Systematic Studies Toward the Synthesis of d-Galactosamine-containing Coumarin Glycosides

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Supporting Information 1

Experimental

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General Experimental

Unless otherwise stated, all reagents used in the following experiments were bought commercially from Acros Organics, Alfa Aesar, Apollo Scientific, Biosynth, Fisher Scientific,

Fluorochem, Glycouniverse, Sigma Aldrich or TCI chemicals and were used without further purification. Reactions were performed under an atmosphere of N_2 either with a Schlenk line or an N_2 filled balloon. Dry solvents were dried and stored under N_2 in Young's flasks over 4 Å molecular sieves. Anhydrous pyridine and THF were purchased from Acros Organics, fitted with AcroSeal™ packaging. For reactions that required heating, DrySyn heating blocks were used as the heat source. Reactions were monitored by thin layer chromatography (TLC) using pre-coated 0.25 mm 60 F_{254} silica gel plates (Merck) and eluent systems outlined in the respective experiments. Visualisation was achieved using UV light (λ = 254 nm), and 10% H_2SO_4 in EtOH or ninhydrin staining followed by heating. Flash column chromatography was performed using silica gel [high purity grade, 60 Å pore size, 40-63 μm particle size]. HRMS were recorded on a ThermoScientific LTQ Orbitrap XL at the ESPRC National Mass Spectrometry Facility at Swansea University. Optical rotations were recorded on a Bellingham + Stanley ADP430 (specific rotation, tube length: 50 mm, concentrations in g per 100 mL). NMR spectra were recorded at 400 MHz on a Bruker AVIII400 spectrometer using deuterated solvent. Chemical shifts are reported in parts per million (ppm), coupling constants (*J*) are reported in Hertz (Hz) and multiplicities are abbreviated as; s (singlet), d (doublet), t (triplet) or m (multiplet) or combinations thereof. Chemical shifts were referenced to tetramethylsilane (TMS, where δ = 0.00 ppm). Assignment of proton and carbon signals follow the numbering system illustrated below:

General Procedure A – Glycosyl imidate synthesis

The starting hemiacetal (1.0 equiv.) was dissolved in DCM (0.1 M) and cooled to 0 °C. To the solution, either Cl_3CCN (3.0 – 20 equiv.) or $ClC(=NPh)CF_3$ (2.0 – 3.0 equiv.) and DBU (0.2 – 1.0 equiv.) were added and the reaction was stirred for 2 – 4 h. The reaction was concentrated

in vacuo (water bath temp. = 30 °C) then purified *via* manual flash column chromatography (neutralised with eluent + 1% Et_3N) to afford either the desired trichloroacetimidate or *N*-phenyltrifluoroacetimidate product. The products were either used directly or stored under N_2 at –20 °C overnight due to the known instability of imidates.

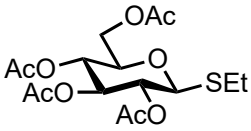
General Procedure B – Glycosylation with coumarins

A solution of glycosyl imidate (1.0 equiv.) and coumarin (1.2 equiv.) were suspended in a solution of DCM/MeCN (10/1, 0.05 M) in a dark environment (using aluminium foil) then pre-dried over 4 Å M.S. for 1 h. The reaction was cooled to –25 °C (using IMS and dry ice) and stirred for 10 min before $BF_3 \cdot Et_2O$ (1.0 equiv.) was added. The reaction was then gradually allowed to warm to 0 °C and after 2 h, TLC analysis (10% Et_2O in DCM) showed full consumption of the glycosyl imidate and the reaction was neutralised with Et_3N prior to filtration. The 4 Å M.S. were washed with DCM (2 ×) and solvents were removed *in vacuo*. The crude material was purified *via* manual flash column chromatography to afford separated anomers of the desired product.

Synthesis of D-Glucopyranosyl compounds

Scheme S1. (i) HBr (33% *v/v* in AcOH), 0 °C to RT, 1 h, 98%; (ii) Ag_2CO_3, Acetone, RT, 2 h, 97%; (iii) Cl_3CCN or $ClC(=NPh)CF_3$, DBU, DCM, 0 °C to RT, 2 h, 94% (**12**), 95%% (**13**); (iv) $P(O)OBu_2OH$, TfOH, DCM, 0 °C, 1 h, 74%, 1/1 α/β; (v) EtSH, $BF_3.Et_2O$, DCM, 0 °C to RT, 87%.

Ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside 9



At 0 °C, ethanethiol (12.3 mL, 167 mmol, 1.3 equiv.) and $BF_3 \cdot Et_2O$ (32 mL, 256 mmol, 2.0 equiv.) were added successively to a solution of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (50.0 g, 128 mmol, 1.0 equiv.) in DCM (250 mL). The reaction mixture was then stirred at RT for a further 3 h before pouring onto sat. aq. $NaHCO_3$ (200 mL) and stirred for 30 min, until effervescence stopped. I_2 (5.60 g, 44.8 mmol, 0.35 equiv.) was added and the solution was stirred for a further 20 min. Subsequently, sat. aq. $Na_2S_2O_3$ (150 mL) was added and following 15 min. of stirring, the organic phase was extracted with DCM (2 × 200 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford the crude product. Recrystallisation with 3/1 hexane/EtOH (200 mL) afforded **9** as colourless crystals (43.4 g, 111 mmol, 87%). Alternatively, the crude syrup can be washed with 10/1 petroleum ether/Et_2O (200 mL) then filtered to afford **9** as a white solid. $\mathbf{R_f}$ 0.38 (2/1 hexane/EtOAc). **m.p.** 82 – 83 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.23 (t, *J* = 9.4 Hz, 1H, H3), 5.09 – 5.03 (m, 2H, H2, H4), 4.50 (d, *J* = 10.0 Hz, 1H, H1), 4.25 (dd, *J* = 12.4, 4.9 Hz, 1H, H6a), 4.14 (dd, *J* = 12.4, 2.4 Hz, 1H, H6b), 3.71 (ddd, *J* = 10.0, 5.0, 2.4 Hz, 1H, H5), 2.79 – 2.64 (m, 2H, SCH_2CH_3), 2.08 (s, 3H, $C(O)CH_3$), 2.06 (s, 3H, $C(O)CH_3$), 2.03 (s, 3H, $C(O)CH_3$), 2.01 (s, 3H, $C(O)CH_3$), 1.28 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.7 (C=O), 170.2 (C=O), 169.4 (C=O), 169.4 (C=O), 83.5 (C1), 75.9 (C5), 73.9 (C3), 69.9 (C2), 68.4 (C4), 62.2 (C6), 24.2

(SCH_2CH_3), 20.7 ($C(O)CH_3$), 20.6 ($C(O)CH_3$), 20.6 ($C(O)CH_3$), 20.5 ($C(O)CH_3$), 14.8 (SCH_2CH_3). **HRMS** m/z (ESI^+) Found $(M+NH_4)^+$ 410.1478, $C_{16}H_{28}NO_9S$ requires 410.1479. These data are in good agreement with literature values.[1]

Di-*n*-butyl (2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl) phosphate 10

Glycosyl imidate **12** (340 mg, 0.690 mmol, 1.0 equiv.) was dissolved in DCM (17 mL) and cooled to 0 °C. Dibutylphosphate (0.27 mL, 1.38 mmol, 2.0 equiv.) and TMSOTf (25 μL, 0.138 mmol, 0.2 equiv.) were added and the reaction was stirred for 1 h then neutralised with Et_3N (0.1 mL). Solvents were removed *in vacuo* then the crude residue was purified *via* manual flash column chromatography (1/1 hexane/EtOAc) to afford phosphate **10** as a colourless oil (264 mg, 0.980 mmol, 71% yield). $\mathbf{R_f}$ 0.25 (1/1 hexane/EtOAc). $[\alpha]_D^{22} =$ + 10.3 (*c* 0.1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.32 – 5.28 (m, 1H, H1), 5.25 – 5.19 (m, 1H, H3), 5.15 – 5.07 (m, 2H, H2, H4), 4.26 (dd, *J* = 12.4, 4.7 Hz, 1H, H6a), 4.16 (dd, *J* = 12.4, 2.3 Hz, 1H, H6b), 4.10 – 4.04 (m, 2H, $OCH_2CH_2CH_2CH_3$), 4.01 (dd, *J* = 8.5, 6.7 Hz, 2H, $OCH_2CH_2CH_2CH_3$), 3.82 (ddd, *J* = 10.0, 4.7, 2.3 Hz, 1H, H5), 2.08 (s, 3H, $C(O)CH_3$), 2.06 (s, 3H, $C(O)\ CH_3$), 2.04 (s, 3H, $C(O)CH_3$), 2.01 (s, 3H, $C(O)CH_3$), 1.70 – 1.60 (m, 4H, 2 × $OCH_2CH_2CH_2CH_3$), 1.39 (dqd, *J* = 14.7, 7.4, 5.6 Hz, 4H, 2 × $OCH_2CH_2CH_2CH_3$), 0.93 (t, *J* = 7.4 Hz, 6H, 2 × $OCH_2CH_2CH_2CH_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.5 (C=O), 170.0 (C=O), 169.4 (C=O), 169.2 (C=O), 96.1 (d, $^2J_{C1\text{-}P}$ = 4.7 Hz, C1) 72.5 (C3), 71.2 (C2), 68.2 (d, $^2J_{CP}$ = 5.8 Hz, $OCH_2CH_2CH_2CH_3$), 68.1 (d, $^2J_{CP}$ = 5.1 Hz, $OCH_2CH_2CH_2CH_3$), 67.9 (C4), 61.6 (C6), 32.1 (d, $^3J_{CP}$ = 5.1 Hz, $OCH_2CH_2CH_2CH_3$) 32.0 (d, $^3J_{CP}$ = 5.3 Hz, $OCH_2CH_2CH_2CH_3$), 20.7 ($C(O)CH_3$), 20.7 ($C(O)CH_3$), 20.6 ($C(O)CH_3$), 20.6 ($C(O)CH_3$), 18.6 ($OCH_2CH_2CH_2CH_3$), 13.5 ($OCH_2CH_2CH_2CH_3$), 13.5 ($OCH_2CH_2CH_2CH_3$). **^{31}P NMR** (162 MHz, $CDCl_3$) δ – 2.96 (h, *J* = 7.0 Hz). These data are in good agreement with literature values.[2]

2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide 11

A solution of compound **8** (2.00 g, 5.12 mmol, 1.0 equiv.) in DCM (17 mL) was cooled to 0 °C and HBr (17 mL, 33% in AcOH) was added dropwise. The reaction was stirred for 1 h in the dark then quenched with ice cold H_2O (40 mL). The phases were separated then the organic phase was washed successively with sat. aq. $NaHCO_3$ (3 × 50 mL) and brine (50 mL). The organic phase was dried over $MgSO_4$, filtered

and concentrated *in vacuo* to afford bromide **11** (2.10 g, 5.10 mmol, 99% yield) as a white foam that was used without further purification. $\mathbf{R_f}$ 0.63 (2/1 hexane/EtOAc). **^{1}H NMR** (400 MHz, $CDCl_3$) 6.57 (d, *J* = 4.0 Hz, 1H, H1), 5.54 (t, *J* = 9.7 Hz, 1H, H3), 5.14 (t, *J* = 9.8 Hz, 1H, H4), 4.81 (dd, *J* = 10.0, 4.0 Hz, 1H, H2), 4.33 – 4.21 (m, 2H, H5, H6a), 4.13 – 4.06 (m, 1H, H6b), 2.07 (s, 3H, C(O)CH_3), 2.07 (s, 3H, C(O)CH_3), 2.02 (s, 3H, C(O)CH_3), 2.01 (s, 3H, C(O)CH_3). **^{13}C NMR** (101 MHz, CDCl3) 170.3 (C=O), 169.9 (C=O), 169.7 (C=O), 169.5 (C=O), 87.0 (C1), 72.2 (C5), 70.2 (C3), 70.1 (C2), 67.6 (C4), 61.2 (C6), 20.8 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3). These data are in good agreement with literature values.[3]

2,3,4,6-Tetra-*O*-acetyl-α/β-D-glucose S1

Glycosyl bromide **11** (2.10 g, 5.10 mmol, 1.0 equiv.) was dissolved in acetone (10 mL) and H_2O (0.3 mL) then cooled to 0 °C, to which Ag_2CO_3 (1.4 g, 5.10 mmol, 1.0 equiv.) was added and the reaction was stirred for 30 min. Following filtration over celite®, solvents were removed *in vacuo* then the crude residue was purified *via* manual flash column chromatography (1/1 hexane/EtOAc) to afford hemiacetal **S1** as a white foam (1.74 g, 4.99 mmol, 98% yield, 1/1 α/β mix). $\mathbf{R_f}$ 0.31 (1/1 hexane/EtOAc). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.54 (dd, *J* = 10.2, 9.4 Hz, 1H, H3-α), 5.47 (t, *J* = 3.7 Hz, 1H, H1-α), 5.26 (t, *J* = 9.6 Hz, 1H, H3-β), 5.09 (ddd, *J* = 10.1, 9.4, 1.8 Hz, 2H, H4-α, H4-β)), 4.93 – 4.86 (m, 2H, H2-α, H2-β), 4.75 (dd, *J* = 8.7, 8.1 Hz, 1H, H1-β), 4.30 – 4.21 (m, 3H, H5-α, H6a-α, H6a-β), 4.14 (ddt, *J* = 11.8, 7.1, 2.4 Hz, 2H, H6b-α, H6b-β), 3.79 (d, *J* = 8.8 Hz, 1H, H1-OH (β)), 3.77 – 3.74 (m, 1H, H5-β), 3.44 (dd, *J* = 3.9, 1.3 Hz, 1H, H1-OH (α)), 2.10 (dd, *J* = 3.4, 1.4 Hz, 12H, 4 × C(O)CH_3), 2.04 (s, 3H, C(O)CH_3), 2.04 (s, 3H, C(O)CH_3), 2.02 (s, 6H, 2 × C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.9 (C=O), 170.9 (C=O), 170.8 (C=O), 170.2 (C=O), 170.2 (C=O), 169.7 (C=O), 169.6 (C=O), 95.6 (C1-β), 90.2 (C1-α) 73.3 (C2-α), 72.2 (C2-β), 72.1 (C5-β), 71.1 (C3-β), 69.9 (C3-α), 68.5 (C4-β), 68.4 (C4-α), 67.3 (C5-α), 61.9 (C6-α), 61.8 (C6-β), 20.8 (C(O)*C*H_3), 20.8 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 20.6 (C(O)*C*H_3). **HRMS** m/z (ESI$^+$) Found $(M+Na)^+$ 371.0952, $C_{14}H_{20}O_{10}Na$ requires $(M+Na)^+$ 371.0949. These data are in good agreement with literature values.[4]

