotein oligosaccharide. In comparison with tetrachlorophthaloyl (TCP) group reported by Fraser-Reid et al.[16] and Schmidt et al.[17], DCPhth seems to be more stable under basic conditions. Combined with conventional Phth, three variants are now available for efficient construction of β-GlcNAc/GalNAc, with the base-lability order of TCP>DCPhth>Phth.

EXPERIMENTAL

General methods: Melting points were determined with a Yanagimoto micro-melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP 370 Polarimeter at 20±3°C. FAB-MS spectra were measured with a JEOL JMS-Hx110 mass spectrometer with *m*-nitrobenzylalcohol as matrix if not stated otherwise. NMR spectra were recorded with either JEOL Ex-270 or Bruker AM-400 spectrometer using Me_4Si as internal standard for $CDCl_3$, d_6-DMSO and CD_3OD solutions. TLC on silica gel 60 F_{254} (Merck, Darmstadt) was used to monitor the reactions and to ascertain the purity of the products. Silica gel column chromatography was performed with Silica Gel 60 (Merck, 63-200 μm) or Spherical Silica Gel 60 N (Kanto, 40-100 or 100-210 μm). N-Iodosuccinimide (NIS) was recrystallized from dioxan-carbon tetrachloride, AgOTf from toluene-hexane. All other reagents were used as received. CH_2Cl_2 and THF were destilled from CaH_2 and Na-benzophenone, respectively. Other solvents were dried and stored over freshly activated molecular sieve 3 or 4 Å which were activated by heating to 180 °C *in vacuo* for 24 h prior to use.

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranose (2): To a suspension of hydrochloride **1** (80.6 g, 0.21 mol) in 1,2-dichloroethane (600 ml), triethylamine (70 ml, 0.5 mol) was added. After portionwise addition of 4,5-dichlorophthalic anhydride (50 g, 0.23 mol), the turbid solution was heated to 50-60°C for 2 h and then evaporated to dryness. The residue was dissolved in pyridine (400 ml) and the solution was cooled to 0°C. Acetic anhydride (190 ml, 2 mol) was added dropwise and the mixture was allowed to warm up gradually to r.t. and stirred for 24 h. The volatiles were removed *in vacuo* and the residue was dissolved in dichloromethane (1 l), washed with water (2×300 ml), 2 N HCl (2× 200 ml) and satd. $NaHCO_3$ solution (400 ml), successively, dried (Na_2SO_4) and evaporated *in vacuo* to leave a syrup which was crystallized from ethanol-diisopropyl ether to give 104 g (91 %) of **2** as colorless crystals. Purification of the mother liquor by silica gel column chromatography (toluene-ethyl acetate 5:1) and crystallization from ethanol-diisopropyl ether gave an additional amount (3 g, 3 %) of **2** (total yield 94%); m.p. 180.5-181.5 °C; $[\alpha]^{20}_D$ +70.9 (*c* 1.0, $CHCl_3$); R_f 0.43 (toluene-ethyl acetate 5:1); ^1H NMR (270 MHz, $CDCl_3$) δ 1.88, 2.01, 2.05, 2.12 (4 s, 3 H each, 4 CH_3CO), 4.01 (ddd, 1 H, 5-H), 4.14 (dd, 1 H, 6-H_a), 4.36 (dd, 1 H, 6-H_b), 4.43 (dd, 1 H, 2-H), 5.22 (dd, 1 H, 4-H), 5.82 (dd, 1 H, 3-H), 6.48 (d, 1 H, 1-H), 7.95 (s, 2 H, DCPhth); $J_{1,2}$ 8.9; $J_{2,3}$ 10.6; $J_{3,4}$ 9.2; $J_{4,5}$ 10.0; $J_{5,6a}$ 2.1; $J_{5,6b}$ 4.1; $J_{6a,b}$ 12.3 Hz.

Anal. Calcd for $C_{22}H_{21}Cl_2NO_{11}$ (546.31): C, 48.37; H, 3.87; N, 2.56; Cl, 12.98. Found: C, 47.95; H, 3.78; N, 2.55; Cl, 12.99.

***p*-Methoxyphenyl 3,4,6-tri-O-acetyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside (3):** Tetraacetate **2** (82 g, 0.15 mol) and 4-methoxyphenol (28 g, 0.225 mol) were dissolved in 1,2-dichloroethane (600 ml) and the flask was flushed with N_2. TMSOTf (1 ml, 6 mmol) was added and the mixture was stirred for 42 h. After being quenched with satd. $NaHCO_3$ solution (200 ml), the mixture was washed with satd. NaCl/$NaHCO_3$ solution (1:1, 3×200 ml), dried (Na_2SO_4) and evaporated *in vacuo* . Crystallization from ethanol-diisopropyl ether afforded 79.7 g (87 %) of **3** as yellow crystals; m.p. 98-100 °C; $[\alpha]^{20}_D$ +63.5 (*c* 1.0, $CHCl_3$); R_f 0.38 ($CHCl_3$-ethyl acetate 9:1); ^1H NMR (270 MHz, $CDCl_3$) δ 1.90, 2.05, 2.11 (3 s, 3 H each, 3 CH_3CO), 3.74 (s, 3 H, $CH_3OC_6H_4$), 3.94 (ddd, 1 H, 5-H), 4.17 (dd, 1 H, 6-H_a), 4.35 (dd, 1 H, 6-H_b), 4.53 (dd, 1 H, 2-H), 5.24 (dd, 1 H, 4-H), 5.78 (dd, 1 H, 3-H), 5.81 (d, 1 H, 1-H); $J_{1,2}$ 8.5; $J_{2,3}$ 10.7; $J_{3,4}$ 9.2; $J_{4,5}$ 10.2; $J_{5,6a}$ 2.5; $J_{5,6b}$ 5.2; $J_{6a,b}$ 12.4 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 20.4, 20.6, 20.7 (3 CH_3CO), 54.9 (C-2), 55.5 ($CH_3OC_6H_4$),

61.9 (C-6), 68.6 (C-4), 70.7 (C-3), 72.0 (C-5), 97.3 (C-1), 114.4, 118.8 ($CH_3OC_6H_4$), 125.8 (DCPhth), 130.4, 139.4 (DCPhth), 150.3, 155.8 ($CH_3OC_6H_4$), 169.3, 170.2, 170.5 (3 CH_3CO).

Anal. Calcd for $C_{27}H_{25}Cl_2NO_{11}$ (610.40): C, 53.13; H, 4.13; N, 2.29; Cl, 11.62. Found: C, 52.92; H, 4.15; N, 2.24; Cl, 11.46.

***p*-Methoxyphenyl 4,6-O-benzylidene-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside (4):** Compound **3** (27.9 g, 45.7 mmol) was dissolved in a mixture of methanol-CH_2Cl_2 (2:1, 300 ml) and treated at 0 °C with 28 % NaOMe solution in methanol (1.5 ml, 7.5 mmol). After 2 h, additional NaOMe solution (1.0 ml, 5.0 mmol) was added, stirring continued for another 2 h and the mixture acidified into ~pH 5 with Amberlyst 15-E resin. Filtration and evaporation of the solvents gave 25 g of a yellow, crystalline mass, which was dissolved in DMF (150 ml) and stirred together with benzaldehyde dimethylacetal (13.5 ml, 90 mmol) and camphorsulphonic acid (2.0 g, 8.6 mmol) at room temperature for 24 h *in vacuo* (10-15 mbar). Benzaldehyde dimethylacetal (6.75 ml, 45 mmol) and camphorsulphonic acid (500 mg, 2.1 mmol) were added and stirring continued for another 36 h. Diluting with CH_2Cl_2 (400 ml) and diethyl ether (100 ml), washing with satd. $NaHCO_3$ solution (200 ml), filtration from insoluble material and further washing with water (2 × 100 ml) and satd. NaCl solution (100 ml), drying (Na_2SO_4) and removal of the solvents *in vacuo* gave a yellow syrup. Coevaporation with toluene-AcOEt (2:1, 3 × 100 ml), crystallisation from hot toluene, washing of the crystals with cold diethyl ether and drying under high vacuum at 50 °C afforded 19.4 g (74 %) of **4** as colorless needles; m.p. 130-132 °C; $[\alpha]^{20}_D$ +22.7 (*c* 1.1, $CHCl_3$); R_f 0.9 ($CHCl_3$-methanol 8:1); ^1H NMR (270 MHz, $CDCl_3$) δ 2.62 (d, 1 H, 3-OH), 3.73 (s, 3 H, $CH_3OC_6H_4$), 3.65 - 3.81 (m, 3 H, 2-H, 4-H, 5-H), 3.87 (dd, 1 H, 6-H_a), 4.41 (dd, 1 H, 6-H_b), 4.47 (dd, 1 H, 2-H), 4.66 (ddd, 1 H, 3-H), 5.59 (s, 1 H, C_6H_5CH), 5.75 (d, 1 H, 1-H); $J_{1,2}$ 8.4; $J_{2,3}$ 10.6; $J_{3,4}$ 8.4; $J_{3,OH}$ 3.4; $J_{5,6b}$ 4.3; $J_{6a,b}$ 10.6 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 55.6 ($CH_3OC_6H_4$), 56.7 (C-2), 66.3 (C-5), 68.4 (C-3), 68.5 (C-6), 81.9 (C-4), 97.9 (C-1), 102.0 (C_6H_5CH), 114.5, 118.5 ($CH_3OC_6H_4$), 125.7 (DCPhth), 126.5, 128.4, 129.4, 130.6, 136.8, 139.2 (C_6H_5CH, DCPhth), 150.4, 155.7 ($CH_3OC_6H_4$), 169.3, 170.2, 170.5 (3 CH_3CO); FAB-MS (positive) *m/z* 573 $[M]^+$.

Anal. Calcd for $C_{28}H_{23}Cl_2NO_8$ (572.40): C, 58.75; H, 4.05; N, 2.45; Cl, 12.39. Found: C, 58.49; H, 4.20; N, 2.38; Cl, 12.17.

