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Electronic Supplementary Information: Glycosidase Activated Release of Fluorescent 1,8-Naphthalimides Probes for Tumor Cell Imaging from Glycosylated ‘pro-probes’

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General Experimental Procedure

Compounds 18-21 were prepared by glycosylation of the commercially available peracetylated glycosides using 3-chloro-1-propanol as the acceptor and BF$_3$OEt$_2$ as the activator (Scheme S1). Following the glycosylation reaction, the alkyl chloride was treated with sodium azide in DMF at 80 °C to introduce the azido group. Deprotection of the glycosides under Zemplén conditions furnished the desired azido-glycosides 7-10 in good yields.

Scheme S1. Synthesis of compounds 7-10.

The synthesis of 11 involved the formation of the lactosyl bromide 27 from peracetylated lactose on treatment with HBr in AcOH (Scheme S2). Compound 29 was obtained on treatment of 27 with sodium azide, followed by deacetylation.

Scheme S2. Synthesis of compound 29.

The naphthalimide motif was synthesised using conditions described by Peng and co-workers\(^1\) by refluxing naphthalic anhydride with propargylamine in ethanol for 6 h to give 31 in 87% yield (Scheme S3). Reduction of the nitro group was first attempted using Pd/C 10 wt.% under H$_2$ atmosphere, which afforded poor yields. Subsequent attempts using SnCl$_2$ as the reducing agent proved to be successful, furnishing 32 in 86% yield. The glycosylated naphthalimides were synthesised using [Cu(MeCN)$_4$]BF$_4$ as catalyst in a Huisgen 1,3-dipolar cycloaddition. However, purification difficulties resulted in poor yields. Naphthalimides easily form aggregates due to $\pi$-$\pi$ stacking interactions, making compounds that possess different polarity, in this case, the glycosylated naphthalimide vs. the non-glycosylated one, very difficult to separate under normal chromatographic conditions. To circumvent this problem, size exclusion column chromatography was
employed. Compound 5 was prepared from the galactosyl naphthalimide 1 in an enzymatic reaction by stirring with β-galactosidase in phosphate buffered saline (PBS) at 30 °C (Scheme S3) giving 5 quantitatively.

Scheme S3. Synthesis of compounds 1-4, 11 and 5.

For the preparation of the related Amonafide derivative 12, peracetylated galactose was reacted with propargyl alcohol using BF$_3$OEt$_2$ as activator (Scheme S4) followed by deacetylation to obtain 34.

Scheme S4. Synthesis of compound 34.

The modified naphthalimide moiety was synthesised in a similar manner starting from 4-bromo-1,8-naphtalic anhydride and reacting it with N,N-dimethylethlenediamine in ethanol at reflux (Scheme S5). Displacement of the bromide using sodium azide proceeded quantitatively. The click reaction using the same conditions previously described for 1-4 gave 12 in 92% yield. Compound 13 was synthesised in a similar enzymatic reaction for the synthesis of compound 5 to furnish the product in 87% yield (Scheme S5).

**Photophysical Studies**

*General Specifications*

**UV/Vis Measurements**

UV-visible absorption spectra and optical density were recorded by means of a Varian CARY 50 spectrophotometer. Solutions were measured in 3 cm (10 mm x 10 mm) cuvettes. The wavelength range was 200-600 nm with a scan rate of 300 nm min\(^{-1}\). Water used in DNA related work was triply distilled, autoclaved and filtered (Millipore, HV, 0.45 µm). PBS was obtained from Sigma Aldrich. Baseline correction measurements were used for all spectra. The ssDNA was obtained from Sigma Aldrich as its sodium salts and it was stored at –20 °C to prevent bacterial growth. The concentrations of ssDNA were accurately determined using quantification by UV-Vis analysis. The DNA concentration per nucleotide was determined spectrophotometrically using the molar extinction coefficient, 6600 M\(^{-1}\)cm\(^{-1}\) at 260 nm for ssDNA.

**Fluorescence Measurements**

Fluorescence measurements were made with a Varian Carey Eclipse Fluorimeter equipped with a 1.0 cm path length quartz cell. The solvents used were of HPLC grade. The concentrations of the compounds under investigation were the same as those used for the UV-visible absorption measurements.

**Results**

A summary of the absorption properties of compounds 1-5, 11-13, along with their respective molar extinction coefficients (ε) is given in Table S1.
### Table S1. Summary of the absorption parameters of 12(a-e), 13, 20 and 21.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>( \lambda_{\text{max}} ) (nm)</th>
<th>( \pi-\pi^* )</th>
<th>ICT (( \varepsilon ) (M(^{-1}) cm(^{-1})) ± 10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>254</td>
<td>275</td>
<td>433 (6,487)</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>254</td>
<td>274</td>
<td>435 (6,372)</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>254</td>
<td>274</td>
<td>434 (12,232)</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>254</td>
<td>273</td>
<td>433 (12,310)</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>253</td>
<td>273</td>
<td>432 (3,689)</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>254</td>
<td>273</td>
<td>434 (8,778)</td>
</tr>
<tr>
<td>7</td>
<td>12</td>
<td>a</td>
<td>a</td>
<td>347 (19,647)</td>
</tr>
<tr>
<td>8</td>
<td>13</td>
<td>a</td>
<td>a</td>
<td>347 (4,876)</td>
</tr>
</tbody>
</table>

* Data could not be registered.

**Effect of Solvent Polarity on the Photophysical Properties**

As was mentioned in section 1.6, the photophysical properties of naphthalimides are governed by an ICT system, which is highly dependent on the solvent, phenomena known as solvatochromic effect. The large excited dipole moment that arises from the ICT can vary depending on the solvent polarity and its hydrogen-bond donor or acceptor capacity. When polar protic solvents are used, proton exchange of the 4-amino moiety may occur, leading to a less energetic excited state and ICT bands shifted towards the red can be observed, as well as lower fluorescence intensity.

As a representative example, the absorption and emission spectra of 1 and 11 were recorded in different solvents to investigate the effect of solvent polarity and are shown in Fig. S1.
Although the optical density (OD) remains relatively unchanged, higher ε values are obtained for both cases in MeOH solution. A moderate hypsochromic shift (ca. 6-15 nm) is observed for both compounds when less polar solvents are used. Although MeOH and MeCN posses same polarity value, proton exchange from the amino nitrogen cannot occur in MeCN, leading to a blue shift (ca. 7-13 nm).

In contrast to the absorption spectra, a quenching of the fluorescence intensity is observed in aqueous solvents, due to the stabilisation of the ICT. However, the blue-shifted behaviour persists for the more apolar solvents. The absorption properties of 1 and 11 for the different solvents are summarised in Table S2.
Table S2. Variation in the ICT band of the UV/Vis spectra of 1 and 11 in different solvents.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>CHCl₃</th>
<th>MeCN</th>
<th>MeOH</th>
<th>H₂O</th>
<th>PBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>425</td>
<td>418</td>
<td>431</td>
<td>434</td>
<td>433</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>a</td>
<td>427</td>
<td>434</td>
<td>434</td>
<td>433</td>
</tr>
</tbody>
</table>

*Data could not be recorded due to solubility issues.

The fluorescence quantum yields ($\Phi_F$) of emission of compounds 1-5 were measured in PBS at pH 7.2 using fluorescein ($\Phi_F = 0.920$ in 0.1 N NaOH) as the primary reference standard, and are presented in Table S3. The study was carried out using dilute solutions of OD 0.05, at the excitation wavelength of 436 nm, so that corrections for self-absorption and of incident and emitted light on the emission intensities were not required. The spectra were recorded using an excitation slit of 20 nm and emission slit of 1.5 nm and the data was collected in the range of 436 – 700 nm. Therefore, the reference and the test samples solutions with identical absorbance at the same excitation wavelength can be assumed to be absorbing the same number of photons.

Table S3. $\Phi_F$ of compounds 1-5 measured using Fluorescein as a reference standard.

<table>
<thead>
<tr>
<th>Compound</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Phi_F$ (± 10%)</td>
<td>12.7</td>
<td>11.6</td>
<td>13.1</td>
<td>11.5</td>
<td>11.8</td>
<td>11.0</td>
</tr>
</tbody>
</table>

$\Phi_F$ values were calculated by comparing the integrated areas underneath the emission band of the spectra using equation S1. Each measurement was repeated twice; calculated quantum yields, following this method, have an error of approximately 10%.

$$\Phi_F(x) = (\Phi_F)_r \cdot A_x / A_r \cdot F_x / F_r \cdot (\eta_x / \eta_r)^2$$

(S1)

where, $x$, $r$, $A$, $F$ and $\eta$ refer to the test sample, reference standard, absorbance, integrated area and the solvent refraction index, respectively.

$\Phi_F$ of compounds 12 and 13 could not be measured as they do not absorb in the same region as the standard fluorescein.
Fig. S2 Concentration studies of compound 1 (a), and 12 (b), respectively, in 10 mM PBS (pH 7.2). All measurements were carried out at rt.

Having investigated the photophysical properties of the compounds, their ability to probe the enzyme cleavage was next evaluated.

