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Research paper

Inhibition of adherence of the yeast *Candida albicans* to buccal epithelial cells by synthetic aromatic glycoconjugates

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ABSTRACT

The yeast *Candida albicans* is an opportunistic fungal pathogen which induces superficial and systemic infections in immunocompromised patients. Adherence to host tissue is critical to its ability to colonise and infect the host. The work presented here describes the synthesis of a small library of aromatic glycoconjugates (AGCs) and their evaluation as inhibitors of *C. albicans* adherence to exfoliated buccal epithelial cells (BECs). We identified a divalent galactoside, ligand **2a**, capable of displacing over 50% of yeast cells already attached to the BECs. Fluorescence imaging indicates that **2a** may bind to structural components of the fungal cell wall.

1. Introduction

The attachment of pathogenic microorganisms to the surface of the host cells is a prequisite for infection [1,2]. The mechanisms that mediate pathogen adherence often involve microbial proteins, known as adhesins, that recognise cell surface biomolecules such as protein receptors and glycans [3]. The development of compounds capable of blocking the adherence of pathogens to host cells is an attractive alternative to traditional antibiotic treatments that rely solely on killing the infective microorganisms [4,5]. There are several examples in which the anti-adherence approach has been exploited successfully to design inhibitors of microbial adherence [6]. Some of these include glycoclusters capable of preventing lung infection caused by *Pseudomonas aeruginosa* [7] and glycoconjugates used in the treatment of conditions caused by pathogenic strains of *Escherichia coli*, such as Crohn's disease [8] and urinary tract infections [9,10]. The lectins involved in the adherence processes in these reports (Lec A and Lec B from *P. auroginosa* and Fim H from *E. coli*, respectively) have been extensively studied and detailed knowledge of their structure and binding specificities is available. This has greatly facilitated the design of high affinity glycoconjugates that can effectively compete with host cell surface ligands [11].

Candida albicans is a dimorphoric yeast that can interconvert from single cells to hyphal forms, and exists in a commensal state in the mucosae and gastrointestinal tract [12]. In immunocompromised patients *C. albicans* induces a range of superficial and systemic infections [13], and is the third leading cause of infections related to medical devices such as catheters [14]. Adherence of *C. albicans* to host cells plays an important role in pathogenesis, as it allows the establishment of a strong link to host cell surfaces and provides a focal point for infection by enabling persistence in harsh environments such as the mouth [15]. Interestingly, this highly adherent organism is also the most pathogenic *Candida* species and the major cause of fungal infections [16], indicating that its highly infectious rate may be related to its strong adherence capacity. In addition, *C. albicans* expresses host regulator binding proteins such as phosphoglycerate mutase (gpm1) [17] and pH-regulated antigen 1 (pra1) [18] that bind to immune regulators such as Factor H and FHL-1 to avoid immune detection, demonstrating that through adherence, *C. albicans* can block activation of immune system

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regulators [19].

The oral cavity, in particular, provides surfaces to which *C. albicans* can adhere, such as buccal epithelial cells (BECs). *C. albicans* is capable of adhering to host cells through the interaction of the yeast cell wall and epithelial cell surfaces [16]. Adherence to abiotic and biotic surfaces is achieved by both non-specific and specific mechanisms: non-specific interactions involve cell surface hydrophobicity (CSH) [20]. CSH does not play a dominant role in the adherence process but has been known to maintain specific interactions between the yeast and the host [21]. Specific adherence mechanisms occur via the binding of adhesins to receptors on the host cell surface through lectin-like and protein-protein interactions [22]. Initial reports indicate that some *C. albicans* adhesins recognise and bind to a broad range of cell surface glycans, which include glycosphingolipids such as lactosylceramide [23] and asialo-GM1,[24] and host oligosaccharides containing fucose [25] (Fuc) and *N*-acetyl-glucosamine (GlcNAc) [26].

These findings provide evidence that cell surface glycans are important receptors for *C. albicans* and warrant the development of anti-adherence ligands that can mimic them, thus disrupting *C. albicans* - epithelial cell interactions. These compounds could represent a promising strategy to overcome fungal infections. However, the lack of structural knowledge of the fungal adhesins that recognise these carbohydrates hampers a focused design approach such as those described earlier. In this study, we opted instead to screen a small library of synthetic glycoconjugates with a diverse presentation of binding epitopes in order to identify structural features that can lead to effective inhibition of fungal adherence. Thus, we herein report the synthesis of aromatic-core glycoconjugates (AGC) which display some of the glycan residues reported to mediate *C. albicans* adherence to epithelial cells and their subsequent evaluation as inhibitors of the adherence of *C. albicans* to BECs.

2. Results and discussion

2.1. Synthesis

There are numerous examples of glycoconjugates built upon aromatic scaffolds, many of which are intended as ligands for adhesins [27], carbohydrate-binding proteins [28] or sensors for the detection of pathogens [29,30]. The popularity of AGCs is partly due to the versatility in functionality and the substitution patterns that can be achieved from readily available starting materials. Thus, we decided to explore 1,3 and 1,3,5 functionalized aromatic derivatives as the starting point in the design of the anti-adherence AGCs library (Scheme 1, Figures SI.1-3).

It is well known that multivalency can be an important factor that modulates carbohydrate-protein interactions [31]. Hence, mono- (compounds **1a**-**c**), di- (compounds **2a**-**f**) and trivalent analogues (compounds **3a**-**c**) were investigated. Carbohydrate moieties present in the epithelial cell surface and reported to bind *C. albicans* adhesins were selected to be grafted onto the aromatic scaffold: these included galactose, fucose, mannose, glucose, *N*-acetyl glucosamine and lactose derivatives. Triazolyl-containing spacer groups of different lengths, generated by means of Copper-Catalyzed Azide-Alkyne Cycloaddition (CuAAC) reactions, connected the glycosides to the central aromatic core. This methodology has been found to be extremely useful and reliable for the efficient synthesis of numerous glycoconjugates [32]. With this modular approach, we were able to readily assemble a small collection of glycoconjugates in which (i) the carbohydrate moiety, (ii) the valency and (iii) the distance between the binding epitopes were varied. This provided sufficient structural diversity for an initial screening of the requirements for fungal anti-adherence activity.

The synthesis of one of the divalent analogues, galactoside **2a**, depicted in Scheme 2, is representative for the synthesis of the other members of the AGCs library. 5-Aminoisophthalic acid was reacted with propanoyl chloride. The resulting dicarboxilic acid was reacted with propargyl amine using freshly prepared 4-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMTMM) to give diamide **6** in 78% yield [33]. The attachment of the carbohydrate moiety to the aromatic scaffold was effected by means of the CuAAC reaction: in this example, 2,3,4,6-tetra-*O*-acetyl-1-β-azido-galactoside [34] was reacted with compound **6** using copper sulphate and sodium ascorbate as the catalytic system. If the cycloaddition was carried out using conventional heating, the reaction times were long (up to 4 days) and the yields were moderate. However, we found that if the reaction was carried out using microwave (MW) irradiation, it proceeded with yields up to 82% for the protected glycoconjugate **7a** and with a drastic reduction in reaction times [35]. The deacetylation of compound **7a** was accomplished under mild basic conditions to give the galactosyl AGC **2a** in 96% yield. Following comparable synthetic schemes (see Supporting Information, Schemes SI.1-3), the remaining mono-, di- and trivalent AGCs were readily prepared in moderate to good yields.

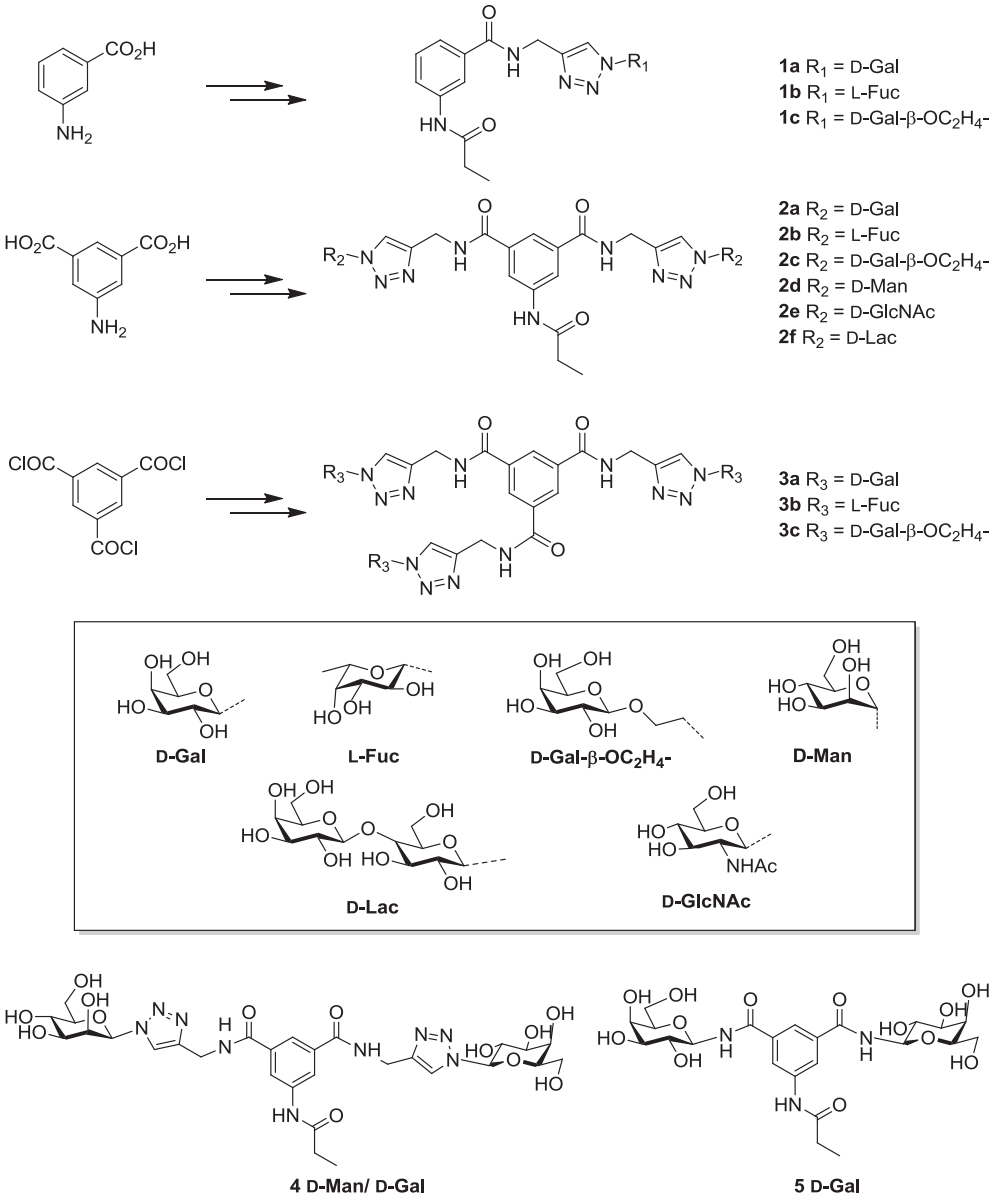
2.2. Biological Evaluation

All of the glycoconjugates (with exception of monovalent fucosyl derivative, compound **1b**) were found to be soluble in water. The toxicity of the compounds against *C. albicans* was firstly evaluated. None of the compounds showed significant ability to inhibit the growth of the yeast cells at the range of concentrations used in the subsequent adherence assays (see Figure SI.4). This implies that any reduction of adherence observed is not due to toxic effects. The ability of the glycoconjugates to inhibit the adherence of *C. albicans* was then evaluated in different assays:

2.2.1. Exclusion assay

The initial adherence assay was performed by treating *C. albicans* with the glycoconjugates, allowing for an incubation period and then exposing the treated yeast cells to the exfoliated BECs. The percentage increase or decrease of the number of *C. albicans* cells adhering to BECs compared to the adherence of the untreated yeast is represented in Table 1.

These results show the impact of the valency effect in the anti-adherence ability of the AGCs: monovalent compounds, in which only one carbohydrate moiety is present, are considerably less active than their di- and trivalent counterparts. In addition, it can be clearly seen that the galactosyl derivatives (**2a**, **2c**, **3a** and **3c**) and the *N*-acetyl glucosamine derivative **2e** are much more efficient at preventing the yeast adherence than any of the other glycoconjugates: in particular, divalent galacoside **2a** was identified as the most active compound of the AGCs library screened, showing a remarkable 80% decrease in adherence of the yeast to the BECs after treatment. Interestingly, compound **4**, a structural analogue of **2a** in which one of the galactosyl moieties has been replaced by mannose, is only capable of producing a 24% reduction in yeast adherence. This highlights the importance of a divalent galactosyl pattern as a recognition motif. The linker connecting the galactosyl moieties to the aromatic scaffold appears to also influence the anti-adherence ability of the glycoconjugates: the more flexible *O*-galactosides **1c**, **2c**, **3c** inhibited yeast adherence less effectively than their respective analogues **1a**, **2a**, **3a**, in which the triazolyl spacer group is directly attached to the anomeric galactosyl carbon. In addition, divalent galactoside **5**, which features no linkers, was only



Scheme 1. Chemical structures and starting materials used in the synthesis of the anti-adherence AGCs library.

able to induce a 26% reduction in adherence of *C. albicans* to BECs. The divalent galactoside **2a** was then evaluated at lower concentrations (Fig. 1a). Significantly, the anti-adherence ability of this compound was maintained at a 100-fold dilution concentration (0.1 mg/mL, 138 μM)).