***p*-Methoxyphenyl 3,6-di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside (6):** A solution of **4** (9.00 g, 15.7 mmol) and benzyl bromide (19.0 ml, 159 mmol) in DMF (250 ml) was stirred for 30 min over freshly activated molecular sieves 4 Å (6.0 g) at 0 °C. Sodium hydride (1.9 g, 55 % oil dispersion, 48 mmol) was added and the mixture was gradually warmed up to 6 °C and stirring was continued at this temperature for 28 h. The reaction was quenched at 0 °C by slowly adding methanol (5 ml) and stirring for 30 min. Diluting with AcOEt (600 ml), washing successively with water-brine (1:1, 2 × 200 ml) and brine (200 ml), drying ($MgSO_4$) and removal of the solvents *in vacuo* gave a colorless syrup, which was coevaporated with toluene to afford crude **5**.

Crude **5** was dissolved in THF (200 ml) and was stirred for 30 min over freshly activated molecular sieves 4 Å (12.0 g) at 0 °C. Sodium cyanoborohydride (10.6 g, 95 %, 159 mmol) and methyl orange (2 mg) were added and the solution acidified with 4 M HCl/dioxane solution. After 7 h, the mixture was poured on ice-water (400 ml), extracted with CH_2Cl_2 (2 × 250 ml) and the organic phase stirred overnight with 2 N HCl (200 ml). Layers were separated and the organic layer was washed successively with 2 N HCl (200 ml), satd. $NaHCO_3$ solution (2 × 200 ml) and water (200 ml). Drying (Na_2SO_4) and evaporation of the solvents left a yellow syrup, which was applied to silica gel column chromatography (toluene-AcOEt 1:0 → 2:1) to afford 5.70 g (55 %) of **6** as yellow foam; $[\alpha]^{20}_D$ +58.2 (*c* 1.1, $CHCl_3$); R_f 0.36 (toluene-AcOEt 5:1); ^1H NMR (270 MHz, $CDCl_3$) δ 3.02 (d, 1 H, 4-OH), 3.70 (s, 3 H, $CH_3OC_6H_4$), 3.72 (m, 1 H, 5-H), 3.82 (m, 2 H, 6-H_2), 3.90 (ddd, 1 H, 4-H), 4.24 (dd, 1 H, 3-H), 4.34 (dd, 1 H, 2-H), 4.52, 4.57, 4.64, 4.80 (4 d, 1 H each, $C_6H_5CH_2$), 5.60 (d, 1 H, 1-H); $J_{1,2}$ 8.2; $J_{2,3}$ 10.7; $J_{3,4}$ 8.4; $J_{4,5}$ 8.7; $J_{4,OH}$ 2.8; J_{CH_2} 11.7, 12.4 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 55.5 ($CH_3OC_6H_4$), 56.6 (C-2), 70.5 (C-6), 73.6 (C-5), 73.8, 74.6 ($C_6H_5CH_2$), 74.4 (C-4), 78.5 (C-3), 97.4 (C-1), 114.5, 118.6 ($CH_3OC_6H_4$), 125.4 (DCPhth), 127.4 - 128.5, 129.0, 137.5, 138.1, 138.7 (C_6H_5CH, DCPhth), 150.6, 155.4 ($CH_3OC_6H_4$).

Anal. Calcd for $C_{35}H_{31}Cl_2NO_8$ (664.54): C, 63.26; H, 4.70; N, 2.11; Cl, 10.67. Found C, 63.50; H, 4.74; N, 2.34; Cl, 10.00.

In a separate experiment, compound **5** was purified by silica gel column chromatography (toluene-AcOEt 50:1) and crystallized from diisopropyl ether into colorless needles; m.p. 111-115 °C; $[\alpha]^{20}_D$ +83.7 (*c* 1.1, $CHCl_3$); R_f 0.72 (toluene-AcOEt 5:1); ^1H NMR (270 MHz, $CDCl_3$) δ 3.71 (s, 3 H, $CH_3OC_6H_4$), ~3.71 (m, 1 H, 5-H), 3.89 (dd, 1 H, 4-H), ~3.90 (m, 1 H, 6-H_a), 4.36 - 4.44 (m, 3 H, 2-H, 3-H, 6-H_b), 4.49, 4.82 (2 d, 1 H each, $C_6H_5CH_2$), 5.65 (s, 1 H, C_6H_5CH), 5.67 (d, 1 H, 1-H); $J_{1,2}$ 7.9; $J_{3,4}$ $J_{4,5}$ 10.2; $J_{5,6}$ 4.9; J_{CH_2} 12.5 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 55.6 ($CH_3OC_6H_4$), 56.0 (C-2), 66.2 (C-5), 68.6

(C-6), 74.2 ($C_6H_5\underline{C}H_2$), 74.4 (C-3), 82.7 (C-4), 97.8 (C-1), 101.4 ($C_6H_5\underline{C}H$), 114.5, 118.5 ($CH_3O\underline{C}_6H_4$), 125.4 (DCPhth), 126.0 - 128.2, 130.5, 137.1, 137.8, 138.8 ($\underline{C}_6H_5CH$, DCPhth), 150.4, 155.6 ($CH_3O\underline{C}_6H_4$). FAB-MS (positive) 663 $[M]^+$.

Anal. Calcd for $C_{35}H_{29}Cl_2NO_8$ (662.52): C, 63.45; H, 4.41; N, 2.11; Cl, 10.70. Found: C, 63.43; H, 4.50; N, 1.93; Cl, 10.70.

***p*-Methoxyphenyl 3,6-di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-4-O-levulinoyl-β-D-glucopyranoside (7)**: To a solution of *p*-methoxyphenyl glycoside **6** (3.31 g, 5.00 mmol) in CH_2Cl_2 (10 ml) and pyridine (30 ml) was added 1 M levulinic anhydride solution in CH_2Cl_2 (25 ml, 25 mmol) and the whole was stirred for 24 h at room temperature. Resulting dark-brown solution was poured on ice-water (200 ml), stirred for 15 min and layers were separated. The organic layer was washed successively with 2 N HCl (3 × 40 ml), satd. $NaHCO_3$ solution (2 × 40 ml) and water (40 ml). After drying (Na_2SO_4), the mixture was evaporated *in vacuo* to furnish a syrup. Purification by silica gel column chromatography ($CHCl_3$-AcOEt 9:1) gave syruppy **7**, which was crystallized from diethyl ether to afford 2.95 g (77 %) of **7** as colorless crystals; m.p. 113-114 °C; $[\alpha]^{20}_D$ +83.8 (*c* 0.9, $CHCl_3$); evaporation of the mother liquor afforded additional 0.71 g (18 %) of colorless material, which was homogeneous judging from TLC; R_f 0.56 (in $CHCl_3$-AcOEt 9:1); ^1H NMR (270 MHz, $CDCl_3$) δ 2.16 (s, 3 H, CH_{3Lev}), 2.50 (t, 2 H, CH_{2Lev}), 2.69 (t, 2 H, CH_{2Lev}), 3.63 (dd, 1 H, 6-H_a), 3.69 (dd, 1 H, 6-H_b), 3.70 (s, 3 H, $CH_3OC_6H_4$), 3.86 (ddd, 1 H, 5-H), 4.30 (d, 1 H, $C_6H_5CH_2$), 4.43 (m, 1 H, 2-H), 4.45 (m, 1 H, 3-H), 4.54 (s, 2 H, $C_6H_5CH_2$), 4.74 (d, 1 H, $C_6H_5CH_2$), 5.20 (m, 1 H, 4-H), 5.59 (m, 1 H, 1-H); $J_{1,2}$ 8.3; $J_{2,3}$ 9.7; $J_{3,4}$ 8.8; $J_{4,5}$ 10.0; $J_{5,6a}$ 6.3; $J_{5,6b}$ 3.3; $J_{6a,b}$ 10.7; J_{CH2Lev} 6.8; J_{CH2} 12.5 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 27.9 (CH_{2Lev}), 29.7 (CH_{3Lev}), 37.6 (CH_{2Lev}), 55.5 ($\underline{C}H_3OC_6H_4$), 55.8 (C-2), 69.3 (C-6), 72.6 (C-4), 73.5 ($C_6H_5\underline{C}H_2$), 73.7 (C-5), 74.4 ($C_6H_5\underline{C}H_2$), 77.5 (C-3), 97.2 (C-1), 114.3, 118.4 ($CH_3O\underline{C}_6H_4$), 125.4 (DCPhth), 127.3 -138.7 ($\underline{C}_6H_5CH$, DCPhth), 150.6, 155.4 ($CH_3O\underline{C}_6H_4$), 171.6 ($CH_2\underline{C}OO$), 206.1 ($CH_3\underline{C}O$).

Anal. Calcd for $C_{40}H_{37}Cl_2NO_{10}$ (762.64): C, 63.00; H, 4.89; N, 1.84; Cl, 9.30; Found: C, 63.07; H, 4.84; N, 2.00; Cl, 9.30.