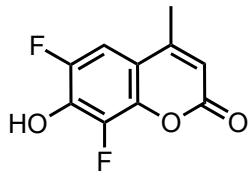
2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate 12

Glycosyl imidate **12** was prepared according to general procedure E. Hemiacetal **S1** (500 mg, 2.87 mmol, 1.0 equiv.), Cl_3CCN (0.9 mL, 8.61 mmol, 3.0 equiv.) and DBU (86 µL, 0.574 mmol, 0.2 equiv.) gave the desired product **13** as a colourless oil (680 mg, 2.76 mmol, 96% yield). During purification, the product was eluted with 1/1 hexane/EtOAc + 1% Et_3N. $\mathbf{R_f}$ 0.64 (1/1 hexane/EtOAc). $[\alpha]_D^{22}$ = + 86.2 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.70 (s, 1H, N*H*) 6.56 (d, *J* = 3.7 Hz, 1H, H1), 5.62 – 5.52 (m, 1H, H3), 5.19 (dd, *J* = 10.3, 9.5 Hz, 1H, H4), 5.14 (dd, *J* = 10.2, 3.7 Hz, 1H, H2), 4.28 (dd, *J* = 12.3, 4.1 Hz, 1H, H6a), 4.24 – 4.19 (m, 1H, H5), 4.16 – 4.09 (m, 1H, H6b), 2.08 (s, 3H, C(O)CH_3), 2.05 (s, 3H, C(O)CH_3), 2.04 (s, 3H, C(O)CH_3), 2.02 (s, 3H, C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6 (C=O), 170.0 (C=O), 169.9 (C=O), 169.5 (C=O), 160.8 (C=N), 92.9 (C1), 90.7 (CCl_3), 70.0 (C5), 69.9 (C3), 69.8 (C2), 67.8 (C4), 61.4 (C6), 21.1 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 20.4 (C(O)*C*H_3). These data are in good agreement with literature values.[5]

***N*-Phenyl-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl) trifluoroacetimidate 13**

Glycosyl imidate **13** was prepared according to general procedure E. Hemiacetal **S1** (200 mg, 0.574 mmol, 1.0 equiv.), PTFACl (0.3 mL, 1.72 mmol, 3.0 equiv.) and DBU (86 µL, 0.574 mmol, 1.0 equiv.) gave the desired product **13** as a white foam (270 mg, 0.545 mmol, 95% yield). During purification, the product was eluted with 5% Et_2O in DCM + 1% Et_3N. $\mathbf{R_f}$ 0.75 (1/1 hexane/EtOAc). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (dtd, *J* = 7.4, 6.4, 1.9 Hz, 2H, Ar-H), 7.17 – 7.10 (m, 1H, Ar-H), 6.82 (dd, *J* = 19.5, 7.9 Hz, 2H, Ar-H), 5.78 (br s, 1H, H1), 5.54 (t, *J* = 9.8 Hz, 1H, H3), 5.27 – 5.23 (br s, 1H, H2), 5.21 – 5.10 (m, 1H, H4), 4.28 (dt, *J* = 12.6, 4.5 Hz, 1H, H6a), 4.18 – 4.10 (m, 2H, H5, H6b), 2.10 (s, 3H, C(O)CH_3), 2.08 (s, 3H, C(O)CH_3), 2.06 (s, 3H, C(O)CH_3), 2.03 (s, 3H, C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.5 (C=O), 170.0 (C=O), 169.7 (C=O), 169.3 (C=O), 142.9 (C=N), 128.9 (Ar-C), 128.9 (Ar-CH), 124.7 (Ar-CH), 119.2 (Ar-CH), 94.5 (C1), 72.5 (C2), 70.2 (C5), 69.8 (C3), 67.7 (C4), 61.4 (C6), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 20.5 (C(O)*C*H_3). These data are in good agreement with literature values.[6]

6,8-Difluoro-7-hydroxy-4-methylcoumarin (DiFMU)



Methanesulfonic acid (15.6 mL, 240 mmol, 25 equiv.) was added dropwise to a solution of 2,4-difluorobenzene-1,3-diol (1.40 g, 9.58 mmol, 1.0 equiv.) and ethyl acetoacetate (1.2 mL, 9.58 mmol, 1.0 equiv.) at 0 °C. The reaction mixture was gradually warmed to RT and stirred for 24 h. TLC analysis (1/1 hexane/EtOAc) showed near conversion of the starting material. The reaction was cooled down to 0 °C and H_2O (20 mL) was added. The resultant precipitate was filtered, washed with cold H_2O (3 × 20 mL) and dissolved with 1 M NaOH (60 mL). The product was re-precipitated by the slow addition of H_2SO_4 until pH 1. This was then filtered and washed again with cold H_2O (3 × 20 mL) before being dissolved in acetone. The solvent was removed *in vacuo* then dried under high vacuum for 6 h to afford **DiFMu** as a yellow solid (1.79 g, 8.43 mmol, 88%). $\mathbf{R_f}$ 0.39 (1/1 hexane/EtOAc). **^{1}H NMR** (400 MHz, MeOD) δ 7.22 (dd, *J* = 11.1, 2.2 Hz, 1H, *H*C=CF), 6.17 (d, *J* = 1.6 Hz, 1H, *H*C=C(CH_3)), 2.37 (d, *J* = 1.2 Hz, 3H, CH_3). **^{13}C NMR** (101 MHz, MeOD) δ 161.7 (C=O)), 154.9 (t, *J* = 2.8 Hz, *C*CH_3), 150.2 (dd, *J* = 240.7, 4.9 Hz, C-F), 140.9 (dd, *J* = 245.4, 6.5 Hz, C-F), 140.8 (dd, *J* = 9.6, 2.3 Hz, *C*(OC(O)R), 139.4 (dd, *J* = 17.9, 12.9 Hz, C-OH), 113.4 (Ar-CH), 112.5 (d, *J* = 8.8 Hz, *C*(CCH_3), 106.7 (dd, *J* = 21.6, 3.3 Hz, C=*C*H), 18.7 (CH_3). **^{19}F NMR** (377 MHz, MeOD) δ −138.37 (t, *J* = 10.3 Hz), −156.26 (dd, *J* = 9.5, 2.3 Hz). **HRMS** (ESI^+) Found $(M+H)^+$ 213.0356, $C_{10}H_7O_3F_2$ requires 213.0285. These data are in good agreement with literature values.[7]

6'-Difluoro-4'-methylumbelliferyl 2,3,4,6-tetra-*O*-acetyl-D-glucopyranoside 14

Compound **14** was prepared according to general procedure B. Trichloroacetimidate **12** (220 mg, 0.379 mmol, 1.0 equiv.), DiFMu (96 mg, 0.455 mmol, 1.2 equiv.) and $BF_3{\cdot}Et_2O$ (7 μL, 0.057 mmol. 0.2 equiv.) afforded compound **15.** Purification using a 10/1 → 5/1 → 3/1 → 1.5 (α-anomer) → 1/1 (β-anomer) hexane/EtOAc gradient isolated **14** (142 mg, 0.262 mmol, 69%) as a pale-yellow oil. $\mathbf{R_f}$ 0.44 (1/1 hexane/EtOAc). $[\alpha]_D^{22}$ = – 8.60 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 10.3, 2.3 Hz, 1H, *H*C=CF), 6.34 (d, *J* = 1.4 Hz, 1H, C*H*C(O), 5.38 – 5.26 (m, 1H, H3), 5.26 – 5.17 (m, 2H, H2, H4), 5.18 (d, *J* = 7.2 Hz, 1H, H1), 4.27 (dd, *J* = 12.4, 4.7 Hz, 1H, H6a), 4.16 – 4.08 (m, 1H, H6b), 3.77 (ddd, *J* = 9.8, 4.7, 2.5 Hz, 1H, H5), 2.40 (d, *J* = 1.3 Hz, 3H, HC=CC*H*$_3$), 2.11 (s, 3H, C(O)CH_3), 2.07 (s, 3H, C(O)CH_3), 2.05 (s, 3H, C(O)CH_3), 2.04 (s,

3H, C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6 (C=O), 170.2 (C=O), 169.3 (C=O), 169.3 (C=O), 158.7 (C=O), 151.4 (d, *J* = 245.0 Hz, C-F), 151.1 (d, *J* = 2.6 Hz, *C*CH_3), 143.29 (d, *J* = 255.8 Hz, C-F), 139.54 (d, *J* = 13.3 Hz, *C*(OC(O)R), 116.8 (d, *J* = 8.6 Hz, *C*H=CCH_3), 115.9 (Ar-CH), 105.8 (dd, *J* = 22.0, 3.9 Hz, C=*C*H), 101.8 (C1), 72.5 (C5), 72.5 (C3), 71.4 (C2), 68.1 (C4), 61.5 (C6), 20.6 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 18.8 (HC=C*C*H_3). **^{19}F NMR** (376 MHz, $CDCl_3$) δ −130.70 (dd, *J* = 10.3, 3.5 Hz), −144.60 (t, *J* = 3.0 Hz). **HRMS** m/z (ESI^+) Found $(M+Na)^+$ 565.1136, $C_{24}H_{24}O_{12}F_2Na$ requires $(M+Na)^+$ 565.1134.

Synthesis of D-Galactopyranosyl compounds

Scheme S2. (i) CSA, MeOH, 50 °C, 2 h; (ii) Ac_2O, pyridine, DMAP, 0 °C to RT, 1 h, 82% over two steps; (iii) $PdCl_2$, DCM/MeOH (1/1), 5 h, 59%; (iv) Ac_2O, pyridine, DMAP, 0 °C to RT, 18 h, 80% (**S5**); (v) TrocCl, DIPEA, DCM, 0 °C, 2 h, 86% (**S6**); (vi) $MeNH_2$ (33% v/v), THF, RT, 1 h, 64% (**S8**), 87% (**S9**); (vii) Cl_3CCN or $ClC(=NPh)CF_3$, DBU, DCM, 0 °C, 75% (**15)**, 80% (**16**), 63% (**17**), 78% (**18**); (ix) DiFMu or 4-MU, $BF_3{\cdot}Et_2O$, DCM/MeCN (10/1), –20 °C to 0 °C, 2 h, 69% (**19**, 1/5 α/β).

Allyl 3,4,6-tri-*O*-acetyl-2-deoxy-*N*-phthalimido-β-D-galactopyranose S3

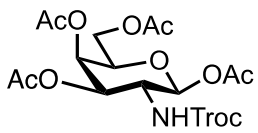
10-Camphorsulfonic acid (53 mg, 0.229 mmol, 0.25 equiv.) was added to a solution of allyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-β-D-galactopyranoside **S2** (400 mg, 0.915 mmol, 1.0 equiv.) in MeOH (9 mL). The reaction was stirred at 40 °C for 3 h until completion, as monitored by TLC analysis (R_f 0.05 (1/1 hexane/EtOAc), then diluted in EtOAc (20 mL) and washed with sat. aq. $NaHCO_3$ (25 mL). The aqueous phase was re-extracted with EtOAc (20 mL) before the combined organic extracts were washed with brine (40 mL) then dried over $MgSO_4$ and filtered. Solvents were removed *in vacuo* and subsequently, the resultant crude residue was dissolved in DCM (9 mL). The solution was cooled to 0 °C then pyridine (0.4 mL, 5.49 mmol, 12 equiv.), DMAP (12 mg, 0.915 mmol, 0.2 equiv.) and Ac_2O (0.17 mL, 1.83 mmol, 4.0 equiv.) were added. The reaction was stirred at RT for 2 h then diluted with DCM (10 mL) and washed successively with 1 M HCl (20 mL), sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL). The organic extract was dried over $MgSO_4$, filtered and concentrated *in vacuo* to obtain a crude syrup which was purified *via* manual flash column chromatography (10/1 → 2/1 hexane/EtOAc) to afford **S3** as a white foam (356 mg, 0.750 mmol, 82% over two steps). **R_f** 0.60 (1/1 hexane/EtOAc). $[\alpha]_D^{22}$ = – 12.2 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (q, *J* = 3.4 Hz, 2H, Ar-H), 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H, Ar-H), 5.79 (dd, *J* = 11.4, 3.4 Hz, 1H, H3), 5.69 (dddd, *J* = 17.0, 10.4, 6.3, 5.1 Hz, 1H, OCH_2CHCH_2), 5.47 (dd, *J* = 3.5, 1.2 Hz, 1H, H4), 5.33 (d, *J* = 8.5 Hz, 1H, H1), 5.15 – 5.01 (m, 2H, OCH_2CHCH_2), 4.56 (dd, *J* = 11.5, 8.5 Hz, 1H, H2), 4.28 (ddt, *J* = 13.0, 5.1, 1.5 Hz, 1H, OCH_2CHCH_2), 4.23 (dd, *J* = 11.2, 6.7 Hz, 1H, H6a), 4.17 (dd, *J* = 11.2, 6.6 Hz, 1H, H6b), 4.09 – 4.01 (m, 2H, H5, OCH_2CHCH_2), 2.18 (s, 3H, $C(O)CH_3$), 2.06 (s, 3H, $C(O)CH_3$), 1.84 (s, 3H, $C(O)CH_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.4 (C=O), 170.3 (C=O), 169.8 (C=O), 134.3 (Ar-CH), 133.3 (OCH_2CHCH_2), 131.5 (Ar-C), 128.2 (Ar-C), 126.4 (Ar-C), 123.7 (Ar-CH), 123.6 (Ar-C), 117.9 (OCH_2CHCH_2), 97.5 (C1), 70.8 (C5), 70.2 (OCH_2CHCH_2), 68.1 (C3), 66.8 (C4), 61.5 (C6), 51.4 (C2), 20.7 ($C(O)CH_3$), 20.7 ($C(O)CH_3$), 20.5 ($C(O)CH_3$). **HRMS** m/z (ESI^+) Found $(M+Na)^+$ 498.1372, $C_{23}H_{25}NO_{10}Na$ requires 498.1376. These data are in good agreement with the literature.[8]