2.2.2. Competitive assay

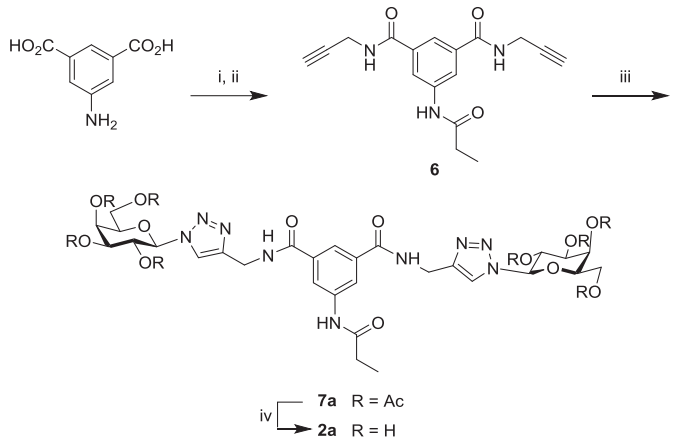
The best performing compound (divalent galactosides **2a**) was then evaluated in a competition assay, in which its anti-adherence ability was tested in the presence of both *C. albicans* and BECs. Co-incubation with compounds **2a** resulted in a reduction in adherence of yeast cells to BECs of 65%, even at the lowest concentration (Fig. 1b).

2.2.3. Displacement assay

A further assay was performed where glycoconjugate **2a** (0.1 mg/mL, 138 μM)) was added to a mixture of *C. albicans* and BECs, which had been previously incubated together. The ability of the compound to reverse the adherence of the yeast to the BECs was then examined. Two controls were used in this assay: control 1 involved the assessment of the binding of *C. albicans* to BECs prior to compound exposure; control 2 involved BECs and adherent yeast cells being re-incubated in PBS for 90 min prior to a second filtration step. It was found that **2a** imparted a reduction in adherence of 56% (compared to the control 1) and 31% (compared to the control 2) (Fig. 1). These results suggest that divalent galactoside **2a** bind effectively to *C. albicans* preventing its interaction with BECs (Fig. 1d).

2.3. Fluorescence imaging

A fluorescently labelled analogue of galactosylated AGC **2a**, compound **8** (Fig. 2), was synthesized to investigate possible sites of interaction of anti-adherence AGCs with *C. albicans* (Scheme SI-6). As controls, *C. albicans* cells with no treatment were imaged under an Olympus Fluoview 1000 confocal microscope to discard yeast



Scheme 2. Synthesis of galactosyl AGC 2a. *Reagents and conditions*: i) C_2H_5COCl, NEt_3, THF, N_2, rt, 22 h, 77%; ii) DMTMM, propargyl amine, DMF, N_2, 16 h, 78%; iii) 2,3,4,6-tetra-*O*-acetyl-1-β-azido-galactoside, $CuSO_4.5H_2O$/Na Asc, CH_3COCH_3/H_2O, 100 °C in MW, 10 min, 84%; iv) methanol, NEt_3, H_2O, 45 °C, 6 h, 94%.

Table 1
Effect of AGCs on adherence of *C. albicans* to BECs (estimated according to exclusion assays, at AGCs concentration = 10 mg/mL. SE in all cases was less than 10% of mean change in adherence).

AGCs	% Increase/Decrease of Adherence
1a D- Gal	- 14.5
1b L- Fuc	- 2
1c D- Gal-β-OC_2H_4	−7.5
2a D-Gal	−80
2b L-Fuc	−8
2c D-Gal-β-OC_2H_4	−35
2d D-Man	+3
2e D-GlcNAc	−45
2f D-Lac	+6.5
3a D-Gal	−45
3b L-Fuc	−30
3c D-Gal-β-OC_2H_4	−42
4 D-Gal/D-Man	−24
5 D-Gal	−26

autofluorescence (Fig. 2a). In addition, *C. albicans* cells were incubated with fluorescein isothiocyanate (FITC, Fig. 2b). Fluorescein derivative galactoside **8** was then co-incubated with *C. albicans* cells and the cells were imaged (Fig. 2c). In this case, strong localized fluorescence can be clearly observed. From these images, it can be deduced that compound **8** is interacting with the surface of the yeast cells.

These results indicate that the valency of the AGCs strongly influences their anti-adherence ability: the monovalent derivatives **1a-c** did not show any significant activity while the trivalent derivatives **3a-c** were moderate inhibitors, with the galactosyl derivatives **3a** and **3c** achieving as high as 45% and 42% reduction of adherence of *C. albicans* to BECs, respectively. Nevertheless, this study was focused in the divalent AGCs based on a 5-aminoisophthalic acid scaffold, which may allow for further synthetic versatility.

The results from the anti-adherence assays highlight the potential of divalent galactosyl AGC 2a as an inhibitor of the adherence of *C. albicans* to BECs. This compound consistently showed the best anti-adherence activity in the three types of assays performed (with up to 80% reduction of adherence in the exclusion assays). Interestingly, divalent compounds analogue in structure to 2a but featuring carbohydrate moieties other than galactose (compounds 2b, **2d-f**) were not as efficient adherence inhibitors as **2a**: the second best performing AGC was the *N*-acetyl glucosamine derivative **2f** (45% reduction of adherence in the exclusion assays). These results suggest that the divalent presentation of the galactose epitopes achieved in compound **2a** is important in mediating adherence to *C. albicans*. Polysaccharides and adhesins present in *C. albicans* cell wall mediate many of the adhesion processes of the yeast [36]. Initial research indicated that the addition of galactose or galactosamine reduced *C. albicans* attachment to buccal mucosal cells *in vitro* [37]. However, this is in contrast to a study in which the pre-treatment of *C. albicans* with galactose failed to inhibit adherence [38]. It has also been reported that *C. albicans* binds specifically to cell surface glycosphingolipids with terminal galactosyl residues such as lactosylceramide [Gal-β-(1–4)-Glc−β-(1-1)Cer] [23] and asialo-GM_1 [Gal-β-(1–3)-GalNAc-β-(1–4)-Gal-β-(1–4)-Glc−β-(1-1)Cer] by means of fimbrial proteins [24]. This study also reports that the synthetic disaccharide derivative GalNAc-β-(1–4)-Gal-β-$O(CH_2)_8CO_2CH_3$ was able to inhibit the binding of *C. albicans* fimbriae to BECs *in vitro*. More recently, a synthetic disaccharide (Fimbrigal-P) also featuring the terminal GalNAc-β-(1–4)-Gal motif, was found to reduce fungal burden in an *in vivo* model of oral candidiasis [39]. However, to the best of our knowledge, there are no Structure-Activity Relationship (SAR) studies of synthetic glycoconjugates regarding inhibition of *C. albicans* adherence that have identified terminal galactosides as key epitopes mediating yeast adhesion. A recent study has linked the binding specificities of some *C. albicans* adhesins (from the Als family) to human cell surface glycans based on glycan array screening results: a predicted glycan determinant for some of these proteins was a di-LacNAc (Gal-β-1,4-GlcNAc) disaccharide [40]. Further studies are currently going on in our laboratory to identify the fungal adhesin that lead compound **2a** may be binding to.

3. Conclusion

In conclusion, this work reports the synthesis of a small library of AGCs designed to conduct a preliminary SAR study on their ability to inhibit the adherence of the pathogenic yeast *C. albicans* to BECs. The anti-adherence assays allowed for the identification of divalent galactosyl derivative **2a** as an efficient inhibitor of *C. albicans* adherence, with **2a** being able to displace over 50% of yeast cells already attached to BECs. The precise three-dimensional presentation of the galactosyl moieties in **2a** appears to be a requirement for efficient adherence inhibition, which suggest that AGC **2a** is interfering with a specific recognition process part of the complex *C. albicans* adherence mechanisms. Fluorescence studies suggest that a potential target for **2a** could be indeed a fungal cell wall adhesin. The synthetic accessibility and high efficacy shown by **2a** in the biological assays make this compound a promising lead for development of new fungal anti-adherence agents, less prone to the appearance of resistance mechanisms than conventional fungicidal treatments.

4. Experimental section

Chemistry. General Methods: All reagents for synthesis were bought commercially and used without further purification. Tetrahydrofuran (THF) was freshly distilled over sodium wire and benzophenone. Dichloromethane (DCM) was freshly distilled over CaH_2 prior to use. Reactions were monitored with thin layer chromatography (TLC) on Merck Silica Gel F_{254} plates. Detection was effected by UV ($\lambda = 254$ nm) or charring in a mixture of 5% sulfuric acid-ethanol. NMR spectra were recorded using Bruker Ascend 500 spectrometer at 293K. All chemical shifts were referenced relative to the relevant deuterated solvent residual peaks. Assignments of the NMR spectra were deduced using ^{1}H NMR and ^{13}C NMR, along with 2D experiments (COSY, HSQC and HMBC).

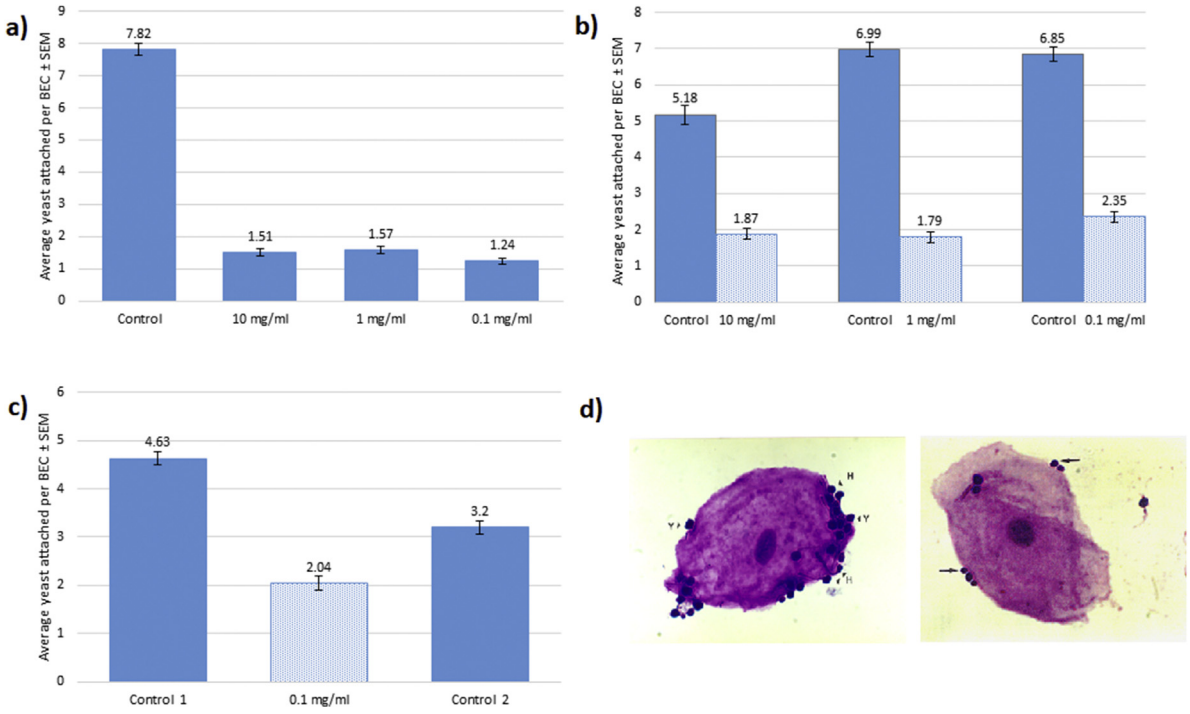


Fig. 1. Effect of divalent galactoside **2a** on the adherence of *C. albicans* to BECs. The data displays average yeast adherence per BEC: a) *Exclusion assay: C. albicans* was preincubated with **2a** (concentrations 10, 1 and 0.1 mg/mL); b) *Competition assay*: *C. albicans,* BECs and **2a** (concentrations 10, 1 and 0.1 mg/mL) were co-incubated; c) *Displacement assay*: *C. albicans* and BECs were co-incubated and compound **2a** (concentration 0.1 mg/mL) was subsequently added; control 1 involved the assessment of the binding of *C. albicans* to BECs prior to compound exposure; control 2 involved BECs and adherent yeast cells being re-incubated in PBS for 90 min prior to a second filtration step; d) Optical microscopy image of *C. albicans* attached to BEC before *(right)* after *(left)* treatment with **2a**.