3,6-Di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-4-O-levulinoyl-β-D-glucopyranosyl trichloroacetimidate (8): To compound **7** (3.40 g, 4.46 mmol) in toluene-acetonitrile-water (50 ml, 4:3:3) ceriumammonium nitrate (CAN, 7.33 g, 13.4 mmol) was added and the mixture was stirred vigorously for 4 h at room temperature. Another portion of CAN (4.90 g, 8.94 mmol) was added and stirring continued for 1 h. The mixture was diluted with AcOEt (150 ml) and washed with water (2 × 50 ml). The aq. layer was back-extracted with AcOEt (2 × 30 ml), and combined organic layers were washed successively with satd. $NaHCO_3$ solution (50 ml) and satd. NaCl solution (50 ml), dried ($MgSO_4$) and evaporated to dryness. Filtration through silica gel (toluene-AcOEt 5:1 → 0:1) afforded 2.39 g (82 %) of the hemiacetal as orange crystalline mass; R_f 0.14 (in toluene-AcOEt 5:1); ^1H NMR (270 MHz, $CDCl_3$) δ 2.15 (s, 3 H, CH_{3Lev}), 2.46 (t, 2 H, CH_{2Lev}), 2.68 (t, 2 H, CH_{2Lev}), 3.14 (d, 1 H, 1-OH), ~3.60 (m, 2 H, 6-H_2), 3.80 (ddd, 1 H, 5-H), 4.11 (dd, 1 H, 2-H), 4.28 (d, 1 H, $C_6H_5CH_2$), 4.44 (dd, 1 H, 3-H), 4.55 (s, 2 H, $C_6H_5CH_2$), 4.71 (d, 1 H, $C_6H_5CH_2$), 5.15 (dd, 1 H, 4-H), 5.32 (dd, 1 H, 1-H); $J_{1,OH}$ 7.3; $J_{1,2}$ 8.5; $J_{2,3}$ 10.8; $J_{3,4}$ 8.9; $J_{4,5}$ 9.9; $J_{5,6a}$ 5.3; $J_{5,6b}$ 3.6; J_{CH2Lev} 6.5; J_{CH2} 12.5 Hz.

A solution of the hemiacetal (2.39 g, 3.64 mmol) and trichloroacetonitrile (3.64 ml, 36.4 mmol) in CH_2Cl_2 (50 ml) was stirred at room temperature for 30 min over freshly activated molecular sieves 4 Å (4.00 g). 1,8-Diazabicyclo-[5.4.0]-7-undecen (DBU, 190 µl, 1.22 mmol) was added and stirring continued for 1 h. Filtration through celite, evaporation and flash chromatography over silica gel (toluene-AcOEt 5:1 containing 1 % triethylamine) afforded 2.27 g (78 %) of trichloroacetimidate **8** as a slightly orange foam; $[\alpha]^{20}_D$ +93.4 (*c* 1.0, $CHCl_3$); R_f 0.32 (in toluene-AcOEt 5:1); ^1H NMR (270 MHz, $CDCl_3$) δ 2.15 (s, 3 H, CH_{3Lev}), 2.47 (dd, 2 H, CH_{2Lev}), 2.67 (dd, 2 H, CH_{2Lev}), 3.64 (dd, 1 H, 6-H_a), 3.70 (dd, 1 H, 6-H_b), 3.95 (ddd, 1 H, 5-H), 4.30 (d, 1 H, $C_6H_5CH_2$), 4.49 (m, 2 H, 2-H, 3-H), 4.53, 4.58, 4.74 (3 d, 1 H each, $C_6H_5CH_2$), 5.27 (dd, 1 H, 4-H), 6.39 (d, 1 H, 1-H), 8.58 (s, 1 H, NH); $J_{1,2}$ 8.3; $J_{3,4}$ 8.2; $J_{4,5}$ 10.1; $J_{5,6a}$ 4.7; $J_{5,6b}$ 3.5; $J_{6a,b}$ 11.3; J_{CH2Lev} 6.8, 12.9 ; J_{CH2} 12.1, 12.4 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 28.0 (CH_{2Lev}), 29.9 (CH_{3Lev}), 37.8 (CH_{2Lev}), 55.0 (C-2), 68.9 (C-6), 72.3 (C-4), 73.6 ($C_6H_5\underline{C}H_2$), 74.6 (C-5, $C_6H_5\underline{C}H_2$), 77.0 (C-3), 93.9 (C-1), 125.6 (DCPhth), 127.5 - 139.0 ($\underline{C}_6H_5CH$, DCPhth), 160.8 (DCPhth), 171.6 ($CH_2\underline{C}OO$), 206.4 ($CH_3\underline{C}O$).

Anal. Calcd for $C_{35}H_{31}Cl_5N_2O_9$ (800.90): C, 52.49; H, 3.90; N, 3.50. Found: C, 52.73; H, 3.93; N, 3.81.

The sample contained ca. 5 % of α-anomer; R_f 0.46 (in toluene-AcOEt 5:1); ^1H NMR (270 MHz, $CDCl_3$) δ 6.36 (d, 1 H, 1-H), 8.55 (s, 1 H, NH); $J_{1,2}$ 3.6 Hz.

p-Methoxyphenyl O-[3,6-di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-4-O-levulinoyl-β-D-glucopyranosyl]-(1→4)-3,6-di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside (9): A solution of compounds **8** (2.20 g, 2.75 mmol) and **6** (1.11 g, 1.67 mmol) in CH_2Cl_2 (30 ml) was stirred under argon at room

temperature for 15 min in the presence of freshly activated molecular sieves 4 Å (2.00 g) and then cooled to -70 °C. Trimethylsilyl trifluoromethanesulphonate (TMSOTf, 40 µl, 0.2 mmol) was added and stirring continued. After 1 h, additional TMSOTf (10 µl, 0.05 mmol) was added and stirring continued for 2.5 h. The suspension was diluted with CH_2Cl_2 (100 ml), filtered quickly through celite and the filtrate was washed successively with satd. $NaHCO_3$ solution (30 ml) and water (30 ml) and dried (Na_2SO_4), followed by evaporation *in vacuo* to furnish a yellowish foam (3.05 g). Purification by silica gel column chromatography (toluene-AcOEt 20:1) afforded 1.58 g (73 %) of **9** as a foam, which was crystallized from ether-*n*-hexane to give yellowish needles; m.p. 91 °C; $[\alpha]^{20}_D$ +34.3 (*c* 1.1, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.13 (s, 3 H, CH_{3Lev}), 2.45 (m, 2 H, CH_{2Lev}), 2.63 (m, 2 H, CH_{2Lev}), ~3.40 (m, 2 H, 5-H, 6-H_a), ~3.50 (m, 2 H, 6-H_b, 6'-H_a), ~3.58 (ddd, 1 H, 5'-H), ~3.58 (m, 1 H, 6'-H_b), 3.66 (s, 3 H, $CH_3OC_6H_4$), 4.13 - 4.20 (m, 3 H, 2'-H, 3-H, 4-H), 4.26 (d, 1 H, $C_6H_5CH_2$), 4.28 (dd, 1 H, 2-H), 4.39 (dd, 1 H, 3'-H), ~4.40 (m, 2 H, $C_6H_5CH_2$), 4.42, 4.44, 4.53, 4.70, 4.84 (5 d, 1 H each, $C_6H_5CH_2$), 5.17 (dd, 1 H, 4'-H), 5.31 (d, 1 H, 1'-H), 5.39 (d, 1 H, 1-H); $J_{1,2}$ 8.1; $J_{1',2'}$ 8.3; $J_{2',3'}$ 8.9; $J_{3',4'}$ 9.1; $J_{4',5'}$ 9.4; $J_{5',6'}$ 3.6; J_{CH_2} 11.9, 12.4, 12.5 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 27.9 (CH_{2Lev}), 29.7 (CH_{3Lev}), 37.6 (CH_{2Lev}), 55.5 ($CH_3OC_6H_4$), 55.9 (C-2), 56.6 (C-2'), 67.9 (C-6), 69.1 (C-6'), 72.9 (C-4', $C_6H_5CH_2$), 73.3 (C-5'), 73.5, 74.3 ($C_6H_5CH_2$), 74.8 (C-5, $C_6H_5CH_2$), 76.2, 77.2 (C-3, C-4), 76.8 (C-3'), 97.1 (C-1'), 97.3 (C-1), 114.3, 118.4 ($CH_3OC_6H_4$), 125.3 (DCPhth), 126.9 - 138.5 ($C_6H_5CH_2$, DCPhth), 150.5, 155.4 ($CH_3OC_6H_4$), 171.5 (CH_2COO), 206.0 (CH_3CO).; FAB-MS (positive) *m/z* 1325.4 $[M+Na]^+$, (negative) *m/z* 1302.3 $[M-H]^-$.

Anal. Calcd for $C_{68}H_{60}Cl_4N_2O_{16}$ (1303.04): C, 62.68; H, 4.64; N, 2.15. Found C, 62.63; H, 4.63; N, 2.14.

***p*-Methoxyphenyl O-[3,6-di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranosyl]-(1→4)-3,6-di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside (10)**: Protected chitobiose **9** (896 mg, 0.690 mmol) was dissolved in pyridine-acetic acid (4:1, 25 ml) and treated with hydrazine monohydrate (344 µl, 6.90 mmol) at room temperature for 40 min. The mixture was diluted with AcOEt (120 ml) and washed successively with satd. $NaHCO_3$ solution (3 × 40 ml) and satd. NaCl solution (40 ml). The aq. phase was back-extracted with AcOEt (60 ml), and combined organic layers were washed succesively with satd. $NaHCO_3$ solution (40 ml) and satd. NaCl solution (40 ml), dried ($MgSO_4$) and evaporated *in vacuo* . The residual syrup was coevaporated with toluene (3 × 10 ml) and CH_2Cl_2 (3 × 10 ml) to afford 820 mg (99 %) of **10** as a beige, crispy foam; $[\alpha]^{20}_D$ +0.84 (*c* 1.0, $CHCl_3$); R_f 0.31 ($CHCl_3$-AcOEt 9:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.09 (d, 1 H, 4'-OH), 3.38 - 3.44 (m, 3 H, 5-H, 5'-H, 6-H_a), 3.54 (br. d, 1 H, 6-H_b), 3.59 (dd, 1 H, 6'-H_a), 3.66 (s, 3 H, $CH_3OC_6H_4$), ~3.74 (dd, 1 H, 6'-H_b), 3.82 (ddd, 1 H, 4'-H), 4.09 (dd, 1 H, 2'-H), 4.13 - 4.23 (m, 3 H, 3-H, 3'-H, 4-H), 4.28 (dd. 1 H, 2-H), 4.40 - 4.52 (m, 6 H, $C_6H_5CH_2$), 4.79, 4.80 (2 d, 1 H each, $C_6H_5CH_2$), 5.27 (d, 1 H, 1'-H), 5.39 (d, 1 H, 1-H); $J_{1,2}$ 8.3; $J_{2,3}$ 10.7; $J_{6a,b}$ 9.2; $J_{1',2'}$ 8.2; $J_{2',3'}$ 10.7; $J_{3',4'}$ 8.3; $J_{4',5'}$ 8.3; $J_{4',OH}$ 2.3; $J_{5',6'a}$ 6.1; $J_{5',6'b}$ 4.3; $J_{6'a,b}$ 9.8; ; J_{CH_2} 11.9, 12.5 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 55.5 ($CH_3OC_6H_4$), 55.9 (C-2), 56.5 (C-2'), 68.0 (C-6), 70.7 (C-6'), 72.9 ($C_6H_5CH_2$), 73.0 (C-5'), 73.7, 74.5 (3 $C_6H_5CH_2$), 74.8 (C-5), 75.2 (C-4'), 75.8, 76.9, 78.3 (C-3, C-4, C-3'), 96.9 (C-1'), 97.3 (C-1), 114.3, 118. 5 ($CH_3OC_6H_4$), 125.3, 125.5 (DCPhth), 127.0 - 138.8 ($C_6H_5CH_2$, DCPhth), 150.5, 155.4 ($CH_3OC_6H_4$), 165.7 (DCPhth).