**Enzymatic Activity Evaluation**

The changes in the absorption and emission spectra of 1 and 12 over time after the addition of β-galactosidase were examined. For compound 1, enzymatic hydrolysis did not lead to a significant change in the ICT absorption band or fluorescence emission over time (Fig. S2a and b). Different concentrations of the enzyme (0.01, 0.1 and 1.0 U) were added to the solution, and the same behaviour was observed. However, the treatment of 12 with 0.1 equiv of the enzyme led to a significantly lower fluorescence intensity (Fig. S3c and d).
Fig. S3 Study of β-galactosidase activity with 1 (0.1 mM) and 12 (0.1 mM), respectively. a) and c) UV/Vis absorption and b) and d) fluorescence (\( \lambda_{\text{max}} = 430 \text{ nm} \)) spectra of 1 and 12, respectively. All the measurements were recorded at 37 °C.

**pH evaluation and pKa determination**

A pH titration study was performed to investigate the influence of a change in pH on the photophysical properties of 12 and 13. The maximum absorption band, ICT band, for compounds 12 and 13 is centred at 347 nm. As shown in Figure S4a and c, an increase in pH resulted in a decrease of absorbance for this band. However, a second band appeared at 298 nm above pH 10, and its absorbance increases with pH (Fig. S3a and c). An isosbestic point is present at 314 nm. The emission spectra were recorded exciting at 298, 314 and 347 nm. As shown in Fig. S3c and d, a significant decrease of the fluorescence intensity occurred above pH 8.
Fig. S4 a) and d) Changes in the UV/Vis absorption of compound 12 (0.1 mM) and compound 13 (0.1 mM), respectively. b) and e) plot of maximum absorbance values at 298 nm and 347 nm vs. pH for graphs a) and d), respectively. c) and f) Changes in fluorescence (λ<sub>exc</sub> = 298 nm, 314 nm and 347 nm) spectra of compound 12 (0.1 mM) and compound 13 (0.1 mM), respectively, in PBS with different pH. All measurements were recorded at rt.
From these luminescence changes the pKa values for compounds 12 and 13 were determined in H2O and PBS (Table S4). pKa values were determined using non-linear regression analysis with ReactLab™.

Table S4. pKa values of compounds 12 and 13 measured in H2O and PBS.

<table>
<thead>
<tr>
<th>Compound</th>
<th>12</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td>pKa</td>
<td>H2O</td>
<td>PBS</td>
</tr>
<tr>
<td></td>
<td>11.474 (±0.011)</td>
<td>11.352 (±0.015)</td>
</tr>
</tbody>
</table>

Biological Studies

General Specifications

Cell culture: HeLa, HepG2 and HCT116 cells were grown in Dulbecco’s Modified Eagle Medium (Glutamax) supplemented with 10% fetal bovine serum and 50 µg/ml penicillin/streptomycin at 37°C in a humidified atmosphere of 5% CO2.

Alamar blue viability assay: HeLa cells were seeded at a density of 5x10^3 cells/well in 96-well plates and treated with the indicated compounds for 24h. Alamar blue (20µl) was then added to each well and incubated at 37°C in the dark for 4 h. Plates were then read on a fluorescence plate reader (SpectraMax Gemini, Molecular Devices) with excitation and emission wavelengths of 544nm and 590nm respectively. Experiments were performed in triplicate on three independent days with activity expressed as percentage cell viability compared to vehicle treated controls. All data points (expressed as means ± S.E.M.) were analysed using GRAPHPAD Prism (Graphpad software Inc., San Diego, CA).

Confocal microscopy: Cells were seeded at a density of 1·10^5 cells/dish in glass bottom wells and treated with compounds (0.1 mM) for 3 h in glucose free medium. For enzyme studies, cells were incubated for a further 1.5 h with 0.1 U of enzyme (β-Galactosidase from Aspergillus oryzae ≥8.0 units/mg). Cells were stained with DRAQ5 (red nuclear stain), followed by viewing using Olympus FV1000 confocal microscopy with a 60X oil immersion lens or Leica SP8 STED confocal microscopy with a 40X oil immersion lens. Image analysis was performed using FluoView Version 7.1 Software. Compounds were excited by a 405 nm argon laser, emission 450-550 nm, DRAQ5 was excited by a 633 nm red helium-neon laser, emission >650 nm. Images are representative of three independent experiments. For some images, compounds were excited with a high, 5-fold increase in laser power, to ensure successful imaging of compounds diluted in cell culture medium, this is noted in the text, where appropriate.

Results

Incubation of HeLa cells with compound 1, 2 and 4 (0.1 mM) for 24 h showed that cellular uptake did not occur and thus the compounds remained outside the cells (Fig. S5).
Fig. S5 Incubation of compounds 1, 2 and 4 (0.1 mM) in HeLa cells for 24 h. Compounds were excited with a high laser power.

A 3 h incubation of HeLa cells with compound 1 at varying concentrations, followed by the subsequent addition of the β-galactosidase enzyme (1.0 U) 1.5 h later, showed that the process is not concentration dependent (however, cell uptake of the released naphthalimide is more difficult to image at lower concentration), (Fig S6).

Fig. S6 Incubation of compound 1 at (0.01 mM), (0.05 mM) and (0.1 mM) in HeLa cells for 3 h, first row and β-galactosidase (1.0 U) for 1.5 h, second row.

A 3 h incubation of relevant cells with compound 12 (0.1 mM) followed by the subsequent addition of the β-galactosidase enzyme (1.0 U) 1.5 h later, analogous to assay performed with compound 1, showed that the naphthalimide moiety had entered the cells upon cleavage of the glycosidic linkage by the glycosidase enzyme (Fig. S7).
**Fig. S7** Incubation of 12 (0.1 mM) in the absence a) and presence b) of 1.0 U of β-galactosidase enzyme in three different cell lines.

Compounds 5 and 13 (0.1 mM) were incubated in the different cell lines for 3 h as positive controls (Fig. S8). Compound 5, led to a bright fluorescence inside the cells due to a rapid internalisation.

**Fig. S8** Incubation of different cell lines with a) 5 (0.1 mM) and b) 13 (0.1 mM) for 3 h.

Compounds 1 and 5 were also subjected to an AlamarBlue viability assay and results demonstrated neither compound to not be toxic (Table S5).
**Table S5.** IC50 values in Hela cells, determined via an Alamar blue viability assay.

<table>
<thead>
<tr>
<th>Compound</th>
<th>IC50 value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;100μM</td>
</tr>
<tr>
<td>2</td>
<td>&gt;100μM</td>
</tr>
<tr>
<td>3</td>
<td>&gt;100μM</td>
</tr>
<tr>
<td>4</td>
<td>&gt;100μM</td>
</tr>
<tr>
<td>5</td>
<td>&gt;100μM</td>
</tr>
</tbody>
</table>
Experimental:

**General Specifications**

Unless otherwise stated; all commercial chemicals were obtained from Sigma-Aldrich or Fluka and used without further purification. Deuterated solvents for NMR use were purchased from Apollo. Dry solvents were distilled under Argon and dried over 4 Å molecular sieves prior to use. Solvents for synthesis purposes were used at GPR grade. Analytical TLC was performed using Merck Kieselgel 60 F254 silica gel plates or Polygram Alox N/UV254 aluminium oxide plates. Visualisation was by UV light (254 nm) by molybdenum staining. NMR spectra were recorded on Bruker DPX–400 Advance spectrometers, operating at 400.13 MHz and 600.1 MHz for 1H NMR; 100.6 MHz and 150.9 MHz for 13C-NMR. Shifts are referenced to the internal solvent signals.\(^{[4]}\) NMR data were processed using Maestrenova software. HRMS spectra were measured on a Micromass LCT electrospray TOF instrument with a WATERS 2690 autosampler and methanol/acetonitrile as carrier solvent. Melting points were determined using a Stuart Scientific Melting Point SMP1 apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer Spectrum One FT-IR Spectrometer equipped with a Universal ATR sampling accessory. Carbohydrate positions are named 1 to 6, starting the count in the anomeric position. In the case of the lactose derivatives, the glycosidase are named A and B, A being the closest one to the naphthalimide.

**General Procedure A; Synthesis of 1-4, 11 and 12.**

Compound 6 (1.1 equiv) and tetrakis(acetonitrile)copper(I)tetrabfluoroborate ([(CH\(_3\)NC\(_2\))\(_2\)Cu]BF\(_4\)) (0.15 eq.) were added to a solution of 7-10, 29 or 37 (1 equiv) in DMF (5 mL) in a microwave vial. The reaction mixture was stirred for 1 h at 115 °C in a microwave reactor. The solvent was removed \textit{in vacuo} and the crude product dissolved in a mixture of MeOH/CH\(_2\)Cl\(_2\) (1:2) and filtered through a plug of Celite\textsuperscript{®} to remove the copper catalyst. The filtrate was concentrated \textit{in vacuo} and purified by SiO\(_2\) column chromatography, previously base treated with Et\(_3\)N, using 20-30% MeOH/EtOH (v/v), to afford the corresponding product.

**General Procedure B; Synthesis of 7-10 and 29.**

The corresponding products 22-25 or 28 (1 equiv) were dissolved in MeOH/NaOMe (0.4 equiv). After stirring overnight at rt, activated DOWEX\textsuperscript{®} 50WX8-200 ion exchange resin was added to the mixture until a neutral pH was measured. The reaction mixture was filtered and the filtrate concentrated \textit{in vacuo}. Column chromatography purification yielded the desired product.