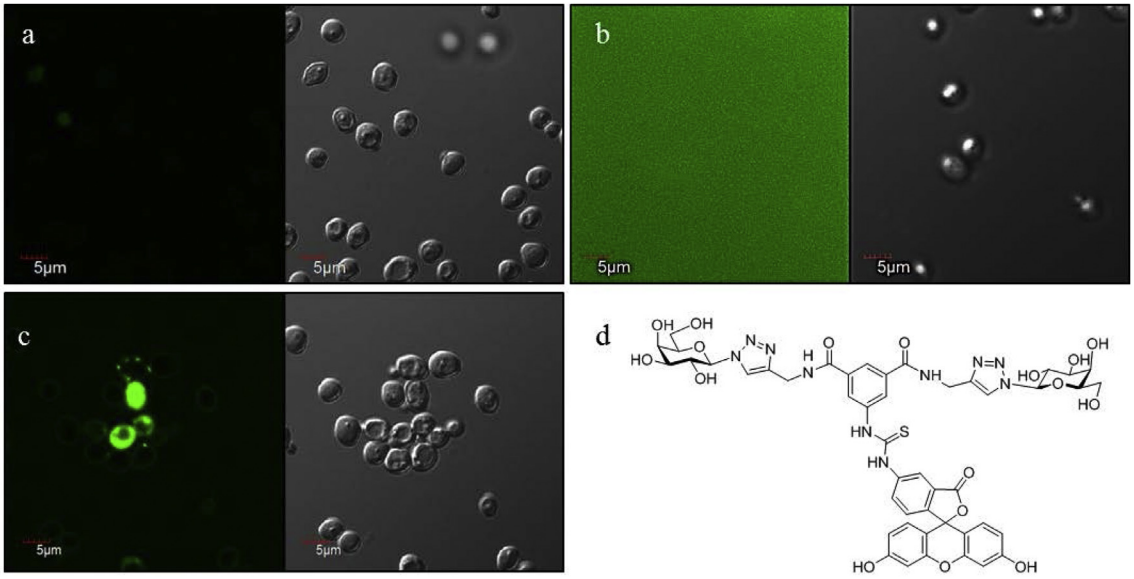


Fig. 2. Confocal microscope images of *C. albicans* cells: *a)* without treatment; *b)* co-incubated with FITC; *c)* co-incubated with fluorescently labelled galactosyl AGC **8**; *d)* chemical structure of galactoside **8**. A wavelength of 488 nm laser was used for excitation and emission was detected at 500–600 nm.

Chemical shifts are reported in ppm. Flash chromatography was performed with Merck Silica Gel 60. Microwave reactions were carried out using a CEM Discover Microwave Synthesizer. Optical rotations were obtained from an AA-100 polarimeter and $[\alpha]_D$ values are given in 10^{-1} cm $[2]\cdot g^{-1}$. High performance liquid chromatography analysis (HPLC, Waters Alliance 2695) was performed in final compounds and indicated purity of 95% based on integrations without the use of an internal standard. High resolution mass spectrometry (HRMS) was performed on an Agilent-LC 1200 Series coupled to a 6210 Agilent Time-Of-Flight (TOF) mass spectrometer equipped with an electrospray source in both positive and negative (ESI+/−) modes. Infrared spectra were obtained as a film on NaCl plates or as KBr disks in the region 4000–400 cm^{-1} on a Perkin Elmer Spectrum 100 FT-IR spectrophotometer. Synthetic schemes and spectroscopic data for all members of the ACG library are provided in the SI.

4.1. General Copper-Catalyzed Azide-Alkyne Cycloaddition (CuAAC) reaction procedures

4.1.1. Method A

Copper sulphate pentahydrate (20 mg) and sodium ascorbate (40 mg) were added to a solution of the acetylated sugar azide (1,25 equiv per propargyl group) and the corresponding propargyl amide scaffold in acetone/water (2:1 ratio). The reaction was allowed to stir at rt until deemed complete by TLC analysis (typically 16–24 h). The solvent was removed *in vacuo*. The residue was dissolved in DCM, washed with water (x3) and dried ($MgSO_4$). The mixture was filtered and the solvent was removed *in vacuo* to yield the crude product, which was purified by silica gel column chromatography (DCM:MeOH 98:2–93:7) to give the corresponding product.

4.1.2. Method B

Copper sulphate pentahydrate (20 mg) and sodium ascorbate (40 mg) were added to a solution of the acetylated sugar azide (1,25 equiv per propargyl group) and the corresponding propargyl amide scaffold in acetonitrile/water (2:1 ratio). The reaction was allowed to stir in the MW at 100 °C until deemed complete by TLC analysis (typically 5–15 min). The solvent was removed *in vacuo*. The residue was dissolved in DCM, washed with water (x3) and dried ($MgSO_4$). The mixture was filtered and the solvent was removed *in vacuo* to yield the crude product, which was purified by silica gel column chromatography (DCM:MeOH 98:2–93:7) to give the corresponding product.

4.1.3. General acetyl ester hydrolysis procedure

The acetylated glycoconjugate was dissolved in methanol/water (2:1 ratio). NEt_3 (0.1 mL) was added and the reaction mixture was allowed to stir at 45 °C until completion (typically 6–18 h). The solution was cooled to rt, Amberlite H^+ was added and the mixture was allowed to stir for 30 min. The solution was filtered and the solvent was removed in the rotatory evaporator and the residue was dried under high vacuum or lyophilized to give the deprotected glycoconjugate.

*4.1.3.1. N,N′-di(prop-2-yn-1-yl)-5-propionamidoisophthalamide (**6**).* 5-aminoisophathalic acid (5 g, 27.6 mmol) was dissolved in anhydrous THF (60 mL) under N_2 and propionyl chloride (2.7 mL, 30.4 mmol) was added dropwise. The mixture was allowed to stir for 5 min and NEt_3 (5 mL, 35.8 mmol) was added slowly. The reaction was left to stir for 22 h. The solvent was removed under reduced pressure, and the residue was dissolved in hot methanol. The insoluble material was filtered off and the filtrate was evaporated in a rotatory evaporator to give 5-propionoamidoisophthalic acid [33], which was used without further purification. (5.03 g, 77%). 5-propionoamidoisophthalic acid (0.78 g, 3.27 mmol) and DMTMM (1.99 g, 7.20 mmol) were suspended in anhydrous DMF (25 mL) under N_2. After 10 min, propargylamine (0.46 mL, 7.2 mmol) was added and the reaction mixture went clear. It was left to stir at rt for 16 h. The reaction mixture was poured into ice/water (30 mL) and the precipitated formed was then filtered and dried on the air to give **6**: white amorphous solid (0.79 g, 78%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.15 (s, 1H, N*H*COC_2H_5), 8.94 (t, J = 5.3 Hz, 2H, N*H*CH_2CCH), 8.18 (s, 2H, Ar–H), 7.93 (s, 1H, Ar–H), 4.11–4.00 (m, 4H, NHC*H*$_2$CCH), 3.13 (s, 2H, NHCH$_2$CC*H*), 2.35 (q, J = 7.5 Hz, 2H, *CH*$_2$CH$_3$), 1.10 (t, J = 7.5 Hz, 3H, CH$_2$*CH*$_3$). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.8 (*CO*C_2H_5), 166.2 (*CO*NHCH$_2$CCH), 140.0 (Ar–C), 135.3 (Ar–C), 121.4 (Ar–CH), 120.7 (Ar–CH), 81.6 (CH$_2$*C*CH), 73.4 (CH$_2$*C*CH), 29.1 (*C*H$_2$CH$_3$), 10.0 (CH$_2$*C*H$_3$). IR (KBr): 3289.16, 3241.00, 3093.06, 2977.14, 2116.87, 1682.50, 1570.58 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{17}H_{17}N_3O_3$ +H^+ $[M+H]^+$ 312.1343, found 312.1361.

*4.1.3.1. N,N′-di-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**7a**).* Prepared from **6** to 2,3,4,6-tetra-*O*-acetyl-1-β-azido-D-galactopyranoside [34], according to Method B: pale yellow amorphous solid (608 mg, 84%). R_f = 0.29 (DCM: methanol 9:1). $[\alpha]_D^{21}$ -4.3 (c 0.7, DCM). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.09 (s, 1H, N*H*COC_2H_5), 8.21 (s, 2H, N*H*CH_2-triaz), 7.97–7.95 (overlapping of 2 s, 4H, Ar–H and triaz-*H*), 7.78 (s, 1H, Ar–H), 5.89 (d, J = 9.2 Hz, 2H, H-1), 5.54 (t, J = 9.7 Hz, 2H, H-2), 5.49 (d, J = 3.2 Hz, 2H, H-4), 5.27 (dd, J = 10.3, 3.2 Hz, 2H, H-3), 4.59 (dd, J = 15.5, 5.2 Hz, 4H, C*H*$_2$-triaz), 4.29 (t, J = 6.5 Hz, 2H, H-5), 4.16–4.05 (m, 4H, H-6 and H-6'), 2.30 (q, J = 7.5 Hz, 2H, C*H*$_2$CH$_3$), 2.14 (s, 3H, OAc), 1.93 (s, 6H, OAc x 2), 1.76 (s, 3H, OAc), 1.06 (t, J = 7.5 Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.4 (*CO*$_2$H$_5$), 170.4 (CO of OAc), 170.2 (CO of OAc), 169.9 (CO of OAc), 169.3 (CO of OAc), 166.9 (*CO*NHCH$_2$-triaz), 145.4 (*C*-triaz), 139.1, 134.7 (each Ar–C), 121.7 (*CH*-triaz), 121.4, 120.9 (each Ar–*CH*), 86.0 (C-1), 73.8 (C-5), 70.8 (C-3), 68.1 (C-2), 67.0 (C-4), 61.2 (C-6), 35.3 (*C*H$_2$-triaz), 30.2 (*C*H$_2$CH$_3$), 20.6(CH$_3$ of OAc), 20.6 (CH$_3$ of OAc), 20.5 (CH$_3$ of OAc), 20.2 (CH$_3$ of OAc), 9.4 (CH$_2$*C*H$_3$). IR (film on NaCl): 3290, 2979, 2940, 2120, 1753, 1655, 1599, 1536 cm^{-1}. HRMS (ESI+): *m/z* calcd. for $C_{45}H_{56}N_9O_{21}$ +H^+ $[M+H]^+$ 1058.3591, found 1058.3602.

*4.1.3.1. N,N′-di-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**7b**).* Prepared from **6** to 2,3,4-tri-*O*-acetyl-1-β-azido-L-fucopyranoside [41] according to Method B: yellow amorphous solid (93 mg, 62%). R_f = 0.44 (DCM:MeOH 9:1). $[\alpha]_D^{19}$ +1.6 (c 0.9, DCM). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.37 (s, 1H, N*H*COC_2H_5), 7.97 (s, 2H, triaz-H), 7.94 (s, 2H, Ar–H), 7.83 (t, J = 5.1 Hz, 2H, CON*H*CH$_2$-triaz), 7.70 (s, 1H, Ar–H), 5.84 (d, J = 9.2 Hz, 2H, H-1), 5.58–5.51 (m, 2H, H-2), 5.38 (d, J = 3.3 Hz, 2H, H-4), 5.27–5.23 (m, 2H, H-3), 4.66 (dd, J = 15.3, 5.7 Hz, 4H, C*H*$_2$-triaz), 4.15 (q, J = 6.4 Hz, 2H, H-5), 2.38 (qd, J = 7.7, 3.7 Hz, 2H, C*H*$_2$CH$_3$), 2.22 (s, 6H, OAc), 1.99 (s, 6H, OAc), 1.83 (s, 6H, OAc), 1.24 (d, J = 6.4 Hz, 6H, H-6), 1.17 (t, J = 7.5 Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.8 (NH*CO*$_2$H$_5$), 170.5 (CO of OAc), 169.9 (CO of OAc), 169.4 (CO of OAc), 166.7 (*CO*NHCH$_2$-triaz), 145.5 (*C*-triaz), 139.1 (Ar–C), 135.0 (Ar–C), 121.4 (*CH*-triaz), 121.2 (Ar–*CH*), 120.5 (Ar–*CH*), 86.3 (C-1), 72.8 (C-5), 71.3 (C-3), 69.9 (C-4), 68.2 (C-2), 35.5 (*C*H$_2$-triaz), 30.4 (*C*H$_2$CH$_3$), 20.7 (CH$_3$ of OAc), 20.5 (CH$_3$ of OAc), 20.3 (CH$_3$ of OAc), 16.1 (C-6), 9.5 (CH$_2$*C*H$_3$). IR (film on NaCl): 3318, 2924, 1749, 1656, 1535 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{41}H_{51}N_9O_{17}$ + H^+ $[M+H]^+$ 942.9130, found 942.9142.

*4.1.3.1. N,N′-di-[2-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-ethyl-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**7c**).* Prepared from **6** and 2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)ethyl azide [42] according to Method B: yellow amorphous solid (545 mg, 82%). R_f = 0.38 (DCM:MeOH 9:1). $[\alpha]_D^{25}$ -9.1 (c 1.1, DCM). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.11 (s, 1H, N*H*COC_2H_5), 8.14 (s, 2H, CON*H*CH$_2$-triaz), 7.96 (s, 2H, Ar–H), 7.64 (d, J = 16.6 Hz, 3H, Ar–H and triaz-H), 5.30 (d, J = 3.2 Hz, 2H, H-4), 5.07 (dd, J = 10.3, 8.1 Hz, 2H, H-2), 4.94 (dd, J = 10.5, 3.2 Hz, 2H, H-3), 4.66–4.36 (m, 10H, C*H*$_2$-triaz and C*H*$_2$CH$_2$O and H-1), 4.15 (dd, J = 13.6, 6.4 Hz, 2H, C*H*O-Gal), 4.09–4.01 (m, 4H, H-6 and H-6'), 3.88 (ap t, J = 6.4 Hz, 4H, C*H*O-Gal and H-5), 2.27 (d, J = 7.0 Hz, 2H, C*H*$_2$CH$_3$), 2.06 (s, 6H, OAc), 1.95 (s, 6H, OAc), 1.89 (d, J = 2.1 Hz, 12H, OAc x2), 1.03 (t, J = 7.3 Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.2 (NH*CO*$_2$H$_5$), 170.4 (CO of OAc), 170.2 (CO of OAc), 170.0 (CO of OAc), 169.7 (CO of OAc), 166.8 (*CO*NHCH$_2$-triaz), 144.7 (*C*-triaz), 139.3 (Ar–C), 134.7 (Ar–C), 123.6 (CH-triaz), 121.1 (Ar–*CH*), 120.2 (Ar–*CH*), 100.8 (C-1), 70.7 (C-5), 70.6 (C-3), 68.5 (C-2), 67.5 (CH$_2$*C*H$_2$O), 66.9 (C-4), 61.1 (C-6), 50.00 (*C*H$_2$CH$_2$O), 35.5 (*C*H$_2$-triaz), 30.2 (*C*H$_2$CH$_3$), 20.7 (CH$_3$ of OAc), 20.6 (CH$_3$ of OAc), 20.6 (CH$_3$ of OAc), 20.5 (CH$_3$ of OAc), 9.5 (CH$_2$*C*H$_3$). IR (film on NaCl): 3311,

3148, 3071, 2980, 1750, 1656, 1599, 1543 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{49}H_{64}N_9O_{23}$ + H^+ $[M+H]^+$ 1146.4115, found 1146.4208.