Anal. Calcd for $C_{63}H_{54}Cl_4N_2O_{14}$ (1204. 94): C, 62.80; H, 4.52; N, 2.32. Found: C, 62.55; H, 4.57; N, 2.91.

2,3,4-Tri-O-acetyl-6-O-benzyl-α-D-galactopyranosyl bromide (12): A mixture of 1,2,3,4-tetra-O-acetyl-6-O-benzyl-D-galactopyranose **11** (3.76 g, 8.58 mmol) and freshly activated molecular sieves 4 Å (sticks, 4 g) in CH_2Cl_2 (80 ml) were stirred for 30 min and then cooled to 0 °C. 30 % HBr/AcOH solution (23 ml, 85.8 mmol) was added dropwise over 5 min and stirring was continued for 45 min. The orange solution was poured into ice-water (250 ml), diluted with CH_2Cl_2 (120 ml), stirred vigorously for 10 min and separated. The org. phase was washed with satd. $NaHCO_3$ solution (2 × 60 ml), 10 % $Na_2S_2O_3$ solution (60 ml) and dried (Na_2SO_4). After evaporation, the crude product was filtered rapidly (10 min) through a short bed of silica gel (toluene-AcOEt-triethylamine 100:10:1) to afford 2.28 g (58 %) of **12** as a clear syrup; $[\alpha]^{20}_D$ +162.6 (*c* 1.3, $CHCl_3$); R_f 0.44 (toluene-AcOEt 5:1 containing 1 % triethylamine); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.00, 2.04, 2.10 (3 s, 3 H each, 3 CH_3CO), 3.48 (dd, 1 H, 6-H_a), 3.55 (dd, 1 H, 6-H_b), 4.42 (d, 1 H, $C_6H_5CH_2$), 4.45 (ddd, 1 H, 5-H), 4.56 (d, 1 H, $C_6H_5CH_2$), 5.03 (dd, 1 H, 2-H), 5.40 (dd, 1 H, 3-H), 5.58 (dd, 1 H, 4-H), 6.70 (d, 1 H, 1-H); $J_{1,2}$ 4.0; $J_{2,3}$ 10.6; $J_{3,4}$ 3.3; $J_{4,5}$ 1.0; $J_{5,6a}$ 6.5; $J_{5,6b}$ 6.2; $J_{6a,b}$ 9.7 Hz.

Anal. Calcd for $C_{19}H_{23}BrO_8$ (459.29): C, 49.49; H, 5.05. Found: C, 48.51; H, 4.91.

Phenyl 2,3,4-tri-O-acetyl-6-O-benzyl-1-thio-D-galactopyranoside (13): Tetraacetate **11** (α/β=1/1.2; 2.40 g, 5.47 mmol) and thiophenol (0.84 ml, 8.2 mmol) were dissolved in CH_2Cl_2 (30 ml) and stirred over freshly activated molecular sieves 4 Å (sticks, 5 g) for 30 min at room temperature. BF_3·OEt_2 (2.1 ml, 16 mmol) was added and stirring continued for 20 h. Additional thiophenol (0.84 ml, 8.2 mmol) and BF_3·OEt_2 (2.1 ml, 16 mmol) were added and, after being stirred for 24 h, the

solution was diluted with CH_2Cl_2 (70 ml), filtered and washed successively with satd. $NaHCO_3$ solution (2 × 25 ml) and water (25 ml), dried (Na_2SO_4) and evaporated *in vacuo*. The residue was purified by silica gel chromatography (toluene-AcOEt 1:0 → 10:1 → 5:1) gave 1.36 g (51 %) β-thiogalactoside **13β** (R_f 0.21) as well as 23 mg (1 %) of slightly impure α-thiogalactoside (R_f 0.26 in toluene-AcOEt 10:1), .

13: $[\alpha]^{20}_D$ -29.3 (*c* 0.5, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 1.97, 2.04, 2.08 (3 s, 3 H each, 3 CH_3CO), 3.50 (dd, 1 H, 6-H_a), 3.61 (dd, 1 H, 6-H_b), 3.90 (ddd, 1 H, 5-H), 4.42, 4.55 (2 d, 1 H each, $C_6H_5CH_2$), 4.74 (dd, 1 H, 1-H), 5.05 (dd, 1 H, 3-H), 5.24 (dd, 1 H, 2-H), 5.49 (d, 1 H, 4-H); $J_{1,2}$ 10.0; $J_{2,3}$ 10.0; $J_{3,4}$ 3.3; $J_{4,5}$ 0.9; $J_{5,6a}$ 6.4; $J_{5,6b}$ 6.3; $J_{6a,b}$ 9.8; J_{CH_2} 11.9 Hz.

Anal. Calcd for $C_{25}H_{28}O_8S$ (488.56): C, 61.46; H, 5.78. Found: C, 61.29; H, 5.80.

α-isomer: ^1H NMR (270 MHz, $CDCl_3$) δ 2.01, 2.06, 2.11 (3 s, 3 H each, 3 CH_3CO), 3.49 (d, 2 H, 6-H_2), 4.39, 4.49 (2 d, 1 H each, $C_6H_5CH_2$), 4.74 (br. dt, 1 H, 5-H), 5.28 (dd, 1 H, 3-H), 5.34 (dd, 1 H, 2-H), 5.56 (dd, 1 H, 4-H), 5.94 (d, 1 H, 1-H), 7.18 - 7.50 (m, 10 H, $C_6H_5CH_2$, C_6H_5S); $J_{1,2}$ 5.0; $J_{2,3}$ 9.4; $J_{3,4}$ 3.0; $J_{4,5}$ 1.3; $J_{5,6}$ 6.3; J_{CH_2} 11.9 Hz.

***p*-Methoxyphenyl 3,6-di-O-benzyl-4-O-chloroacetyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside (15)**: Compound **6** (100 mg, 0.15 mmol) was dissolved in a mixture of CH_2Cl_2 (3 ml) and pyridine (1 ml) and chloroacetyl chloride (60 µl, 0.75 mmol) was added at room temperature. The mixture was stirred for 1 h, poured on ice-water (30 ml) and diluted with CH_2Cl_2 (40 ml). Layers were separated and the organic layer was washed successively with 2 N HCl (2 × 15 ml) and satd. $NaHCO_3$ solution (15 ml) and dried (Na_2SO_4). Evaporation under reduced pressure left a yellowish syrup, which was purified by silica gel column chromatography (toluene-AcOEt 5:1) to afford 91 mg (82 %) of **15** as a yellow foam; $[\alpha]^{20}_D$ +78.0 (*c* 0.7, $CHCl_3$); R_f 0.63 (toluene-AcOEt 5:1); ^1H NMR (270 MHz, $CDCl_3$) δ 3.65 (d, 2 H, 6-H_2), 3.71 (s, 3 H, $CH_3OC_6H_4$), 3.81 (d, 2 H, $ClCH_2CO$), 3.85 (ddd, 1 H, 5-H), 4.33 (d, 1 H, $C_6H_5CH_2$), 4.44 (m, 1 H, 2-H), 4.47 (m, 1 H, 3-H), 4.55 (s, 2 H, $C_6H_5CH_2$), 4.65 (d, 1 H, $C_6H_5CH_2$), 5.26 (m, 1 H, 4-H), 5.59 (m, 1 H, 1-H); $J_{1,2}$ 8.3; $J_{2,3}$ 9.0; $J_{3,4}$ 8.8; $J_{4,5}$ 9.9; $J_{5,6}$ 5.0; J_{CH_2} 12.4 Hz.

Anal. Calcd for $C_{37}H_{32}Cl_3NO_9$ (741.03): C, 59.97; H, 4.35; N, 1.89. Found: C, 59.14; H, 4.25; N, 1.82.