**General Procedure C; Synthesis of 18-19**

To a stirred solution of the corresponding peracetylated sugar (1 equiv) and 3-chloro-1-propanol (2 equiv) in anhydrous CH\(_2\)Cl\(_2\), BF\(_3\)Et\(_2\)O (2.5 equiv) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature (rt). After reaction completion the mixture was poured into ice water and stirring continuously until the ice was melted. After phase separation, the water layer was extracted with CH\(_2\)Cl\(_2\) (3 x 100 mL). The combined organic phases were washed with aqueous NaHCO\(_3\) solution (100 mL), brine (100
mL), dried over MgSO₄ and the solvent evaporated in vacuo. Purification of the crude product by SiO₂ column chromatography furnished the product.

**General Procedure D; Synthesis of 22-25**

The corresponding 2,3,4,6-tetra-O-acetyl-1-α-(3-chloropropyl)-β-D-glycopyranoside (1 equiv) was dissolved in DMF (0.05 M) and NaN₃ (4 equiv) was added in one portion. The mixture was stirred for 18 h at 80 °C, allowed to cool and poured into ice water and extracted with EtOAc (3×100 mL). The combined organic layers were washed with water (200 mL) and brine (200 mL), dried over MgSO₄ and concentrated in vacuo. Purification using SiO₂ column chromatography gave the corresponding product.

**N-((1-(3-(β-d-galactopyranosyl)-(1-4)-O-β-d-glucopyranosyloxy)propyl)-1H-1,2,3-triazol-4-yl)methyl)-4-amino-1,8-naphthalimide (1)**

Following general procedure A, 7 (312 mg, 1.20 mmol), 6 (327 mg, 1.30 mmol), [(CH₃CN)₄Cu]BF₄ (66.00 mg, 0.18 mmol) and DMF (15 mL). Compound 1 was obtained as an orange powder (345 mg, 58%).

Rf = 0.13 (25% MeOH/EtOAc)

[α]T = 18.82 deg cm² g⁻¹

δH (400 MHz, CD₃OD): 7.99 (s, 1H, H-10), 7.78 (d, J₁₆,₁₄ = 7.8 Hz, 1H, H-16), 7.71 (d, J₁₄,₁₆ = 7.8 Hz, 1H, H-14), 7.55 (d, J₁₂,₁₃ = 8.4 Hz, 1H, H-12), 7.03 (app. t, 1H, H-15), 6.33 (d, J₁₃,₁₂ = 8.4 Hz, 1H, H-13), 5.16 – 5.06 (m, 2H, H-11, H-11’), 4.57 (t, J₉,₈ = 6.7 Hz, 2H, H-9, H-9’), 4.05 (d, J₁₁,₁₂ = 8.4 Hz, 1H, H-1), 3.92 – 3.84 (m, 1H, H-6), 3.73 (d, J₄,₃ = 3.5 Hz, 1H, H-4), 3.70 - 3.53 (m, 3H, H-2, H-8, H-8’), 3.30 – 3.25 (m, 1H, H-5), 3.20 (dd, J₃,₂ = 9.9 Hz, J₃,₄ = 3.5 Hz, 1H, H-3), 2.24 - 2.24 (m, 2H, H-7, H-7’).

δC (100 MHz, CD₃OD): 165.8 (CO), 164.8 (CO), 153.4 (q, Ar-C), 144.6 (q, Ar-C), 135.2 (C-12), 132.5 (C-16), 129.9 (C-15), 129.6, 126.1 (C-10), 124.9 (C-14), 120.8, 119.4, 109.8, 107.9 (C-13), 104.0 (C-1), 75.9 (C-5), 73.5 (C-3), 71.6 (C-2), 69.4 (C-6), 67.2 (C-4), 61.7 (C-7), 47.9 (C-9), 35.6 (C-11), 30.4 (C-8).

νmax (ATR)/cm⁻¹: 1045 (C-N), 1409 (N=N), 1559 (ar. C-C), 1656 (C=O), 3363 (OH/NH₂).


**N-((1-(3-(β-d-glucopyranosyl)propyl)-1H-1,2,3-triazol-4-yl)methyl)-4-amino-1,8-naphthalimide (2):**

Following general procedure A, 8 (60.00 mg, 0.23 mmol), 6 (62.50 mg, 0.25 mmol), [(CH₃CN)₄Cu]BF₄ (13.00 mg, 0.03 mmol) and DMF (5 mL). An orange powder was obtained (108 mg, 91%).

Rf = 0.14 (25% MeOH/EtOAc)

[α]T = 46.20 deg cm² g⁻¹
δ_H (600 MHz, D_2O): 7.99 (s, 1H, H-10), 7.52 (d, _J_{16,14} = 7.1 Hz, 1H, H-16), 7.44 (d, _J_{14,16} = 7.1 Hz, 1H, H-14), 7.32 (d, _J_{12,13} = 8.2 Hz, 1H, H-12), 6.77 (app. t, 1H, H-15), 6.10 (d, _J_{13,12} = 8.2 Hz, 1H, H-13), 5.00 (s, 2H, H-11), 4.58 (t, _J_{9,8} = 7.26 Hz, 2H, H-9, H-9'), 4.32 (d, _J_{1,2} = 7.9 Hz, 1H, H-1), 3.92 -3.88 (m, 1H, H-8), 3.82 – 3.79 (m, 1H, H-6), 3.65 – 3.62 (m, 1H, H-6'), 3.59 – 3.55 (m, 1H, H-8'), 3.38 - 3.23 (m, 4H, H-2, H-3, H-4, H-5), 2.26 – 2.19 (m, 2H, H-7, H-7').

δ_C (150 MHz, D_2O): 163.9 (CO), 162.8 (CO), 151.6 (1, Ar-C), 142.9 (q, Ar-C), 133.8 (C-16), 130.9 (C-12), 128.7 (C-14), 125.3 (C-10), 123.3 (C-15), 117.4, 108.4 (C-13), 106.2, 101.7 (C-1), 75.9, 72.9, 69.6, 66.0 (C-8), 60.4 (C-6), 46.9 (C-9), 34.54 (C-11), 29.7 (C-7).

ν_max (ATR)/cm^-1: 1033 (C-N), 1379 (N=N), 1584 (ar. C-C), 1672 (C=O), 3371 (OH/NH_2).

HRMS (m/z – ESI): Found: 514.1946, ([M+H]^+·C_{24}H_{28}N_{5}O_{8}, Required: 514.1938).

N-((1-(3-(β-d-galactopyranosyl)-(1-4)-O-β-d-glucopyranosyloxy)propyl)-1H-1,2,3-triazol-4-yl)methyl)-4-amino-1,8-naphthalimide (3)

Following general procedure A, 9 (110.00 mg, 0.15 mmol), 6 (42.00 mg, 0.17 mmol), [(CH_3CN)_4Cu]BF_4 (8.40 mg, 0.02 mmol) and DMF (5 mL). Orange powder precipitated (68.00 mg, 67%).

R_f = 0.12 (50%MeOH/EtOAc)

[α]_T = 36.1336 deg cm^2 g^-1

δ_H (600 MHz, CD_3OD): 8.56 (dd, _J_{16,15} = 7.2 Hz, _J_{16,14} = 1.1 Hz, 1H, H-16), 8.52 (dd, _J_{14,15} = 8.4 Hz, 1H, H-14), 8.31 (d, _J_{12,13} = 8.4 Hz, 1H, H-12), 7.99 (s, 1H, H-10), 7.66 (dd, _J_{15,14} = 8.4 Hz, 1H, H-15), 6.90 (d, _J_{13,12} = 8.4 Hz, 1H, H-13), 5.43 (s, 2H, H-11, H-11'), 4.52 (t, _J_{9,8} = 6.6 Hz, 2H, H-9, H-9'), 4.36 (d, _J_{9b,8} = 7.6 Hz, 1H, H-1a), 4.16 (d, _J_{1b,2b} = 7.7 Hz, 1H, H-1b), 3.91 – 3.78 (m, 5H), 3.73 (dd, _J = 11.4, 4.7 Hz, 1H), 3.64 – 3.54 (m, 2H), 3.55 – 3.48 (m, 2H), 3.22 (dd, _J = 9.3, 7.7 Hz, 1H), 3.11 (q, _J = 7.3 Hz, 2H), 2.17 – 2.11 (m, 2H, H-7, H-7').

δ_C (150 MHz, CD_3OD): 134.4 (C-16), 131.33 (C-Ar), 129.00 (C-Ar), 128.7 (C-13), 124.1 (C-10), 123.8 (C-Ar), 103.9 (C-1a), 102.7 (C-1b), 79.0, 77.9, 75.5, 73.3, 71.0, 68.7, 65.3, 60.3, 46.9 (C-9), 29.1 (C-7).

ν_max (ATR)/cm^-1: 1014 (C-N), 1407 (N=N), 1518 (ar. C-C), 1660 (C=O), 3257 (OH/NH_2).

HRMS (m/z - ESI): Found: 698.2290, ([M+Na]^+·C_{30}H_{37}N_{5}O_{13}Na, Required: 698.2286).

N-((1-(3-(α-d-mannopyranosyloxy)propyl)-1H-1,2,3-triazol-4-yl)methyl)-4-amino-1,8-naphthalimide (4)

Following general procedure A, 10 (50.00 mg, 0.18 mmol), 6 (51.20 mg, 0.20 mmol), [(CH_3CN)_4Cu]BF_4 (10.00 mg, 0.03 mmol) and DMF (5 mL). Product 4 afforded as an orange powder (75.00 mg, 78%).