***N*-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-galactopyranose S5**

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-amino-β-D-galactopyranose hydrochloride **S4** (300 mg, 0.782 mmol, 1.0 equiv.) was dissolved in DCM (4 mL) and cooled to 0 °C. To this solution, Et_3N (0.3 mL, 2.35

mmol, 3.0 equiv.) and Ac_2O (1 mL) were added successively then the reaction was gradually warmed to RT and stirred for 16 h. The reaction was diluted with DCM (20 mL) then washed with 1 M HCl (20 mL), sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford compound **S5** as a white solid (296 mg, 0.756 mmol, 97% yield). $\mathbf{R_f}$ 0.63 (7/1/1 EtOAc/MeOH/H_2O). $[\alpha]_D^{22}$ = + 3.80 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.69 (d, *J* = 8.8 Hz, H1), 5.38 (m, 2H, H4, N*H*), 5.07 (dd, *J* = 11.3, 3.2 Hz, 1H, H3), 4.45 (dt, *J* = 9.2, 11.1 Hz, 1H, H2), 4.20-4.08 (m, 2H, H6a, H6b), 4.03-4.00 (m, 1H, H5), 2.16 (s, 3H, C(O)CH_3), 2.12 (s, 3H, C(O)CH_3), 2.04 (s, 3H, C(O)CH_3), 2.03 (s, 3H, C(O)CH_3), 1.93 (s, 3H, C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1 (C=O), 170.3 (C=O), 170.0 (C=O), 169.9 (C=O), 169.5 (C=O), 93.0 (C1), 71.7 (C5), 70.5 (C3), 66.4 (C4), 61.2 (C6), 50.1 (C2), 23.4 (C(O)*C*H_3), 20.9 (C(O)*C*H_3), 20.8 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.7 (C(O)*C*H_3). **HRMS** m/z (ESI^+) Found $(M+Na)^+$ 412.1225, $C_{16}H_{23}NO_{10}Na$ requires 412.1220. These data are in good agreement with literature values.[9]

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-*N*-(2,2,2-trichloroethoxycarbonylamino)-β-D-galactopyranose S6

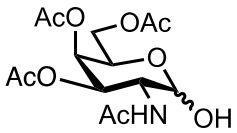


To a solution of **S4** (18 g, 46.9 mmol, 1.0 equiv.) in DCM (190 mL) at 0 °C, DIPEA (20.4 mL, 117 mmol, 2.5 equiv.) and TrocCl (13 mL, 93.8 mmol, 2.0 equiv.) were added. The reaction mixture was stirred at RT for 2 h before sat. aq. NH_4Cl (200 mL) was added, and the resultant aqueous phase was washed with DCM (100 mL). The combined organic phases were washed with brine (250 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude material was purified *via* manual flash silica plug (10/1 → 2/1 hexane/EtOAc) to afford **S6** as a white foam (20.5 g, 39.4 mmol, 86%). $\mathbf{R_f}$ 0.72 (1/1 hexane/EtOAc)**.** $[\alpha]_D^{22}$ = +13.3 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.77 (d, *J* = 8.8 Hz, 1H, H1), 5.44 (d, *J* = 9.6 Hz, 1H, N*H*), 5.41 (dd, *J* = 3.4, 1.1 Hz, 1H, H4), 5.16 (dd, *J* = 11.3, 3.3 Hz, 1H, H3), 4.77 – 4.69 (m, 2H, CH_2-Troc), 4.18 – 4.07 (m, 4H, H2, H5, H6a, H6b), 2.18 (s, 3H, C(O)*C*H_3), 2.13 (s, 3H, C(O)*C*H_3), 2.05 (s, 3H, C(O)*C*H_3), 2.01 (s, 3H, C(O)*C*H_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.3 (C=O), 170.5 (C=O), 170.2 (C=O), 169.4 (C=O), 154.4 (C=O, Troc), 95.5 (CCl_3), 92.6 (C1), 74.4 (CH_2-Troc), 71.7 (C3), 70.1 (C5), 66.4 (C4), 61.3 (C6), 51.7 (C2), 20.9 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3). **HRMS** m/z (ESI^+) Found $(M+NH_4)^+$ 539.0583, $C_{17}H_{26}Cl_3N_2O_{11}$ requires 539.0602.

3,4,6-Tri-*O*-acetyl-2-deoxy-*N*-phthalimido-α/β-D-galactopyranose S7

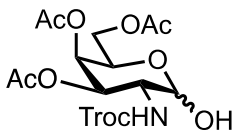
Compound **S6** (350 mg, 0.737 mmol, 1.0 equiv.) was dissolved in DCM/MeOH (1/1, 36 mL) and $PdCl_2$ (78 mg, 0.442 mmol, 0.6 equiv.) was added. The reaction was stirred for 5 h at RT then filtered over celite® and washed with DCM (30 mL). The crude residue was concentrated *in vacuo* then purified *via* manual flash column chromatography (100% DCM → 20% Et_2O in DCM) which afforded hemiacetal **S7** as a colourless oil (1/3 α/β mix, 190 mg, 0.435 mmol, 59%). $\mathbf{R_f}$ 0.40 (1/1 hexane/EtOAc). **^{1}H NMR β anomer** (400 MHz, $CDCl_3$) δ 7.86 (td, *J* = 4.8, 2.7 Hz, 2H, Ar-H), 7.75 (dd, *J* = 5.5, 3.1 Hz, 2H, Ar-H), 5.88 (dd, *J* = 11.5, 3.4 Hz, 1H, H3), 5.54 – 5.46 (m, 2H, H1, H4), 4.49 (dd, *J* = 11.5, 8.4 Hz, 1H, H2), 4.22 – 4.12 (m, 3H, H5, H6a, H6b), 3.54 (br s, 1H, C1-OH), 2.20 (s, 3H, $C(O)CH_3$), 2.07 (s, 3H, $C(O)CH_3$), 1.86 (s, 3H, $C(O)CH_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.5 (C=O), 170.3 (C=O), 169.8 (C=O), 168.1 (C=O), 134.6 (Ar-CH), 134.4 (Ar-C), 123.7 (Ar-CH), 123.7 (Ar-C), 93.2 (C1), 71.2 (C5), 67.8 (C3), 66.8 (C4), 61.7 (C6), 52.9 (C2), 20.7 ($C(O)CH_3$), 20.7 ($C(O)CH_3$), 20.5 ($C(O)CH_3$). **HRMS** m/z (ESI^+) Found $(M+Na)^+$ 458.1068, $C_{20}H_{21}NO_{10}Na$ requires 458.1063.

3,4,6-Tri-*O*-acetyl-2-deoxy-*N*-acetamido-α/β-D-galactopyranose S8

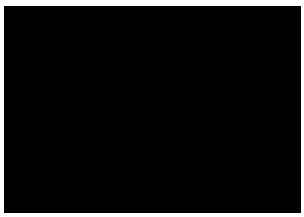


A solution of **S5** (300 mg, 0.666 mmol, 1.0 equiv.) in $MeNH_2$ (0.6 mL, 33% *v/v*) and THF (4.8 mL) was stirred at RT for 1 h. The reaction mixture was co-evaporated with MeCN (10 mL) and concentrated *in vacuo*. Hemiacetal **S8** was obtained as a white foam (1/6 α/β mix, 184 mg, 0.406 mmol, 64%) and used without further purification. $\mathbf{R_f}$ 0.53 (7/1/1 EtOAc/MeOH/H_2O). **^{1}H NMR β anomer** (400 MHz, $CDCl_3$) δ 5.96 (d, *J* = 9.5 Hz, 1H, NH), 5.37 (dd, *J* = 3.3, 1.3 Hz, 1H, H4), 5.29 (app. t, *J* = 2.8 Hz, 1H, H1), 5.24 (dd, *J* = 11.3, 3.2 Hz, 1H, H3), 4.92 – 4.87 (br s, 1H, C1-OH), 4.52 (ddd, *J* = 11.3, 9.6, 3.5 Hz, 1H, H2), 4.42 (td, *J* = 6.6, 1.3 Hz, 1H, H5), 4.18 – 4.00 (m, 2H, H6a, H6b), 2.15 (s, 3H, $C(O)CH_3$), 2.03 (s, 3H, $C(O)CH_3$), 1.98 (s, 3H, $C(O)CH_3$), 1.96 (s, 3H, $C(O)CH_3$). **^{13}C NMR β anomer** (101 MHz, $CDCl_3$) δ 171.0 (C=O), 170.7 (C=O), 170.5 (C=O), 170.5 (C=O), 92.1 (C1), 68.2 (C3), 67.6 (C4), 66.4 (C5), 62.1 (C6), 48.2 (C2), 23.3 ($C(O)CH_3$), 23.0 ($C(O)CH_3$), 20.8 ($C(O)CH_3$), 20.8 ($C(O)CH_3$), 20.7 ($C(O)CH_3$). These data are in good agreement with literature values.[10]

3,4,6-Tri-*O*-acetyl-2-deoxy-*N*-(2,2,2-trichloroethoxycarbonylamino)-α/β-D-galactopyranose S9



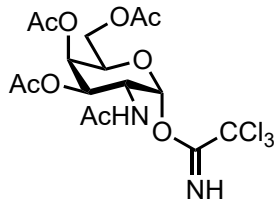
Acetate **S6** (310 mg, 0.595 mmol, 1.0 equiv.) was dissolved in THF (6 mL) and cooled to 0 °C before $MeNH_2$ (0.5 mL, 33% *v/v*) was added. The reaction was stirred for 30 min then diluted with EtOAc (20 mL) and washed successively with 1 M HCl (20 mL), sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Hemiacetal **S9** was obtained as a white foam (2/1 α/β mix, 269 mg, 0.517 mmol, 87%) and used without further purification. $\mathbf{R}_f$ 0.65 (1/1 hexane/EtOAc). **^{1}H NMR α anomer** (400 MHz, $CDCl_3$) δ 5.47 (d, *J* = 10.0 Hz, 1H, NH), 5.42 (dd, *J* = 3.3, 1.3 Hz, 1H, H4), 5.37 (d, *J* = 3.7 Hz, 1H, H1), 5.26 (dd, *J* = 11.2, 3.3 Hz, 1H, H3), 4.83 (d, *J* = 12.0 Hz, 1H, CH_2), 4.64 (d, *J* = 12.0 Hz, 1H, CH_2), 4.46 (td, *J* = 6.6, 1.4 Hz, 1H, H5), 4.28 (ddd, *J* = 11.2, 10.0, 3.5 Hz, 1H, H2), 4.15 – 4.05 (m, 2H, H6a, H6b), 2.03 (s, 3H, C(O)CH_3), 2.01 (s, 3H, C(O)CH_3), 1.95 (s, 3H, C(O)CH_3). **^{13}C NMR α anomer** (101 MHz, $CDCl_3$) δ 171.2 (C=O), 170.7 (C=O), 170.6 (C=O), 170.4 (C=O), 95.5 (CCl_3), 92.2 (C1), 74.5 (CH_2CCl_3), 68.5 (C3), 67.6 (C4), 66.4 (C5), 61.9 (C6), 50.2 (C2), 26.5 (C(O)*C*H_3), 23.0 (C(O)*C*H_3), 20.7 (C(O)*C*H_3). **HRMS** (ESI^+) Found $(M+Na)^+$ 502.0034, $C_{15}H_{20}Cl_3NO_{10}Na$ requires 502.0045.



3,4,6-Tri-*O*-acetyl-2-deoxy-*N*-acetamido-α-D-galactopyranosyl trichloroacetimidate 15

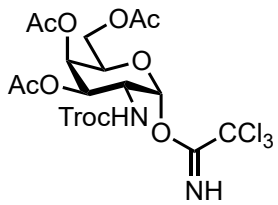
Glycosyl imidate **15** was prepared according to General Procedure **A**. Hemiacetal **S7** (100 mg, 0.230 mmol, 1.0 equiv.), Cl_3CCN (70 μL, 0.689 mmol, 3.0 equiv.) and DBU (10 μL, 0.069 mmol, 0.3 equiv.) gave the desired product **15** as a white foam (93 mg, 0.161 mmol, 70%). During purification, the product was eluted with 10% Et_2O in DCM + 1% Et_3N. $\mathbf{R_f}$ 0.70 (5/1 DCM/MeOH). $[\alpha]_D^{22}$ = + 30.2 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.63 (s, 1H, N*H*), 7.87 – 7.74 (m, 4H, Ar-CH), 6.48 (d, 1H, *J* = 3.8 Hz, H1), 5.91 (dd, 1H, *J* = 11.5 Hz, 3.4 Hz, H3), 5.55 (d, 1H, *J* = 3.5 Hz, H4), 4.79 (dd, 1H, *J* = 11.5, 8.9 Hz, H2), 4.28 – 4.20 (m, 3H, H5, H6a, H6b), 2.22 (s, 3H, C(O)CH_3), 2.05 (s, 3H, C(O)CH_3), 1.89 (s, 3H, C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.9 (C=O), 170.3 (C=O), 170.1 (C=O), 160.8 (C=N), 95.2 (C1), 90.8 (CCl_3), 68.9 (C5), 67.4 (C3), 65.5 (C4), 61.8 (C6), 49.6 (C2), 20.9 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3). These data were in good agreement with literature values.[11]

3,4,6-Tri-*O*-acetyl-2-deoxy-*N*-acetamido-α-D-galactopyranosyl trichloroacetimidate 16



Glycosyl imidate **16** was prepared according to General Procedure **A**. Hemiacetal **S8** (180 mg, 0.419 mmol, 1.0 equiv.), Cl_3CCN (0.1 mL, 1.26 mmol, 3.0 equiv.) and DBU (19 µL, 0.126 mmol, 0.3 equiv.) gave the desired product **16** as a white foam (159 mg, 0.281 mmol, 67%). During purification, the product was eluted with 5/1 DCM/MeOH + 1% Et_3N. $\mathbf{R_f}$ 0.70 (5/1 DCM/MeOH). $[\alpha]_D^{22}$ = +95.5 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.79 (s, 1H, NH), 6.41 (d, *J* = 3.6 Hz, 1H, H1), 5.57 (d, *J* = 9.2 Hz, 1H, NHAc), 5.49 (dd, *J* = 3.3, 1.3 Hz, 1H, H4), 5.31 – 5.25 (m, 1H, H3), 4.80 (ddd, *J* = 11.5, 9.2, 3.7 Hz, 1H, H2), 4.36 (ddd, *J* = 6.9, 6.1, 1.2 Hz, 1H, H5), 4.18 (dd, *J* = 11.3, 6.6 Hz, 1H, H6a), 4.07 (dd, *J* = 11.3, 6.6 Hz, 1H, H6b), 2.19 (s, 3H, C(O)CH_3), 2.04 (s, 3H, C(O)CH_3), 2.02 (s, 3H, C(O)CH_3), 1.95 (s, 3H, C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.0 (C=O), 170.3 (C=O), 170.2 (C=O), 170.1 (C=O), 160.4 (C=N), 95.5 (C1), 90.9 (CCl_3), 69.2 (C5), 67.9 (C3), 66.7 (C4), 61.4 (C6), 47.5 (C2), 23.2 (C(O)*C*H_3), 20.8 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3). These data are in good agreement with literature values.[12]