***p*-Methoxyphenyl 4-O-acetyl-3,6-di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside (14)**: A solution of **6** (100 mg, 0.15 mmol) in CH_2Cl_2 (3 ml) and pyridine (1 ml) was cooled to 0 °C. Acetic anhydride (71 µl, 0.75 mmol) was added and the solution stirred for 20 h at room temperature. The mixture was poured on ice-water (10 ml), diluted with CH_2Cl_2 (30 ml) and layers separated. The organic layer was washed successively with 2 N HCl (2 × 10 ml) and satd. $NaHCO_3$ solution (10 ml), dried (Na_2SO_4) and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (toluene-AcOEt 5:1) to afford 92 mg (87 %) of **14** as a colorless foam; $[\alpha]^{20}_D$ +88.3 (*c* 1.0, $CHCl_3$); R_f 0.50 (toluene-AcOEt 5:1); ^1H NMR (270 MHz, $CDCl_3$) δ 2.01 (s, 3 H, CH_3CO), 3.62 (dd, 1 H, 6-H_a), 3.64 (dd, 1 H, 6-H_b), 3.70 (s, 3 H, $CH_3OC_6H_4$), 3.84 (ddd, 1 H, 5-H), 4.29 (d, 1 H, $C_6H_5CH_2$), 4.44 (m, 1 H, 2-H), 4.45 (m, 1 H, 3-H), 4.53 (s, 2 H, $C_6H_5CH_2$), 4.68 (d, 1 H, $C_6H_5CH_2$), 5.18 (m, 1 H, 4-H), 5.58 (m, 1 H, 1-H); $J_{1,2}$ 8.3; $J_{2,3}$ 9.4; $J_{3,4}$ 8.9; $J_{4,5}$ 9.9; $J_{5,6a}$ 5.5; $J_{5,6b}$ 4.1; $J_{6a,b}$ 10.9; J_{CH_2} 12.5 Hz.

Anal. Calcd for $C_{37}H_{33}Cl_2NO_9$ (706.575): C, 62.90; H, 4.71; N, 1.98. Found: C, 62.67; H, 4.66; N, 1.89.

***p*-Methoxyphenyl 3,6-di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside (6)**

From monochloroacetate 15: A solution of monochloroacetate **15** (85 mg, 0.12 mmol) in CH_2Cl_2-MeOH (1:1, 2 ml) was stirred with freshly activated molecular sieves 3 Å for 20 min. Thiourea (11.5 mg, 0.15 mmol) was added and stirring continued for 3 d at room temperature. Additional portion of thiourea (11.5 mg, 0.15 mmol) was added and, after stirring for 4 d, the mixture was diluted with CH_2Cl_2 (30 ml), filtered through a pad of celite and evaporated. The residual orange solid was subjected to silica gel column chromatography (toluene-AcOEt) to afford 64 mg (83 %) of **6** as colorless foam.

From acetate 14: Compound **14** (40 mg, 0.057 mmol) was dissolved in CH_2Cl_2-MeOH(2 ml, 1:1) and cooled to 0 °C. NaOMe solution in MeOH (28 %, 6 µl, 0.03 mmol) was added and stirring continued for 22 h. After adding another NaOMe solution (5 µl, 0.025 mmol) the mixture was stirred for 10 h at room temperature, neutralized with Amberlyst 15-E (H^+, strongly acidic), filtered and evaporated to dryness to leave 36 mg (96 %) of crude **6** as a colorless foam. Purification by silica gel column chromatography (toluene-AcOEt 5:1) gave 22 mg (58 %) of **6**.

***p*-Methoxyphenyl O-[2,3,4-tri-O-acetyl-6-O-benzyl-β-D-galactopyranosyl]-(1→4)-3,6-di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside (16)**

Method A (by AgOTf promoted glycosylation with 12): A suspension of silver triflate (1.57 g, 6.12 mmol), compound **6** (2.03 g, 3.06 mmol) and freshly activated molecular sieves 4 Å (3 g) in CH_2Cl_2 (15 ml) was stirred under argon

with exclusion of light for 30 min and then cooled to -40 °C. Galactosyl bromide **12** (2.32 g, 5.05 mmol) was added as a solution in CH_2Cl_2 (10 ml) and stirring continued for 4 h. The reaction mixture was quenched by addition of satd. $NaHCO_3$ solution (10 ml), diluted with CH_2Cl_2 (120 ml) and filtered through a short pad of celite. Washing with satd. $NaHCO_3$ solution (2 × 30 ml), 10 % $Na_2S_2O_3$ solution (30 ml) and drying (Na_2SO_4) and removal of the solvent *in vacuo* afforded 3.65 g of a slightly yellow foam. Purification by silica gel column chromatography (toluene-AcOEt 10:1 → 6:1) gave 2.13 g (67 %) **16** as a colorless foam; $[\alpha]^{20}_D$ +30.1 (*c* 1.1, $CHCl_3$); R_f 0.07 (toluene-AcOEt 10:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.97 (s, 6 H each, 2 CH_3CO), 2.01 (s, 3 H, CH_3CO), 3.29 (dd, 1 H, 6'-H_a), 3.43 (dd, 1 H, 6'-H_b), 3.58 - 3.68 (m, 2 H, 5-H, 5'-H), 3.71 (s, 3 H, $CH_3OC_6H_4$), 3.76 (m, 2 H, 6-H_2), 4.10 (dd, 1 H, 4-H), 4.26 (dd, 1 H, 3-H), 4.30 (d, 1 H, $C_6H_5CH_2$), 4.36 (dd, 1 H, 2-H), 4.42 (d, 1 H, $C_6H_5CH_2$), 4.49 (d, 2 H, $C_6H_5CH_2$), 4.58 (d, 1 H, 1'-H), 4.76, 4.82 (2 d, 1 H each, $C_6H_5CH_2$), 4.88 (dd, 1 H, 3'-H), 5.13 (dd, 1 H, 2'-H), 5.40 (dd, 1 H, 4'-H), 5.55 (d, 1 H, 1-H); $J_{1,2}$ 8.1; $J_{2,3}$ 10.9; $J_{3,4}$ 8.1; $J_{4,5}$ 9.9; $J_{1',2'}$ 7.9; $J_{2',3'}$ 10.3; $J_{3',4'}$ 3.5; $J_{4',5'}$ < 1; $J_{5',6'a}$ 7.6; $J_{5',6'b}$ 5.6; $J_{6'a,b}$ 9.2; J_{CH_2} 11.9, 12.2, 12.5 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 20.5, 20.7 (CH_3CO), 55.5 ($CH_3OC_6H_4$), 55.9 (C-2), 67.0 (C-6'), 67.3 (C-6), 67.4 (C-4'), 69.7 (C-2'), 71.0 (C-3'), 71.9 (C-5'), 73.4, 73.6, 74.6 ($C_6H_5CH_2$), 75.0 (C-5), 76.8 (C-3), 77.6 (C-4), 97.4 (C-1), 100.3 (C-1'), 114.3, 118.6 ($CH_3OC_6H_4$), 125.2 (DCPhth), 129.0 - 138.6 ($C_6H_5CH_2$), 150.6, 155.4 ($CH_3OC_6H_4$), 169.2, 169.9, 170.0 (CH_3CO); FAB-MS (positive) *m/z* 1066. 3 $[M+Na]^+$.

Anal. Calcd for $C_{54}H_{53}Cl_2NO_{16}$: C, 62.19; H, 5.12; N, 1.34; Cl, 6.80. Found: C, 62.16; H, 5.08; N, 1.36; Cl, 6.70.

Method B (by NIS/TfOH promoted glycosylation with 13): A solution of **6** (643 mg, 0.97 mmol) and **13** (612 mg, 1.25 mmol) in CH_2Cl_2 (15 ml) was stirred under argon with freshly activated molecular sieves 4 Å (1.5 g) for 20 min and cooled to 0 °C. Then, *N*-iodosuccinimide (NIS, 543 mg, 2.42 mmol) was added, stirring continued for another 20 min and trifluoromethanesulfonic acid (TfOH, 43 µl, 0.48 mmol) added. After 1 h, the reaction was quenched with triethylamine (0.25 ml). Dilution with CH_2Cl_2 (120 ml), filtration through celite, and washing successively with satd. $NaHCO_3$ solution (20 ml) and 10 % $Na_2S_2O_3$ solution (2 × 20 ml) and drying (Na_2SO_4) furnished, after removal of the solvent *in vacuo*, 1.2 g of a brown foam. Purification by silica gel column chromatography (toluene-AcOEt 20:1 → 10:1 → 6:1) gave 827 mg (82 %) of **16** as a slightly orange foam.

***p*-Methoxyphenyl O-[6-O-benzyl-β-D-galactopyranosyl]-(1→4)-3,6-di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside (17):** Compound **16** (2.13 g, 2.04 mmol) was dissolved in CH_2Cl_2-MeOH(40 ml, 1:1) containing freshly activated molecular sieves 3 Å (sticks, 6 g) stirred for 1h and and cooled to 0 °C. Sodium methoxide (21 mg, 0.39 mmol) was added, the mixture was allowed to stand for 24 h at 0 °C and was then brought to pH 5 by addition of Amberlyst 15-E. Insoluble materials were filtered off and the filtrate was evaporated *in vacuo* to afford 1.82 g of crude product. Separation by silica gel chromatography ($CHCl_3$-MeOH 20:1) and collection of fractions with R_f 0.25 gave 730 mg (39 %) **17** as a yellowish foam. Fractions contaminated with impurities were collected and purified again by silica gel column chromatography ($CHCl_3$-AcOEt 50:1) to afford additional 645 mg (35 %) **17** (total yield 74%); $[\alpha]^{20}_D$ +69.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$, 5 dr. D_2O) δ 3.45 (dd, 1 H, 3'-H), 3.49 (dd, 1 H, 5'-H), 3.63 (dd, 1 H, 6'-H_a), ~3.65 (m, 2 H, 5-H, 2'-H), 3.71 (s, 3 H, $CH_3OC_6H_4$), 3.29 (dd, 1 H, 6'-H_b), 3.83 (dd, 1 H, 6-H_a), 3.96 (d, 1 H, 4'-H), 4.05 (dd, 1 H, 6-H_b), 4.17 (m, 1 H, 4-H), 4.30 - 4.41 (m, 2 H, 2-H, 3-H), 4.42 - 4.51 (m, 2 H, $C_6H_5CH_2$), 4.58 (d, 1 H, 1'-H), 4.59 (d, 1 H, $C_6H_5CH_2$), 4.74 (d, 2 H, $C_6H_5CH_2$), 4.88 (d, 2 H, $C_6H_5CH_2$), 5.53 (d, 1 H, 1-H); $J_{1,2}$ 8.3; $J_{3,4}$ 8.3; $J_{4,5}$ 9.9; $J_{5,6a}$ 1.8; $J_{5,6b}$ 3.5; $J_{6a,b}$ 11.7; $J_{1',2'}$ 7.6; $J_{2',3'}$ 9.4; $J_{3',4'}$ 3.5; $J_{4',5'}$ < 1; $J_{5',6'a}$ 5.5; $J_{5',6'b}$ 5.6; $J_{6'a,b}$ 10.1; J_{CH_2} 11.9, 12.2 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 55.5 ($CH_3OC_6H_4$), 55.9 (C-2), 68.0 (C-6), 69.0 (C-4'), 69.4 (C-6'), 72.4, 74.9 (C-2', C-5), 73.3 (C-5'), 73.5 ($C_6H_5CH_2$), 73.7 (C-3'), 74.8 ($C_6H_5CH_2$), 78.3 (C-3), 78.4 (C-4), 97.4 (C-1), 103.5 (C-1'), 114.3, 118.6 ($CH_3OC_6H_4$), 125.3 (DCPhth), 129.0 - 138.5 ($C_6H_5CH_2$), 150.5, 155.4 ($CH_3OC_6H_4$), 165.9 (DCPhth).