R_f = 0.12 (10% MeOH/EtOAc)
$\alpha_l T = 143.7371 \text{ deg cm}^2 \text{ g}^{-1}$

$\delta_H$ (600 MHz, CD$_2$OD): 8.49 (dd, $J_{16,15} = 7.3$ Hz, $J_{16,15} = 1.2$ Hz, 1H, H-16), 8.45 (dd, $J_{14,15} = 8.4$ Hz, $J_{14,16} = 1.2$ Hz, 1H, H-14), 8.24 (d, $J_{12,13} = 8.4$ Hz, 1H, H-12), 7.84 (s, 1H, H-10), 7.58 (dd, $J_{15,14} = 8.4$ Hz, $J_{15,16} = 7.3$ Hz, 1H, H-15), 6.82 (d, $J_{13,12} = 8.4$ Hz, 1H, H-13), 5.36 (s, 2H, H-11, H-11'), 4.42 (d, $J_{1,2} = 2.0$ Hz, 1H, H-1), 4.40 (td, $J = 6.9, 3.0$ Hz, 2H, H-9, H-9'), 3.76 – 3.66 (m, 3H, H-6, H-8, H-3), 3.64 – 3.57 (m, 2H, H-6', H-2), 3.52 (app. t, 1H, H-4), 3.45 – 3.39 (m, 2H, H-8', H-5), 2.14 – 2.05 (m, 2H, H-7, H-7').

$\delta_C$ (150 MHz, CD$_2$OD): 133.2 (C-16), 131.2 (C-12), 128.8 (C-13), 124.7 (C-10), 124.0 (C-15), 108.4 (C-14), 99.9 (C-1), 70.3, 69.6, 66.7, 64.7 (C-6), 60.7 (C-8), 48.7, 47.9 (C-9), 34.6 (C-11), 28.8 (C-7).

$\nu_{\text{max}}$ (ATR)/cm$^{-1}$: 1534 (ar. C-C), 1636 (C=O), 2490, 3352 (OH/NH$_2$).

HRMS ($m/z$ - ESI): Found: 352.1401, ([M+H]$^+$, C$_{18}$H$_{18}$N$_5$O$_3$, Required: 352.1404).

**N-(3'-propanol)-1H-1,2,3-triazol-4-yl)methyl)-4-amino-1,8-naphthalimide** (5)

Compound 1 (55.00 mg, 0.11 mmol, 1.00 equiv) was dissolved in 5 mL of NaOAc buffer (10 mM, pH = 5) and a solution of galactosidase enzyme (2 mL, 1.4 g/L, 0.01 U) in NaOAc buffer (10 mM, pH = 5) was added. The reaction was stirred at 30 °C overnight. Solvent was evaporated in vacuo and product purified using SiO$_2$ chromatography column (4% MeOH/EtOAc, v/v).

Compound 5 was obtained as an orange powder (29 mg, 99%).

$R_f = 0.6$ (10% MeOH/EtOAc)

$\delta_H$ (400 MHz, CD$_2$OD): 8.56 (dd, $J_{10,9} = 7.3$ Hz, $J_{10,8} = 1.1$ Hz, 1H, H-10), 8.53 (dd, $J_{8,9} = 8.2$ Hz, $J_{8,10} = 1.1$ Hz, 1H, H-8), 8.32 (d, $J_{6,7} = 8.4$ Hz, 1H, H-6), 7.91 (s, 1H, H-4), 7.66 (app. t, 1H, H-9), 6.90 (d, $J_{7,6} = 8.4$ Hz, 1H, H-7), 5.43 (s, 2H, H-5, H-5'), 4.46 (t, $J_{3,2} = 7.0$ Hz, 2H, H-3), 3.54 (t, $J_{1,2} = 6.1$ Hz, 2H, H-1), 2.12 – 2.03 (m, 2H, H-2).

$\delta_C$ (100 MHz, CD$_2$OD): 166.0 (CO), 165.4 (CO), 154.8 (q, Ar-C), 145.5 (q, Ar-C), 135.8 (C-6), 132.8 (C-10), 130.43 (C-8), 125.28 (C-9), 124.9 (C-4), 123.4 (q, Ar-C), 121.2 (q, Ar-C), 109.7 (C-7), 59.3 (C-1), 49.0 (C-3), 35.9 (C-5), 33.9 (C-2).

$\nu_{\text{max}}$ (ATR)/cm$^{-1}$: 1033 (C-N), 1260 (N=N), 1660 (C=O), 3248 (OH/NH$_2$).

HRMS ($m/z$ - ESI): Found: 352.1401, ([M+H]$^+$, C$_{18}$H$_{18}$N$_5$O$_3$, Required: 352.1404).

**N-Propargyl-4-amino-1,8-naphthalimide** (6) [1]

A solution of SnCl$_2$ (4.77 g, 25.6 mmol, 7.00 equiv) in HCl (10 mL) was carefully added to a stirred suspension of 31 (1.00 g, 3.60 mmol, 1.00 equiv) in EtOH (40 mL). The reaction mixture was stirred for 2 h at rt and quenched with an aqueous solution containing 10% NaHCO$_3$ (150 mL). The mixture was filtered and the collected solids given into CH$_2$Cl$_2$ (500 mL). Filtration followed by washing the residue with CH$_2$Cl$_2$ (200 mL) and drying off the residue in vacuo afforded the product 6 as orange powder (895 mg, 86%).

$R_f = 0.33$ (50% EtOAc/Hex)
HRMS (m/z - ESI): Found: 249.0661 (M-Na). C_{15}H_{11}N_2O_2 Required: 249.0664.

1-O-(3-azidopropyl)-β-d-galactopyranoside (7) \textsuperscript{\textsuperscript{[10]}}

Following general procedure B, 22 (1.15 g, 2.66 mmol) and NaOMe (72.00 mg, 1.33 mmol) and MeOH (60 mL). Purification using 10% MeOH/EtOAc (v/v) gave 7 as a colourless oil (625 mg, 90%).

\[ \delta_H(400\ MHz,\ DMSO):\ 8.64\ (d,\ J_{8,6} = 7.3\ Hz,\ 1H,\ H-8),\ 8.45\ (d,\ J_{6,8} = 7.3\ Hz,\ 1H,\ H-8),\ 8.21\ (d,\ J_{4,5} = 8.4\ Hz,\ 1H,\ H-4),\ 7.67\ (app.\ t,\ 1H,\ H-7),\ 7.53\ (br.\ s,\ 2H,\ NH_2),\ 6.85\ (d,\ J_{5,4} = 8.4\ Hz,\ 1H,\ H-5),\ 4.73\ (d,\ J_{3,1} = 2.4\ Hz,\ 2H,\ H-3),\ 3.06\ (t,\ J_{1,3} = 2.4\ Hz,\ 1H,\ H-1). \]

HRMS (m/z - ESI): Found: 286.1015, (\[M+Na\]^+. C_{9}H_{17}N_{3}O_{6}Na, Requires: 286.015).

1-O-(3-azidopropyl)-β-d-glucopyranoside (8) \textsuperscript{\textsuperscript{[11]}}

Following general procedure B, 23 (1.36 g, 3 mmol), NaOMe (72 mg, 1.33 mmol) and MeOH (50 mL). The product was recrystallised from hexane yielding a colourless oil (524 mg, 67%).

\[ \delta_H(400\ MHz,\ CD_3OD):\ 4.48\ (d,\ J = 8.7\ Hz,\ 1H,\ H-1),\ 4.30\ (d,\ J = 7.5\ Hz,\ 1H),\ 3.86\ (dd,\ J = 12.3, 4.0\ Hz,\ 1H),\ 3.77\ –\ 3.73\ (m,\ 1H),\ 3.73\ –\ 3.69\ (m,\ 1H),\ 3.64\ (dd,\ J = 11.4, 4.0\ Hz,\ 1H),\ 3.57\ –\ 3.39\ (m,\ 6H). \]

HRMS (m/z - ESI): Found: 262.1049, ([M-H]^-. C_{9}H_{16}N_{3}O_{6}, Requires: 262.1039).