*4.1.3.1. N,N′-di-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**7d**).* Prepared from **6** to 2,3,4,6-tetra-*O*-acetyl-1-α-azido-D-mannopyranoside [43] according to Method B: sticky, yellow amorphous solid (110 mg, 82%). R_f = 0.42 (DCM:MeOH 9:1). $[\alpha]_D^{22}$ +3 (c 1, DCM). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.93 (s, 1H, N*H*COC_2H_5), 8.23 (s, 2H, N*H*CH_2-triaz), 7.94 (s, 2H, triaz-H), 7.78 (s, 2H, Ar—H), 7.55 (s, 1H, Ar—H), 6.11 (s, 2H, H-1), 5.99 (s, 2H, H-2), 5.90 (d, *J* = 9.8 Hz, 2H, H-3), 5.41 (t, *J* = 9.6 Hz, 2H, H-4), 4.65—4.54 (m, 4H, C*H*$_2$-triaz), 4.27 (dd, *J* = 12.5, 2.9 Hz, 2H, H-6), 4.05 (dd, *J* = 12.4, 3 Hz, 2H, H-6'), 3.97 (dd, *J* = 6.0, 3.5 Hz, 2H, H-5), 2.48—2.33 (m, 4H, C*H*$_2$$CH_3$), 2.17 (d, *J* = 1.2 Hz, 6H, OAc), 2.06 (d, *J* = 1.6 Hz, 6H, OAc), 2.02—1.96 (m, 12H, OAc x2), 1.14 (dd, *J* = 9.4, 5.5 Hz, 6H, CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.5 (*C*OC_2H_5), 170.7 (*C*O of OAc), 170.0 (*C*O of OAc), 169.9 (*C*O of OAc), 169.7 (*C*O of OAc), 166.6 (*C*ONHCH$_2$-triaz), 145.6 (*C*-triaz), 138.9 (Ar—C), 134.4 (Ar—C), 123.5 (*C*H-triaz), 121.4 (Ar—*C*H), 120.2 (Ar—*C*H), 84.2 (C-1), 71.8 (C-5), 69.3 (C-3), 68.3 (C-2), 65.6 (C-4), 61.7 (C-6), 35.1 (C*H*$_2$-triaz), 30.3 (CH_2CH_3), 20.8 (CH_3 of OAc), 20.7 (CH_3 of OAc), 20.7 (CH_3 of OAc), 20.6 (CH_3 of OAc), 20.4 (CH_3 of OAc), 9.5 (CH_2CH_3). IR (film on NaCl): 3429, 2115, 1748, 1646 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{45}H_{56}N_9O_{21}$ + H^+ $[M+H]^+$ 1058.3591, found 1058.3593.

*4.1.3.1. N,N′-di-(2-Acetamido-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucopyranosyl-1,2,3-triazol-4-ylmethylamide)-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**7e**).* Prepared from **6** and 2-acetamido-2-deoxy-,3,4,6-tri-*O*-acetyl-1-β-azido-D-glucopyranoside [44] according to Method B: yellow amorphous solid (60 mg, 42%). R_f = 0.36 (DCM:MeOH 9:1). $[\alpha]_D^{26}$ -30 (c 0.4, DCM). ^{1}H NMR (500 MHz, d_5-Pyr): δ 10.87 (s, 1H, NH), 9.88 (t, *J* = 5.6 Hz, 2H, NH), 9.74 (d, *J* = 9.0 Hz, 2H, NH), 8.90 (s, 2H, triaz-H), 8.62 (s, 2H, Ar—H), 8.57 (s, 1H, Ar—H), 6.77 (d, *J* = 9.9 Hz, 2H, H-1), 6.06 (t, *J* = 9.6 Hz, 2H, H-3 or 4), 5.61 (t, *J* = 9.7 Hz, 2H, H-2), 5.23—5.14 (m, 2H, H-3 or 4), 4.48 (dd, *J* = 12.3, 5.0 Hz, 2H, H-6), 4.38 (d, *J* = 8.2 Hz, 2H, H-5), 4.32 (d, *J* = 12.3 Hz, 2H, H-6'), 2.43 (q, *J* = 7.5 Hz, 2H, C*H*$_2$$CH_3$), 2.10 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.89 (s, 3H, OAc), 1.72 (s, 3H, OAc), 1.19 (t, *J* = 7.6 Hz, 3H, CH_2C*H*$_3$). IR (ATR): 3305, 3078, 2924, 2850, 1743, 1667, 1651, 1529 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{45}H_{57}N_{11}O_{19}$ + H^+ $[M+H]$+1056.3910, found 1056.3942.

*4.1.3.1. N,N′-di-[{4-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-2,3,6-tri-O-acetyl-β-D-glucopyranosyl}-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**7f**).* Prepared from **6** and 4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-1-β-azido-D-glucopyranoside [45] according to Method B: sticky, yellow amorphous solid (102 mg, 72%). R_f = 0.62 (DCM:MeOH 9:1). $[\alpha]_D^{22}$ 11 (c 1, DCM). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.55 (s, 1H, N*H*COC_2H_5), 7.93—7.84 (m, 6H, N*H*CH_2-triaz, triaz-H and Ar—H), 7.68 (s, 1H, Ar—H), 5.84 (d, *J* = 9.2 Hz, 2H, H-1 Gal), 5.53—5.45 (m, 2H, H-2 Gal), 5.40 (dd, *J* = 11.2, 7.2 Hz, 2H, H-3 Gal), 5.35 (dd, *J* = 7.0, 3.5 Hz, 2H, H-4 Glc), 5.11 (dd, *J* = 10.3, 7.9 Hz, 2H, H-2 Glc), 5.02—4.96 (m, 2H, H-3 Glc), 4.63 (dd, *J* = 6.8, 4.3 Hz, 4H, C*H*$_2$-triaz), 4.57 (d, *J* = 7.9 Hz, 2H, H-1 Glc), 4.47 (dd, *J* = 11.1, 7.8 Hz, 2H, H-6 Glc), 4.18—4.05 (m, 6H, H-6′ Glc and H-6 and H-6' (Gal)), 4.04—3.99 (m, 2H, H-4 Gal), 3.93 (dd, *J* = 14.4, 8.4 Hz, 4H, H-5 Gal and H-5 Glc), 2.40 (q, *J* = 7.2 Hz, 2H, C*H*$_2$$CH_3$), 2.19—1.92 (m, 42H, OAc x14), 1.81 (s, 3H), 1.19 (t, *J* = 7.5 Hz, 2H, CH_2C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.1 (*C*OC_2H_5), 170.4 (*C*O of OAc), 170.1 (*C*O of OAc), 170.1 (*C*O of OAc), 169.6 (*C*O of OAc), 169.5 (*C*O of OAc), 169.1 (*C*O of OAc), 166.6 (*C*ONHCH$_2$-triaz), 145.6 (C-triaz), 138.9 (Ar—C), 134.7 (Ar—C), 121.5 (CH-triaz), 121.2 (Ar—*C*H), 120.7 (Ar—*C*H), 101.1 (C-1 Glc), 85.5 (C-1 Gal), 76.0 (C-5 Gal), 75.6 (C-4 Gal), 72.6 (C-3 Gal), 70.9 (C-3 Glc), 70.8 (C-2 Gal), 70.7 (C-5 Glc), 69.1 (C-2 Glc), 66.7 (C-4 Glc), 61.9 (C-6 Glc), 60.8 (C-6 Gal), 35.5 (C*H*$_2$-triaz), 30.4 (CH_2CH_3), 20.7 (CH_3 of OAc), 20.6 (CH_3 of OAc), 20.6 (CH_3 of OAc), 20.5 (CH_3 of OAc), 20.4 (CH_3 of OAc), 20.3, 9.5 (CH_2CH_3). IR (film on NaCl): 3293, 2942, 1749, 1656, 1599, 1537 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{69}H_{88}N_9O_{37}$ + H^+ $[M+H]^+$ 1634.5281, found 1634.5287.

*4.1.3.1. N,N′-di-(β-D-galactopyranosyl-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**2a**).* White amorphous solid (60 mg, 94%). $[\alpha]_D^{25}$ +12.7 (c 0.5, H_2O). ^{1}H NMR (500 MHz, D_2O): δ 8.24 (s, 2H, triaz-H), 7.85 (s, 2H, Ar—H), 7.79 (s, 1H, Ar—H), 5.66 (d, *J* = 8.8 Hz, 2H, H-1), 4.64 (s, 4H, C*H*$_2$-triaz), 4.20 (t, *J* = 9.2 Hz, 2H, H-2), 4.08 (d, *J* = 8.6 Hz, 2H, H-4), 3.97 (s, 2H, H-5), 3.86 (d, *J* = 9.7 Hz, 2H, H-3), 3.75 (d, *J* = 4.7 Hz, 2H, H-6 and H-6'), 2.37 (d, *J* = 7.4 Hz, 2H, C*H*$_2$$CH_3$), 1.12 (t, *J* = 7.3 Hz, 3H, CH_2C*H*$_3$). ^{13}C NMR (125 MHz, D_2O): δ 176.8 (*C*OC_2H_5), 169.0 (*C*ONHCH$_2$-triaz), 145.2 (*C*-triaz), 138.2, 134.6 (Ar—*C*), 123.0 (*C*H-triaz), 122.9, 122.1 (Ar—CH), 88.1 (C-1), 78.3 (C-5), 72.9 (C-3), 69.8 (C-2), 68.6 (C-4), 60.9 (C-6), 35.1 (C*H*$_2$-triaz), 29.9 (CH_2CH_3), 9.2 (CH_2CH_3). IR (KBr): 3368, 2940, 2121, 1649, 1598, 1546 cm^{-1}. HRMS (ESI+): *m/z* calcd. for $C_{29}H_{40}N_9O_{13}$ +H^+ $[M+H]$+722.2746, found 722.2730.

*4.1.3.1. N,N′-di-(β-L-fucopyranosyl-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**2b**).* Pale yellow amorphous solid (76 mg, 92%). $[\alpha]_D^{23}$ +4.3 (c 0.4, H_2O). ^{1}H NMR (500 MHz, D_2O): δ 8.22 (d, *J* = 4.1 Hz, 2H, triaz-H), 7.88 (d, *J* = 1.5 Hz, 2H, Ar—H), 7.81 (s, 1H, Ar—H), 5.65—5.61 (d, *J* = 9.2 Hz, 2H, H-1), 4.65 (s, 4H, C*H*$_2$-triaz), 4.15 (t, *J* = 9.5 Hz, 2H, H-2), 4.08—4.02 (m, 2H, H-5), 3.90—3.82 (m, 4H, H-3 and H-4), 2.37 (q, *J* = 7.6 Hz, 2H, C*H*$_2$$CH_3$), 1.25—1.22 (m, 6H, C6—*H*$_3$), 1.12 (t, *J* = 7.6 Hz, 3H, CH_2C*H*$_3$). ^{13}C NMR (125 MHz, D_2O): δ 176.6 (*C*OC_2H_5), 168.7 (*C*ONHCH$_2$-triaz), 144.8 (*C*-triaz), 138.2 (Ar—C), 134.4 (Ar—C), 123.0 (*C*H-triaz), 122.7 (Ar—CH), 121.9 (Ar—*C*H), 88.1 (C-1), 74.4 (C-5), 73.1 (C-3), 71.2 (C-4), 69.5 (C-2), 35.0 (C*H*$_2$-triaz), 29.9 (CH_2CH_3), 15.5 (C-6), 9.1 (CH_2CH_3). IR (ATR): 3261, 2917, 2851, 1646, 1601, 1536 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{29}H_{39}N_9O_{11}$ + H^+ $[M+H]^+$ 690.6910, found 690.6923.