Anal. Calcd for $C_{48}H_{47}Cl_2NO_{13}$ (916.80): C, 62.88; H, 5.17; N, 1.53; Cl, 7.73. Found: C, 62.79; H, 5.10; N, 1.44; Cl 7.73.

***p*-Methoxyphenyl O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-non-2-ulopyranosyl) onate]-(2→3)-(2,4-di-O-acetyl-6-O-benzyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside (24) and corresponding β-isomer (25)**

Metod A (via sialylation with methyl thioglycoside 21): A solution of compounds **17** (907 mg, 0.99 mmol) and **21** (1.29 g, 2.47 mmol) in CH_3CN (50 ml) was stirred under argon with freshly activated molecular sieves 3 Å (1.5 g) for 30 min and brought to -40 °C. After addition of *N*-iodosuccinimide (NIS, 850 mg, 3.46 mmol), stirring was continued for 30 min, followed by the addition of trifluoromethanesulfonic acid (TfOH, 93 µl, 1.05 mmol). The mixture was kept at -40 °C for 22 h, then additional amounts of sialyl donor **21** (155 mg, 0.30 mmol), NIS (111 mg, 0.50 mmol) and TfOH (31 µl, 0.35 mmol) were added. After being stirred for additional 4 h, the reaction was quenched by the addition of triethylamine (0.4 ml). Dilution

with CH_2Cl_2 (200 ml), filtration through celite, and washing successively with satd. $NaHCO_3$ solution (3 × 30 ml) and 10 % $Na_2S_2O_3$ solution (3 × 30 ml), drying (Na_2SO_4) and removal of the solvents *in vacuo* gave 2.17 g of crude mixture. The mixture was subjected to size exclusion chromatography on Biobeads SX-1 (3.5 × 60 cm, in 3 portions, toluene) to remove reagents and monosaccharide by-products afforded 1.27 g of an orange foam.

This material was dissolved in CH_2Cl_2 (30 ml) and pyridine (4 ml) containing 4-dimethylaminopyridine (4-DMAP, 75 mg, 0.61 mmol) followed by the addition of acetic anhydride (4 ml). After stirring for 21 h, the mixture was quenched with MeOH (5 ml) and stirred for 60 min. Removal of volatiles under reduced pressure and coevaporation with toluene (3 × 30 ml) gave a syrup, which was separated by silica gel chromatography (toluene-EtOH 20:1) gave 738 mg (48%) of sialylated product **24** (R_f 0.30) and 276 mg(19 %) of **25** (R_f 0.39), together with 105 mg (10 %) of acetylated lactosamine **16**.

24: $[\alpha]^{20}_D$ +24.7 (*c* 1.7, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.74 (dd, 1 H, 3"-H_{ax}), 1.86, 1.98, 2.00, 2.01, 2.08, 2.12, 2.24 (7 s, 3 H each, 7 CH_3CO), 2.59 (dd, 1 H, 3"-H_{eq}), 3.31 (dd, 1 H, 6'-H_a), 3.41 (dd, 1 H, 6'-H_b), 3.65 (dd, 1 H, 6"-H), 3.69 (s, 3 H, $CH_3OC_6H_4$), 3.70 - 3.80 (m, 2 H, 5-H, 6-H_a), 3.82 (dd, 1 H, 5'-H), 3.85 (s, 3 H, CH_3OOC), 3.96 (d, 1 H, 6-H_b), 4.01 (dd, 1 H, 9"-H_a), 4.06 (dd, 1 H, 4-H), 4.07 (ddd, 1 H, 5"-H), 4.31 (d, 1 H, $C_6H_5CH_2$), 4.32 (dd, 2 H, 2-H, 3-H), 4.35 (dd, 1 H, 9"-H_b), 4.45 (d, 2 H, $C_6H_5CH_2$), 4.58 (d, 1 H, $C_6H_5CH_2$), 4.58 (dd, 1 H, 3'-H), 4.68, 4.88 (d, 1 H each, $C_6H_5CH_2$), 4.90 (d, 1 H, 1'-H), ~4.90 (m, 1 H, 4"-H), 5.01 (dd, 1 H, 4'-H), 5.07 (dd, 1 H, 2'-H), 5.10 (d, 1 H, 5"-NH), 5.39 (dd, 1 H, 7"-H), 5.54 (m, 1 H, 1-H), 5.60 (ddd, 1 H, 8"-H); $J_{1,2}$ 8.2; $J_{3,4}$ 10.5; $J_{4,5}$ 10.5; $J_{5,6b}$ < 1.0; $J_{6a,b}$ 9.5; $J_{1',2'}$ 7.7; $J_{2',3'}$ 10.0; $J_{3',4'}$ 3.1; $J_{4',5'}$ < 0.5; $J_{5',6'a}$ 7.0; $J_{5',6'b}$ 5.7; $J_{6'a,b}$ 9.8; $J_{3"eq,ax}$ 12.6; $J_{3"ax,4"}$ 12.5; $J_{3"eq,4"}$ 4.7; $J_{4",5"}$ 10.5; $J_{5",6"}$ 10.7; $J_{6",7"}$ 2.6; $J_{7",8"}$ 9.0; $J_{8",9"a}$ 5.9; $J_{8",9"b}$ 2.8; $J_{9"a,b}$ 12.4; J_{CH2} 11.6, 12.2 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 20.7, 21.0, 21.3, 23.1 (CH_3CO), 37.5 (C-3"), 49.1 (C-5"), 53.2 (CH_3OOC), 55.5 ($CH_3OC_6H_4$), 56.0 (C-2), 62.3 (C-9"), 67.2 (C-7"), 67.9 (C-6', C-8"), 68.0 (C-4'), 68.4 (C-6), 69.4 (C-4"), 71.0 (C-2'), 71.8 (C-3', C-5'), 72.1 (C-6"), 73.1, 73.3, 74.8 ($C_6H_5CH_2$), 75.5 (C-5), 77.6 (C-3), 78.1 (C-4), 96.9 (C-2"), 97.2 (C-1), 100.5 (C-1'), 114.3, 118.5 ($CH_3OC_6H_4$), 125.3 (DCPhth), 126.9 - 138.7 ($C_6H_5CH_2$), 150.7, 155.3 ($CH_3OC_6H_4$), 165.6 (DCPhth), 167.8 (C-1"), 169.6, 169.7, 170.1, 170.3, 170.4, 170.5, 170.9 (CH_3CO); $J_{C-1"-H-3"ax}$ 6.1 Hz; FAB-MS (negative) *m/z* 1474.4 $[M-H]^-$.

Anal. Calcd for $C_{72}H_{78}Cl_2N_2O_{27}$ (1474.31): C, 58.66; H, 5.33; N, 1.90. Found: C, 58.47; H, 5.30; N, 1.86.

25: $[\alpha]^{20}_D$ +28.4 (*c* 1.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.80 (dd, 1 H, 3"-H_{ax}), 1.90, 1.91, 1.99, 2.00, 2.11 (5 s, 3 H each, 5 CH_3CO), 2.14 (s, 6 H, 2 CH_3CO), 2.46 (dd, 1 H, 3"-H_{eq}), 3.36 (dd, 1 H, 6'-H_a), 3.47 (dd, 1 H, 6'-H_b), 3.61 (ddd, 1 H, 5-H), 3.70 (s, 3 H, $CH_3OC_6H_4$), ~3.72 (dd, 1 H, 6-H_a), ~3.83 (dd, 1 H, 6-H_b), 3.84 (s, 3 H, CH_3OOC), 3.86 (dd, 1 H, 9"-H_a), 3.98 (ddd, 1 H, 5'-H), ~4.02 (ddd, 1 H, 5"-H), 4.04 (dd, 1 H, 4-H), 4.26 (dd, 1 H, 3-H), 4.33 (dd, 1 H, 2-H), 4.38, 4.46, 4.52, 4.61, 4.65 (5 d, 1 H each, $C_6H_5CH_2$), 4.67 (d, 1 H, 1'-H), ~4.68 (d, 1 H, 6"-H), 4.72 (dd, 1 H, 3'-H), 4.85 (d, 1 H, $C_6H_5CH_2$), 5.04 (ddd, 1 H, 4"-H), 5.10 (dd, 1 H, 9"-H_b), 5.22 (dd, 1 H, 2'-H), 5.29 (ddd, 1 H, 8"-H), 5.38 (br.d, 2 H, 4'-H, 7"-H), 5.53 (d, 1 H, 1-H), 5.65 (d, 1 H, 5"-NH); $J_{1,2}$ 8.3; $J_{2,3}$ 10.7; $J_{3,4}$ 7.8; $J_{4,5}$ 9.9; $J_{5,6a}$ 4.8; $J_{1',2'}$ 8.2; $J_{2',3'}$ 10.6; $J_{3',4'}$ 3.4; $J_{4',5'}$ < 0.5; $J_{5',6'a}$ 6.7; $J_{5',6'b}$ 6.5; $J_{6'a,b}$ 9.8; $J_{3"eq,ax}$ 13.2; $J_{3"ax,4"}$ 11.7; $J_{3"eq,4"}$ 4.6; $J_{4",5"}$ 10.3; $J_{5",NH}$ 10.3; $J_{6",7"}$ < 1.0; $J_{7",8"}$ 2.9; $J_{8",9"a}$ 9.4; $J_{8",9"b}$ 2.7; $J_{9"a,b}$ 12.2;J_{CH2} 12.2, 12.7 Hz.

Anal. Calcd for $C_{72}H_{78}Cl_2N_2O_{27}$ (1474.31): C, 58.66; H, 5.33; N, 1.90. Found: C, 58.27; H, 5.28; N, 1.82.

Method B (via sialylation with phenylthio glycoside 22): A solution of lactosamine **17** (497 mg, 0.54 mmol) and α-thioglycoside **22** (791 mg, 1.35 mmol) in CH_3CN-CH_2Cl_2 (27.5 ml, 10:1) was stirred under argon with freshly activated molecular sieves 3 Å (500 mg) for 30 min and brought to -40 °C. After addition of N-iodosuccinimide (NIS, 760 mg, 3.39 mmol), stirring was continued for 30 min and then trifluoromethanesulfonic acid (TfOH, 14 µl, 0.163 mmol) was added. The mixture was kept at -40 °C for 6 h, stirred at -10 °C for 18 h and was then quenched by addition of triethylamine (0.25 ml). Aqueous work-up, the mixture was processed as described in Method A to afford 305 mg (42 %) of **24**, 166 mg (23 %) of **25**, and 65 mg (13 %) of **16**, .

Method C (via sialylation with phosphite 23): Compounds **17** (572 mg, 0.62 mmol) and **23** (954 mg, 1.56 mmol) were dissolved in CH_3CN (25 ml), that contained freshly activated molecular sieves 3 Å (500 mg), and stirred under argon for 30 min. The mixture was cooled to -40 °C, followed by the addition of trimethylsilyl trifluoromethanesulfonate (TMSOTf, 11 µl, 62 µmol), and the stirring was continued at the same temperature. After 2.5 h, the same amount (11 µl, 62 µmol) of TMSOTf was added and the mixture was kept at -40 °C for 6 h and was quenched by the addition of triethylamine (0.5 ml). Dilution with CH_2Cl_2 (100 ml), filtration through a bed of celite and removal of the solvents *in vacuo* gave 1.59 of a pale yellow foam, which was processed as described in Method A to give 291 mg (32 %) of **24**, 177 mg (19 %) of **25**, and 139 mg (21 %) of **16**.

***p*-Methoxyphenyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside (18)**: Compound **3** (610 mg, 1.0 mol) was added to a stirred solution of ethylenediamine (670 µl, 10 mmol) in MeOH (20 ml). After 2 h, the clear solution was evaporated to dryness at 30 °C, dissolved in CH_2Cl_2 (5 ml)-pyridine (5 ml) and cooled to 0 °C. Acetic anhydride (5

ml) was added and the mixture allowed to stand for 18 h. Resulting mixture was pouring on ice-water (50 ml), diluted with CH_2Cl_2 (100 ml), and washed successively with 2 N HCl (30 ml) and satd. $NaHCO_3$ solution (2 × 30 ml), drie (Na_2SO_4) and evaporated *in vacuo* to afford 427 mg of a colorless solid. Adsorptive filtration through silica gel ($CHCl_3$-MeOH 20:1) furnished 325 mg (72 %) of **18** as a colorless solid; $[\alpha]^{20}_D$ -12.3 (1.1, $CHCl_3$); R_f 0.22 ($CHCl_3$-MeOH 20:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.97, 2.04, 2.06, 2.08 (4 s, 3 H each, 4 CH_3CO), 3.76 (s, 3 H, $CH_3OC_6H_4$), 3.81 (ddd, 1 H, 5-H), 4.08 (ddd, 1 H, 2-H), 4.15 (dd, 1 H, 6-H_a), 4.29 (dd, 1 H, 6-H_b), 5.13 (dd, 1 H, 4-H), 5.15 (d, 1 H, 1-H), 5.39 (dd, 1 H, 3-H), 5.69 (d, 1 H, 2-NH); $J_{1,2}$ 8.4; $J_{2,3}$ 10.5; $J_{3,4}$ 9.4; $J_{4,5}$ 9.8; $J_{5,6a}$ 2.4; $J_{5,6b}$ 5.3; $J_{6a,b}$ 12.1 Hz.

Anal. Calcd for $C_{21}H_{27}NO_{10}$ (453.44): C, 55.63; H, 6.00; N, 3.09. Found: C, 55.64; H, 5.98; N, 3.17.

***p*-Methoxyphenyl O-[2,3,4-tri-O-acetyl-6-O-benzyl-β-D-galactopyranosyl]-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (19):** A solution of **16** (137 mg, 130 μmol) in MeOH (5 ml) was stirred with ethylenediamine (176 μl, 2.63 mmol) at room temperature for 20 h. The mixture was evaporated to dryness at 30 °C and coevaporated with toluene (3 × 5 ml). Acetylation in pyridine (1.5 ml) by addition of acetic anhydride (1.5 ml) and 4-dimethylaminopyridine (4-DMAP, 2 mg, 16.4 μmol) for 2 h at room temperature, quench with MeOH (2 ml), stirring for 20 min and evaporation to dryness gave crude **19**; adsorptive filtration through silica gel ($CHCl_3$-AcOEt 15:1) gave 88 mg (77 %) of **19** as a colorless foam; $[\alpha]^{20}_D$ -53.3 (*c* 1.0, $CHCl_3$); R_f 0.03 ($CHCl_3$-AcOEt 15:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.98, 1.99, 2.02, 2.03 (4 s, 3 H each, 4 CH_3CO), 3.40 (dd, 1 H, 6'-H_a), 3.46 (dd, 1 H, 6'-H_b), 3.68 (d, 1 H, 6-H_a), ~3.70 (m, 1 H, 5'-H), 3.76 (s, 3 H, $CH_3OC_6H_4$), ~3.77 (ddd, 1 H, 5-H), 3.88 (dd, 1 H, 6-H_b), 3.98 (dd, 1 H, 3-H), 4.05 (dd, 1 H, 4-H), 4.14 (ddd, 1 H, 2-H), 4.34, 4.37 (2 d, 1 H each, $C_6H_5CH_2$), 4.48 (d, 1 H, 1'-H), ~4.49, 4.53, 4.70, 4.75 (4 d, 1 H each, $C_6H_5CH_2$), 4.96 (dd, 1 H, 3'-H), 5.13 (dd, 1 H, 2'-H), 5.27 (d, 1 H, 1-H), 5.46 (d, 1 H, 4'-H), 6.17 (d, 1 H, 2-NH) ; $J_{1,2}$ 4.8; $J_{2,3}$ 5.1; $J_{2,NH}$ 8.9; $J_{3,4}$ 5.2; $J_{4,5}$ 5.0; $J_{5,6a}$ 4.8; $J_{5,6b}$ 5.5; $J_{6a,b}$ 9.6; $J_{1',2'}$ 7.9; $J_{2',3'}$ 10.5; $J_{3',4'}$ 3.2; $J_{4',5'}$ < 1; $J_{5',6'a}$ 8.7; $J_{5',6'b}$ 6.1; $J_{6'a,b}$ 9.2; J_{CH_2} 11.7, 11.9, 12.2 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 20.5, 20.6, 20.8, 23.3 (CH_3CO), 51.3 (C-2), 55.5 ($CH_3OC_6H_4$), 66.7 (C-6'), 67.2 (C-4'), 69.0 (C-6), 69.3 (C-2'), 70.6 (C-3'), 72.0 (C-5'), 72.7, 73.4 ($C_6H_5CH_2$), 73.4, 76.1 (C-3, C-4, C-5), 98.5 (C-1), 99.7 (C-1'), 114.4, 117.8 ($CH_3OC_6H_4$), 127.5 - 138.3 ($C_6H_5CH_2$), 151.1, 154.9 ($CH_3OC_6H_4$), 169.8, 170.0, 170.2 (CH_3CO).

Anal. Calcd for $C_{48}H_{55}NO_{15}$ (885.96): C, 65.07; H, 6.26; N, 1.58. Found: C, 64.59; H, 6.28; N, 1.58.

***p*-Methoxyphenyl O-(2-acetamido-4-O-acetyl-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (20):** To a solution of **9**(68 mg, 52 μmol) in MeOH (1 ml) was added ethylenediamine (525 μl, 7.8 mmol) and the mixture stirred at 50 °C for 20 h. Removal of volatile components under reduced pressure and coevaporation with toluene (5 ml) gave a yellow syrup, which was acetylated in CH_2Cl_2 (2 ml) and pyridine (0.5 ml) by treatment with acetic anhydride (0.5 ml) and 4-DMAP (1 mg, 8.2 μmol) for 20 h. After being quenched with MeOH (0.5 ml), the mixture was stirred for 30 min and evaporated *in vacuo* to afford a crude product, which was purified by elution from silica gel ($CHCl_3$-MeOH 1:0 → 50:1) to afford 41 mg (84 %) **20** as a colorless, crystalline mass. Recrystallization from hot methanol furnished colorless needles; m.p. 242-243 °C; $[\alpha]^{20}_D$ -36.0 (*c* 1.1, $CHCl_3$); R_f 0.55 in $CHCl_3$-MeOH 20:1; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.74, 1.93, 1.99 (3 s, 3 H each, 3 CH_3CO), 3.35 - 3.54 (m, 3 H, 5'-H, 6'-H_2), 3.67 - 3.71 (m, 2 H, 6-H_a, 3'-H), 3.75 (s, 3 H, $CH_3OC_6H_4$), 3.76 - 3.85 (m, 3 H, 5-H, 6-H_b, 2'-H), 3.89 (dd, 1 H, 3-H), 4.04 (dd, 1 H, 4-H), 4.28 (ddd, 1 H, 2-H), 4.36, 4.43 (2 d, 1 H each, $C_6H_5CH_2$), 4.45 (s, 2 H, $C_6H_5CH_2$), 4.46 (d, 1 H, 1'-H), 4.49, 4.60, 4.64, 4.78 (4 d, 1 H each, $C_6H_5CH_2$), 5.08 (d, 1 H, 2'-NH), 5.10 (dd, 1 H, 4'-H), 5.16 (d, 1 H, 1-H), 6.57 (d, 1 H, 2-NH); $J_{1,2}$ 4.8; $J_{2,3}$ 4.8; $J_{2,NH}$ 9.0; $J_{3,4}$ 4.5; $J_{4,5}$ 4.1; $J_{1',2'}$ 4.6; $J_{2',NH}$ 7.6; $J_{3',4'}$ 7.9; J_{CH_2} 11.6, 11.7 Hz; ^{13}C NMR (67.80 MHz, $CDCl_3$) δ 20.9, 23.0, 23.4 (CH_3CO), 50.5 (C-2), 55.0 (C-2'), 55.6 ($CH_3OC_6H_4$), 69.3 (C-6'), 69.8 (C-6), 71.1 (C-4'), 72.0, 72.3 ($C_6H_5CH_2$), 72.9 (C-5'), 73.2, 73.5 ($C_6H_5CH_2$), 73.6 (C-4), 74.6 (C-5), 76.5 (C-3), 78.0 (C-3'), 98.9 (C-1), 99.7 (C-1'), 114.4, 117.8 ($CH_3OC_6H_4$), 127.4 - 137.7 ($C_6H_5CH_2$), 151.2, 155.0 ($CH_3OC_6H_4$), 169.8, 170.5, 170.8 (CH_3CO).

Anal. Calcd for $C_{53}H_{60}N_2O_{13}$ (933.06): C, 68.23; H, 6.48; N, 3.00. Found: C, 67.69; H, 6.39; N, 3.08.

***p*-Methoxyphenyl O-[2'-acetamidoethyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-non-2-ulopyranosyl) onamide]-(2→3)-(2,4-di-O-acetyl-6-O-benzyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (26):** Trisaccharide **24** (60 mg, 40 μmol) was added to a solution of ethylenediamine (120 μl, 1.8 mmol) in MeOH (1 ml) and stirred at room temperature for 3 d. The mixture was freed from reagent and solvent by evaporation at 30 °C, acetylated in pyridine (0.5 ml) by addition of acetic anhydride (0.3 ml) and 4-DMAP (1.0 mg, 8.2 μmol) and stirring for 20 h at room temperature. Quenching with MeOH (0.5 ml), stirring for 30 min and evaporation to dryness gave crude **29**; elution from silica gel ($CHCl_3$-MeOH 20:1) gave 39 mg (71 %) of **29** as a colorless film; $[\alpha]^{20}_D$ -31.9 (*c* 0.8, $CHCl_3$); R_f 0.11 in $CHCl_3$-MeOH 20:1; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.86 (dd, 1 H, 3"-

H_{ax}), 1.91, 1.96, 1.98, 2.00 (4 s, 3 H each, 4 CH_3CO), 2.03 (s, 9 H, 3 CH_3CO), 2.10, 2.13 (2 s, 3 H each, 2 CH_3CO), 2.37 (dd, 1 H, 3"-H_{eq}), 3.30 - 3.50 (m, 6 H, $NHCH_2CH_2NH$, 2 ring protons), 3.68 - 3.78 (m, 2 H, ring protons), 3.75 (s, 3 H, $CH_3OC_6H_4$), 3.92 - 4.10, 4.25 (2 m, 7 and 1 H, ring protons), 4.32 (dd, 1 H, 3'-H), 4.34 (d, 1 H, $C_6H_5CH_2$), 4.38 (dd, 1 H, 9"-H_b), 4.43 (s, 2 H, $C_6H_5CH_2$), 4.53 (d, 1 H, $C_6H_5CH_2$), 4.63 (d, 1 H, 1'-H), 4.68, 4.77 (2 d, 1 H each, $C_6H_5CH_2$), 5.01 (dd and m , 2 H, 2'-H, 4"-H), 5.24 (d, 1 H, 1-H), 5.29 (dd, 1 H, 7"-H), 5.32 (d, 1 H, 4'-H), 5.64 (ddd, 1 H, 8"-H), 5.87 (br. d, 1 H, 5"-NH), 6.26 (d, 1 H, 2-NH), 6.43 (br. t, 1 H, $NHCH_2CH_2NH$); $J_{1,2}$ 4.6; $J_{2,NH}$ 8.9; $J_{1',2'}$ 8.0; $J_{2',3'}$ 10.5; $J_{3',4'}$ 2.8; $J_{4',5'}$ < 1.0; $J_{3"eq,ax}$ 12.7; $J_{3"eq,4"}$ 4.6; $J_{5",NH}$ 9.2; $J_{7",8"}$ 6.6;$J_{8",9"a}$ 5.6; $J_{8",9"b}$ 2.3; $J_{9"a,b}$ 12.2; J_{CH_2} 11.6, 11.7 Hz.

Anal. Calcd for $C_{69}H_{86}N_4O_{26}$ (1387.45): C, 59.73; H, 6.25; N, 4.04. Found: C, 59.31; H, 6.22; N, 4.08.

***p*-Methoxyphenyl O-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-non-2-ulopyranosylonic acid]-(2→3)-(6-O-benzyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (27)**: Trisaccharide 24 (107 mg, 72.6 μmol) was heated under reflux in the presence of lithium iodide (291 mg, 2.18 mmol) in pyridine (15 ml) under argon for 6 h. The dark yellow solution was evaporated to dryness, coevaporated with AcOEt (3 × 20 ml) and dissolved in AcOEt (60 ml). Washing of the org. phase with 2 N HCl (3 × 5 ml), satd. NaCl solution (2 × 5 ml), drying ($MgSO_4$) and concentration *in vacuo* afforded 98 mg (92 %) of the corresponding carboxylic acid as a bright yellow film; R_f 0.26 in $CHCl_3$-MeOH 8:1.

To the solution of the free acid in MeOH (4 ml) was added ethylenediamine (224 μl, 3.34 mmol) and the mixture warmed to 50 °C for 8 h. Evaporation of the volatile components under reduced pressure gave 118 mg of free amine (R_f 0.13 - 0.27 in $CHCl_3$-MeOH 2:1), which was *N*-acetylated by stirring in MeOH (10 ml) with acetic anhydride (600 μl) for 24 h at room temperature. The mixture was freed from the solvents *in vacuo*, dissolved in MeOH (5 ml) and treated with NaOMe (25 mg, 0.48 mmol) at 0 °C for 3 d. The solution was brought to pH 4-5 with Amberlyst 15-E, filtered and evaporated to give 83 mg of a yellowish glass which was purified by silica gel column chromatography ($CHCl_3$-EtOH-AcOH 4:1:0 → 3:1:0 → 2:1:0 → 12:6:1). From the resulting solid (54.4 mg), 39.3 mg were further purified by size exclusion chromatography on Sephadex LH-20 with MeOH to give 25.8 mg (46 % from 24) of 30 as a colorless powder; $[\alpha]^{20}_D$ -0.4 (*c* 1.7, CH_3OH); R_f 0.13 in $CHCl_3$-MeOH 2:1; ^1H NMR (400 MHz, $CDCl_3$) δ 1.72 (dd, 1 H, 3"-H_{ax}), 1.79, 1.90 (2 s, 3 H each, 2 CH_3CO), 2.75 (br. dd, 1 H, 3"-H_{eq}), 3.40j (m, 2 H, 6'-H_2), ~3.54 (m, 1 H, 2'-H), 3.62 (s, 3 H, $CH_3OC_6H_4$), ~3.63 (m, 1 H, 3-H), ~3.95 (dd, 1 H, 2-H), 3.50 (m, 13 H, ring protons), 4.17, 4.31 (d, 1 H each, $C_6H_5CH_2$), 4.38 (d, 1 H, 1'-H), 4.44 (d, 1 H, $C_6H_5CH_2$), 4.51 (d, 2 H, $C_6H_5CH_2$), 4.84 (d, 1 H, 1-H), 4.95 (d, 1 H, $C_6H_5CH_2$); $J_{1,2}$ 8.3; $J_{1',2'}$ 7.8; $J_{3"eq,ax}$ 12.2; $J_{3"eq,4"}$ 3.9; $J_{3"ax,4"}$ 12.2; J_{CH_2} 11.2, 11.7, 12.2 Hz; ^{13}C NMR (100.40 MHz, $CDCl_3$) δ 22.7, 23.0 ($\underline{C}H_3CO$), 30.7 (C-3"), 54.2 (C-5"), 56.0 ($\underline{C}H_3OC_6H_4$), 69.1, 69.6, 69.8, 70.7, 71.2, 72.9, 74.2, 74.4, 74.8, 75.0, 75.2, 76.4, 77.9, 78.2, 82.1 (ring C, $C_6H_5\underline{C}H_2$), 101.8 (C-2", C-1), 104.6 (C-1'), 115.5, 119.3 ($CH_3O\underline{C}_6H_4$), 128.3 - 129.4, 139.6, 19.8, 140.6 ($\underline{C}_6H_5CH_2$), 153.0, 156.7 ($CH_3O\underline{C}_6H_4$), 173.4, 175.6 ($CH_3\underline{C}O$); ESI-MS (positive) *m/z* 1073.3 $[M+Na]^+$.

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