3-Azidopropyl(β-O-d-galactopyranosyl)-(1-4)-O-β-d-glucopyranoside (9) \textsuperscript{\textsuperscript{[12]}}

Following general procedure B, compound 24 (0.27 g, 0.37 mmol), NaOMe (30 mg, 0.15 mmol) and MeOH (50 mL). Solvent removal affords compound 9 (158 mg, quantitative) as a white foam.

\[ \delta_H(600\ MHz,\ CD_3OD):\ 4.36\ (d,\ J = 7.7\ Hz,\ 1H,\ H-1b),\ 4.28\ (d,\ J = 7.8\ Hz,\ 1H,\ H-1a),\ 3.98\ –\ 3.92\ (m,\ 1H,\ H-6a),\ 3.92\ –\ 3.87\ (m,\ 1H,\ H-6b),\ 3.86\ –\ 3.75\ (m,\ 3H,\ H-6'b,\ H-7,\ H-7'),\ 3.69\ (dd,\ J = 4.6\ Hz,\ J = 11.3\ Hz,\ 1H,\ H-4b),\ 3.76\ –\ 3.62\ (m,\ H-6'a),\ 3.60\ –\ 3.38\ (m,\ 7H,\ H-3a,\ H-4a,\ H-2b,\ H-3b,\ H-5b,\ H-9,\ H-9'),\ 3.24\ (app.\ t,\ 1H,\ H-2a),\ 1.89\ -1.84\ (m,\ 2H,\ H-8,\ H-8'). \]

HRMS (m/z - ESI): Found: 424.1560, ([M-Na]^-. C_{15}H_{28}N_{3}O_{11}, Requires: 424.1567).
1-O-(3-azidopropyl)-α-d-mannopyranoside (10)\(^5\)

Following general procedure B, 25 (423 mg, 0.98 mmol), NaOMe (21.60 mg, 0.40 mmol) and MeOH (40 mL). Purification using 10\% MeOH/EtOAc (v/v) yielded to a colourless oil (220 mg, 85\%). 

\[ R_f = 0.48 \text{ (70\% Hex/EtOAc)} \]

\[ \delta_H (400 MHz, D_2O): 4.87 (d, J = 2.3 Hz, 1H, H-1), 3.98 – 3.94 (m, 1H, H-2), 3.93 – 3.72 (m, 4H, H-6, H-6', H-7, H-7'), 3.70 – 3.57 (m, 3H, H-3, H-4, H-5), 3.50 – 3.41 (m, 2H, H-9, H-9'), 1.99 – 1.84 (m, 2H, H-8, H-8'). \]


N-((1-(β-d-galactopyranosyl)-(1-4)-O-β-d-glucopyranosyloxy)-1H-1,2,3-triazol-4-yl)methyl)-4-amino-1,8-naphthalimide (11)

Following general procedure A, 29 (55.00 mg, 0.15 mmol), 6 (42.00 mg, 0.17 mmol), [(CH\(_3\)CN)\(_4\)Cu]BF\(_4\) (8.40 mg, 0.02 mmol) and DMF (5 mL). Compound 12 obtained as an orange powder (80 mg, 87\%).

\[ R_f = 0.07 \text{ (50\% MeOH/EtOAc, base treated with Et}_3N\).} \]

\[ \delta_H (400 MHz, D_2O): 8.27 (s, 1H, H-7), 7.60 (d, J_{13,11} = 7.1 Hz, 1H, H-13), 7.42 (d, J_{11,13} = 7.1 Hz, 1H, H-11), 7.37 (d, J_{9,10} = 8.4 Hz, 1H, H-9), 6.79 (br. s, 1H, H-12), 6.07 (d, J_{10,9} = 8.4 Hz, 1H, H-10), 5.84 (d, J_{1a,2a} = 9.2 Hz, 1H, H-1a), 5.08 (s, 2H, H-3), 4.53 (d, J_{1b,2b} = 7.8 Hz, 1H, H-1b), 4.12 (app. t, 1H), 3.99 – 3.85 (m, 4H), 3.84 – 3.74 (m, 2H), 3.73 – 3.66 (m, 1H), 3.60 (dd, J = 9.9, 7.7 Hz, 1H), 3.32 – 3.25 (m, 1H), 3.23 – 3.16 (m, 1H), 1.34 - 1.25 (m, 1H).

\[ \delta_C (100 MHz, D_2O): 164.4 (CO), 163.5 (CO), 151.1 (q, Ar-C), 133.9 (C-9), 131.4 (C-13), 126.9 (C-11), 124.4 (C-7), 122.3 (C-12), 118.0 (q, Ar-C), 109.3 (C-10), 108.5 (q, Ar-C), 102.4 (C-1), 86.9 (C-1'), 77.2, 76.8, 74.9, 72.0, 71.5, 68.1, 67.4, 59.3, 48.3, 36.4, 30.8. \]

\[ \nu_{max} \text{(ATR)/cm}^{-1}: 1033 \text{ (C-N)}, 1422 \text{ (N=N)}, 1575 \text{ (ar-C)}, 2854, 2924. \]

HRMS (m/z - ESI): Found: 618.2043, ([M+H] + \(C_{27}H_{32}N_5O_{12}\); Required: 618.2047).

N-(2-(dimethylamino)ethyl)-4-(5-((β-d-glucopyranosyl)methyl)-1H-1,2,3-triazol-5-yl) 1,8-naphthalimide (12)

Following general procedure A, 34 (70.00 mg, 0.22 mmol) 37 (100.50 mg, 0.26 mmol), [(CH\(_3\)CN)\(_4\)Cu]BF\(_4\) (10.00 mg, 0.02 mmol) and DMF (15 mL). Compound 12 obtained as an orange powder (34 mg, 29\%).

\[ R_f = 0.22 \text{ (MeOH).} \]

\[ [\alpha]_T = 21.08 \text{ deg cm}^2 \text{ g}^{-1} \]

\[ 20 \]
\[ \delta_H \text{(400 MHz, CD}_{3}\text{OD): } 8.74 \text{ (d, } J_{10,9} = 7.8 \text{ Hz, } 1H, \text{-H-10), } 8.71 \text{ (dd, } J_{11,12} = 7.3 \text{ Hz, } J_{11,13} = 1.1 \text{ Hz, } 1H, \text{-H-11), } 8.64 \text{ (s, } 1H, \text{-H-8), } 8.26 \text{ (dd, } J_{13,12} = 8.6 \text{ Hz, } J_{13,11} = 1.1 \text{ Hz, } 1H, \text{-H-13), } 8.03 \text{ (d, } J_{9,10} = 7.8 \text{ Hz, } 1H, \text{-H-9), } 7.95 \text{ (dd, } J_{12,13} = 8.6 \text{ Hz, } J_{13,11} = 7.3 \text{ Hz, } 1H, \text{-H-12), } 5.17 \text{ (d, } J_{7,7'} = 12.7 \text{ Hz, } 1H, \text{-H-7), } 5.03 \text{ (d, } J_{7,7'} = 12.7 \text{ Hz, } 1H, \text{-H-7'}, 4.48 \text{ (d, } J_{1,2} = 7.6 \text{ Hz, } 1H, \text{-H-1), } 4.39 \text{ (t, } J_{14,15} = 6.8 \text{ Hz, } 2H, \text{-H-14), } 3.86 \text{ (dd, } J_{4,3} = 3.3 \text{ Hz, } J_{4,5} = 1.0 \text{ Hz, } 1H, \text{-H-4), } 3.87 \text{ – 3.74 (m, } 2H, \text{-H-6, H-6'), } 3.66 \text{ – 3.59 (m, } 2H, \text{-H-2, H-5), } 3.53 \text{ (dd, } J_{3,2} = 9.7 \text{ Hz, } J_{3,4} = 3.3 \text{ Hz, } 1H, \text{-H-3), } 2.77 \text{ (t, } J_{15,14} = 6.8 \text{ Hz, } 2H, \text{-H-15), } 2.40 \text{ (s, } 6H, \text{-H-16).}
\]

\[ \delta_C \text{(100 MHz, CD}_{3}\text{OD): } 146.9 \text{ (CO), } 139.5 \text{ (CO), } 132.9 \text{ (C-11), } 131.7 \text{ (C-10), } 130.5 \text{ (C-13), } 129.8 \text{ (C-12), } 128.0 \text{ (C-8), } 125.3 \text{ (C-9), } 104.6 \text{ (C-1), } 76.9 \text{ (C-2 or C-5), } 74.9 \text{ (C-3), } 72.5 \text{ (C-2 or C-5), } 70.4 \text{ (C-4), } 65.2 \text{ (C-7), } 57.7 \text{ (C-15), } 45.8 \text{ (C-16), } 38.9 \text{ (C-14).}
\]

\[ \nu_{\text{max}} \text{(ATR)/}\text{cm}^{-1}: 1047 \text{ (C-N), } 1435 \text{ (N=N), } 1589 \text{ (ar. C-C), } 1655 \text{ (C=O), } 2496, 3368 \text{ (OH/NH}_2\text{).}
\]

HRMS (m/z - ESI): Found: 528.2092, ([M+H]+, C_{25}H_{30}N_{5}O_{8}, Required: 528.2094).

\[ N-(2'-(dimethylamino)ethyl)-4-(4'-hydroxymethyl)-1''',2''',3'''-triazol-1''-yl)-1,8-naphthalimide (13)
\]

Compound 12 (45.00 mg, 0.08 mmol, 1 equiv) was dissolved in 5 mL of NaOAc buffer (10 mM, pH = 5) and galactosidase enzyme (1 mg, 8 u/mg, 0.01 U) was added. The reaction was stirred at 30 °C overnight. Solvent was evaporated in vacuo and product purified by SiO\textsubscript{2} chromatography column using 15% MeOH/EtOAc (v/v). Compound 13 was obtained as an orange powder (27.0 mg, 87%).