*4.1.3.1. N,N′-di-[2-O-(β-D-galactopyranosyl)-ethyl-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**2c**).* Pale brown amorphous solid (55 mg, 91%). $[\alpha]_D^{20}$ +2.9 (c 0.3, H_2O). ^{1}H NMR (500 MHz, D_2O): δ 8.10 (s, 2H, triaz-H), 8.00 (d, *J* = 1.5 Hz, 2H, Ar—H), 7.93 (s, 1H, Ar—H), 4.73—4.67 (m, 8H, C*H*$_2$-triaz and C*H*$_2$$CH_2$), 4.39—4.27 (m, 4H, H-1 and C*H*CH_2), 4.18—4.10 (m, 2H, C*H*CH_2), 3.90 (dd, *J* = 3.4, 0.8 Hz, 2H, H-4), 3.77—3.68 (m, 4H, H-6 and H-6'), 3.68—3.61 (m, 2H, H-5), 3.59 (dd, *J* = 9.9, 3.4 Hz, 2H, H-3), 3.48 (dd, *J* = 10.0, 7.8 Hz, 2H, H-2), 2.47 (q, *J* = 7.6 Hz, 2H, C*H*$_2$$CH_3$), 1.20 (td, *J* = 7.6, 1.6 Hz, 3H, CH_2C*H*$_3$). ^{13}C NMR (125 MHz, D_2O): δ 176.8 (*C*OC_2H_5), 168.8 (*C*ONHCH$_2$-triaz), 144.3 (*C*-triaz), 138.1 (Ar—C), 134.6 (Ar—C), 124.8 (*C*H-triaz), 123.0 (Ar—*C*H), 122.1 (Ar—CH), 103.0 (C-1), 75.1 (C-5), 72.6 (C-3), 70.6 (C-2), 68.5 (C-4), 60.9 (C-6), 35.0 (C*H*$_2$-triaz), 29.9 (CH_2CH_3), 9.2 (CH_2CH_3). IR (KBr): 3365, 3323, 3117, 3053, 2977, 2942, 2882, 1691, 1651, 1614, 1564 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{33}H_{48}N_9O_{15}$ + H^+ $[M+H]^+$ 810.3270, found 810.3322.

*4.1.3.1. N,N′-di-(α-D-mannopyranosyl-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**2d**).* Pale yellow amorphous solid (42 mg, 88%). $[\alpha]_D^{22}$ +19.1 (c 0.4, H_2O). ^{1}H NMR (500 MHz, D_2O): δ 8.14 (s, 2H, triaz-H), 7.85 (s, 2H, Ar—H), 7.78 (s, 1H, Ar—H), 6.08 (s, 2H, H-1), 4.75 (s, 2H, H-2), 4.64 (s, 4H, C*H*$_2$-triaz), 4.14 (dd, *J* = 9.0, 3.2 Hz, 2H, H-3), 3.86—3.74 (m, 6H, H-4 and H-6 and H-6'), 3.38—3.29 (m, 2H, H-5), 2.37 (q, *J* = 7.6 Hz, 2H, C*H*$_2$$CH_3$), 1.12 (t, *J* = 7.6 Hz, 3H, CH_2C*H*$_3$). ^{13}C NMR (125 MHz, D_2O): δ 176.4 (*C*OC_2H_5), 168.5 (*C*ONHCH$_2$-triaz), 145.0 (*C*-triaz), 138.2

(Ar–*C*), 134.4 (Ar–*C*), 123.7 (*C*H-triaz), 122.4 (Ar–*C*H), 121.7 (Ar–*C*H), 86.7 (C-1), 76.2 (C-5), 70.6 (C-3), 68.3 (C-2), 66.6 (C-4), 60.5 (C-6), 35.0 (CH_2-triaz), 29.9 (CH_2CH_3), 9.1 (CH_2CH_3). IR (KBr): 3375, 2941, 1649, 1555 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{29}H_{40}N_9O_{13}$ + H^+ $[M+H]^+$ 722.2746, found 722.2740.

*4.1.3.1. N,N′-di-(2-Acetamido-2-deoxy-β-D-glucopyranosyl-1,2,3-triazol-4-ylmethylamide)-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**2e**).* Pale yellow amorphous solid (34 mg, 75%). $[\alpha]_D^{22}$ -5.2 (c 0.3, H_2O). ^1H NMR (500 MHz, D_2O): δ 8.20 (s, 2H, triaz-H), 8.01 (t, *J* = 3.9 Hz, 2H, Ar–H), 7.96–7.89 (m, 1H, Ar–H), 5.86 (d, *J* = 9.7 Hz, 2H, H-1), 4.72–4.66 (m, 4H, CH_2-triaz), 4.27 (t, *J* = 10.0 Hz, 2H, H-2), 4.01–3.64 (m, 10H, H-3, H-4, H-5, H-6 and H-6‘), 2.48 (q, *J* = 7.6 Hz, 2H, CH_2CH$_3$), 1.79 (s, 3H, NHAc), 1.21 (t, *J* = 7.6 Hz, 3H, CH_2CH_3). ^{13}C NMR (125 MHz, D_2O): δ 176.8 (*C*OC_2H_5), 174.1 (*C*O of NHAc), 168.9 (*C*ONHCH$_2$-triaz), 123.2 (Ar–*C*H), 122.8 (CH-triaz), 122.2 (Ar–CH), 86.4 (C-1), 78.9 (C-5), 73.5 (C-3), 69.3 (C-4), 60.4 (C-6), 55.4 (C-2), 35.0 (CH_2-triaz), 30.0 (CH_2CH_3), 21.6 (CH_3 of NHAc), 9.2 (CH_2CH_3). IR (ATR): 3370, 2943, 1648, 1557 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{33}H_{45}N_{11}O_{13}$ + Na^+ $[M+Na]^+$ 826.3096, found 826.3102.

*4.1.3.1. N,N′-di-[{4-O-β-D-galactopyranosyl-β-D-glucopyranosyl}-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**2f**).* White amorphous (65 mg, 90%). $[\alpha]_D^{17}$ +1.5 (c 0.6, H_2O). ^1H NMR (500 MHz, D_2O): δ 8.16 (s, 2H, triaz-H), 7.91 (s, 2H, Ar–H), 7.84 (s, 1H, Ar–H), 5.72 (d, *J* = 9.2 Hz, 2H, H-1 Glc), 4.64 (s, 4H, CH_2-triaz), 4.45 (d, *J* = 7.8 Hz, 2H, H-1 Gal), 4.00 (t, *J* = 9.0 Hz, 2H, H-2 Glc), 3.93–3.87 (m, 3H, H-6 Glc and H-4 Gal), 3.85–3.79 (m, 4H, H-3 Glc, H-4 Glc, H-5 Glc and H-6′ Glc), 3.78–3.65 (m, 4H, H-6 Gal, H-6′ Gal and H-5 Gal), 3.65–3.57 (m, 2H, H-3 Gal), 3.56–3.49 (m, 2H, H-2 Gal), 2.38 (q, *J* = 7.6 Hz, 1H, CH_2CH$_3$), 1.12 (dd, *J* = 9.4, 5.8 Hz, 3H, CH_2CH_3). ^{13}C NMR (125 MHz, D_2O): δ 168.8 (*C*ONHCH$_2$-triaz), 145.0 (*C*-triaz), 138.2 (Ar–*C*), 134.4 (Ar–*C*), 123.1 (CH-triaz), 122.8 (Ar–CH), 102.8 (C-1 Gal), 87.2 (C-1 Glc), 77.6 (C-4/5 Glc), 77.2 (C-4/5 Glc), 75.3 (C-5 Gal), 74.4 (C-3 Glc), 72.4 (C-3 Gal), 71.9 (C-2 Glc), 70.9 (C-2 Gal), 68.5 (C-4 Gal), 61.0 (C-6 Gal), 59.7 (C-6 Glc), 35.0 (CH_2-triaz), 29.8 (CH_2CH_3), 9.1 (CH_2CH_3). IR (KBr): 3412, 2923, 2125, 1644, 1548 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{41}H_{60}N_9O_{23}$ + H^+ $[M+H]^+$ 1046.3802, found 1046.2788.

*4.1.3.1. N-(prop-2-yn-1-yl)-3-propionamidobenzamide (**9**).* 3-aminobenzoic acid (2 g, 14.6 mmol) was dissolved in anhydrous THF (15 mL) under N_2 and propionyl chloride (3.19 mL, 36.5 mmol) was added dropwise. The mixture was allowed to stir for 5 min and NEt_3 (6.1 mL, 43.8 mmol) was added slowly. The reaction was left to stir for 16 h. The solvent was removed *in vacuo*. The crude mixture was dissolved in ethyl acetate (30 mL), washed with 0.5 M HCl (30 mL), and dried ($MgSO_4$). The mixture was filtered and the solvent was removed under reduced pressure to yield the product 3-(propionylamino) benzoic acid as an off-white amorphous (0.637 g, 23%) which was used without further purification. This acid (0.307 g, 1.59 mmol) and TBTU (0.56 g, 1.75 mmol) were dissolved in anhydrous DMF (15 mL) under N_2. NEt_3 (0.3 mL, 2.38 mmol) was added, and the reaction mixture was stirred for 10 min on ice. Propargylamine (0.15 mL, 2.38 mmol) was added, and the reaction was stirred for 16 h at rt. The solvent was removed *in vacuo*. The crude mixture was dissolved in ethyl acetate (30 mL), washed with 0.5 M HCl (30 mL), sat. $NaHCO_3$ (30 mL) and brine (30 mL), and dried ($MgSO_4$). The mixture was filtered and the solvent was removed in the rotatory evaporator to yield product **9**: pale yellow amorphous (0.359 g, 98%). ^1H NMR (500 MHz, DMSO-d_6): δ 9.99 (s, 1H, N*H*CH$_2$CCH), 8.86 (s, 1H, N*H*COC_2H_5), 8.04 (s, 1H, Ar–H), 7.77 (d, *J* = 8.2 Hz, 1H, Ar–H), 7.48 (d, *J* = 7.7 Hz, 1H, Ar–H), 7.37 (t, *J* = 7.9 Hz, 1H, Ar–H), 4.03 (dd, *J* = 5.5, 2.4 Hz, 2H, CH_2CCH), 3.10 (t, *J* = 2.3 Hz, 1H, CH_2CCH), 2.32 (q, *J* = 7.5 Hz, 2H, CH_2CH_3), 1.08 (t, *J* = 7.5 Hz, 3H, CH_2CH_3). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.6 (*C*OC_2H_5), 166.4 (CONHCH$_2$-triaz), 139.9 (Ar–C), 135.0 (Ar–C), 129.1 (Ar–CH), 122.3 (Ar–CH), 121.8 (Ar–CH), 118.9 (Ar–CH), 81.8 (CH_2CCH), 73.2 (CH_2CCH), 30.0 (CH_2CH$_3$), 29.0 (CH_2CCH), 10.1 (CH_2CH_3). IR (KBr): 3365, 3321, 3298, 3117, 2977, 2942, 1690, 1652, 1562 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{13}H_{15}N_2O_2$ +H^+ $[M+H]^+$ 231.1134, found 231.1135.

*4.1.3.1. N-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-1,2,3-triazol-4-ylmethylamide)-N′-propyl-3-aminobenzene-1-carboxamide (**10a**).* Prepared from **9** to 2,3,4,6-tetra-*O*-acetyl-1-β-azido-D-galactopyranoside [34], according to Method A: Off-white amorphous solid (235 mg, 83%). R_f = 0.45 (DCM:MeOH 9:1). $[\alpha]_D^{19}$ -6.9 (c 0.9, DCM). ^1H NMR (500 MHz, $CDCl_3$): δ 8.62 (s, 1H, N*H*COC_2H_5), 7.95 (s, 1H, triaz-H), 7.89–7.78 (m, 2H, Ar–H x2), 7.72 (s, 1H, N*H*CH$_2$-triaz), 7.48 (d, *J* = 7.4 Hz, 1H, Ar–H), 7.28 (t, *J* = 7.8 Hz, 1H, Ar–H), 5.91 (d, *J* = 9.2 Hz, 1H, H-1), 5.56 (m, 2H, H-2 and H-4), 5.34–5.24 (m, 2H, H-3), 4.68 (dd, *J* = 14.5, 3.5 Hz, 2H, CH_2-triaz), 4.31 (t, *J* = 6.1 Hz, 1H, H-5), 4.15 (dd, *J* = 11.5, 6.8 Hz, 2H, H-6 and H-6‘), 2.39 (q, *J* = 7.4 Hz, 2H, CH_2CH$_3$), 2.18 (s, 3H, OAc), 2.00 (s, 6H, OAc x2), 1.82 (s, 3H, OAc), 1.18 (t, *J* = 7.5 Hz, 3H, CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.0 (NH*C*OC_2H_5), 170.4 (CO of OAc), 170.1 (CO of OAc), 169.9 (CO of OAc), 169.1 (CO of OAc), 167.5 (*C*ONHCH$_2$-triaz), 145.4 (C-triaz), 138.8 (Ar–C), 134.5 (Ar–C), 129.1 (Ar–CH), 123.1 (Ar–CH), 122.3 (Ar–CH), 121.6 (CH-triaz), 118.5 (Ar–CH), 86.1 (C-1), 73.9 (C-5), 70.8 (C-3), 68.0 (C-2), 66.9 (C-4), 61.2 (C-6), 35.3 (CH_2-triaz), 30.4 (CH_2CH_3), 20.6 (CH_3 of OAc), 20.6 (CH_3 of OAc), 20.5 (CH_3 of OAc), 20.2 (CH_3 of OAc), 9.6 (CH_2CH_3). IR (film on NaCl): 3311, 2980, 1753, 1652, 1591, 1553 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{27}H_{34}N_5O_{11}$ +H^+ $[M+H]^+$ 604.2255, found 604.2262.

*4.1.3.1. N-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl-1,2,3-triazol-4-ylmethylamide)-N′-propyl-3-aminobenzene-1-carboxamide (**10b**).* Prepared from **9** to 2,3,4-tri-*O*-acetyl-1-β-azido-L-fucopyranoside [41] according to Method A: Off-white amorphous solid (90 mg, 76%). R_f = 0.56 (DCM:MeOH 9:1). $[\alpha]_D^{20}$: +16.1 (c 1, DCM). ^1H NMR (500 MHz, $CDCl_3$): δ 8.32 (s, 1H, N*H*COC_2H_5), 7.90 (s, 1H, triaz-H), 7.87 (d, *J* = 8.0 Hz, 1H, Ar–H), 7.77 (s, 1H, Ar–H), 7.46 (m, 2H, Ar–H and N*H*CH$_2$-triaz), 7.28 (t, *J* = 8.0 Hz, 1H, Ar–H), 5.78 (d, *J* = 9.2 Hz, 1H, H-1), 5.52–5.46 (m, 1H, H-2), 5.35 (d, *J* = 2.9 Hz, 1H, H-4), 5.24 (dd, *J* = 10.3, 3.4 Hz, 1H, H-3), 4.66 (dd, *J* = 15.2, 5.6 Hz, 2H, CH_2-triaz), 4.11 (q, *J* = 6.4 Hz, 1H, H-5), 2.37 (q, *J* = 7.5 Hz, 2H, CH_2CH$_3$), 2.20 (s, 3H, OAc), 1.97 (s, 3H, OAc), 1.81 (s, 3H, OAc), 1.26–1.13 (m, 6H, C6–H_3 and CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.8 (*C*OC_2H_5), 169.5 (CO of OAc), 168.9 (CO of OAc), 168.2 (CO of OAc), 166.4 (*C*ONHCH$_2$-triaz), 144.3 (CH-triaz), 137.8 (Ar–C), 133.6 (Ar–C), 128.2 (Ar–CH), 122.1 (Ar–CH), 121.4 (Ar–CH), 120.4 (CH-triaz), 117.4 (Ar–CH), 85.3 (C-1), 71.7 (C-5), 70.2 (C-3), 68.9 (C-4), 67.2 (C-2), 34.4 (CH_2-triaz), 29.5 (CH_2CH$_3$), 19.7 (CH_3 of OAc), 19.5 (CH_3 of OAc), 19.3 (CH_3 of OAc), 15.0 (C-6), 8.6 (CH_2CH_3). IR (film on NaCl): 3308, 3146, 3085, 2985, 2941, 2248, 1750, 1647, 1591, 1553 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{25}H_{32}N_5O_9$ + H^+ $[M+H]^+$ 546.2200, found 546.2197.

*4.1.3.1. N-[2-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-ethyl-1,2,3-triazol-4-ylmethylamide)-N′-propyl-3-aminobenzene-1-carboxamide (**10c**).* Prepared from **9** and *2-O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)ethyl azide [42] according to Method A: Off-white amorphous solid (97 mg, 88%). R_f = 0.36 (DCM:MeOH 9:1). $[\alpha]_D^{23}$ -3.1 (c 1, DCM). ^1H NMR (500 MHz, $CDCl_3$): δ 8.41 (s, 1H, N*H*COC_2H_5), 7.90 (d, *J* = 8.0 Hz, 1H, Ar–*H*), 7.80 (s, 1H, Ar–*H*), 7.63 (s, 1H, triaz-*H*), 7.56 (t, *J* = 5.1 Hz, 1H, N*H*CH$_2$-triaz), 7.46 (d, *J* = 7.7 Hz, 1H, Ar–*H*), 7.27 (t, *J* = 8 Hz, 1H, Ar–*H*), 5.34 (dd, *J* = 3.4, 1.0 Hz, 1H, H-4), 5.11 (dd, *J* = 12.5, 6.2 Hz, 1H, H-2), 4.96 (dd, *J* = 10.5, 3.4 Hz, 1H,

H-3), 4.69–4.59 (m, 2H, C*H*$_2$-triaz), 4.56–4.44 (m, 2H, C*H*$_2$CH$_2$O), 4.42 (d, J = 7.9, 1H, H-1), 4.18 (dt, *J* = 10.5, 4.1 Hz, 1H, C*H*O-Gal), 4.08 (dd, *J* = 11.3, 6.6 Hz, 2H, H-6 and H-6'), 3.95–3.85 (m, 2H, C*H*O-Gal and H-5), 2.36 (q, *J* = 7.5 Hz, 2H, C*H*$_2$CH$_3$), 2.09 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.93 (s, 3H, OAc), 1.90 (s, 3H, OAc), 1.16 (t, *J* = 7.6 Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, CDCl$_3$): δ 172.8 (*C*OC$_2$H$_5$), 170.4 (CO of OAc), 170.2 (CO of OAc), 170.0 (CO of OAc), 169.7 (CO of OAc), 167.3 (*C*ONHCH$_2$-triaz), 144.5 (*C*-triaz), 138.9 (Ar–C), 134.6 (Ar–C), 129.1 (Ar–*C*H), 123.8 (CH-triaz), 123.0 (Ar–*C*H), 122.2 (Ar–*C*H), 118.5 (Ar–*C*H), 100.9 (C-1), 70.9 (C-5), 70.6 (C-3), 68.6 (C-2), 67.5 (CH$_2$*C*H$_2$O-Gal), 66.9 (C-4), 61.2 (C-6), 50.1 (*C*H$_2$CH$_2$O-Gal), 35.5 (*C*H$_2$-triaz), 30.5 (*C*H$_2$CH$_3$), 20.6 (CH$_3$ of OAc), 20.6 (CH$_3$ of OAc), 20.6 (CH$_3$ of OAc), 20.5 (CH$_3$ of OAc), 9.6 (CH$_2$*C*H$_3$). IR (film on NaCl): 3312, 3146, 2980, 2941, 2250, 2111, 1750, 1649, 1591, 1552 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{29}H_{37}N_5O_{12}$ + H$^+$ [M+H]$^+$ 648.2517, found 648.2581.

*4.1.3.1. N-(β-D-galactopyranosyl-1,2,3-triazol-4-ylmethylamide)-N′-propyl-3-aminobenzene-1-carboxamide (**1a**).* White amorphous solid (73 mg, 92%). $[\alpha]_D^{19}$ +11.6 (c 0.7, H$_2$O). ^{1}H NMR (500 MHz, D$_2$O): δ 8.09 (s, 1H, triaz-H), 7.55 (t, *J* = 1.8 Hz, 1H, Ar–H), 7.34 (ddd, *J* = 8.0, 2.1, 1.0 Hz, 1H, Ar–H), 7.32–7.29 (m, 1H, Ar–H), 7.21 (t, *J* = 7.9 Hz, 1H, Ar–H), 5.53 (d, *J* = 9.2 Hz, 1H, H-1), 4.48 (s, 2H, C*H*$_2$-triaz), 4.07 (t, *J* = 9.5 Hz, 1H, H-2), 3.93 (dd, *J* = 3.3, 0.6 Hz, 1H, H-4), 3.83 (td, *J* = 6.0, 0.8 Hz, 1H, H-5), 3.72 (dd, *J* = 9.8, 3.3 Hz, 1H, H-3), 3.62 (d, *J* = 6.1 Hz, 2H, H-6 and H-6'), 2.24–2.18 (q, *J* = 7.7 Hz, 2H, C*H*$_2$CH$_3$), 0.99 (t, *J* = 7.6 Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, D$_2$O): δ 176.5 (NHCOC$_2$H$_5$), 169.7 (*C*ONHCH$_2$-triaz), 145.0 (*C*-triaz), 137.5 (Ar–C), 133.7 (Ar–C), 129.4 (Ar–*C*H), 124.8 (Ar–*C*H), 123.5 (Ar–*C*H), 123.1 (*C*H-triaz), 119.8 (Ar–*C*H), 88.2 (C-1), 78.3 (C-5), 72.9 (C-3), 69.8 (C-2), 68.6 (C-4), 60.9 (C-6), 34.9 (*C*H$_2$-triaz), 29.8 (*C*H$_2$CH$_3$), 9.2 (CH$_2$*C*H$_3$). IR (ATR): 3268, 1643, 1588, 1542 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{19}H_{26}N_5O_7$ +H$^+$ [M+H]$^+$ 436.1882, found 436.1826.

*4.1.3.1. N-(β-L-fucopyranosyl-1,2,3-triazol-4-ylmethylamide)-N′-propyl-3-aminobenzene-1-carboxamide (**1b**).* Yellow amorphous solid (63 mg, 94%). $[\alpha]_D^{23}$ -6.3 (c 0.6, H$_2$O). ^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 10.02 (s, 1H, N*H*COC$_2$H$_5$), 9.01 (t, *J* = 5.6 Hz, 1H, N*H*CH$_2$-triaz), 8.07 (m, 2H, triaz-H and Ar–H), 7.82 (d, *J* = 8.2 Hz, 1H, Ar–H), 7.56 (d, *J* = 7.7 Hz, 1H, Ar–H), 7.40 (t, *J* = 7.9 Hz, 1H, Ar–H), 5.47 (d, *J* = 9.2 Hz, 1H, H-1), 5.20 (d, *J* = 5.9 Hz, 1H, OH), 4.96 (d, *J* = 5.4 Hz, 1H, OH), 4.67 (d, *J* = 5.7 Hz, 1H, OH), 4.61–4.49 (m, 2H, C*H*$_2$-triaz), 3.99 (dd, *J* = 15.0, 9.1 Hz, 1H, H-2), 3.89 (q, *J* = 6.4 Hz, 1H, H-5), 3.56 (m, 2H, H-3 and H-4), 2.36 (q, *J* = 7.6 Hz, 2H, C*H*$_2$CH$_3$), 1.16 (d, *J* = 6.4 Hz, 3H, C6–*H*$_3$), 1.12 (t, *J* = 7.5 Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 172.6 (*C*OC$_2$H$_5$), 166.7 (*C*ONHCH$_2$-triaz), 145.6 (C-triaz), 139.9 (Ar–C), 135.3 (Ar–C), 129.1 (Ar–*C*H), 122.3 (Ar–*C*H), 122.0 (Ar–*C*H), 122.0 (*C*H-triaz), 119.0 (Ar–*C*H), 88.5 (C-1), 74.4 (C-3), 73.7 (C-5), 71.6 (C-4), 69.5 (C-2), 35.4 (*C*H$_2$-triaz), 30.0 (*C*H$_2$CH$_3$), 16.9 (C-6), 10.1 (CH$_2$*C*H$_3$). IR (KBr): 3401, 2925, 1645, 1589, 1542 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{19}H_{25}N_7O_7$ + H$^+$ [M+H]$^+$ 436.1832, found 436.1849.

*4.1.3.1. N-[2-O-(β-D-galactopyranosyl)-ethyl-1,2,3-triazol-4-ylmethylamide)-N′-propyl-3-aminobenzene-1-carboxamide (**1c**).* Off-white amorphous solid (104 mg, 87%). $[\alpha]_D^{24}$ +3.8 (c 1, MeOH). ^{1}H NMR (500 MHz, D$_2$O): δ 8.00 (s, 1H, triaz-H), 7.75 (s, 1H, Ar–H), 7.56–7.53 (m, 2H, Ar–H), 7.40 (t, *J* = 7.8 Hz, 1H, Ar–H), 4.50–4.46 (m, 4H, C*H*$_2$-triaz and C*H*$_2$CH$_2$), 4.29–4.20 (m, 2H, H-1 and C*H*CH$_2$), 4.15–4.10 (m, 1H, C*H*CH$_2$), 3.89 (s, 1H, H-4), 3.80–3.40 (m, 5H, H-6, H-6', H-2, H-3 and H-5), 2.33 (s, 2H, C*H*$_2$CH$_3$), 1.08 (s, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, D$_2$O) δ 176.9 (*C*OC$_2$H$_5$), 168.8 (*C*ONHCH$_2$-triaz), 144.4 (*C*-triaz), 137.3 (Ar–C), 134.0 (Ar–C), 130.7 (Ar–*C*H), 129.6, 127.8 (Ar–*C*H), 126.6 (Ar–*C*H), 125.2 (*C*H-triaz), 123.8, 122.1 (Ar–*C*H), 103.0 (C-1), 75.1 (C-5), 72.6 (C-3), 70.6 (C-2), 68.5 (C-4), 67.8 (*C*H$_2$CH$_2$), 60.9 (C-6), 50.8 (*C*H$_2$CH$_2$), 34.8 (*C*H$_2$-triaz), 29.8 (*C*H$_2$CH$_3$), 9.3 (CH$_2$*C*H$_3$). IR (KBr): 3400, 2934, 2615, 1648, 1590, 1549 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{21}H_{29}N_5O_8$ + H$^+$ [M+H]$^+$ 480.2094, found 480.2107.

*4.1.3.1. N,N′,N″-tri-(2,3,4,-tri-O-acetyl-β-L-fucopyranosyl-1,2,3-triazol-4-ylmethylamide)-benzene-1,3,5-tricarboxamide (**12b**).* Prepared from **11** [46] and 2,3,4-tri-*O*-acetyl-1-β-azido-L-fucopyranoside [41] according to Method A: yellow amorphous solid (93 mg, 72%). $[\alpha]_D^{20}$ +24.7 (c 0.9, DCM). ^{1}H NMR (500 MHz, CDCl$_3$): δ 8.22 (s, 3H, Ar–H), 8.06 (s, 3H, N*H*CH$_2$-triaz), 8.00 (s, 3H, triaz-H), 5.89 (d, *J* = 9.2 Hz, 3H, H-1), 5.55 (t, *J* = 9.7 Hz, 3H, H-2), 5.36 (d, *J* = 3.0 Hz, 3H, H-4), 5.25 (dd, *J* = 10.2, 3.3 Hz, 3H, H-3), 4.68 (dd, *J* = 58.5, 10.9 Hz, 6H, C*H*$_2$-triaz), 4.17 (q, *J* = 6.2 Hz, 3H, H-5), 2.21 (s, 9H, OAc), 1.98 (s, 9H, OAc), 1.77 (s, 9H, OAc), 1.21 (d, *J* = 6.3 Hz, 9H, C6–H$_3$). ^{13}C NMR (125 MHz, CDCl$_3$): δ 169.5 (CO of OAc), 168.9 (CO of OAc), 168.2 (CO of OAc), 165.1 (*C*ONHCH$_2$-triaz), 144.4 (*C*-triaz), 127.7 (Ar–CH), 120.6 (CH-triaz), 85.3 (C-1), 71.7 (C-5), 70.2 (C-3), 68.9 (C-4), 67.2 (C-2), 34.4 (*C*H$_2$-triaz), 19.7 (CH$_3$ of OAc), 19.6 (CH$_3$ of OAc), 19.3 (CH$_3$ of OAc), 15.0 (C-6). IR (KBr): 3411, 2989, 2942, 2115, 1751, 1659, 1537 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{52}H_{67}N_{12}O_{20}$ + H$^+$ [M+H]$^+$ 1179.4595, found 1179.4610.

*4.1.3.1. N,N′,N″-tri-[2-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-ethyl-1,2,3-triazol-4-ylmethylamide)-benzene-1,3,5-tricarboxamide (**12c**).* Prepared from **11** and 2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)ethyl azide [42] according to Method A: Off-white amorphous solid (69 mg, 50%). $[\alpha]_D^{23}$ -5.8 (c 0.7, DCM). ^{1}H NMR (500 MHz, CDCl$_3$): δ 8.22 (s, 3H, N*H*CH$_2$-triaz), 8.16 (s, 3H, triaz-*H*), 7.67 (s, 3H, Ar–*H*), 5.34 (d, *J* = 3.2 Hz, 3H, H-4), 5.12 (dd, *J* = 10.4, 8.0 Hz, 3H, H-2), 4.98 (dd, *J* = 10.5, 3.4 Hz, 3H, H-3), 4.79–4.50 (m, 12H, C*H*$_2$-triaz and C*H*$_2$CH$_2$O), 4.47 (d, *J* = 7.9 Hz, 3H, H-1), 4.28–4.18 (m, 3H, C*H*O-Gal), 4.09 (dd, *J* = 11.3, 6.6 Hz, 6H, H-6 and H-6'), 4.00–3.86 (m, 6H, C*H*O-Gal and H-5), 2.11 (s, 9H, OAc), 2.00 (s, 9H, OAc), 1.93 (s, 18H, OAc x 2). ^{13}C NMR (125 MHz, CDCl$_3$): δ 170.4 (CO of OAc), 170.1 (CO of OAc), 170.0 (CO of OAc), 169.7 (CO of OAc), 165.9 (*C*ONHCH$_2$-triaz), 144.7 (*C*-triaz), 134.6 (Ar–C), 128.5 (*C*H-triaz), 123.6 (Ar–*C*H), 100.9 (C-1), 70.6 (C-5), 68.6 (C-3), 67.5 (C-2), 67.0 (CH$_2$*C*H$_2$O-Gal), 61.2 (C-4), 50.1 (C-6), 35.5 (*C*H$_2$-triaz), 20.7 (CH$_3$ of OAc), 20.6 (CH$_3$ of OAc), 20.6 (CH$_3$ of OAc), 20.5 (CH$_3$ of OAc). IR (film on NaCl): 3391, 2939, 1748, 1661, 1537 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{66}H_{84}N_{12}O_{33}$ + H$^+$ [M+H]$^+$ 1573.5342, found 1574.5422.

*4.1.3.1. N, N′, N″-tri-(β-D-galactopyranosyl-1,2,3-triazol-4-ylmethylamide)-benzene-1,3,5-tricarboxamide (**3a**).* Prepared from *N,N′,N″*-tri-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-1,2,3-triazol-4-ylmethylamide)-benzene-1,3,5-tricarboxamide (**12a**) [47]. Yellow amorphous solid (63 mg, 89%). $[\alpha]_D^{23}$ +11.1 (c 0.6, H$_2$O). ^{1}H NMR (500 MHz, D$_2$O): δ 8.24 (s, 3H, triaz-*H*), 8.19 (s, 3H, Ar–*H*), 5.65 (d, *J* = 9.2 Hz, 3H, H-1), 4.64 (s, 6H, C*H*$_2$-triaz), 4.19 (t, *J* = 9.5 Hz, 3H, H-2), 4.06 (d, *J* = 3.2 Hz, 3H, H-4), 3.96 (t, *J* = 6.1 Hz, 3H, H-5), 3.85 (dd, *J* = 9.8, 3.3 Hz, 3H, H-3), 3.74 (d, *J* = 6.0 Hz, 6H, H-6 and H-6'). ^{13}C NMR (125 MHz, D$_2$O): δ 168.1 (*C*ONHCH$_2$-triaz), 144.8 (C-triaz), 134.3 (Ar–*C*), 129.2 (Ar–*C*H), 123.2 (CH-triaz), 88.2 (C-1), 78.3 (C-5), 73.0 (C-3), 69.8 (C-2), 68.6 (C-4), 60.9 (C-6), 35.1 (*C*H$_2$-triaz). IR (KBr): 3402, 1658, 1539, cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{36}H_{48}N_{12}O_{18}$ + H$^+$ [M+H]$^+$ 937.3288, found 937.3201.

*4.1.3.1. N,N′,N″-tri-(β-L-fucopyranosyl-1,2,3-triazol-4-ylmethylamide)-benzene-1,3,5-tricarboxamide (**3b**).* Yellow amorphous solid (53 mg, 88%). $[\alpha]_D^{21.5}$ -5.6 (c 0.5, H$_2$O). ^{1}H NMR (500 MHz, D$_2$O): δ 8.26 (s, 3H, Ar–*H*), 8.25 (s, 3H, triaz-*H*), 5.66 (d, *J* = 9.2 Hz, 3H, H-1), 4.70 (s, 6H, C*H*$_2$-triaz), 4.19 (t, *J* = 9.4 Hz, 3H, H-2), 4.10–4.06 (m, 3H, H-5), 3.91 (dd, *J* = 3.4, 0.8 Hz, 3H, H-4), 3.88

(dd, $J = 9.7$, 3.4 Hz, 3H, H-3), 1.28–1.26 (m, 9H, C6–H_3). ^{13}C NMR (125 MHz, D_2O): δ 168.3 (*C*ONHCH$_2$-triaz), 144.9 (C-triaz), 134.3 (Ar–*C*), 129.2 (Ar–*C*H), 123.0 (CH-triaz), 88.1 (C-1), 74.4 (C-5), 73.1 (C-3), 71.2 (C-4), 69.5 (C-2), 35.1 (*C*H$_2$-triaz), 15.6 (C-6). IR (KBr): 3381, 1659, 1536 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{38}H_{54}N_{12}O_{15}$ + Na^+ $[M+Na]^+$ 941.3729, found 941.3709.

*4.1.3.1. N,N′,N″-tri-[2-O-(β-D-galactopyranosyl)-ethyl-1,2,3-triazol-4-ylmethylamide)-benzene-1,3,5-tricarboxamide (**3c**).* Pale yellow amorphous solid (34 mg, 83%). $[\alpha]_D^{20}$ +5.9 (c 0.7, H_2O). ^{1}H NMR (500 MHz, D_2O): δ 8.31 (bs, 3H, triaz-H), 8.18 (s, 2H, Ar–H), 8.12 (s, 1H, Ar–H), 4.71 (bs, 6H, C*H*$_2$-triaz), 4.58–4.56 (m, 3H, C*H*CH$_2$), 4.37–4.26 (m, 6H, H-1 and C*H*CH$_2$), 4.12 (m, 3H, C*H*CH$_2$), 3.96–3.90 (m, 3H, C*H*CH$_2$), 3.87 (d, $J = 3.3$ Hz, 3H, H-4), 3.76–3.68 (m, 6H, H-6 and H-6'), 3.65–3.60 (m, 3H, H-5), 3.59–3.56 (m, 3H, H-3), 3.49–3.42 (m, 3H, H-2). ^{13}C NMR (125 MHz, D_2O): δ 167.8 (*C*ONHCH$_2$-triaz), 143.8 (C-triaz), 134.4 (Ar–C), 129.3 (CH-triaz), 125.3 (Ar–*C*H), 124.9 (Ar–*C*H) 103.0 (C-1), 96.5, 75.1 (C-5), 72.8 (H-3), 72.6, 71.9, 70.6 (C-2), 68.6 (C-4), 67.8 (*C*H$_2$CH$_2$), 61.0, 60.9 (C-6), 60.0, 53.1, 51.0 (*C*H$_2$CH$_2$), 34.8 (*C*H$_2$-triaz). IR (ATR): 3267, 2931, 1655, 1537 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{42}H_{60}N_{12}O_{21}$ + H^+ $[M+H]^+$ 1069.4074, found 1069.4091.

*4.1.3.1. N-(2,3,4,6-tetra-O-acetyl-β-D-mannopyranosy)l-1,2,3-triazol-4-ylmethylamide-N′-prop-2-yn-1-yl-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**13**).* **6** (435 mg, 1.40 mmol) and 2,3,4,6-tetra-*O*-acetyl-1-α-azido-mannoside [43] (131 mg, 0.349 mmol) were reacted according to Method B: yellow amorphous solid (91 mg, 34%). $R_f = 0.45$ (DCM:MeOH 9:1). $[\alpha]_D^{23}$ +12.1 (c 0.9, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.15 (s, 1H, N*H*COC$_2$H$_5$), 8.13 (s, 1H, N*H*CH$_2$-triaz), 8.07 (s, 1H, Ar–H), 8.02 (s, 1H, Ar–H), 7.87 (s, 1H, triaz-H), 7.78 (s, 1H, Ar–H), 7.68 (s, 1H, N*H*CH$_2$-triaz), 6.04 (s, 1H, H-1), 5.91–5.84 (m, 2H, H-2 and H-3), 5.40 (t, $J = 9.5$ Hz, 1H, H-4), 4.73–4.58 (m, 2H, C*H*$_2$-triaz), 4.27 (dd, $J = 12.5$, 4.7 Hz, 1H, H-6), 4.13 (s, 2H, C*H*$_2$CCH), 4.03 (d, $J = 10.6$ Hz, 1H, H-6'), 3.96–3.87 (m, 1H, H-5), 2.36 (q, $J = 7.4$ Hz, 2H, C*H*$_2$CH$_3$), 2.19 (d, $J = 7.6$ Hz, 1H, CH$_2$CC*H*), 2.17 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.02 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.11 (t, $J = 7.5$ Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.5 (*C*OC$_2$H$_5$), 170.6 (*C*O of OAc), 170.0 (*C*O of OAc), 169.7 (*C*O of OAc), 169.6 (*C*O of OAc), 166.8 (*C*ONHCH$_2$-triaz), 166.7 (*C*ONHCH$_2$-triaz), 145.4 (*C*-triaz), 139.3 (Ar–C), 134.6 (Ar–C), 123.4 (*C*H-triaz), 121.4 (Ar–*C*H x2), 120.7 (Ar–*C*H), 84.0 (C-1), 79.7 (CH$_2$*C*CH), 71.9 (C-5), 69.3 (C-2/C-3), 68.3 (C-2/C-3), 65.6 (C-4), 61.7 (C-6), 35.3 (*C*H$_2$-triaz), 30.3 (CH$_2$*C*CH), 29.7 (*C*H$_2$CH$_3$), 29.3 (*C*H$_2$CCH), 20.8 (CH$_3$ of OAc), 20.7 (CH$_3$ of OAc), 20.7 (CH$_3$ of OAc), 20.6 (CH$_3$ of OAc), 9.4 (CH$_2$*C*H$_3$). IR (film on NaCl): 3289, 3082, 2981, 1751, 1653, 1598, 1535 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{29}H_{39}N_9O_{13}$ + Na^+ $[M+Na]^+$ 744.2565, found 744.2575.

*4.1.3.1. N-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-1,2,3-triazol-4-ylmethylamide-N′-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-1,2,3-triazol-4-ylmethylamide- N″-propyl-5-aminobenzene-1,3-dicarboxamide (**14**).* **13** (77 mg, 0.112 mmol) and 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl azide [34] (50 mg, 0.134 mmol) were reacted according to Method B: yellow amorphous solid (100 mg, 84%). $R_f = 0.48$ (DCM:MeOH 9:1). $[\alpha]_D^{21}$ +9.0 (c 1, DCM). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.89 (s, 1H, NH), 8.20 (s, 1H, NH), 8.14 (s, 2H, triaz-H), 8.02 (m, 3H, Ar–H x2 and NH), 7.81 (s, 1H, Ar–H), 6.22 (d, $J = 1.8$ Hz, 1H, (H-1 Man)), 6.12 (dd, $J = 3.6$, 2.0 Hz, 1H, H-2 (Man)), 6.09–6.02 (m, 2H, H-3 (Man) and H-1 (Gal)), 5.75 (t, $J = 9.7$ Hz, 1H, H-2 (Gal)), 5.67 (dd, $J = 3.3$, 0.7 Hz, 1H, H-4 (Gal)), 5.55 (dd, $J = 12.5$, 6.8 Hz, 1H, H-2 (Gal)), 5.44–5.39 (m, 1H, H-3 (Gal)), 4.87–4.71 (m, 4H, C*H*$_2$-triaz x2), 4.47–4.39 (m, 2H, H-6 (Man) and H-5 (Gal)), 4.29 (dd, $J = 11.5$, 6.5 Hz, 2H, H-6 and H-6' (Gal)), 4.22–4.15 (m, 1H, H-6' (Man)), 4.09 (ddd, $J = 9.6$, 4.4, 2.5 Hz, 1H, H-5 (Man)), 2.52 (q, $J = 7.4$ Hz, 2H, C*H*$_2$CH$_3$), 2.32 (d, $J = 4.0$ Hz, 6H, OAc x2), 2.20 (s, 3H, OAc), 2.16 (s, 3H, OAc), 2.14 (s, 3H, OAc), 2.12 (s, 6H, OAc x2), 1.96 (s, 3H, OAc), 1.28 (t, $J = 7.5$ Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.4 (*C*OC$_2$H$_5$), 170.8 (*C*O of OAc), 170.5 (*C*O of OAc), 170.3 (*C*O of OAc), 170.0 (*C*O of OAc), 170.0 (*C*O of OAc), 169.8 (*C*O of OAc), 169.4 (*C*O of OAc), 166.9 (*C*ONHCH$_2$-triaz), 166.8 (*C*ONHCH$_2$-triaz), 145.8 (C-triaz), 145.7 (C-triaz), 139.2 (Ar–C), 134.9 (Ar–C), 134.8 (Ar–C), 123.6 (Ar–CH), 121.6 (CH-triaz), 120.7 (Ar–CH), 86.3 (C-1 Gal), 84.2 (C-1 Man), 74.1 (C-5 Gal), 72.0 (C-5 Man), 71.0 (C-3 Gal), 69.4 (C-3 Man), 68.5 (C-2 Man), 68.2 (C-2 Gal), 67.1 (C-4 Gal), 65.8 (C-4 Man), 61.9 (C-6 Man), 61.3 (C-6 Gal), 35.6 (*C*H$_2$-triaz), 35.4 (*C*H$_2$-triaz), 30.5 (*C*H$_2$CH$_3$), 20.9 (CH$_3$ of OAc), 20.8 (CH$_3$ of OAc), 20.8 (CH$_3$ of OAc), 20.8 (CH$_3$ of OAc), 20.7 (CH$_3$ of OAc), 20.4 (CH$_3$ of OAc), 9.6 (CH$_2$*C*H$_3$). IR (film on NaCl): 3311, 3147, 3082, 2981, 1750, 1657, 1599, 1548 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{45}H_{56}N_9O_{21}$ + H^+ $[M + H^+]$: 1058.3591, found 1058.3607.

*4.1.3.1. N-β-D-galactopyranosyl-1,2,3-triazol-4-ylmethylamide-N′-α-D-mannopyranosyl-1,2,3-triazol-4-ylmethylamide)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**4**).* Pale yellow amorphous solid (84 mg, 89%). $[\alpha]_D^{26}$ +13.1 (c 0.8, H_2O). ^{1}H NMR (500 MHz, D_2O): δ 8.23 (s, 1H, triaz-H), 8.14 (s, 1H, triaz-H), 7.85 (s, 1H, Ar–H), 7.83 (s, 1H, Ar–H), 7.77 (s, 1H, Ar–H), 6.07 (d, $J = 2.2$ Hz, 1H, H-1 Man), 5.65 (d, $J = 9.2$ Hz, 1H, H-1 Gal), 4.72 (dd, $J = 6.4$, 3.6 Hz, 1H, H-2 Man), 4.62 (s, 4H, C*H*$_2$-triaz x2), 4.18 (t, $J = 9.5$ Hz, 1H, H-2 Gal), 4.10 (dd, $J = 9.0$, 3.4 Hz, 1H, H-3 Man), 4.06 (d, $J = 3.2$ Hz, 1H, H-4 Gal), 3.96 (t, $J = 6.0$ Hz, 1H, H-5 Gal), 3.85 (dd, $J = 9.8$, 3.2 Hz, 1H, H-3 Gal), 3.81–3.70 (m, 5H, H-4 Man, H-6, H-6′ Gal, H-6, H-6′ Man), 3.30 (ddd, $J = 8.9$, 5.1, 1.7 Hz, 1H, H-5 Man), 2.35 (q, $J = 7.6$ Hz, 2H, C*H*$_2$CH$_3$), 1.10 (t, $J = 7.6$ Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (125 MHz, D_2O): δ 176.3 (*C*OC$_2$H$_5$), 168.4 (*C*ONHCH$_2$-triaz), 144.7 (C-triaz), 138.2 (Ar–C), 134.2 (Ar–C), 123.8 (*C*H-triaz), 123.1 (*C*H-triaz), 122.3 (Ar–*C*H), 121.7 (Ar–*C*H), 88.2 (C-1 Gal), 86.8 (C-1 Man), 78.3 (C-5 Gal), 76.2 (C-2 Man), 72.9 (C-3 Gal), 70.5 (C-3 Man), 69.8 (C-2 Gal), 68.6 (C-4 Gal), 68.3 (C-2 Man), 66.6 (C-4 Man), 60.9 (C-6 Gal), 60.5 (C-6 Man), 35.0 (*C*H$_2$-triaz), 34.9 (*C*H$_2$-triaz), 29.8 (*C*H$_2$CH$_3$), 9.1 (CH$_2$*C*H$_3$). IR (ATR): 3259, 2922, 2597, 1648, 1600, 1536 cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{29}H_{39}N_9O_{13}$ + Na^+ $[M+Na]$+744.2565, found 744.2575.

*4.1.3.1. N,N′-di-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**15**).*

5-Propionamidoisophthalic acid (0.133 g, 5.61 mmol) and TBTU (0.396 g, 1.23 mmol) were dissolved in DMF (10 mL) under N_2. NEt_3 (0.312 mL, 2.24 mmol) was added and the mixture was allowed to stir for 15 min. 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosylamine [48] (0.487 g, 1.40 mmol) was dissolved in DMF (5 mL) and was added to the reaction mixture. The solution was stirred for 24 h. The crude mixture was dissolved in DCM (30 Ml), washed with 0.5 M HCl (30 mL), sat. $NaHCO_3$ (30 mL) and brine (30 mL), and dried ($MgSO_4$). The mixture was filtered and the solvent was removed *in vacuo* to yield the crude product, which was purified by silica gel column chromatography (EtOAc) to give the pure product. Yellow amorphous solid (343 mg, 68%). $R_f = 0.64$ (DCM:MeOH 9:1) $[\alpha]_D^{25}$ -18.1 (c 1.1, DCM). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (s, 1H, NH), 8.23 (s, 2H, Ar–H), 7.86 (s, 1H, Ar–H), 7.54 (d, $J = 9.1$ Hz, 2H, NH), 5.59 (t, $J = 8.9$ Hz, 2H, H-1), 5.47 (d, $J = 1.5$ Hz, 2H, H-4), 5.31–5.29 (m, 4H, H-2 and H-3), 4.20 (t, $J = 6.6$ Hz, 2H, H-5), 4.16–4.05 (m, 4H, H-6 and H6'), 2.42 (q, $J = 7.5$ Hz, 2H), 2.17 (s, 6 H CH$_3$ of OAc), 2.01 (s, 6H, CH$_3$ of OAc), 1.99 (s, 6H, CH$_3$ of OAc), 1.97 (s, 6H, CH$_3$ of OAc). ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.8 (*C*OC$_2$H$_5$), 171.3 (*C*O of OAc), 170.5 (*C*O of OAc), 170.2 (*C*O of OAc), 170.1 (*C*O of OAc), 166.2 (*C*ONH-Gal), 139.7 (Ar–C), 134.3 (Ar–C), 121.9 (Ar–*C*H), 120.7 (Ar–*C*H), 79.0 (C-1), 72.4 (C-5), 71.1 (C-2/3), 68.6 (C-2/3), 67.4 (C-4), 61.3 (C-6), 30.5 (*C*H$_2$CH$_3$), 20.8 (CH$_3$ of OAc), 20.7 (CH$_3$ of OAc), 20.7 (CH$_3$ of OAc),

20.6 (CH_3 of OAc), 9.4 (CH_2CH_3). IR (film on NaCl): 3338, 1750, 1602, 1535, cm^{-1}. HRMS (ESI+): *m/z* calcd for $C_{39}H_{50}N_3O_{21} + H^+$ $[M+H]^+$ 896.2931, found 896.2956.

*4.1.3.1. N, N′-di-(β-D-galactopyranosyl)-N″-propyl-5-aminobenzene-1,3-dicarboxamide (**5**).* White amorphous solid (26 mg, 96%). $[\alpha]_D^{20}$ +10.0 (c 1, MeOH). ^{1}H NMR (500 MHz, D_2O): δ 8.04 (d, J = 1.4 Hz, 2H, Ar–H), 8.03 (d, J = 1.5 Hz, 1H, Ar–H), 5.10 (d, J = 8.4 Hz, 2H, H-1), 3.97 (d, J = 3.0 Hz, 2H, H-4), 3.82 (t, J = 6.2 Hz, 2H, H-5), 3.79–3.67 (m, 8H, H-2, H-3, H-6, H-6′), 2.47–2.37 (m, 2H, CH_2CH_3), 1.19–1.11 (m, 3H, CH_2CH_3). ^{13}C NMR (126 MHz, D_2O) δ 176.9 (COC_2H_5), 170.2 (CONH-Gal), 137.6 (Ar–C), 134.4 (Ar–C), 124.1 (Ar–CH), 123.0 (Ar–CH), 80.5 (C-1), 77.0 (C-5), 73.5 (C-3), 69.3 (C-2), 68.7 (C-4), 61.0 (C-6), 29.9 (CH_2CH_3) 9.2 (CH_2CH_3). HRMS (ESI+): *m/z* calcd for $C_{23}H_{34}N_3O_{13} + H^+$ $[M+H]^+$ 560.2086, found 560.2072.Biology

4.1.4. Sample Preparation

All glycoconjugates (with exception of monovalent fucosyl derivative, compound **1b**) were dissolved in water at the required concentration (10 mg/mL) and dilutions from these stock solutions were performed as appropriate. Compound **1b** was dissolved in DMSO and diluted with water to the required concentration (10 mg/mL), ensuring that the final DMSO content was below 10%. Dilutions from this stock solution were performed as appropriate.

4.1.5. Fungal Strain

C. albicans was maintained on sabouraud dextrose agar and cultures were grow to the stationary phase ($1–2 \times 10^8$/ml) overnight in YEPD broth (1% (w/v) yeast extract, 2% (w/v) bacteriological peptone, 2% (w/v) glucose) at 30 °C and 200 rpm. Stationary phase yeast cells were harvested, washed with PBS and resuspended at a density of 1×10^8/mL in PBS.

4.1.5.1*Buccal epithelial cells*

Buccal epithelial cells (BECs) were harvested from healthy volunteers by gently scraping the inside of the cheek with a sterile tongue depressor. Cells were washed in PBS and resuspended at a density of 5×10^5/ml.

4.1.6. Adherence assays

Yeast cells were mixed with BECs in a ratio of 50:1 in a final volume of 2 mL and incubated at 30 °C and 200 rpm for 90 min. The BEC/yeast cell mixture was harvested by passing through a polycarbonate membrane containing 30 μm pores which trapped the BECs but allowed unattached yeast cells to pass through. This was washed x 2 with 10 mL PBS and cells remaining on the membrane were collected and placed on glass slides which were left to air dry overnight. The cells were heat fixed and stained using 0.5% (w/v) crystal violet, rinsed using cold water to remove any surplus stain and left to air dry for 30 min. The number of *C. albicans* cells adhering to a sample of 200 BECs per treatment was assessed microscopically. In the *exclusion assay* the yeast cells were incubated for 90 min in the presence of each compound (10 mg/mL). After this time the cells were harvested and washed twice with PBS before being resuspended in 1 mL PBS before being mixed with BECs (as described). In the *competition assay* format yeast cells, BECs and compound (10, 1 or 0.1 mg/mL) were co-incubated for 90 min prior to harvesting. In the *displacment assay* adherence was allowed to occur by mixing the yeast cells and BECs together. BECs and adherent yeast cells were harvested and re-incubated with the compound (0.1 mg/mL) for a further 90 min after which time the level of adherence was measured.

4.1.7. Statistics

All experiments were performed on three independent occasions. In each assay the number of yeast cells adhering to 200 randomly chosen BECs was determined. Results are mean ± SEM.

4.2. Fluorescence imaging

An Olympus Fluoview FV1000 confocal microscope was employed to visualise the binding of the fluorescently labelled galactoside **8** to the *C. albicans* cell surface. A wavelength of 488 nm laser was used for excitation and emission was detected at 500–600 nm.

Associated content

Electronic Supporting Information (ESI) is available free of charge via the Internet at http://pubs.acs.org. It includes detailed optimized experimental procedures for the synthetic materials and spectroscopic data.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejmech.2018.10.011.

Abbreviations

Asc	ascorbic
Triaz	triazolyl
YEPD	Yeast extract Peptone Dextrose

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