3,4,6-Tri-*O*-acetyl-2-deoxy-*N*-(2,2,2-trichloroethoxycarbonylamino)-α-D-galactopyranosyl trichloroacetimidate 17

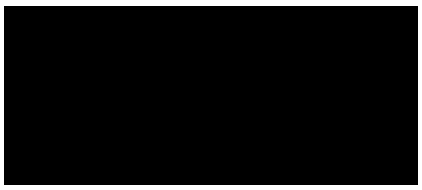


Glycosyl imidate **17** was prepared according to General Procedure **A**. Hemiacetal **S9** (280 mg, 0.622 mmol, 1.0 equiv.), Cl_3CCN (0.2 mL, 1.87 mmol, 3.0 equiv.) and DBU (28 µL, 0.187 mmol, 0.3 equiv.) gave the desired product **17** as an off-white foam (240 mg, 0.392 mmol, 63% yield). During purification, the product was eluted with 5% Et_2O in DCM + 1% Et_3N. $\mathbf{R_f}$ 0.67 (1/1 hexane/EtOAc). $[\alpha]_D^{22}$ = +90.2 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.80 (s, 1H, NH), 6.46 (d, *J* = 3.7 Hz, 1H, H1), 5.52 (dd, *J* = 3.2, 1.4 Hz, 1H, H4), 5.31 – 5.25 (m, 1H, H3), 5.14 (d, *J* = 9.6 Hz, 1H, NH), 4.80 – 4.68 (m, 2H, CH_2-Troc), 4.53 (ddd, *J* = 11.4, 9.6, 3.7 Hz, 1H, H2), 4.41 – 4.34 (m, 1H, H5), 4.18 (dd, *J* = 11.4, 6.7 Hz, 1H, H6a), 4.08 (dd, *J* = 11.3, 6.6 Hz, 1H, H6b), 2.19 (s, 3H, C(O)CH_3), 2.03 (s, 3H, C(O)CH_3), 2.02 (s, 3H, C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.7 (C=O), 170.3 (C=O), 170.1 (C=O), 160.5 (C=N), 154.3 (C=O), 95.3 (C1), 90.8 (CCl_3), 74.7 (CH_2-Troc), 69.2 (C5), 67.9 (C3), 66.7 (C4), 61.3 (C6), 49.6 (C2), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 20.6 (C(O)*C*H_3). These data are in good agreement with literature values.[13]

***N*-Phenyl (3,4,6-tri-*O*-acetyl-2-deoxy-*N*-(2,2,2-trichloroethoxycarbonylamino)-α-D-galactopyranosyl) trifluoroacetimidate 18**

Glycosyl imidate **18** was prepared according to General Procedure **A**. Hemiacetal **S9** (400 mg, 0.835 mmol, 1.0 equiv.), PTFACl (0.45 mL, 2.51 mmol, 3.0 equiv.) and DBU (0.1 mL, 0.835 mmol, 1.0 equiv.) gave the desired product **18** as an off-white foam (425 mg, 0.654 mmol, 78% yield). During purification, the product was eluted with 5% Et_2O in DCM + 1% Et_3N. $\mathbf{R_f}$ 0.71 (4/1 toluene/acetone). $[\alpha]_D^{22}$ = +30.5 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.9 Hz, 2H, Ar-H), 7.16 – 7.11 (m, 1H, Ar-H), 6.82 (d, *J* = 7.7 Hz, 1H, Ar-H), 6.38 (br s, 1 H, H1) 5.53 – 5.46 (m, 1H, H4), 5.35 – 5.23 (m, 1H, H3), 4.84 (d, *J* = 12.0 Hz, 1H, CH_2-Troc), 4.68 (d, *J* = 12.1 Hz, 1H, CH_2-Troc), 4.55 – 4.44 (m, 1H, H2), 4.28 (t, *J* = 6.4 Hz, 1H, H5), 4.13 (tt, *J* = 10.6, 5.3 Hz, 2H, H6a, H6b), 2.18 (s, 3H, C(O)CH_3), 2.06 (s, 3H, C(O)CH_3), 2.02 (2 × s, 6H, 2 × C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.7 (C=O), 170.3 (C=O), 170.1 (C=O), 154.4 (C=O), 142.9 (C=N), 129.4 (Ar-C), 129.2 (Ar-CH), 128.9 (Ar-CH), 127.4 (Ar-CH), 124.8 (CF_3), 120.6 (Ar-CH), 119.2 (Ar-CH), 95.3 (CCl_3), 74.7 (CH_2-Troc), 69.1 (C5), 67.7 (C3), 66.7 (C4), 61.4 (C6), 49.3 (C2), 20.7 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3). **^{19}F NMR** (377 MHz, $CDCl_3$) δ −71.6 (s).

6'-Difluoro-4'-methylumbelliferyl 3,4,6-tri-*O*-acetyl-2-deoxy-*N*-(2,2,2-trichloroethoxycarbonylamino)- α/β-D-galactopyranoside 19



Compound **19** was prepared according to General Procedure **B**. Trichloroacetimidate **18** (220 mg, 0.379 mmol, 1.0 equiv.), DiFMu (72 mg, 0.455 mmol, 1.0 equiv.) and $BF_3{\cdot}Et_2O$ (7 μL, 0.057 mmol. 0.2 equiv.) afforded crude compound **19** as a 1/4 α/β mixture. Purification using a 10/1 → 5/1 → 3/1 → 1.5 (α-anomer) → 1/1 (β-anomer) hexane/EtOAc gradient isolated **α-19** (60 mg, 0.089 mmol, 14% yield) as a pale-yellow oil and **β-19** (120 mg, 0.178 mmol, 57%) as a white solid. **α-anomer**: $\mathbf{R_f}$ 0.44 (1/1 hexane/EtOAc). $[\alpha]_D^{22}$ = + 65.8 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 10.5, 2.2 Hz, 1H, *H*C=CF), 6.36 (d, *J* = 1.5 Hz, 1H, C*H*C(O)), 5.60 – 5.54 (m, 2H, H1, H4), 5.53 (d, *J* = 9.9 Hz, 1H, N*H*), 5.44 (dd, *J* = 11.4, 3.1 Hz, 1H, H3), 4.85 (d, *J* = 12.0 Hz, 1H, CH_2-Troc), 4.73 (d, *J* = 12.0 Hz, 1H, CH_2-Troc), 4.71 – 4.66 (m, 1H, H5), 4.53 (ddd, *J* = 11.5, 9.9, 3.5 Hz, 1H, H2), 4.22 (dd, *J* = 11.4, 6.0 Hz, 1H, H6a), 4.02 (dd, *J* = 11.4, 6.8 Hz, 1H, H6b), 2.41 (d, *J* = 1.3 Hz, 3H, HC=C*C*H_3), 2.19 (s, 3H, C(O)CH_3), 2.04 (s, 6H, C(O)CH_3). **^{13}C NMR** (101

MHz, $CDCl_3$) δ 170.6 (C=O), 170.4 (C=O), 170.1 (C=O), 158.5 (C=O), 154.5 (C=O), 151.3 (d, *J* = 250.8 Hz, C-F), 150.9 (*C*CH_3), 141.7 (d, *J* = 256.4 Hz, C-F), 139.5 (*C*(OC(O)R), 117.4 (Ar-CH), 102.2 (C1, $^1J_{1CH}$ = 183.5 Hz from coupled HSQC), 95.3 (CCl_3), 74.8 (CH_2-Troc), 69.0 (C5), 67.5 (C3), 67.2 (C4), 61.6 (C6), 50.1 (C2), 21.1 (C(O)*C*H_3), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 18.8 (CH=C*C*H_3). **^{19}F NMR** (377 MHz, $CDCl_3$) δ −131.43 (dd, *J* = 10.4, 3.3 Hz), −144.64 (s). **HRMS** Found $(M+NH_4)^+$ 691.0680, $C_{25}H_{28}Cl_3F_2N_2O_{12}$ requires $(M+NH_4)^+$ 691.0670.

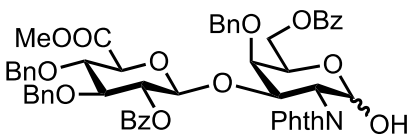
β-anomer: R_f 0.38 (1/1 hexane/EtOAc). $[\alpha]_D^{22}$ = – 6.86 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.14 (dd, *J* = 10.4, 2.2 Hz, 1H, *H*C=CF), 6.32 (d, *J* = 1.6 Hz, 1H, C*H*C(O)), 5.75 (d, *J* = 9.1 Hz, 1H, N*H*), 5.43 (dd, *J* = 3.4, 1.2 Hz, 1H, H4), 5.35 (dd, *J* = 11.5, 3.3 Hz, 1H, H3), 5.33 – 5.29 (d, *J* = 8.3 Hz, 1H, H1), 4.81 (d, *J* = 12.0 Hz, 1H, CH_2-Troc), 4.69 (d, *J* = 12.0 Hz, 1H, CH_2-Troc), 4.21 – 4.10 (m, 3H, H2, H6a, H6b), 4.03 – 3.97 (m, 1H, H5), 2.40 (d, *J* = 1.3 Hz, 3H, C(O)CH_3), 2.21 (s, 3H, C(O)CH_3), 2.03 (s, 3H, C(O)CH_3), 2.01 (s, 3H, C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.5 (C=O), 170.3 (C=O), 170.3 (C=O) 158.8 (C=O), 154.4 (C=O), 151.5 (d, *J* = 249.2 Hz, C-F), 151.3 (br s, *C*CH_3), 143.3 (d, *J* = 255.2 Hz, C-F), 139.4 (d, *J* = 10.3 Hz, *C*(OC(O)R), 116.6 (d, *J* = 8.8 Hz, *C*H=CCH_3) 115.7 (Ar-CH), 105.8 (dd, *J* = 22.0, 3.7 Hz, C=*C*H), 102.4 (C1, $^1J_{1CH}$ = 168.8 Hz from coupled HSQC), 95.5 (CCl_3), 74.5 (CH_2-Troc), 71.4 (C5), 69.4 (C3), 66.3 (C4), 60.9 (C6), 53.0 (C2), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 18.8 (HC=C*C*H_3). **^{19}F NMR** (376 MHz, $CDCl_3$) δ −130.15 (d, *J* = 7.8 Hz), −144.61 (s). **HRMS** m/z (ESI^+) Found $(M+NH_4)^+$ 691.0675, $C_{25}H_{28}Cl_3F_2N_2O_{12}$ - requires 691.0676.

Synthesis of D-GalN disaccharide compounds

Synthesis towards building blocks **S11** – **S13** was reported previously within our group in 17 – 19 steps.[15] With these in hand, allylic deprotection of **S11** – **S13** was achieved with $PdCl_2$ in DCM/MeOH in 78% - 88% yields to give hemiacetals **S14** – **S16**. These disaccharides were converted to their corresponding α-TCAI or α-PTFA imidates (Scheme 4.5) in the presence of DBU to afford **29** – **32** in 59% - 81% yields. *N.B.* An excess of reagents was often required to drive the reaction to completion.

Scheme S3 (i) $PdCl_2$, MeOH/DCM (1/1), RT, 6 h, 79% (**S13**), 88% (**S14**), 78% (**S15**); (ii) Cl_3CCN or $ClC(=NPh)CF_3$, DBU, DCM, 0 °C, 2 h, 74% (**20**), 59% yield (**21**), 73% yield (**22**), 81% yield (**23**).

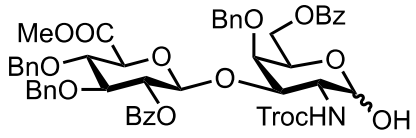
Methyl (3,4-di-*O*-benzyl-2-*O*-benzoyl-D-glucopyranosyl)uronate-β(1→3)-4-*O*-benzyl-6-*O*-benzoyl-2-deoxy-*N*-phthalimido-β-D-galactopyranoside S13



Disaccharide **S10** (334 mg, 0.324 mmol, 1.0 equiv.) was dissolved in a solution of DCM/MeOH (1/1, 16 mL) at RT. To this solution, $PdCl_2$ (35 mg, 0.194 mmol, 0.6 equiv.) was added and the reaction was stirred at RT for 6 h until complete then filtered over celite® and washed with DCM (20 mL). The filtrate was concentrated *in vacuo* and the crude residue was purified using manual flash column chromatography (2/1 hexane/EtOAc) to afford **S13** (1/2 α/β mixture) as a sticky white foam (249 mg, 0.256 mmol, 79%). $\mathbf{R_f}$ 0.50 (1/1 hexane/EtOAc). **^{1}H NMR** (400 MHz, $CDCl_3$) **β anomer** δ 7.95 – 7.91 (m, 5H, Ar-H α:β mix), 7.57 – 7.44 (m, 14H, Ar-H α:β mix), 7.42 (dddd, *J* = 8.6, 5.6, 2.9, 1.7 Hz, 1H, Ar-H α:β mix), 7.39 – 7.25 (m, 13H, Ar-H α:β mix), 7.22 (dddd, *J* = 8.3, 6.7, 3.3, 2.0 Hz, 8H, Ar-H α:β mix), 7.12 – 7.00 (m,

5H, Ar-H α:β mix), 7.02 – 6.92 (m, 7H, Ar-H α:β mix), 5.31 – 5.20 (m, 2H, H2'-β), 5.12 (dd, *J* = 11.7, 4.7 Hz, 2H, CH_2-OBn), 5.03 (d, *J* = 8.4 Hz, 1H, H1-β), 4.96 – 4.84 (m, 2H, H3-β), 4.82 – 4.69 (m, 7H, H1'-β, 6 × CH_2-OBn), 4.65 (d, *J* = 11.0 Hz, 1H, CH_2-OBn), 4.65 – 4.57 (m, 2H, H2-β, CH_2-OBn), 4.51 (d, *J* = 7.0 Hz, 1H, CH_2-OBn), 4.47 (d, *J* = 6.5 Hz, 1H, CH_2-OBn), 4.46 – 4.38 (m, 2H, H5-β, H6a-β), 4.29 – 4.15 (m, 2H, H4-β, H6b-β), 4.07 – 3.98 (m, 1H, H5'-β), 3.99 – 3.90 (m, 2H, H4'-β), 3.77 (t, *J* = 9.0 Hz, 1H, H3'-β), 3.59 (s, 3H, OCH_3). **^{1}H NMR** (400 MHz, $CDCl_3$) **α-anomer selected signals** δ 5.39 – 5.28 (m, 1H, H2'-α), 5.31 – 5.20 (m, 2H, H1-α), 5.00 (d, *J* = 8.0 Hz, 1H, H1'-α), 4.96 – 4.84 (m, 2H, H2-α), 4.33 – 4.27 (m, 1H, H4-α), 4.10 (d, *J* = 9.6 Hz, 1H, H5'-α), 3.99 – 3.90 (m, 2H, H4-α), 3.91 – 3.81 (m, 1H, H3'-α), 3.58 (s, 3H, OCH_3). **^{13}C NMR** (101 MHz, $CDCl_3$**) β-anomer** δ 168.3 (C=O), 166.1 (C=O), 164.3 (C=O), 138.4 (Ar-C), 137.7 (Ar-C), 137.5 (Ar-C), 133.1 (Ar-C), 132.6 (Ar-C), 129.9 (Ar-CH), 129.7 (Ar-CH), 129.7 (Ar-CH), 129.3 (Ar-CH), 129.1 (Ar-CH), 128.4 (Ar-CH), 128.4 (Ar-CH), 128.3 (Ar-CH), 128.3 (Ar-CH), 128.2 (Ar-CH), 127.9 (Ar-CH), 127.7 (Ar-CH), 127.7 (Ar-CH), 127.7 (Ar-CH), 127.6 (Ar-CH), 102.1 (C1'-β), 93.8 (C1-β), 81.8 (C3'-β), 79.4 (C4'), 77.6 (C3-β) 75.6 (C4-β), 75.1 (CH_2-OBn), 74.7 (C4-β), 74.2 (C5'), 73.8 (CH_2-OBn), 73.6 (CH_2-OBn), 72.6 (CH_2-OBn), 72.5 (C4), 68.5 (C5-β) 63.3 (C6-β), 54.5 (C2-β), 52.4 (OCH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) **α-anomer selected signals** δ 168.5 (C=O), 166.0 (C=O), 164.2 (C=O), 138.2 (Ar-C), 137.5 (Ar-C), 137.3 (Ar-C), 132.9 (Ar-C), 132.5 (Ar-C), 129.7 (Ar-CH), 129.3 (Ar-CH), 129.0 (Ar-CH), 128.9 (Ar-CH), 128.9 (Ar-CH), 128.4 (Ar-CH), 128.4 (Ar-CH), 128.3 (Ar-CH), 128.2 (Ar-CH), 128.1 (Ar-CH), 127.9 (Ar-CH), 127.9 (Ar-CH), 127.8 (Ar-CH), 127.7 (Ar-CH), 127.7 (Ar-CH), 101.7 (C1'-α), 92.9 (C1-α), 81.6 (C3'-α), 79.6 (C4'), 75.2 (C4), 75.1 (CH_2-OBn), 75.0 (CH_2-OBn), 74.7 (CH_2-OBn), 74.6 (CH_2-OBn), 74.2 (C5'), 73.5 (CH_2-OBn), 72.3 (CH_2-OBn), 63.1 (C6-α), 52.4 (OCH_3), 51.8 (C2-α). **HRMS** m/z (ESI^+) Found $(M+NH_4)^+$ 995.3598, $C_{56}H_{55}N_2O_{15}$ requires 995.3602.

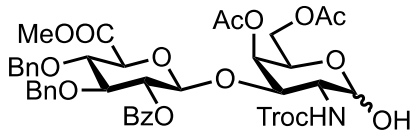
Methyl (3,4-di-*O*-benzyl-2-*O*-benzoyl-D-glucopyranosyl)uronate-β(1→3)-4-*O*-benzyl-6-*O*-benzoyl-2-deoxy-*N*-2,2,2-trichloroethoxycarbonylamino-β-D-galactopyranoside S14



Disaccharide **S11** (815 mg, 0.857 mmol, 1.0 equiv.) was dissolved in DCM/MeOH (1/1, 43 mL) and $PdCl_2$ (91 mg, 0.514 mmol, 0.6 equiv.) was added. The reaction was stirred for 5 h until complete then filtered over celite® and washed with DCM (50 mL). The filtrate was concentrated *in vacuo* then the crude residue was purified *via* manual flash column chromatography (100% DCM → 10% Et_2O in DCM) which afforded hemiacetal **S14** as a white

solid (747 mg, 0.754 mmol, 88%). **R_f** 0.50 (4/1 toluene/acetone). **m.p.** 165 – 166 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 – 7.94 (m, 4H, Ar-H), 7.62 – 7.51 (m, 2H, Ar-H), 7.43 (td, *J* = 7.8, 1.6 Hz, 4H, Ar-H), 7.37 – 7.21 (m, 10H, Ar-H), 7.16 – 7.06 (m, 5H, Ar-H), 5.39 (t, *J* = 8.3 Hz, 1H, H2'), 5.23 (app. d, *J* = 12.2 Hz, 1H, H1'), 5.03 (d, *J* = 11.4 Hz, 1H, CH_2-OBn), 4.91 (d, *J* = 8.3 Hz, 1H, H1), 4.80 – 4.58 (m, 5H, 4 × CH_2-OBn, 1 × CH_2-Troc), 4.48 – 4.22 (m, 4H, H2, H5, H6a, H6b), 4.11 – 3.98 (m, 4H, H3, H4, H4', H5'), 3.84 (t, *J* = 8.6 Hz, 1H, H3'), 3.65 (s, 3H, OCH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.6 (C=O), 166.2 (C=O), 164.9 (C=O), 154.0 (C=O), 138.3 (Ar-C), 137.5 (Ar-C), 137.4 (Ar-C), 133.3 (Ar-C), 133.1 (Ar-C), 129.9 (Ar-CH), 129.8 (Ar-CH), 129.8 (Ar-CH), 128.6 (Ar-CH), 128.5 (Ar-CH), 128.5 (Ar-CH), 128.4 (Ar-CH), 128.4 (Ar-CH), 128.3 (Ar-CH), 128.3 (Ar-CH), 128.1 (Ar-CH), 128.1 (Ar-CH), 128.0 (Ar-CH), 127.8 (Ar-CH), 127.6 (Ar-CH), 101.5 (C1'), 95.6 (CCl_3), 92.7 (C1), 81.8 (C3'), 79.3 (C4'), 77.2 (C3), 75.6 (CH_2-OBn), 75.3 (CH_2-OBn) 75.1 (CH_2-OBn), 74.7 (CH_2-Troc), 74.3 (C4), 73.9 (C5'), 73.2 (C2'), 68.6 (C5), 63.3 (C6), 52.5 (OCH_3), 51.4 (C2). **HRMS** m/z (ESI^+) Found $(M+NH_4)^+$ 1039.2550, $C_{51}H_{54}Cl_3N_2O_{15}$ requires 1039.2950.

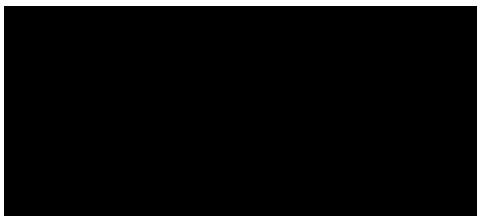
Methyl (3,4-di-*O*-benzyl-2-*O*-benzoyl-D-glucopyranosyl)uronate-β(1→3)-4,6-di-*O*-acetyl-2-deoxy-*N*-2,2,2-trichloroethoxycarbonylamino-β-D-galactopyranoside S15



Disaccharide **S12** (220 mg, 0.231 mmol, 1.0 equiv.) was dissolved in DCM/MeOH (1/1, 12 mL) and $PdCl_2$ (25 mg, 0.014 mmol, 0.6 equiv.) was added. The reaction was stirred for 5 h at RT then filtered over celite® and washed with DCM (20 mL). The crude residue was concentrated *in vacuo* then purified *via* manual flash column chromatography (100% DCM → 15% Et_2O in DCM) which afforded hemiacetal **S15** as a white foam (155 mg, 0.180 mmol, 78%). **R_f** 0.37 (4/1 toluene/acetone). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 – 7.95 (m, 2H, Ar-H), 7.61 – 7.52 (m, 1H, Ar-H), 7.43 (t, *J* = 7.6 Hz, 2H, Ar-H), 7.37 – 7.17 (m, 5H, Ar-H), 7.14 (s, 5H, Ar-H), 5.48 (d, *J* = 2.5 Hz, 1H, H4), 5.36 (d, *J* = 9.5 Hz, 1H, N*H*), 5.26 – 5.21 (m, 2H, H1, H2'), 4.86 (d, *J* = 6.7 Hz, 1H, H1'), 4.75 (d, *J* = 10.9 Hz, 1H, CH_2-OBn), 4.69 – 4.58 (m, 4H, 3 × CH_2-OBn, 1 × CH_2-Troc), 4.34 (t, *J* = 6.4 Hz, 1H, H5), 4.25 – 4.08 (m, 4H, H2, H3, CH_2-Troc, H6a), 4.07 – 3.96 (m, 3H, H4', H5', H6b), 3.87 – 3.81 (m, 1H, C1-OH), 3.75 (s, 4H, H3', OCH_3), 2.04 (s, 6H, 2 × C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.8 (C=O), 170.2 (C=O), 169.0 (C=O), 164.9 (C=O), 154.13 (C=O), 137.6 (Ar-C), 137.5 (Ar-C), 133.3 (Ar-C), 129.8 (Ar-CH), 128.4 (Ar-CH), 128.4 (Ar-CH), 128.3 (Ar-CH), 128.0 (Ar-CH), 128.0 (Ar-CH), 127.9 (Ar-CH), 127.9 (Ar-CH), 127.7 (Ar-CH), 100.0 (C1'), 95.5 (CCl_3), 92.3

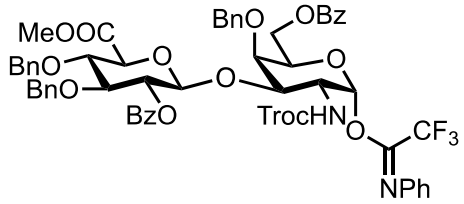
(C1), 81.8 (C3'), 78.7 (C4'), 75.0 (CH_2-OBn), 74.4 (CH_2-OBn), 74.3 (CH_2-Troc), 74.1 (C5'), 72.9 (C2'), 72.4 (C3), 69.1 (C4), 67.3 (C5), 62.8 (C6), 52.6 (OCH_3), 51.3 (C2), 20.8 (C(O)*C*H_3), 20.6 (C(O)*C*H_3). **HRMS** (ESI^+) Found $(M+Na)^+$ 934.1602, $C_{41}H_{44}Cl_3NO_{16}Na$ requires 934.1618.

Methyl(3,4-di-*O*-benzyl-2-*O*-benzoyl-D-glucopyranosyl)uronate-β(1→3)-4-*O*-benzyl-6-*O*-benzoyl-2-deoxy-*N*-phthalimido-α-D-galactopyranosyl trichloroacetimidate 20



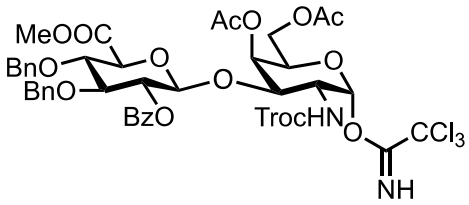
Glycosyl imidate **20** was prepared according to General Procedure **A**. Hemiacetal **S13** (190 mg, 0.194 mmol, 1.0 equiv.), Cl_3CCN (0.4 mL, 3.89 mmol, 20 equiv.) and DBU (6 μL, 0.039 mmol, 0.2 equiv.) gave the desired product **20** as an off-white foam (161 mg, 0.144 mmol, 74% yield). During purification, the product was eluted with 2% Et_2O in DCM + 1% Et_3N. $\mathbf{R_f}$ 0.74 (1/1 hexane/EtOAc). $[\alpha]_D^{22}$ = +82.8 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.42 (s, 1H, N*H*), 7.96 – 7.91 (m, 2H, Ar-H), 7.70 – 7.64 (m, 1H, Ar-H), 7.56 – 7.49 (m, 6H, Ar-H), 7.46 – 7.19 (m, 13H, Ar-H), 7.13 – 7.01 (m, 5H, Ar-H), 6.98 – 6.94 (m, 2H, Ar- H), 6.23 (d, *J* = 2.6 Hz, 1H, H1), 5.30 – 5.24 (m, 1H, H2'), 5.16 (d, *J* = 11.6 Hz, 1H, CH_2-OBn), 4.98 (dd, *J* = 11.3, 2.6 Hz, 1H, H2), 4.90 (dd, *J* = 11.3, 2.6 Hz, 1H, H3), 4.79 (d, *J* = 11.7 Hz, 1H, CH_2-OBn), 4.77 – 4.70 (m, 1H, CH_2-OBn), 4.64 – 4.57 (m, 2H, H1', CH_2-OBn), 4.51 – 4.47 (m, 2H, H6a, CH_2-OBn), 4.31 (dd, *J* = 11.0, 6.8 Hz, 1H, H6b), 4.26 (dd, *J* = 2.7, 1.2 Hz, 1H, H4), 4.13 – 4.08 (m, 1H, H5), 4.04 (d, *J* = 9.6 Hz, 1H, H5'), 3.94 (dd, *J* = 9.6, 8.7 Hz, 1H, H4'), 3.77 (t, *J* = 9.0 Hz, 1H, H3'), 3.60 (s, 3H, OCH_3). Selected **^{13}C NMR** data from HSQC (101 MHz, $CDCl_3$) δ 133.4 (Ar-CH), 132.7 (Ar-CH), 129.9 (Ar-CH), 129.1 (Ar-CH), 128.4 (Ar-CH), 128.4 (Ar-CH), 128.4 (Ar-CH), 128.1 (Ar-CH), 127.7 (Ar-CH), 123.2 (Ar-CH), 122.8 (Ar-CH), 102.4 (C1'), 94.3 (C1), 81.7 (C3'), 79.2 (C4'), 77.5 (C3), 75.0 (CH_2-OBn), 75.0 (CH_2-OBn), 74.7 (CH_2-OBn), 74.7 (C4), 74.3 (C5'), 73.6 (C2'), 73.2 (C5), 62.7 (C6), 52.5 (OCH_3), 51.1 (C2).

Methyl(3,4-di-*O*-benzyl-2-*O*-benzoyl-D-glucopyranosyl)uronate-β(1→3)-*N*-phenyltrifluoroacetimidoyl-4-*O*-benzyl-6-*O*-benzoyl-2-deoxy-*N*-2,2,2-trichloroethoxycarbonylamino-α-D-galactopyranoside 22



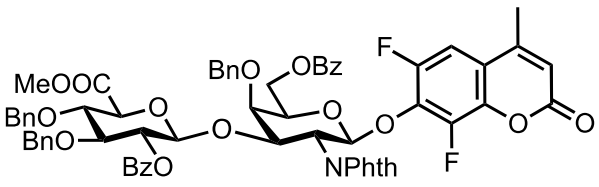
Glycosyl imidate **22** was prepared according to General Procedure **A**. Hemiacetal **S14** (330 mg, 0.347 mmol, 1.0 equiv.), PTFFACl (0.1 mL, 0.694 mmol, 2.0 equiv.) and DBU (52 μL, 0.348 mmol, 1.0 equiv.) gave the desired product **22** as a white foam (300 mg, 0.253 mmol, 73% yield). During purification, the product was eluted with 5% Et_2O in DCM + 1% Et_3N. $[\alpha]_D^{22}$ = +22.6 (*c* 1, $CHCl_3$). **R_f** 0.74 (1/1 hexane/EtOAc). $[\alpha]_D^{22}$ = +10.8 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 – 7.97 (m, 2H, Ar-H), 7.94 – 7.89 (m, 1H, Ar-H), 7.61 – 7.55 (m, 1H, Ar-H), 7.44 (ddd, *J* = 15.9, 7.8, 2.2 Hz, 4H, Ar-H), 7.35 – 7.23 (m, 10H, Ar-H), 7.21 – 7.16 (m, 5H, Ar-H), 7.14 – 7.11 (m, 5H, Ar-H), 7.07 – 7.02 (m, 1H, Ar-H), 6.65 (dd, *J* = 12.9, 8.0 Hz, 1H, Ar-H), 5.42 – 5.37 (m, 1H, H2'), 5.28 (d, *J* = 8.8 Hz, 1H, NH), 5.01 (d, *J* = 11.4 Hz, 1H, CH_2-OBn), 4.98 – 4.91 (m, 2H, H1, CH_2-OBn), 4.81 – 4.73 (m, 2H, H1', CH_2-OBn), 4.70 – 4.60 (m, 3H, CH_2-OBn), 4.51 – 4.47 (m, 2H, H2, CH_2-Troc), 4.39 (dt, *J* = 11.8, 5.4 Hz, 1H, H6a), 4.24 – 4.13 (m, 3H, H3, H4, H6b), 4.05 – 3.98 (m, 2H, H4', H5'), 3.94 (d, *J* = 12.2 Hz, 1H, CH_2-Troc), 3.87 (t, *J* = 8.8 Hz, 1H, H3'), 3.72 (s, 3H, OCH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.3 (C=O), 166.0 (C=O), 164.9 (C=O), 153.7 (C=O), 143.1 (C=N), 137.9 (Ar-C), 137.4 (Ar-C), 137.4 (Ar-C), 137.3 (Ar-C), 137.2 (Ar-C), 133.5 (Ar-C), 133.2 (Ar-CH), 133.0 (Ar-CH), 129.9 (Ar-CH), 129.8 (Ar-CH), 129.8 (Ar-CH), 129.7 (Ar-CH), 129.3 (Ar-CH), 128.9 (Ar-CH), 128.7 (Ar-CH), 128.6 (Ar-CH), 128.5 (Ar-CH), 128.4 (Ar-CH), 128.4 (Ar-CH), 128.3 (Ar-CH), 128.1 (Ar-CH), 128.1 (Ar-CH), 128.0 (Ar-CH), 127.9 (Ar-CH), 124.3 (CF_3) 119.2 (Ar-CH), 102.2 (C1'), 100.7 (C1), 95.6 (CCl_3), 81.5 (C3'), 79.4 (C4'), 75.2 (CH_2-OBn), 75.2 (CH_2-OBn), 75.1 (CH_2-OBn), 74.8 (C4), 74.4 (CH_2-Troc), 74.4 (C5'), 73.2 (C2'), 71.0 (C3), 63.1 (C6), 52.6 (OCH_3), 52.5 (C2). **^{19}F NMR** (377 MHz, $CDCl_3$) δ −75.5 (s). **HRMS** m/z (ESI$^+$) Found $(M+NH_4)^+$ 1210.2867, $C_{59}H_{54}Cl_3N_2O_{15}F_3$ requires 1210.2886.

Methyl (3,4-di-*O*-benzyl-2-*O*-benzoyl-D-glucopyranosyl)uronate-β(1→3)-Trichloroacetimidate-4,6-*O*-acetyl-2-deoxy-2-*N*-2,2,2-trichloroethoxycarbonylamino-D-galactopyranoside 23



Glycosyl imidate **23** was prepared according to General Procedure **A**. Hemiacetal **S15** (155 mg, 0.170 mmol, 1.0 equiv.), Cl_3CCN (51 µL, 0.509 mmol, 3.0 equiv.) and DBU (8 µL, 0.051 mmol, 0.3 equiv.) gave the desired product **23** as an off-white foam (145 mg, 0.138 mmol, 81% yield). During purification, the product was eluted with 1/1 hexane/EtOAc + 1% Et_3N. $\mathbf{R_f}$ 0.50 (4/1 toluene/acetone). $[\alpha]_D^{21}$ = +88.4 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 8.3, 1.3 Hz, 2H, Ar-H), 7.62 – 7.52 (m, 1H, Ar-H), 7.43 (t, *J* = 7.8 Hz, 2H, Ar-H), 7.33 – 7.23 (m, 5H, Ar-H), 7.12 (qd, *J* = 5.0, 2.5 Hz, 5H, Ar-H), 6.45 (d, *J* = 3.6 Hz, 1H, H1), 5.54 – 5.52 (m, 1H, H4), 5.31 (dd, *J* = 8.5, 7.4 Hz, 1H, H2'), 5.24 (d, *J* = 8.3 Hz, 1H, NH), 4.87 (d, *J* = 7.4 Hz, 1H, H1'), 4.78 – 4.70 (m, 3H, CH_2-OBn), 4.62 (dd, *J* = 11.0, 9.7 Hz, 2H, 1 × CH_2-Troc, 1 × CH_2-OBn), 4.39 (ddd, *J* = 10.9, 8.4, 3.5 Hz, 1H, H2), 4.30 – 4.25 (m, 2H, H5, CH_2-Troc), 4.21 – 4.12 (m, 2H, H3, H6a), 4.06 (d, *J* = 9.7 Hz, 1H, H5'), 3.96 – 3.92 (m, 2H, H4', H6b), 3.80 (t, *J* = 8.6 Hz, 1H, H3'), 3.73 (s, 3H, OCH_3), 2.02 (s, 3H, C(O)CH_3), 2.01 (s, 3H, C(O)CH_3). Selected **^{13}C NMR** data from HSQC (101 MHz, $CDCl_3$) δ 133.4 (Ar-CH), 129.9 (Ar-CH), 128.4 (Ar-CH), 128.4 (Ar-CH), 128.1 (Ar-CH), 128.1 (Ar-CH), 99.6 (C1'), 95.4 (C1), 81.7 (C3'), 78.9 (C4'), 75.0 (CH_2-OBn), 75.0 (CH_2-OBn), 74.3 (CH_2-Troc), 74.3 (C5'), 72.5 (C3), 72.5 (C2'), 69.7 (C5), 67.6 (C4), 62.0 (C6), 52.5 (OCH_3), 50.7 (C2), 20.9 (C(O)*C*H_3), 20.8 (C(O)*C*H_3).

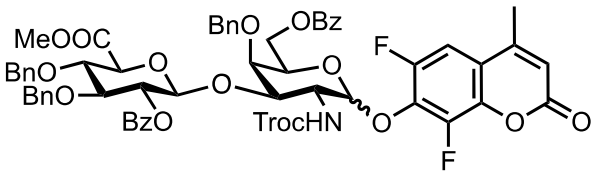
6',8'-Difluoro-4'-methylumbelliferyl (methyl (3,4-di-*O*-benzyl-2-*O*-benzoyl-D-glucopyranosyl)uronate)-β(1→3)-4-*O*-benzyl-6-*O*-benzoyl-2-deoxy-*N*-phthalimido-β-D-galactopyranoside 24



Compound **24** was prepared according to General Procedure **B**. Trichloroacetimidate **20** (161 mg, 0.144 mmol, 1.2 equiv.), DiFMu (26 mg, 0.116 mmol, 1.0 equiv.) and $BF_3{\cdot}Et_2O$ (2 µL, 0.017 mmol. 0.2 equiv.) afforded compound β-**27** (95 mg, 0.101 mmol, 70% yield) as white foam. Purification was achieved using a 10/1 → 2/1 → 1.5 → 1/1 hexane/EtOAc gradient. $\mathbf{R_f}$ 0.34 (5% Et_2O in DCM). $[\alpha]_D^{25}$ = +23.2 (*c* 1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 – 7.85 (m, 2H, Ar-H), 7.73 (d, *J* = 7.5 Hz, 1H, Ar-H), 7.57 – 7.49 (m, 4H, Ar-H), 7.44

– 7.33 (m, 6H, Ar-H), 7.32 – 7.27 (m, 3H, Ar-H), 7.21 (dd, *J* = 7.7, 1.8 Hz, 2H, Ar-H), 7.16 – 7.02 (m, 5H, Ar-H), 6.98 – 6.94 (m, 2H, Ar-H), 6.86 (dd, *J* = 10.2, 2.1 Hz, 1H, Ar-H), 6.20 (d, *J* = 1.4 Hz, 1H, (*H*C=C(CH_3)), 5.47 (d, *J* = 8.4 Hz, 1H, H1), 5.27 (dd, *J* = 9.3, 7.8 Hz, 1H, H2'), 5.16 (d, *J* = 11.7 Hz, 1H, CH_2-OBn), 5.01 (dd, *J* = 11.3, 8.4 Hz, 1H, H2), 4.87 (dd, *J* = 11.3, 2.7 Hz, 1H, H3), 4.82 – 4.70 (m, 3H, H1', CH_2-OBn), 4.65 – 4.57 (m, 2H, CH_2-OBn), 4.50 (d, *J* = 11.0 Hz, 1H, CH_2-OBn), 4.44 (dd, *J* = 11.2, 7.0 Hz, 1H, H6a), 4.26 – 4.19 (m, 2H, H4, H6b), 4.04 (d, *J* = 9.6 Hz, 1H, H5'), 3.98 – 3.90 (m, 2H, H4', H5), 3.78 (t, *J* = 9.0 Hz, 1H, H3'), 3.62 (s, 3H, OCH_3), 2.24 (d, *J* = 1.3 Hz, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.4 (C=O), 166.0 (C=O), 164.2 (C=O), 158.7 (C=O), 151.5 (d, *J* = 249.1 Hz, C-F), 151.0 (t, *J* = 2.6 Hz, *C*CH_3), 143.32 (d, *J* = 251.5 Hz, C-F), 139.2 (dd, *J* = 10.5, 2.9 Hz, *C*(OC(O)R), 138.2 (Ar-C), 137.5 (Ar-C), 137.3 (Ar-C), 133.0 (Ar-C), 132.7 (Ar-C), 130.9 (Ar-CH), 129.7 (Ar-CH), 129.6 (Ar-CH), 129.4 (Ar-CH), 129.1 (Ar-CH), 129.1 (Ar-CH), 128.4 (Ar-CH), 128.4 (Ar-CH), 128.3 (Ar-CH), 128.2 (Ar-CH), 128.2 (Ar-CH), 127.9 (Ar-CH), 127.9 (Ar-CH), 127.8 (Ar-CH), 127.7 (Ar-CH), 116.40 (d, *J* = 8.7 Hz, *C*(CCH_3)), 115.5 (Ar-CH), 105.5 (dd, *J* = 22.2, 3.8 Hz, *C*=CH), 102.3 (C1'), 100.6 (C1, $^1J_{1CH}$ = 169.4 Hz from coupled HSQC), 81.6 (C3'), 79.3 (C4'), 77.2 (C3), 75.1 (CH_2-OBn), 75.0 (CH_2-OBn), 74.7 (CH_2-OBn), 74.3 (C4), 74.2 (C5'), 73.5 (C2'), 72.9 (C5), 62.7 (C6), 52.5 (OCH_3), 52.1 (C2), 18.6 (CH_3). **^{19}F NMR** (377 MHz, $CDCl_3$) δ −129.6 (dd, *J* = 10.1, 3.6 Hz), −144.1 (br s). **HRMS** m/z (ESI^+) Found $(M+NH_4)^+$ 1189.3783, $C_{66}H_{59}N_2O_{17}F_2$ requires 1189.3776.

6',8'-Difluoro-4'-methylumbelliferyl (methyl 3,4-di-*O*-benzyl-2-*O*-benzoyl-D-glucopyranosyl)uronate-β(1→3)-4-*O*-benzyl-6-*O*-benzoyl-2-deoxy-*N*-2,2,2-trichloroethoxycarbonylamino-α/β-D-galactopyranoside 25



Compound **25** was prepared according to General Procedure **B**. Glycosyl imidate **22** (300 mg, 0.252 mmol, 1.0 equiv.), DiFMu (52 mg, 0.280 mmol, 1.2 equiv.) and $BF_3{\cdot}Et_2O$ (28 μL, 0.228 mmol., 1.0 equiv.) afforded crude compound **25** as a 2/1 α/β mixture. Purification using a 100% DCM → 5% Et_2O in DCM (α-anomer) → 6% Et_2O in DCM (β-anomer) gradient isolated **α-25** (131 mg, 0.109 mmol, 48% yield) and **β-25** (70 mg, 0.057 mmol, 25%) as white foams. $\mathbf{R_f}$ 0.62 (α), 0.55 (β) (10% Et_2O in DCM). $[\alpha]_D^{22}$ = +56.2 (α); +17.8 (β) (*c* 1, $CHCl_3$). **α-anomer: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 – 8.01 (m, 2H, Ar-H), 7.93 – 7.89 (m, 2H, Ar-H), 7.61 – 7.56 (m, 1H, Ar-H), 7.49 – 7.45 (m, 1H), 7.45 – 7.29 (m, 10H,

Ar-H), 7.17 – 7.10 (m, 9H, Ar-H), 6.93 – 6.88 (m, 1H, Ar-H (5')), 6.25 – 6.23 (m, 1H, (C(CH_3)C*H*)), 5.55 (d, *J* = 3.7 Hz, 1H, H1), 5.45 – 5.40 (m, 2H, H2', N*H*), 5.05 (d, *J* = 11.5 Hz, 1H, CH_2-OBn), 5.00 (d, *J* = 7.8 Hz, 1H, H1'), 4.82 – 4.76 (m, 2H, CH_2-OBn), 4.70 – 4.61 (m, 5H, H2, 2 × CH_2-OBn, 2 × CH_2-Troc), 4.56 – 4.51 (m, 1H, H5), 4.31 (d, *J* = 7.6 Hz, 1H, H6a), 4.23 – 4.20 (m, 2H, H3, H6b), 4.13 (br s, 1H, H4), 4.04 – 4.02 (m, 2H, H4', H5'), 3.89 (t, *J* = 8.7 Hz, 1H, H3'), 3.74 (s, 3H, OCH_3), 2.35 (s, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.5 (C=O), 166.0 (C=O), 164.9 (C=O), 158.6 (C=O), 151.73 (d, *J* = 249.8 Hz, C-F), 150.9 (*C*CH_3), 143.9 (d, *J* = 252.5 Hz), 139.4 (d, *J* = 10.0 Hz, *C*(OC(O)R), 137.9 (Ar-C), 137.4 (Ar-C), 137.4 (Ar-C), 137.3 (Ar-C), 133.0 (Ar-C), 129.9 (Ar-CH), 129.6 (Ar-CH), 129.0 (Ar-CH), 128.6 (Ar-CH), 128.5 (Ar-CH), 128.4 (Ar-CH), 128.3 (Ar-CH), 128.3 (Ar-CH), 128.3 (Ar-CH), 128.2 (Ar-CH), 128.1 (Ar-CH), 128.1 (Ar-CH), 128.0 (Ar-CH), 128.0 (Ar-CH), 125.3 (Ar-CH), 116.6 (d, *J* = 9.0 Hz, *C*(CCH_3)), 115.3 (Ar-CH), 105.9 (d, J_{CF} = 23.9 Hz, C=*C*H), 102.2 (C1, $^1J_{1CH}$ = 178.7 Hz from coupled HSQC), 101.7 (C1', $^1J_{1CH}$ = 164.9 Hz from coupled HSQC), 95.5 (CCl_3), 81.6 (C3'), 79.3 (C4'), 75.4 (C3), 75.2 (CH_2-OBn), 75.1 (CH_2-OBn), 74.8 (CH_2-OBn), 74.7 (CH_2-Troc), 74.4 (C4), 74.4 (C5'), 73.2 (C2'), 71.0 (C5), 63.9 (C6), 52.5 (OCH_3), 50.9 (C2), 18.6 (CH_3). **^{19}F NMR** (377 MHz, $CDCl_3$) δ −130.7 (dd, *J* = 10.9, 3.7 Hz), −144.6 (s). **HRMS** m/z (ES^+) Found $(M+Na)^+$ 1238.2326, $C_{61}H_{54}Cl_3F_2NO_{17}Na$ requires 1238.2317.

β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 7.9, 1.4 Hz, 2H, Ar-H), 7.87 – 7.83 (m, 2H, Ar-H), 7.66 – 7.58 (m, 1H, Ar-H), 7.52 – 7.23 (m, 14H, Ar-H), 7.13 (s, 5H, Ar-H), 6.94 (dd, *J* = 10.5, 2.2 Hz, 1H, Ar-H (5')), 6.26 (d, *J* = 1.4 Hz, 1H, (C(CH_3)C*H*)), 5.54 (d, *J* = 9.6 Hz, 1H, H1), 5.40 (dd, *J* = 9.4, 7.9 Hz, 1H, H2'), 5.15 (d, *J* = 6.8 Hz, 1H, N*H*), 5.00 (d, *J* = 11.5 Hz, 1H, CH_2-OBn), 4.82 – 4.61 (m, 7H, H1', H3, 1 × CH_2-Troc, 4 × CH_2-OBn), 4.56 (d, *J* = 11.8 Hz, 1H, CH_2-Troc), 4.38 (dd, *J* = 11.3, 7.3 Hz, 1H, H6a), 4.15 (dd, *J* = 11.4, 5.6 Hz, 1H, H6b), 4.06 – 3.97 (m, 3H, H4, H4', H5'), 3.83 (t, *J* = 6.2 Hz, 1H, H5), 3.78 – 3.74 (m, 1H, H3'), 3.69 (s, 3H, OC*H*$_3$), 3.59 (q, *J* = 8.7 Hz, 1H, H2), 2.30 (d, *J* = 1.3 Hz, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.5 (C=O), 165.9 (C=O), 164.9 (C=O), 158.8 (C=O), 153.9 (C=O), 151.0 (br s, CCH_3), 141.8 (d, *J* = 251.2 Hz, C-F), 139.4 (*C*(OC(O)R) 137.9 (Ar-C), 137.5 (Ar-C), 137.4 (Ar-C), 133.5 (Ar-CH), 133.0 (Ar-CH), 131.6 (Ar-C), 129.8 (Ar-C), 129.7 (Ar-CH), 129.6 (Ar-CH), 129.2 (Ar-CH), 128.7 (Ar-CH), 128.6 (Ar-CH), 128.5 (Ar-CH), 128.5 (Ar-CH), 128.4 (Ar-CH), 128.3 (Ar-CH), 128.3 (Ar-CH), 128.3 (Ar-CH), 128.1 (Ar-CH), 128.1 (Ar-CH), 127.9 (Ar-CH), 127.8 (Ar-CH), 116.0 (*C*(CCH_3)) 115.5 (Ar-CH), 105.6 (d, *J* = 22.2 Hz, C=*C*H), 102.2 (C1', $^1J_{1CH}$ = 163.5 Hz from coupled HSQC), 99.9 (C1, $^1J_{1CH}$ =

166.8 Hz from coupled HSQC), 94.8 (CCl_3), 81.5 (C3'), 79.6 (C4'), 76.8 (C3), 75.2 (CH_2-OBn), 75.1 (CH_2-OBn), 74.8 (CH_2-OBn), 74.4 (CH_2-Troc), 74.2 (C5'), 74.2 (C4), 73.3 (C2'), 72.9 (C5), 62.9 (C6), 55.3 (OCH_3), 52.6 (C2), 18.7 (CH_3). **^{19}F NMR** (377 MHz, $CDCl_3$) δ −130.3 (dd, *J* = 10.7, 4.0 Hz), −144.7 (s). **HRMS** m/z (ESI^+) Found $(M+NH_4)^+$ 1235.2756, $C_{61}H_{54}Cl_3NO_{17}F_2$ requires 1235.2754.

_N_-Trichloroacetyl (methyl (3,4-di-_O_-benzyl-2-_O_-benzoyl-D-glucopyranosyl)uronate-β(1→3)-4-_O_-benzyl-6-_O_-benzoyl-2-deoxy-_N_-2,2,2-trichloroethoxycarbonylamino-α-D-galactopyranosyl)amide S16

Amide **S16** was generated as an undesired side product from the reaction of imidate **21** with DiFMu using General Procedure **B**. Glycosyl imidate **21** (91 mg, 0.078 mmol, 1.1 equiv.), DiFMu (15 mg, 0.070 mmol, 1.0 equiv.) and $BF_3{\cdot}Et_2O$ (2 μL, 0.014 mmol., 0.2 equiv.) afforded amide **S16** (40 mg, 0.033 mmol, 47% yield) as a white foam. **R_f** 0.53 (4/1 toluene/acetone). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 – 7.82 (m, 5H, Ar-H), 7.58 – 7.53 (m 3H, Ar-H), 7.47 – 7.22 (m, 12H, Ar-H), 7.11 (br s, 5H, Ar-H), 6.59 (br s, 1H, NH-amide), 5.65 (d, *J* = 7.8 Hz, 1H, NH-Troc), 5.44 – 5.30 (m, 2H, H2, H2'), 5.18 – 5.09 (m, 1H, H3), 4.98 (d, *J* = 7.8 Hz, 1H, H1'), 4.92 (dd, *J* = 11.3, 2.2 Hz, 1H, CH_2-OBn), 4.78 (d, *J* = 10.7 Hz, 1H, CH_2-OBn), 4.74 – 4.69 (m, 2H, H1, CH_2-OBn), 4.66 – 4.59 (m, 4H, 3 × CH_2-OBn, 1 × CH_2-Troc), 4.56 (d, *J* = 12.0 Hz, 1H, CH_2-Troc), 4.49 (d, *J* = 11.0 Hz, 1H, CH_2-OBn), 4.42 (dd, *J* = 11.1, 6.1 Hz, 1H, H6a), 4.28 (dd, *J* = 11.1, 7.1 Hz, 1H, H6b), 4.11 – 3.93 (m, 5H, H2, H4, H4', H5, H5'), 3.85 (t, *J* = 8.8 Hz, 1H, H3'), 3.66 (s, 3H, OCH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.4 (C=O), 166.0 (C=O), 165.1 (C=O), 163.4 (C=O), 155.3 (C=O, Troc), 137.9 (Ar-C), 137.8 (Ar-C), 137.5 (Ar-C), 137.4 (Ar-C), 137.3 (Ar-C), 137.2 (Ar-C), 133.5 (Ar-CH), 133.4 (Ar-CH), 129.8 (Ar-CH), 129.8 (Ar-CH), 129.7 (Ar-CH), 129.3 (Ar-CH), 128.7 (Ar-CH), 128.5 (Ar-CH), 128.4 (Ar-CH), 128.4 (Ar-CH), 128.3 (Ar-CH), 128.1 (Ar-CH), 128.0 (Ar-CH), 127.9 (Ar-CH), 127.8 (Ar-CH), 101.9 (C1), 100.8 (C1'), 95.2 (CCl_3), 91.6 (CCl_3), 81.5 (C3), 81.2 (C3'), 79.2 (C4'), 75.2 (CH_2-OBn), 75.2 (CH_2-OBn), 75.1 (CH_2-OBn), 74.8 (CH_2-Troc), 74.4 (C5'), 74.3 (C4), 73.2 (C2'), 72.1 (C5), 62.5 (C6), 52.9 (C2), 52.7 (OCH_3). **HRMS** m/z (ESI^+) Found $(M+Na)^+$ 1189.1223, $C_{53}H_{50}Cl_6N_2O_{15}Na$ requires 1189.1240.

4'-Methylumbelliferyl (methyl (3,4-di-*O*-benzyl-2-*O*-benzoyl-D-glucopyranosyl)uronate)-β(1→3)-4-*O*-benzyl-6-*O*-benzoyl-2-deoxy-*N*-2,2,2-trichloroethoxycarbonylamino-α/β-D-galactopyranoside 26

Compound **26** was prepared according to General Procedure **B**. Glycosyl imidate **22** (222 mg, 0.186 mmol, 1.0 equiv.), 4-methylumbelliferone (40 mg, 0.223 mmol, 1.2 equiv.) and $BF_3{\cdot}Et_2O$ (23 μL, 0.186 mmol., 1.0 equiv.) afforded crude compound **26** as a 1/1 α/β mixture. Purification using a 100% DCM → 5% Et_2O in DCM (α-anomer) → 7% Et_2O in DCM (β-anomer) gradient isolated **α-26** (77 mg, 0.065 mmol, 35% yield) and **β-26** (90 mg, 0.076 mmol, 41%) as white foams. $\mathbf{R_f}$ 0.69 (α-anomer), 0.62 (β-anomer, 10% Et_2O in DCM). $[\alpha]_D^{22}$ = +74.1 (α); +10.9 (β) (*c* 1, $CHCl_3$). **α-anomer: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.7 Hz, 2H, Ar-H), 7.80 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.66 – 7.51 (m, 1H, Ar-H), 7.49 – 7.42 (m, 3H, Ar-H), 7.37 – 7.23 (m, 12H, Ar-H), 7.18 – 7.02 (m, 6H, Ar-H), 7.00 (d, *J* = 2.4 Hz, 1H, Ar-H), 6.94 (dd, *J* = 8.8, 2.4 Hz, 1H, Ar-H), 6.11 (d, *J* = 1.5 Hz, 1H, C=CH), 5.66 (d, *J* = 3.5 Hz, 1H, H1), 5.46 – 5.38 (m, 1H, H2'), 5.04 (dd, *J* = 11.0, 9.2 Hz, 2H, H1', CH_2-OBn), 4.80 (d, *J* = 10.9 Hz, 1H, CH_2-Troc), 4.76 (d, *J* = 11.3 Hz, 1H, CH_2-OBn), 4.71 – 4.48 (m, 6H, H2, 3 × CH_2-OBn, 1 × CH_2-Troc), 4.33 (dd, *J* = 11.2, 7.8 Hz, 1H, H6a), 4.27 – 4.13 (m, 5H, H3, H4, H5, H5', H6b), 4.08 – 4.02 (m, 1H, H4'), 3.89 (t, *J* = 8.6 Hz, 1H, H3'), 3.73 (s, 3H, OCH_3), 2.28 (d, *J* = 1.3 Hz, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.5 (C=O), 165.94 (C=O), 165.0 (C=O), 160.9 (*C*OC(O)), 158.8 (C=O), 154.66 (*C*CH_3), 152.04 (C=O), 137.36 (Ar-C), 137.28 (Ar-C), 133.02 (Ar-CH), 129.95 (Ar-C), 129.5 (Ar-C), 128.7 (Ar-C), 128.6 (Ar-CH), 128.5 (Ar-CH), 128.5 (Ar-CH), 128.5 (Ar-CH), 128.4 (Ar-CH), 128.4 (Ar-CH), 128.3 (Ar-CH), 128.3 (Ar-CH), 128.2 (Ar-CH), 128.1 (Ar-CH), 128.1 (Ar-CH), 128.0 (Ar-CH), 128.0 (Ar-CH), 127.8 (Ar-CH), 127.7 (Ar-CH), 125.6 (Ar-CH), 155.1 (*C*(CCH_3)) 113.0 (Ar-CH, coumarin), 101.4 (C1', $^1J_{1CH}$ = 165.3 Hz, from coupled HSQC), 96.8 (C1, $^1J_{1CH}$ = 179.8 Hz, from coupled HSQC), 95.5 (CCl_3), 81.6 (C3'), 79.3 (C4'), 76.3 (C3), 75.2 (C5'), 75.1 (CH_2-OBn), 75.0 (CH_2-OBn), 74.8 (CH_2-OBn), 74.4 (C4), 74.0 (CH_2-Troc), 73.1 (C2'), 69.8 (C5), 63.5 (C6), 52.7 (OCH_3), 50.8 (C2), 18.5 (CH_3). **HRMS** (ESI^+) Found $(M+NH_4)^+$ 1197.2959, $C_{61}H_{60}Cl_3N_2O_{17}$ requires 1197.2952.

β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.05 (m, 2H, Ar-H), 7.97 (d, *J* = 7.4 Hz, 2H, Ar-H), 7.65 – 7.59 (m, 1H, Ar-H), 7.57 – 7.54 (m, 1H, Ar-H), 7.48 (td, *J* = 7.6, 3.6 Hz, 3H, Ar-H), 7.44 – 7.40 (m, 3H, Ar-H), 7.36 – 7.26 (m, 9H, Ar-H), 7.12 (s, 5H, Ar-H), 6.91 (dd, *J* =

6.5, 2.4 Hz, 2H, Ar-H), 6.82 (ddd, *J* = 8.8, 4.8, 2.4 Hz, 2H, Ar-H), 6.13 (d, *J* = 1.4 Hz, 1H, C=CH), 5.53 (d, *J* = 8.5 Hz, 1H, H1), 5.42 (dd, *J* = 9.2, 7.8 Hz, 1H, H2'), 5.26 (d, *J* = 7.0 Hz, 1H, N*H*), 5.02 (d, *J* = 11.4 Hz, 1H, CH_2-OBn), 4.83 – 4.62 (m, 6H, 1 × CH_2-Troc, 5 × CH_2-OBn), 4.55 – 4.46 (m, 2H, H3, CH_2-Troc), 4.39 (dd, *J* = 11.5, 8.0 Hz, 1H, H6a), 4.21 (dd, *J* = 11.6, 4.6 Hz, 1H, H6b), 4.08 – 4.02 (m, 3H, H4, H4', H5'), 3.97 (br s, 1H, H5), 3.81 (td, *J* = 9.7, 5.5 Hz, 1H, C3'), 3.71 (s, 3H, OCH_3), 3.64 (br s, 1H, H2), 2.31 (d, *J* = 1.3 Hz, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.5 (C=O), 166.2 (C=O), 164.9 (C=O), 161.9 (C=O, coumarin), 160.1 (*C*OC(O)), 159.7 (Ar-C, coumarin), 155.1 (C=O, Troc), 154.7 (*C*CH_3), 137.8 (Ar-C), 137.5 (Ar-C), 137.4 (Ar-C), 133.5 (Ar-C), 133.3 (Ar-C), 129.9 (Ar-CH), 129.7 (Ar-CH), 129.7 (Ar-CH), 129.5 (Ar-CH), 129.1 (Ar-CH), 128.7 (Ar-CH), 128.5 (Ar-CH), 128.4 (Ar-CH), 128.3 (Ar-CH), 128.3 (Ar-CH), 128.3 (Ar-CH), 128.2 (Ar-CH), 128.1 (Ar-CH), 128.1 (Ar-CH), 128.0 (Ar-CH), 128.0 (Ar-CH), 125.9 (Ar-CH, coumarin), 113.3 (Ar-CH, coumarin), 111.4 (C=*C*H), 103.3 (Ar-CH, coumarin), 102.4 (C1', $^1J_{1CH}$ = 162.7 Hz, from coupled HSQC), 96.7 (C1, $^1J_{1CH}$ = 166.9 Hz, from coupled HSQC), 95.6 (CCl_3), 81.5 (C3'), 79.5 (C4'), 77.2 (C3), 75.2 (CH_2-OBn), 75.2 (CH_2-OBn), 74.7 (CH_2-OBn), 74.5 (C5'), 74.3 (C4), 74.0 (CH_2-Troc), 73.3 (C2'), 72.8 (C5), 63.5 (C6), 54.5 (C2), 52.6 (OCH_3), 18.6 (CH_3). **HRMS** (ESI^+) Found $(M+NH_4)^+$ 1197.2946, $C_{61}H_{60}Cl_3N_2O_{17}$ requires 1197.2952.

6',8'-Difluoro-4'-methylumbelliferyl (methyl 3,4-di-*O*-benzyl-2-*O*-benzoyl-D-glucopyranosyl)uronate-β(1→3)-4,6-*O*-acetyl-2-deoxy-*N*-2,2,2-trichloroethoxycarbonylamino-α/β-D-galactopyranoside 27

Compound **27** was prepared according to General Procedure **B**. Glycosyl imidate **23** (137 mg, 0.129 mmol, 1.0 equiv.), DiFMu (32 mg, 0.155 mmol, 1.2 equiv.) and $BF_3{\cdot}Et_2O$ (5 μL, 0.039 mmol., 0.3 equiv.) afforded crude compound **27** as a 1.5/1 α/β mix. Purification using a 100% DCM → 4% Et_2O in DCM (α-anomer) → 5% Et_2O in DCM (β-anomer) gradient isolated **α-27** (50 mg, 0.045 mmol, 35% yield) as a yellow oil and **β-27** (40 mg, 0.036 mmol, 28%) as a white foam. $\mathbf{R_f}$ 0.46 (α), 0.41 (β) (4/1 toluene/acetone). $[\alpha]_D^{25}$ = +78.4 (α), +26.2 (β) (*c* 1, $CHCl_3$). **β-anomer: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 – 7.96 (m, 2H, Ar-H), 7.64 – 7.55 (m, 1H, Ar-H), 7.47 (dd, *J* = 8.3, 7.1 Hz, 2H, Ar-H), 7.37 – 7.20 (m, 5H, Ar-H), 7.19 – 7.15 (m, 1H, Ar-H), 7.13 – 7.09 (m, 4H, Ar-H), 7.07 (dd, *J* = 10.6, 2.1 Hz, 1H, *H*C=CF), 6.29 (d, *J* = 1.4 Hz, 1H, C*H*C(O)), 5.48 (d, *J* = 8.4 Hz, 1H, H1), 5.45 – 5.43 (m, 1H, H4), 5.25 (dd, *J* =

8.7, 7.3 Hz, 1H, H2'), 4.78 – 4.73 (m, 2H, H1', CH_2-OBn), 4.71 (d, *J* = 11.2 Hz, 1H, CH_2-OBn), 4.64 – 4.59 (m, 3H, H3, 2 × CH_2-OBn), 4.48 (d, *J* = 12.1 Hz, 1H, CH_2-Troc), 4.17 – 4.07 (m, 2H, H6a, CH_2-Troc), 4.05 – 3.94 (m, 3H, H4', H5', H6b), 3.92 – 3.86 (m, 1H, H5), 3.76 – 3.70 (m, 4H, H3', OCH_3), 3.61 – 3.54 (m, 1H, H2), 2.35 (s, 3H, CH_3), 2.11 (s, 3H, C(O)CH_3), 2.00 (s, 3H, C(O)CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.5 (C=O), 170.1 (C=O), 168.5 (C=O), 164.9 (C=O), 158.8 (C=O), 153.8 (C=O, Troc), 151.2 (d, *J* = 248.0 Hz, C-F), 151.1 (br s, *C*CH_3), 142.4 (d, *J* = 249.0 Hz, C-F), 137.6 (Ar-C), 137.5 (Ar-C), 133.5 (Ar-C), 129.8 (Ar-CH), 129.0 (Ar-CH), 128.7 (Ar-CH), 128.5 (Ar-CH), 128.3 (Ar-CH), 128.2 (Ar-CH), 128.1 (Ar-CH), 127.9 (Ar-CH), 127.8 (Ar-CH), 125.3 (Ar-CH), 116.3 (d, *J* = 8.1 Hz, *C*(CCH_3)), 115.6 (Ar-CH), 105.8 (dd, *J* = 25.7 Hz, C=*C*H) 101.0 (C1'), 100.4 (C1), 95.4 (CCl_3), 81.5 (C3'), 78.9 (C4'), 75.1 (CH_2-OBn), 74.8 (CH_2-OBn), 74.4 (C5'), 73.9 (CH_2-Troc), 73.6 (C3), 73.2 (C2'), 72.1 (C5), 68.3 (C4), 62.1 (C6), 55.3 (C2), 52.6 (OCH_3), 20.7 (C(O)*C*H_3), 20.6 (C(O)*C*H_3), 18.7 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$) δ −130.7 (d, *J* = 7.8 Hz), −144.9 (s). **HRMS** m/z (ESI^+) Found $(M+NH_4)^+$ 1125.2229, $C_{51}H_{52}N_2O_{18}Cl_3F_2$ requires 1125.2229. **α-anomer**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 – 7.96 (m, 4H, Ar-H), 7.61 – 7.55 (m, 1H, Ar-H), 7.47 – 7.41 (m, 2H, Ar-H), 7.33 – 7.29 (m, 4H, Ar-H), 7.19 – 7.10 (m, 6H, Ar-H), 6.32 (d, *J* = 1.4 Hz, 1H, C=C*H*), 5.75 (d, *J* = 7.1 Hz, 1H, NH), 5.63 – 5.60 (m, 1H, H4), 5.50 (d, *J* = 3.6 Hz, 1H, H1), 5.32 – 5.27 (m, 1H, H2'), 4.94 – 4.90 (m, 1H, H1'), 4.77 (d, *J* = 10.0 Hz, 1H, CH_2-OBn), 4.66 (d, *J* = 12.0 Hz, 1H, CH_2-OBn), 4.62 – 4.56 (m, 3H, H3, 2 × CH_2-OBn), 4.45 (ddd, *J* = 11.0, 9.2, 3.6 Hz, 1H, H2), 4.34 (d, *J* = 12.0 Hz, 1H, CH_2-Troc), 4.27 (dq, *J* = 11.0, 4.0 Hz, 2H, H6a, H6b), 4.17 (d, *J* = 12.1 Hz, 1H, CH_2-Troc), 4.10 – 3.91 (m, 4H, H4, H4', H5, H5'), 3.79 (s, 4H, H3', OCH_3), 2.37 (d, *J* = 1.3 Hz, 3H, CH_3), 2.05 (d, *J* = 1.3 Hz, 6H, 2 × C(O)CH_3). Selected **^{13}C NMR** data from HSQC (101 MHz, $CDCl_3$) δ 133.2 (Ar-CH), 129.7 (Ar-CH), 128.4 (Ar-CH), 128.1 (Ar-CH), 127.9 (Ar-CH), 127.9 (Ar-CH), 127.9 (Ar-CH), 115.8 (C=*C*H), 105.8 (Ar-CH), 102.3 (C1'), 99.5 (C1), 81.6 (C3'), 78.5 (C4'), 74.9 (CH_2-OBn), 74.7 (CH_2-OBn), 74.7 (CH_2-Troc), 74.1 (C5'), 73.1 (C5), 72.4 (C2'), 69.5 (C3), 68.4 (C4), 62.4 (C6), 52.6 (OCH_3), 50.9 (C2), 20.5 (C(O)*C*H_3), 20.5 (C(O)*C*H_3), 18.6 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$) δ −131.06 (dd, *J* = 10.4, 3.4 Hz), −144.55 (d, *J* = 3.3 Hz). **HRMS** m/z (ESI^+) Found $(M+NH_4)^+$ 1125.2232, $C_{51}H_{52}N_2O_{18}Cl_3F_2$ requires 1125.2229.

References

1 T. Holmstrøm and C. M. Pedersen, *Eur J Org Chem*, 2020, **2020**, 4612–4615.

2 G. Soldaini, F. Cardona and A. Goti, *Org Lett*, 2005, **7**, 725–728.

3 D. Sondag, F. F. J. de Kleijne, S. Castermans, I. Chatzakis, M. van Geffen, C. van't Veer, W. L. van Heerde, T. J. Boltje and F. P. J. T. Rutjes, *Chem Eur J*, 2024, **30**, e202302547.

4 J. Dinkelaar, M. D. Witte, L. J. van den Bos, H. S. Overkleeft and G. A. van der Marel, *Carbohydr Res*, 2006, **341**, 1723–1729.

5 J. Porter, D. Parisi, T. Miller, A. N. Cheallaigh and G. J. Miller, *Carbohydr Res*, 2023, **530**, 108854.

6 M. Thomas, J. P. Gesson and S. Papot, *J Org Chem*, 2007, **72**, 4262–4264.

7 C. Hedberg, F. J. Dekker, M. Rusch, S. Renner, S. Wetzel, N. Vartak, C. Gerding-Reimers, R. S. Bon, P. I. H. Bastiaens and H. Waldmann, *Angew. Chem. Int. Ed.*, 2011, **50**, 9832–9837.

8 S. Sabesan and R. U. Lemieux, *Can J Chem*, 1984, **62**, 644-654.

9 M. Dowlut, D. G. Hall and O. Hindsgaul, *J Org Chem*, 2005, **70**, 9809–9813.

10 M. A. Probert, J. Zhang and D. R. Bundle, *Carbohydr. Res.*, 1996, **296**, 149-170.

11 S. K. Sarkar and N. Roy, *J Carbohydr Chem*, 2003, **22**, 285–296.

12 S. W. Khan, S. Nayab, M. N. Umar, M. Khan, A. Iqbal, N. Ahmad, H. ur Rashid, M. I. Ali Shah, N. Gulfam, M. Zahoor, R. Ullah and E. A. Ali, *Open Chem*, 2024, **22**, 20230195.

13 B. Sun, A. V. Pukin, G. M. Visser and H. Zuilhof, *Tetrahedron Lett*, 2006, **47**, 7371–7374.

14 H. S. Wootton, S. S. Berry, E. L. Ferguson, C. S. Mahon and G. J. Miller, *Eur. J. Org. Chem.*, 2024, **27,** e202400587.

15 H. Tanaka, Y. Iwata, D. Takahashi, M. Adachi and T. Takahashi, *J Am Chem Soc*, 2005, **127**, 1630–1631.