\[ R_f = 0.33 \text{ (MeOH)}
\]

\[ \delta_H \text{(400 MHz, CD}_{3}\text{OD): } 8.76 \text{ (d, } J_{5,4} = 7.8 \text{ Hz, } 1H, \text{-H-5), } 8.73 \text{ (dd, } J_{6,7} = 7.3 \text{ Hz, } J_{6,8} = 1.0 \text{ Hz, } 1H, \text{-H-6), } 8.51 \text{ (s, } 1H, \text{-H-9), } 8.26 \text{ (dd, } J_{8,7} = 8.6 \text{ Hz, } J_{8,6} = 1.0 \text{ Hz, } 1H, \text{-H-8), } 8.04 \text{ (d, } J_{4,5} = 7.8 \text{ Hz, } 1H, \text{-H-4), } 7.95 \text{ (dd, } J_{7,8} = 8.6 \text{ Hz, } J_{7,6} = 7.3 \text{ Hz, } 1H, \text{-H-7), } 4.89 \text{ (br. s, } 2H, \text{-H-10, H-10'), } 4.45 \text{ (t, } J_{3,2} = 6.6 \text{ Hz, } 2H, \text{-H-3), } 3.00 \text{ (t, } J_{2,3} = 6.6 \text{ Hz, } 2H, \text{-H-2), } 2.58 \text{ (s, } 6H).
\]

\[ \delta_C \text{(150 MHz, CD}_{3}\text{OD): } 165.5 \text{ (CO), } 164.9 \text{ (CO), } 149.9 \text{ (q, Ar-C), } 139.8 \text{ (q, Ar-C), } 133.2 \text{ (C-6), } 131.9 \text{ (C-5), } 130.7 \text{ (C-8), } 129.8 \text{ (C-7), } 128.0 \text{ (q, Ar-C), } 126.7 \text{ (C-9), } 125.3 \text{ (C-4), } 124.2 \text{ (q, Ar-C), } 57.6 \text{ (C-10), } 56.5 \text{ (C-2), } 45.0 \text{ (C-1), } 37.9 \text{ (C-3).}
\]

\[ \nu_{\text{max}} \text{(ATR)/}\text{cm}^{-1}: 949.9, 1010 \text{ (C-N), } 1638 \text{ (C=O), } 3360 \text{ (OH/NH}_2\text{).}
\]

HRMS (m/z - ESI): Found: 366.1563, ([M+H]+, C_{19}H_{20}N_{5}O_{3}, Required: 366.1566).

\[ 2,3,4,6-Tetra-O-acetyl-1-O-(3-chloropropyl)-\beta-D-galactopyranoside (18) [5]
\]

Following general procedure C, 1,2,3,4,6-penta-O-acetyl-\beta-D-galactose (4.00 g, 10.24 mmol), 3-chloro-1-propanol (1.72 mL, 20.48 mmol), BF\textsubscript{3}·Et\textsubscript{2}O (3.16 mL, 25.60 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (40 mL). Reaction time; 72 h. Purification using 17% EtOAc/Hexane (v/v) afforded 18 as pale yellow oil (1.40 g, 32%).

\[ R_f = 0.58 \text{ (40% } \text{CH}_2\text{Cl}_2/\text{Hexane)}
\]
δ_H (400 MHz, CDCl₃): 5.38 (d, J₃,₄ = 3.3 Hz, 1H, H-3), 5.22 – 5.12 (m, 1H, H-2), 5.01 (dd, J₄,₅ = 10.4 Hz, J₃,₄ = 3.3 Hz, 1H, H-4), 4.46 (d, J₁,₂ = 7.9 Hz, 1H, H-1), 4.23 – 4.05 (m, 2H, H-6, H-6’), 4.03 – 3.94 (m, 1H, H-7), 3.91 (app. t, 1H, H-5), 3.74 – 3.63 (m, 1H, H-7’), 3.60 (dd, J = 6.8, 5.5 Hz, 2H, H-9, H-9’), 2.14 (s, 3H, OCOCH₃), 2.08 (m, 2H, H-8, H-8’), 2.06, 2.04, 1.97 (s, 9H, OCOCH₃).


2,3,4,6-Tetra-O-acetyl-1-O-(3-chloropropyl)-β-D-glucopyranoside (19)[6]

Following procedure C, 1,2,3,4,6-penta-O-acetyl-β-D-glucose (4.00 g, 10.24 mmol), 3-chloro-1-propanol (1.72 mL, 20.48 mmol), BF₃·Et₂O (6.29 mL, 50.00 mmol, 5 equiv) in CH₂Cl₂ (50 mL). Reaction time: 14 h. Purification using 17% EtOAc/Hexane (v/v) afforded 19 as pale yellow oil (1.29 g, 30%).

R_f = 0.62 (40% EtOAc/Hexane)

δ_H (600 MHz, CDCl₃): 5.07 (app. t, 1H, H-3), 4.92 (app. t, 1H, H-4), 4.82 (dd, J = 9.8 Hz, J₂,₁ = 8.0 Hz, 1H, H-2), 4.40 (d, J₁,₂ = 8.0 Hz, 1H, H-1), 4.13 (dd, J = 12.3, 4.9 Hz, 1H, H-6), 4.02 – 3.95 (m, 2H, H-6’, H-5), 3.90 – 3.77 (m, 2H, H-7, H-7’), 3.64 – 3.52 (m, 2H, H-9, H-9’), 3.51 – 3.41 (m, 2H, H-8, H-8’), 1.93, 1.91, 1.88, 1.85 (4 s, 12H, OCOCH₃).


3-chloropropyl 4-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (20)[7]

Following procedure C, 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (4.00 g, 5.90 mmol) dissolved in CH₂Cl₂ (50 mL), BF₃·Et₂O (1.80 mL, 14.75 mmol) was added at 0 °C. Reaction time: 3 days. Purification using 37% EtOAc/Hexane (v/v) a colourless oil (1.25 g, 30%).

R_f = 0.6 (60% EtOAc/Hex).

δ_H (400 MHz, CDCl₃): 5.34 (d, J₃ = 3.3 Hz, 1H, H-4b), 5.19 (app. t, 1H, H-3a), 5.10 (app. t, 1H, H-2b), 4.95 (dd, J = 8.0 Hz, J = 10.4 Hz, 1H, H-2b), 4.88 (app. t, 1H, H-2a), 4.44 - 4.52 (m, 3H, H-1a, H-1b, H-6b), 4.05 – 4.15 (m, 3H, H-6a, H-5b, H-6’b), 3.92 – 3.99 (m, 1H, H-6’a), 3.87 (app. t, 1H, H-5a), 3.79 (app. t, 1H, H-4a), 3.64 – 3.72 (m, 1H, H-7), 3.56 – 3.64 (m, 3H, H-7’, H-9, H-9’), 2.15, 2.12, 2.06, 2.05, 2.05, 2.04, 1.96 (s, 3H, OCOCH₃), 1.26 (app. t, 2H, H-8, H-8’).


2,3,4,6-Tetra-O-acetyl-1-O-(3-chloropropyl)-α-D-mannopyranoside (21)[5]

Following procedure C, 1,2,3,4,6-penta-O-acetyl-α-D-mannose (6.00 g, 15.30 mmol), 3-chloro-1-propanol (6.40 mL, 76.70 mmol, 5 equiv), BF₃·Et₂O (13.16 mL, 107.10 mmol, 7 equiv) in dry CH₂Cl₂ (50 mL). Reaction time: 14 h.
Purification using 27% EtOAc/Hexane (v/v) afforded 21 as pale yellow oil (2.90 g, 45%).

R$_f$ = 0.68 (60% EtOAc/Hexane)

δ (400 MHz, CDCl$_3$): 5.31 – 5.27 (m, 2H, H-3, H-4), 5.26 – 5.24 (m, 1H, H-2), 4.82 (d, $J_{1, 2} = 1.7$ Hz, 1H, H-1), 4.28 (dd, $J = 12.2, 5.4$ Hz, 1H, H-6), 4.16 – 4.09 (m, 2H, H-6' and H-5), 4.02 – 3.97 (m, 1H, H-7), 3.94 – 3.88 (m, 2H, H-8, H-8'), 3.69 – 3.64 (m, 1H, H-7'), 3.63 – 3.55 (m, 2H, H-9 and H-9'), 2.16, 2.10, 2.05, 1.99 (s, 3H, OCOCH$_3$).

HRMS (m/z - ESI): Found: 447.1030, ([M+Na]$^+$). C$_{17}$H$_{25}$O$_{10}$NaCl, Required: 447.1034.

2,3,4,6-Tetra-O-acetyl-1-O-(3-azidopropyl)-β-D-galactopyranoside (22)

Following procedure D, 18 (1.37 g, 3.23 mmol) and NaN$_3$ (800 mg, 12.27 mmol) and DMF (50 mL). Purification using 17% EtOAc/Hexane (v/v) gave the product as pale yellow oil (1.15 g, 83%).

R$_f$ = 0.40 (40% EtOAc/Hexane)

δ (400 MHz, CDCl$_3$): 5.38 (d, $J_{4, 3} = 3.3$ Hz, 1H, H-4), 5.19 (dd, $J_{2, 3} = 10.5$ Hz, $J_{2, 1} = 8.0$ Hz, 1H, H-2), 5.01 (dd, $J_{3, 2} = 10.5$ Hz, $J_{3, 4} = 3.3$ Hz, 1H, H-3), 4.46 (d, $J_{1, 2} = 8.0$ Hz, 1H, H-1), 4.08 – 4.21 (m, 2H, H-6, H-6'), 4.00 – 3.88 (m, 2H, H-7, H-5), 3.63 – 3.56 (m, 1H, H-7'), 3.41 – 3.32 (m, 2H, H-9, H-9'), 2.14, 2.06, 2.04, 1.98, 1.95 – 1.76 (m, 2H, H-8, H-8').


2,3,4,6-Tetra-O-acetyl-1-O-(3-azidopropyl)-β-D-glucopyranoside (23)

Following general procedure D, 19 (1.29 g, 3.04 mmol) and NaN$_3$ (790 mg, 12.2 mmol) and DMF (50 mL). Solvent evaporation gave the product as colourless oil (1.35 g, 99%).

R$_f$ = 0.31 (40% EtOAc/Hexane)

δ (400 MHz, CDCl$_3$): 5.11 (app. t, 1H, H-3), 4.97 (app. t, 1H, H-4), 4.88 (dd, $J = 9.6$ Hz, $J_{2, 1} = 8.0$ Hz, 1H, H-2), 4.43 (d, $J_{1, 2} = 8.0$ Hz, 1H, H-1), 4.16 (dd, $J = 12.3, 4.8$ Hz, 1H, H-6), 4.04 (dd, $J = 12.3, 2.5$ Hz, 1H, H-6'), 3.88 – 3.82 (m, 2H, H-6, H-6'), 3.66 – 3.60 (m, 1H, H-7), 3.57 – 3.48 (m, 1H, H-7'), 3.30 – 3.24 (m, 2H, H-8, H-8'), 1.98, 1.95, 1.92, 1.90 (s, 3H, OCOCH$_3$), 1.78-1.70 (m, 2H, H-7, H-7').

HRMS (m/z-ESI): Found: 454.1444, ([M+Na]$^+$). C$_{17}$H$_{25}$N$_3$O$_{10}$Na, Required: 454.1438.

3-Azidopropyl-4-O-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (24)

Following general procedure D, 20 (290 mg, 0.40 mmol) and NaN$_3$ (104 mg, 1.60 mmol) in DMF (20 mL). Purification using 35% EtOAc/Hexane (v/v) afforded 24 as a pale yellow oil (270 g, 95%).

R$_f$ = 0.55 (60% EtOAc/Hex)
δ_H (600 MHz, CDCl_3): 5.34 (d, J = 3.3 Hz, 1H, H-4b), 5.19 (app. t, 1H, H-3a), 5.10 (app. t, 1H, H-3b), 4.95 (dd, J = 8.0 Hz, J = 10.4 Hz, 1H, H-2b), 4.88 (app. t, 1H, H-2a), 4.44 - 4.52 (m, 3H, H-1a, H-1b, H-6b), 4.05 - 4.15 (m, 3H, H-6a, H-5b, H-6’b), 3.84 – 3.82 (m, 2H, H-6’a, H-7), 3.79 (app. t, 1H, H-4a), 3.55 – 3. 62 (m, 2H, H-5a, H-7’), 3.30 – 3.39 (m, 2H, H-9, H-9’), 2.15, 2.12, 2.06, 2.06, 2.04, 2.04 1.96 (s, 3H, OCOCH_3), 1.76 – 1.82 (m, 2H, H-8, H-8’).

**HRMS (m/z - ESI):** Found: 742.2278, ([M+Na]^+. C_{29}H_{41}N_3O_{18}Na, Required: 742.2283).

2,3,4,6-tetra-O-acetyl-1-O-(3-azidopropyl)-α-D-mannopyranoside (25) [5]

Following general procedure D, 21 (1.22 g, 2.87 mmol) and NaN_3 (150 mg, 11.48 mmol) and DMF (60 mL). Purification using 27% EtOAc/Hexane (v/v) yielded 25 as a pale yellow oil (430 g, 40%).

R_f = 0.48 (30%EtOAc/Hexane)

δ_H (600 MHz, CDCl_3): 5.37 – 5.26 (m, 2H, H-3, H-5), 5.25 – 5.21 (m, 1 H, H-2), 4.81 (d, J_{1,2} = 2.5 Hz, 1H, H-1), 4.27 (dd, J = 8.2 Hz, J = 18.4 Hz, 1H, H-7), 4.14 – 4.07 (m, 1H, H-7’), 4.0 0 – 3.92 (m, 1H, H-4), 3.85 – 3.77 (m, 1H, H-6), 3.56 – 3.48 (m, 1H, H-6’), 3.4 3 (app. t, 2H, H-9, H-9’), 1.98 – 1.83 (m, 2H, H-8, H-8’).

**HRMS (m/z - ESI):** Found: 454.1143, ([M+Na]^+. C_{17}H_{25}N_3O_{10}Na, Required: 454.1438).

1-Bromo-(2,3,4,6-Tetra-O-acetyl-1-O-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-2,3,6-tri-O-acetyl-α-D-glucopyranoside (27). [13]

Hydrobromic acid (2.04 mL, 35.4 mmol, 6.00 equiv) is added at 0 °C to peracetylated lactose (4.00 g, 5.90 mmol, 1.00 equi v) in 60 mL of CH_2Cl_2. After 1 h of stirring at 0 °C, the mixture was let to stirred overnight at rt. The reaction mixture was filtered off and quenched with NaHCO_3 until orange colour disappeared. The aqueous phase was extracted with EtOAc (100 mL) and the combined organic layers dried under MgSO_4. Solvent removed in vacuo led to 27, obtained as a colourless oil (1.94 g, 48%).

R_f = 0.54 (50% EtOAc/Hex)

δ_H (400 MHz, CD_3Cl): 6.53 (d, J_{1b,2b} = 4.0 Hz, 1H, H-1b), 6.25 (d, J = 3.5 Hz, 1H, H-1a), 5.60 – 5.50 (m, 1H, H-3b), 5.46 (dd, J = 10.2 Hz, J = 9.3 Hz, 1H), 5.38- 5.34 (m, 1H) 5.16 – 5.10 (m, 2H), 5.04 - 4.95 (m, 2H), 4.76 (dd, J = 10.0 Hz, J_{2b,1b} = 4.0 Hz, 1H, H-2b), 4.55 – 4.45 (m, 2H, H-6a, H-6’a), 4.24 – 4.04 (m, 2H), 2.17, 2.15, 2.13, 2.09, 2.06, 2.06, 1.97, (s, 3H, OCOCH_3).

**HRMS (m/z - ESI):** Found: 721.0950, ([M+Na]^+. C_{26}H_{35}O_{17}Na^+Br, Required: 721.0955).


A mixture containing 27 (1.90 g, 2.70 mmol, 1.00 equiv), sodium azide (85 mg, 13.60 mmol, 5.00 equiv), tetrabutylammonium hydrogensulphate (923.17 mg, 4.08 mmol, 1.50 equiv) and 40 mL of NaHCO_3/CH_2Cl_2 (1:1), was stirred overnight at rt. The organic layer was diluted with CH_2Cl_2, washed with water and brine, dried over
Mg$_2$SO$_4$, filtered off and concentrated. Column chromatography of the residue on silica gel (35%EtOAc/Hexane) gave the product as a white foam (890 mg, 49%).

**R$_f$** = 0.73 (60% EtOAc/Hex)

δ$_H$ (600 MHz, CDCl$_3$): 5.26 (dd, $J_{4b, 3b} = 3.5$ Hz, $J = 1.1$ Hz, 1H, H-4b), 5.12 (app. t, 1H, H-3a), 5.01 (dd, $J_{2b, 3b} = 10.4$ Hz, $J = 7.8$ Hz, 1H, H-2b), 4.88 (dd, $J_{3b, 2b} = 10.4$ Hz, $J_{3b, 4b} = 3.5$ Hz, 1H, H-3b), 4.76 (dd, $J = 9.5$ Hz, $J_{2a, 1a} = 8.8$ Hz, 1H, H-2a), 4.58 (d, $J_{1a, 2a} = 8.8$ Hz, 1H, H-1a), 4.47 – 4.39 (m, 2H, H-6a, H-4a), 4.38 – 4.32 (m, 1H, H-5a), 2.06, 2.04, 1.98, 1.97, 1.96, 1.95 (s, 3H, OCOCH$_3$).

**HRMS** (m/z - ESI): Found: 684.1870, ([M+Na]$^+$, C$_{26}$H$_{35}$N$_3$O$_{17}$Na, Required: 684.1864).

1-Azide-((β-D-galactopyranosyl)-(1-4)-O-β-D-glucopyranoside (29)$^{[13]}$

Following general procedure B, compound 28 (890 mg, 1.30 mmol) was dissolved in 25% NaOMe/MeOH solution (60 mL). Compound 29 (386 mg, 86%) was obtained without further purification as a white foam.

**R$_f$** = 0.70 (30% Hex/EtOAc).

δ$_H$ (400 MHz, CD$_2$OD): 4.48 (d, $J = 8.7$ Hz, 1H, H-1a), 4.30 (d, $J = 7.5$ Hz, 1H, H-1b), 3.86 (dd, $J = 12.3$, 2.4 Hz, 1H), 3.80 (dd, $J = 12.3$, 4.0 Hz, 1H), 3.77 – 3.73 (m, 1H), 3.73 – 3.68 (m, 1H), 3.64 (dd, $J = 11.4$, 4.0 Hz, 1H), 3.57 – 3.50 (m, 3H), 3.50 – 3.39 (m, 4H).

**HRMS** (m/z - ESI): Found: 390.1132, ([M+Na]$^+$, C$_{12}$H$_{22}$N$_3$O$_{10}$Na, Required: 390.1135).

N-Propargyl-4-nitro-1,8-naphthalimide (31)$^{[1]}$

2-Propyn-1-amine (0.30 mL, 4.60 mmol, 1.10 equiv) was added to a sparingly soluble solution of 4-nitro-1,8-naphthalic anhydride (1.00 g, 4.19 mmol, 1.00 equiv) in ethanol (25 mL). After 6 h refluxing under argon, the reaction was cooled to room temperature, filtered and washed with cool ethanol (10 mL). The residue was dried in vacuo to afford the product 31 as a brown powder (1.01 g, 87%).

**R$_f$** = 0.45 (40 % EtOAc:Hex).

δ$_H$ (400 MHz, CDCl$_3$): 8.86 (d, $J_{6, 8} = 7.8$ Hz, 1H, H-6), 8.79 (d, $J_{6, 8} = 7.8$ Hz, 1H, H-8), 8.74 (d, $J_{5, 6} = 8.0$ Hz, 1H, H-5), 8.41 (d, $J_{6, 5} = 8.0$ Hz, 1H, H-6), 8.01 (app. t, 1H, H-7), 4.97 (d, $J_{3, 1} = 2.4$ Hz, 2H, H-3), 2.22 (t, $J_{1, 3} = 2.4$ Hz 1H, H-1).

**HRMS** (m/z - ESI): Found: 303.03792 ([M+Na]$^+$, C$_{15}$H$_{8}$N$_2$O$_4$Na, Required: 303.0376).
2,3,4,6-Tetra-O-acetyl-1-O-(propargyl)-β-D-galactopyranoside (33) \[14\]

\[
\begin{align*}
&\text{AcO} \quad \text{AcO} \\
&\text{O} \quad \text{O} \\
&\text{O} \quad \text{O} \\
&\text{9} \quad \text{8} \\
&\text{7} \quad \text{6} \\
&\text{5} \quad \text{4} \\
&\text{3} \quad \text{2} \\
&\text{1} \quad \text{2,3,4,6-penta-O-acetyl-β-D-galactose (3.00 g, 7.70 mmol, 1 equiv) and propargyl alcohol (1.84 mL, 30.80 mmol, 4 equiv) and BF}_3 \cdot \text{Et}_2 \text{O (4.72 mL, 38.50 mmol, 5.00 equiv) were stirred overnight in anhydrous CH}_2 \text{Cl}_2 (40 mL).}
\end{align*}
\]

The crude product was purified by SiO\(_2\) column chromatography SiO\(_2\) using 17\% EtOAc/Hexane (v/v), affording 33 as pale colourless oil (1.76 g, 60%).

\[R_f = 0.75 \text{ (50\% EtOAc/Hexane)}\]

\[\delta H (400 MHz, CDCl}_3): 5.39 (dd, \text{J}_4, 3 = 3.5 Hz, \text{J}_{4,5} = 1.1 Hz, 1H, H-4), 5.21 (dd, \text{J}_{2,3} = 10.4 Hz, \text{J}_{2,1} = 7.9 Hz, 1H, H-2), 5.05 (dd, \text{J}_{1,2} = 10.4 Hz, \text{J}_{3,4} = 3.5 Hz, 1H, H-3), 4.73 (d, \text{J}_{1,2} = 7.9 Hz, 1H, H-1), 4.38 \text{ (d, \text{J}_{7,9} = 2.4 Hz, 2H, H-7)}, 4.22 - 4.07 (m, 2H, H-6, H-6'), 4.02 - 3.87 (m, 1H, H-5), 2.46 (t, \text{J}_{9,7} = 2.4 Hz, 1H, H-9), 2.14, 2.07, 2.05, 1.98 (s, 3H, OCOCH}_3).\]

\[\text{HRMS } (m/z - \text{ESI}): \text{ Found: 409.1108, } [\text{M+Na}^+] \text{ C}_{17} \text{H}_{22} \text{O}_{10} \text{Na, Required: 409.1111).}\]

Propargyl-β-D-galactopyranoside (34) \[14\]

Following general procedure C, 33 (1.30 g, 3.36 mmol) and NaOMe (72.00 mg, 1.33 mmol) were stirred in MeOH (60 mL). Purification using 15\% EtOH/Hexane (v/v) gave the product as a colourless oil (674 mg, 92%).

\[R_f = 0.68 \text{ (50\% MeOH/ EtOAc)}\]

\[\delta H (600 MHz, D}_2 \text{O): 4.59 (d, \text{J}_{1,2} = 7.9 Hz, 1H, H-1), 4.55 - 4.44 (m, 2H, H-7), 3.94 (dd, \text{J}_{4,3} = 3.5 Hz, \text{J}_{4,5} = 1.0 Hz, 1H, H-4), 3.84 - 3.70 (m, 3H, H-6, H-6', H-5), 3.68 (dd, \text{J}_{3,4} = 9.9 Hz, \text{J}_{3,5} = 3.5 Hz, 1H, H-3), 3.54 (dd, \text{J}_{2,3} = 9.9 Hz, \text{J}_{2,1} = 7.9 Hz, 1H, H-2), 2.93 (t, \text{J}_{9,7} = 2.4 Hz, 1H, H-9).\]

\[\text{HRMS } (m/z - \text{ESI): } \text{ Found: 241.0685, } [\text{M+Na}^+] \text{ C}_{9} \text{H}_{14} \text{N}_2 \text{O}_6 \text{Na, Requires: 241.0688).}\]

N-(2-(dimethylamino)ethyl)-4-Bromo-1,8-naphthalimide (36) \[15\]

\[\text{Following general procedure C, 33 (1.30 g, 3.36 mmol) and NaOMe (72.00 mg, 1.33 mmol) were stirred in MeOH (60 mL). Purification using 15\% EtOH/Hexane (v/v) gave the product as a colourless oil (674 mg, 92%).}\]

\[R_f = 0.68 \text{ (50\% MeOH/ EtOAc)}\]

\[\delta H (400 MHz, CDCl}_3): 8.66 (dd, \text{J}_{5,4} = 7.3 Hz, \text{J}_{5,3} = 1.1 Hz, 1H, H-5), 8.58 (dd, \text{J}_{3,4} = 8.5 Hz, \text{J}_{3,5} = 1.1 Hz, 1H, H-3), 8.41 (d, \text{J}_{1,2} = 7.9 Hz, 1H, H-1), 8.04 (d, \text{J}_{2,1} = 7.9 Hz, 1H, H-2), 7.85 (dd, \text{J}_{3,4} = 8.5 Hz, \text{J}_{3,5} = 7.3 Hz, 1H, H-3), 4.41 (t, J = 6.8 Hz, 2H, CH}_2), 2.91 (br. s, 2H, CH}_2), 2.54 (s, 6H, H-8).\]

\[\text{HRMS } (m/z - \text{ESI): } \text{ Found: 347.0392 } [\text{M+H}^+] \text{ C}_{18} \text{H}_{16} \text{N}_2 \text{O}_2 ^{79}\text{Br Required: 347.0395).}\]
Compound 36 (190 g, 0.55 mmol, 1.00 equiv), NaN₃ (143 mg, 2.2 mmol, 4 equiv) were stirred in DMF (25 mL) at 80 °C overnight. Solvent was removed in vacuo and the crude was dissolved in hot methanol, subsequent hot filtration removed NaBr salt. Solvent removal and further purification using SiO₂ chromatography column gave the product as brown oil (1.70 g, neat).

Rᵣ = 1.6 (20% MeOH/EtOAc).

δ_H (400 MHz, CD₃OD): 8.58 (dd, J₃,₄ = 7.3 Hz, J₃,₅ = 1.1 Hz, 1H, H-3), 8.54 (d, J₂,₁ = 8.0 Hz, 1H, H-2), 8.48 (dd, J₅,₄ = 8.4 Hz, J₅,₃ = 1.1 Hz, 1H, H-5), 7.80 (dd, J₄,₅ = 8.4 Hz, J₄,₃ = 7.3 Hz, 1H, H-4), 7.64 (d, J₁,₂ = 8.0 Hz, 1H, H-1), 4.33 (t, J = 7.0 Hz, 2H, CH₂), 2.72 (t, J = 7.0 Hz, 2H, CH₂), 2.38 (s, 6H, H-8).

δ_C (100 MHz, CD₃OD): 166.3 (CO), 165.6 (CO), 154.6 (q, Ar-C), 135.6 (C-1), 132.6 (C-5), 131.4 (q, Ar-C), 130.5 (C-3), 125.2 (C-4), 123.0 (q, Ar-C), 120.9 (q, Ar-C), 109.6 (C-2), 57.7 (C-7), 45.5 (C-8), 38.1 (C-6).

HRMS (m/z - ESI): Found: 310.1299, ([M+H]⁺, C₁₆H₁₆NO₂, Required: 310.1304).
• NMR Spectra

Compound 1

$^1$H-NMR of compound 1.

$^{13}$C-NMR of compound 1.
Compound 2

$^1$H-NMR of compound 2.

HSQC-NMR of compound 2.
Compound 3

$^1$H-NMR of compound 3.

$^{13}$C-NMR of compound 3.
Compound 4

$^1$H-NMR of compound 4.

$^{13}$C-NMR of compound 4.
Compound 5

**H-NMR of compound 5.**

**C-NMR of compound 5.**
Compound 11

$^{1}H$-NMR of compound 11.

$^{13}C$-NMR of compound 11.
Compound 12

$^1$H-NMR of compound 12.

$^{13}$C-NMR of compound 12.
Compound 13

$^1$H-NMR of compound 13.

$^{13}$C-NMR of compound 13.
References: