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Exploring a glycosylation methodology for the synthesis of hydroxamate-modified alginate building blocks†

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Alginate, an anionic polysaccharide, is an important industrial biomaterial naturally harvested from seaweed. Many of its important physicochemical properties derive from the presence of charged carboxylate groups presented as uronic acids within the polysaccharide backbone. An ability to modify these carboxylates with alternate functional groups would enable the design and implementation of new alginate systems possessing different physicochemical properties. We present herein our approach to the chemical synthesis of alginate disaccharides, modified at the carboxylate C6 position with bioisosteric hydroxamate residues. The synthesis and utilisation of C6-hydroxamate donor and acceptor building blocks enables a first access to protected α- and β-linked hydroxamate-containing disaccharides, additionally equipped with a functional tether at the reducing terminus. The evaluation of these building blocks for chemical glycosylation demonstrates the incorporation of bioisosteric functional groups into an alginate disaccharide backbone and highlights the important contribution of both acceptor and donor reactivity underpinning uronate glycosylations.

1. Introduction

Alginate, **1**, a heterogenous polysaccharide composed of β-1,4-linked D-mannuronic acid (M) and its C5 epimer α-L-guluronic acid (G) (Fig. 1), was first extracted from brown algae (*Phaeophyceae*) in the late nineteenth century and has been commercially available since the early twentieth century. It is also produced by two genera of bacteria, *Pseudomonas* and *Azotobacter*, and the study of alginate biochemistry and biosynthesis has, to date, largely focused on the *Pseudomonas* genera. This is owed to the prevalence of *Pseudomonas aeruginosa* in causing chronic infections for cystic fibrosis patients, contributing to a reduction in lung function and increased mortality rates.[1]

Within alginate sub-structure the relative proportions of M and G units, their homo- or hetereopolymeric block-groupings and the possibility for acetylation at the C2 and/or C3 positions of M residues produces a structurally diverse biopolymer. This structural microheterogeneity varies depending on the alginate source and consequently affects the viscosity and gel-forming capacity of the final polysaccharide material. Such physicochemical properties mean that alginate has also found important use as an industrial biomaterial, currently sourced from marine algae, where it is applied as a stabiliser, viscosifier and gelling agent across the food, beverage, paper and pharmaceutical industries.[2–5] Alginate is therefore something of a double-edged sword from the perspective of its deleterious role in microbial infections countered by its profound utility as a biomaterial.

As part of a program to develop accessing next-generation alginate materials, through the provision of modified oligosaccharide sequences with improved or altered functional group properties, we targeted a bottom-up synthetic approach to provide structurally defined, modified alginate building blocks. Utilisation of such an approach for both chemical[6–9] and automated[10] syntheses of poly-M and GM-containing algi-

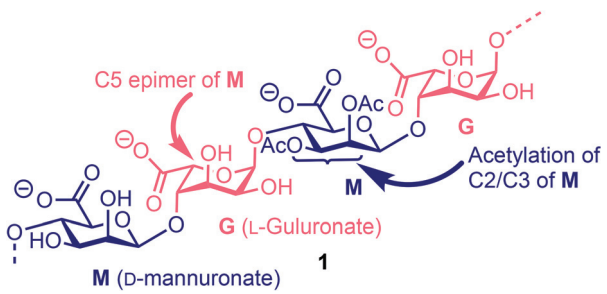

Fig. 1 Chemical structure of the alginate polysaccharide **1** showing constituent M and G residues and C2/C3 acetylation for one M residue.

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nate oligosaccharides have been reported, which provides essential understanding of the glycosylation chemistry required to assemble such complex materials.[11] The assembly of β-1,4-linked mannuronates is challenging, owing to the required 1,2-*cis* linkage and the presence of a carboxylate oxidation level at C6. Uronate donors were typically classed as inferior donors compared to their unoxidised counterparts, due to the electron withdrawing effect of the C6 group making them less reactive. Recently Codée's group have countered this general classification and demonstrated a highly β-selective glycosylation methodology for the assembly of alginate oligosaccharides. They proposed that a C5-carboxylate ester in the mannuronate donor prefers to occupy an axial position in the oxocarbenium half-chair intermediate (Fig. 2a), which undergoes reaction with the acceptor, delivering the required 1,2-*cis* linked glycosylation products with excellent diastereoselectivity.[11,12]

Inspired by this work we envisaged that incorporating changes to the parent monosaccharide component (through modification of the carboxylate residue) could enable the assembly of modified alginate oligosaccharides using a glycosylation approach similar to that seen for the native system. We chose to investigate a bioisosteric carboxylate replacement (Fig. 2b), with a view to providing C6-modified alginates with new functional properties; in this case as possible siderophores through the known ion-chelating abilities of a hydroxamic acid.[13] Hydroxamic acid incorporation at C6 in glycosides has been harnessed to produce biodegradable surfactants with good chelating properties for the removal of contaminant metals in wastewater; Kovensky and co-workers demonstrated that hydroxamic acid derivatives exhibited improved iron extraction compared to native C6-carboxylic acids.[14] We report herein our approach to the first examples of hydroxamate modified alginate disaccharide building blocks and discuss the initial data arising from utilising C6-modified mannuronates for glycosylation.

2. Results and discussion

2.1. Synthesis of monosaccharide building blocks

We envisaged our synthetic methodology to derive from a common precursor that could give access to several different mannuronate building blocks (donors and acceptors), for glycosylation and assembly into longer systems. We also wished to incorporate capability for immobilisation or conjugation through a reducing-end tether, as has been employed successfully for many carbohydrate fragment syntheses.[15–17] Accordingly, we identified carboxylate **3**, reported by Codèe for automated alginate oligosaccharide synthesis,[10] as our starting point. Thioglycoside hydroxamate donors **5** and **6** were prepared on multi-gram scale from **3** (Scheme 1). To install the C6-hydroxamate group we investigated coupling of carboxylate **3** with *O*-benzyl hydroxylamine using PyBOP as the activating reagent. This reaction proceeded smoothly and in good yield (81%) and was followed by benzyl protection of the hydroxamate nitrogen. We evaluated coupling of **3** directly with *N*,*O*-dibenzyl hydroxylamine to avoid this subsequent protection step, but this reagent, more basic than *O*-benzyl hydroxylamine, triggered a competing C4–C5 elimination and so was abandoned. Similarly, use of an acetyl group to protect the hydroxamate nitrogen proved problematic, being readily

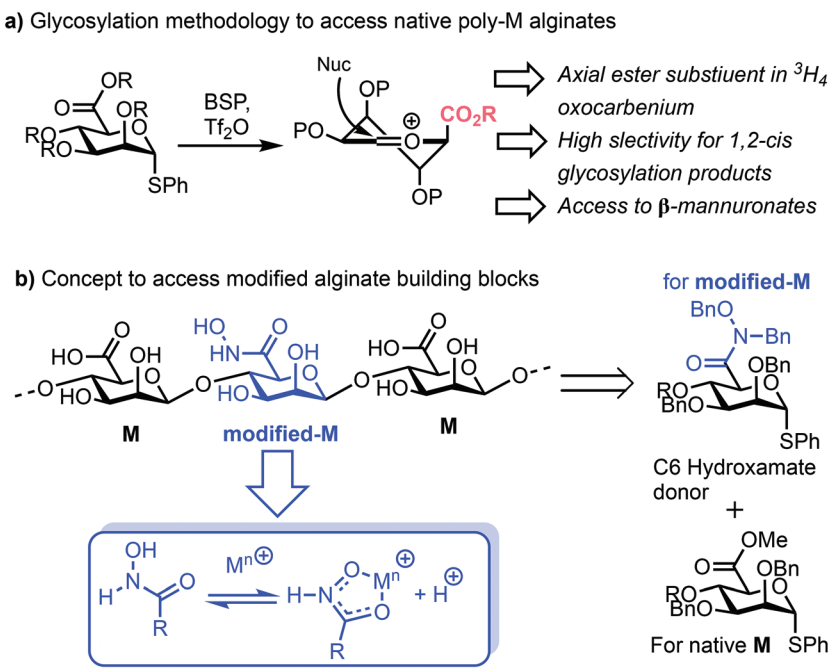
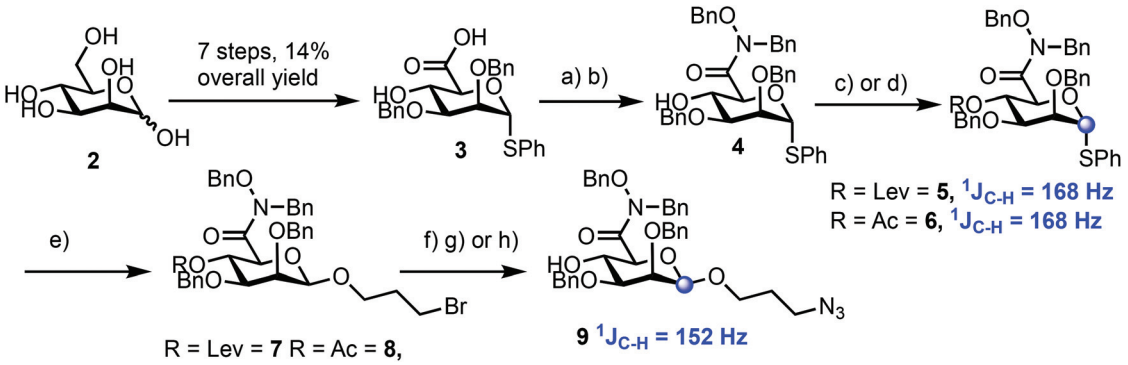


Fig. 2 (a) Glycosylation chemistry to access β-mannuronates (b) building blocks required for assembly of modified alginates. R = protecting group *e.g.* Bn, Lev.



Scheme 1 (a) BnO–NH_2, PyBOP, DIPEA, DCM, rt, 3 h, 81% (b) K_2CO_3, BnBr, DMF, RT, 2 h, 42% (c) Ac_2O, pyridine DCM, rt, 24 h, 68% (d) Lev_2O, pyridine, DCM, rt, 24 h, 88% (e) for R = Ac, $HO(CH_2)_3Br$, Ph_2SO, TTBP, Tf_2O, DCM, −90 °C to −20 °C, 1 h, 89%, for R = Lev, Ph_2SO, TTBP, Tf_2O, $HO(CH_2)_3Br$, DCM, −90 °C to −20 °C, 1 h, 85% (f) For R = Ac, NaN_3, acetone, 76%, for R = Lev, NaN_3, acetone, 54% (g) For R = Ac, $Na_{(s)}$, MeOH, RT, 24 h, 61%. (h) For R = Lev, $H_2NNH_2{\cdot}H_2O$, pyridine/AcOH (4/1), 30 min, 55%. Anomeric $^1J_{C-H}$ coupling constants shown in blue to support later assignment of glycosylation stereochemistry.

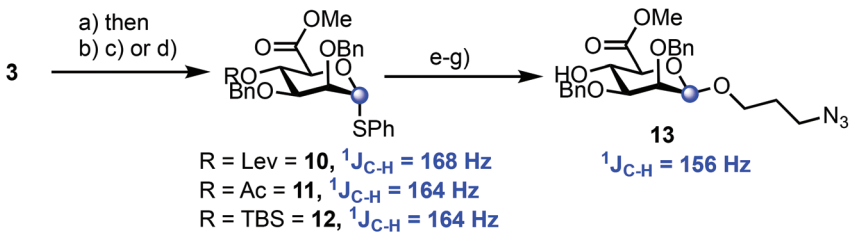
cleaved under the reaction conditions needed for thioglycoside donor activation to access **7** or **8**. Following successful coupling and *N*-Bn protection, *O*-4 was protected as either a levulinoyl or acetyl ester to deliver thioglycoside donors **5** and **6** (Scheme 1).

Both **5** and **6** were additionally manipulated into a reducing end acceptor, to allow iteration with appropriate donors. Thioglycoside activation using Ph_2SO–Tf_2O allowed glycosylation with 3-bromopropanol, installing the precursor to a reducing-end, conjugable linker within **7** and **8**. Initial attempts using NIS or NBS to activate **5** or **6** for reaction with 3-bromopropanol failed, with *N*-Bn deprotection observed, followed by the formation of an α-linked glycosylation product, possibly through anchimeric assistance of the now deprotected nitrogen blocking the top face of the intermediate. S_N2 displacement of alkyl bromides **7** and **8** was completed using sodium azide, followed by appropriate *O*-4 deprotection to deliver hydroxamate acceptor **9**.

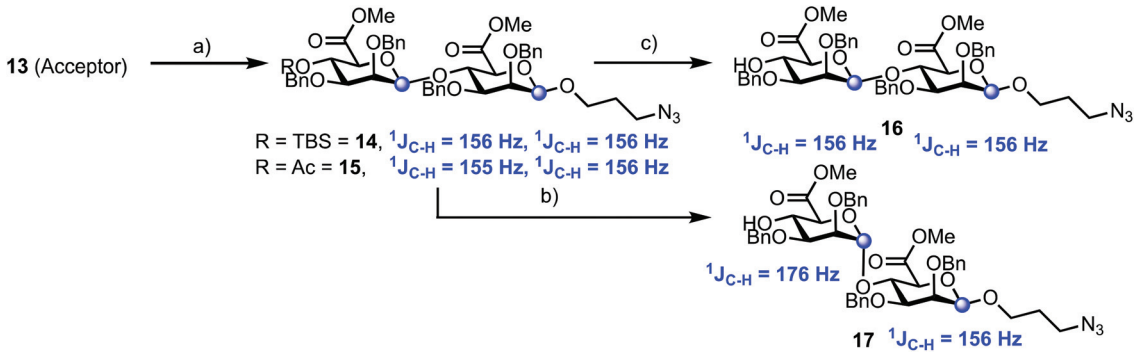
With C6-modified donor and acceptor building blocks **5**, **6** and **9** in hand we also completed the synthesis of native mannuronate donor (**10–12**) and acceptor **13** materials from **3** (Scheme 2), delivering a small matrix of appropriate building blocks to subsequently explore modified alginate disaccharide synthesis.

2.2. Synthesis of C6-hydroxamate-modified disaccharides

For comparative purposes we first completed a synthesis of native mannuronate disaccharides **14** and **15**,[8] glycosylating native acceptor **13** with either of donors **11** or **12** using NIS/TMSOTf activation (Scheme 3). Confirmation of the desired 1,2-*cis* glycosylation products **14** and **15** was made through comparison of the anomeric $^1J_{C-H}$ coupling constants, which closely matched those previously reported for **15**.[8] Whilst proceeding with *O*-4-deprotection of disaccharides **14** and **15** we observed that removal of the *O*-4 acetyl group from **15** using NaOMe delivered a product whose analytical data were not consistent with the literature reported for the expected product **16** (which was accessed form an *O*-4 Lev deprotection using hydrazine).[8] ^{1}H NMR analysis of our material (**17**) showed $H_{1'}$ at 5.43 ppm instead of the reported 4.73 ppm. Moreover, coupled HSQC data showed $^1J_{C1-H1}$ = 156 Hz and $^1J_{C1'-H1'}$ = 176 Hz. These data suggested that the reaction conditions had liberated the C4-*OH* (observed at 2.95 ppm), but also altered the anomeric integrity at the non-reducing end of the disaccharide. ESI-MS analysis found the sodium adduct of **17** and comparison to a disaccharide containing L-guluronic acid as the non-reducing end monomer ruled out C5 epimerisation ($H_{1'Gul}$ = 5.24 ppm).[8] An n*O*e experiment using **17** and irradiat-



Scheme 2 (a) MeI, K_2CO_3, DMF rt, 24 h, 77% (b) Lev_2O, pyridine, 18 h, 78% (c) Ac_2O, pyridine, 3 h, 78% (d) TBDMSOTf, imidazole, DMAP, DMF, RT, 24 h, 70% (e) for R = Ac, Ph_2SO, TTBP, Tf_2O, $HO(CH_2)_3Br$, DCM, −60 to −90 °C, 1 h, 66% (f) NaN_3, acetone, 55 °C, 48 h, 97% (g) $Na_{(s)}$, MeOH, RT, 24 h, 87%. Anomeric $^1J_{C-H}$ coupling constants shown in blue.



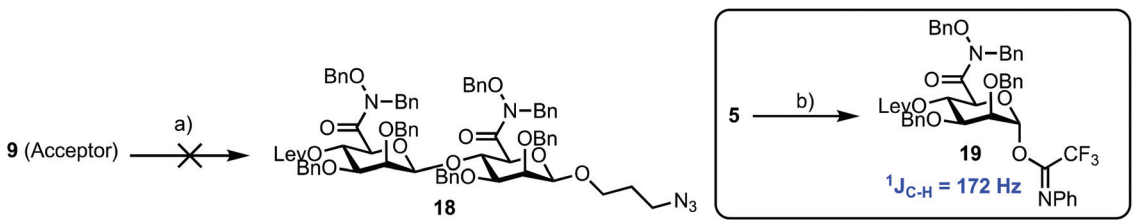
Scheme 3 (a) For **11**, NIS, TMSOTf, CH_2Cl_2, −60 °C, 30 min, 56%, for **12**, NIS, TMSOTf, CH_2Cl_2, −60 °C, 30 min, 61%, (b) NaOMe, MeOH, 2 h, 46% (c) for **14** AcCl, MeOH, 18 h, 40%. Anomeric $^1J_{C-H}$ coupling constants shown in blue.

ing $H_{1'}$ (5.43 ppm) showed transfer to H_4 (see ESI†), but not to $H_{5'}$. Comparatively, an n*O*e experiment for **16** showed transfer from $H_{1'}$ to $H_{5'}$ but not to H_4, supporting a change in the disaccharide linkage stereochemistry from β to α for **17** under these reaction conditions. To investigate this unusual observation further, we repeated the experiment and stopped the deprotection after 1 h, neutralising with Amberlite as before. ^{13}C NMR clearly showed a mixture of α- and β-linked products (see ESI†), suggesting the anomerisation was underway, but not complete. We took this material and stirred it overnight in MeOH with Amberlite (observed pH = 5–6), but no further change was observed by ^{13}C NMR, suggesting that the reaction time and/or pH and for 4-*O*-Ac deprotection were causing this unwanted reaction. At present we cannot fully explain why this occurred under these conditions beyond being able to report the observed data; an $E1_{CB}$ elimination from the reducing end uronate, mutarotation of the released hemi-acetal to the α-anomer, followed by re-addition to the bottom face of the elimination product could deliver **17** from **15.** Alternative attempts to remove the acetate group in **15** with NH_3 or triethylamine in methanol at room temperature and 35 °C were unsuccessful, recovering only starting material. Comparatively, when *O*-4 TBS disaccharide **14** was treated with AcCl in MeOH at room temperature the reaction proceeded in 40% yield to deliver **16** whose anomeric integrity was confirmed as expected (Scheme 3).

We next attempted to apply the established glycosylation methodology using hydroxamate donor **5** and hydroxamate acceptor **9** (Scheme 4). We had previously confirmed that donor pre-activation with Ph_2SO/Tf_2O was successful in delivering β-linked products **7** and **8** in high yields (Scheme 1). This same activation protocol was thus applied in the glycosylation of **9** with **5**, but unfortunately disaccharide **18** was not formed (Scheme 4).

Variations to the reaction conditions using Ph_2SO/Tf_2O were scrutinised, but still did not deliver **18**. For this pre-activation protocol we generally observed acceptor, amounts of hydrolysed donor and formation of a polar, baseline material, suggesting that donor **5** was undergoing an alternative reaction. Despite isolating the baseline material, we were unable to characterise this side-product. Evaluation of several further glycosylation conditions, including BSP/Tf_2O, DMTST and inverse glycosylation, all failed to produce **18**.

Based on these observations, we synthesised an *N*-phenyltrifluoroacetimidate (*N*-PhTFA) donor **19** from **5** *via* the hemiacetal (Scheme 4) and used this directly for glycosylation with **9**. *tert*-Butyldimethylsilyl trifluoromethanesulphonate (TBDMSOTf) was employed as the activator, as it had been used successfully for activation of the native *N*-PhTFA mannuronate donor.[10] This glycosylation returned mostly unreacted **9** (87%) and a small amount of the anomeric *tert*-butyldimethylsilanol adduct of donor **5** (16%). We next attempted pre-activation of donors **5** or **10** prior to the addition of the α-thio acceptors (**9** or **13**). However, this reaction was only successful when an acceptor with a primary C6-OH was used, not with **9** or **13**. As we had evaluated several unsuccessful approaches to effect glycosylation towards a hydroxamate disaccharide, we next investigated the reactivity of modified C6 donor **5** and acceptor **9** systems with native mannuronate building blocks **10** and **13.**



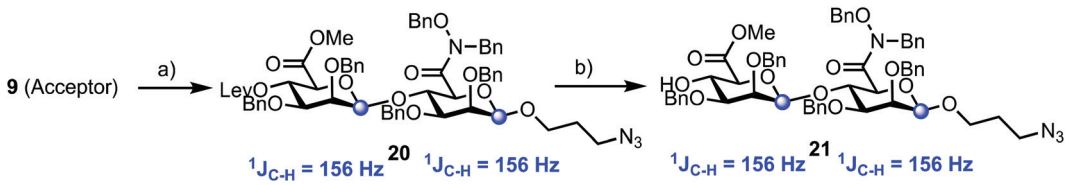
Scheme 4 (a) **5**, Ph_2SO/Tf_2O or BSP/Tf_2O or Me_2S_2/Tf_2O or NIS/TMSOTf, see Table 1 in ESI† for details of reaction conditions attempted (b) (i) NIS, AgOTf, DCM/H_2O, 75% (ii) *N*-PhTFA-Cl, K_2CO_3, H_2O, acetone, 68%. Anomeric $^1J_{C-H}$ coupling constants shown in blue.

2.3. Synthesis of mixed C6-hydroxamate disaccharides

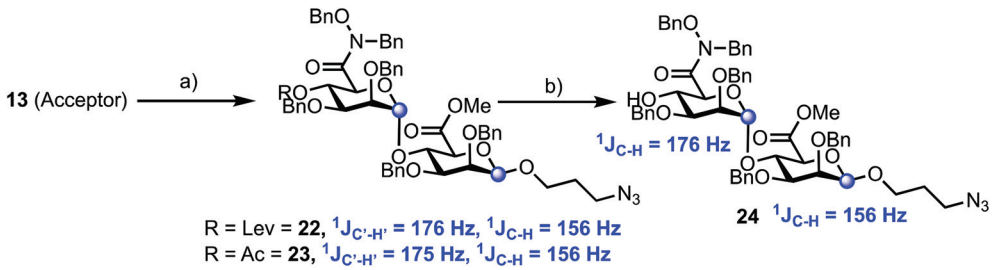
The coupling of hydroxamate acceptor **9** with mannuronate donor **10** using an NIS/TMSOTf promoter system produced β-linked disaccharide **20** in 55% yield, as indicated by the observed $^{1}J_{C-H}$ coupling constants (Scheme 5). This result suggested the balance of both donor and acceptor reactivity during glycosylation was improved, relative to forming **18**, possibly through the known reactivity of mannuronate donor **10**.[8,10] C6-modified alginate disaccharide **20** could be conveniently 4-*O*-deprotected, using hydrazine hydrate, to regenerate acceptor capability in the form of **21** in good yield (81%).

We also attempted the reverse reaction, using donors **5** or **6** with mannuronate acceptor **13** (Scheme 6). Using donor **6**, TLC analysis indicated the formation of a complex mixture after 30 min at 0 °C. Purification yielded **23** in low yield (12%). A coupled HSQC spectrum showed $^{1}J_{C1-H1}$ = 156 Hz for the reducing end (C_1, ^{13}C δ 99.5 ppm) and $^{1}J_{C1'-H1'}$ = 176 Hz for the non-reducing end linkage ($C_{1'}$, ^{13}C δ 102.0 ppm), suggesting an α-linkage had formed as the major product (9/1 as adjudged by ^{1}H NMR). This glycosylation was repeated using donors **5** and **6** at different temperatures and for different periods of time (1 h at −40 °C, 2 h at −25 °C, 3 h at −20 °C and 30 min at −10 °C). The yields obtained were however only slightly improved with **22** isolated in a maximum 30%, alongside recovered **13** (14%). Subsequent *O*-4-deprotection of **22** or **23** was effected using hydrazine or sodium methoxide giving **24** in acceptable yields (76% from **22** and 54% from **23**) and noting that the anomerisation issues observed for deprotecting **15** were not repeated. Here we generally found 4-*O*-Lev deprotection to be better yielding at disaccharide level, compared to 4-*O*-Ac.

In isolating α-linked disaccharides **22** and **23**, we propose that the inclusion of a protected hydroxamate group enabled its participation in the reaction through blocking the top face of the donor. This may proceed through a bicyclic glycosyl cation of type **25**, illustrated in Fig. 3, or through coordination of the hydroxamate oxygen to the anomeric carbon (not



Scheme 5 (a) **10**, NIS, TMSOTf, CH_2Cl_2, −40 °C, 60 min, 55% (b) $H_2NNH_2{\cdot}H_2O$, pyridine/AcOH (4/1), 30 min, 81%. Anomeric $^{1}J_{C-H}$ coupling constants shown in blue.



Scheme 6 (a) **6**, NIS, TMSOTf, CH_2Cl_2, 0 °C, 30 min, 12% or **5**, NIS, TMSOTf, CH_2Cl_2, −40 °C to −10 °C, 6.5 h, 30% (b) for R = Ac, $Na_{(s)}$, MeOH, RT, 16 h, 54%, For **22**, $H_2NNH_2{\cdot}H_2O$, pyridine/AcOH (4/1), 30 min, 76%. Anomeric $^{1}J_{C-H}$ coupling constants shown in blue.

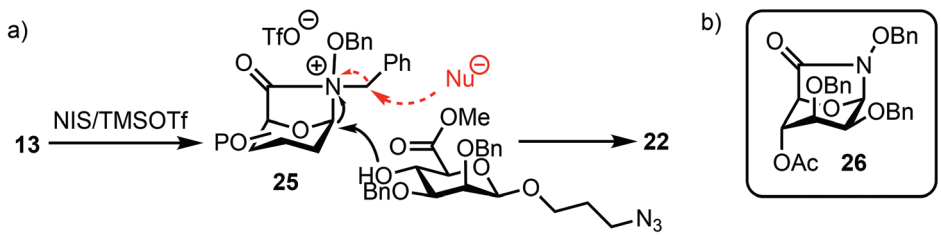


Fig. 3 (a) A possible glycosyl intermediate **25** formed during glycosylation to **22**, blocking the top face of the donor (b) cyclic amide **26**. A $^{1}C_4$ conformation was indicated through analysis of the ^{1}H coupling constants *e.g.* H4 δ 5.06 (app. t, J = 1.9 Hz).

shown). As the yields for this reaction were generally poor and coincided with recovered acceptor, we hypothesised that an alternative pathway may exist for the reaction, giving rise to a cyclic product with loss of *N*-Bn (Fig. 3, red dotted pathway). This arose from earlier experiments using an *N*-Ac protected hydroxamate donor (attempting to install the anomeric linker group) where we isolated and characterised bicyclic *N*-linked hydroxamate **26**. We were however unable to isolate any of **26** from the reaction to form **22** and also confirmed through HRMS and HMBC analyses of **22** that the *N*-Bn remained intact. Additionally, we did not detect *N*- to *O*-4 Bn transfer between **6** and **13** and at this juncture are unable to fully explain the lower than average yield for these glycosylations.

The results of these experiments using C6-hydroxamate modified glycosyl donors and acceptors indicate there is a delicate balance of reactivity contributed from both reaction components. From this initial data we conclude that modified acceptor **9** can be used effectively with native mannuronate donors to deliver β-1,4-linked **20** in acceptable yields. A subsequent small scale iteration attempt to the trisaccharide using modified donor **6** and acceptor **21** switched the linkage stereochemistry to α and proceeded in poor yield (14%). This implies a redundancy for the formation of multiple β-1,4-linkages. Similarly, use of native acceptor **13** with modified donor **6** gave α-linked products and in low yield, but glycosylation of **5** or **6** with a more reactive primary alcohol acceptor was successful. We are currently evaluating approaches to alternative C6-hydroxamate building blocks that will deliver capability for β-linked elongation beyond disaccharide level and will report on this in due course.

4. Conclusion

Elucidating new chemical methodologies to modify carbohydrate monomer building blocks is underpinning to their glycosylation to create longer oligo- and polysaccharides that contain non-native functional groups. This will contribute to the development of next-generation carbohydrate-based materials with improved or altered physicochemical properties and will enable the essential study of polysaccharide architectures in more detail.[18] Targeting the provision of modified alginate oligosaccharides, we have described our approach to access C6-hydroxamate derivatives of native mannuronic acid. Bioisosteric hydroxamate donor and acceptor monosaccharides were successfully synthesised and enabled the first preparations of related disaccharide species (in protected form). Of note is an observed switch between the ability to deliver α- or β-linked glycosylation products, depending on donor/acceptor pairing when using these non-native building blocks.

5. Experimental section

5.1. General methods and materials

All reagents and solvents which were available commercially were purchased from Acros, Alfa Aesar, Fisher Scientific, or Sigma Aldrich. All reactions in non-aqueous solvents were conducted in oven dried glassware under a nitrogen atmosphere with a magnetic stirring device. Solvents were purified by passing through activated alumina columns and used directly from a Pure Solv-MD solvent purification system and were transferred under nitrogen. Reactions requiring low temperatures used the following cooling baths: −78 °C (dry ice/acetone), −30 °C (dry ice/acetone), −15 °C (NaCl/ice/water) and 0 °C (ice/water). Infra-red spectra were recorded neat on a PerkinElmer Spectrum 100 FT-IR spectrometer; selected absorbtion frequencies (ν_{max}) are reported in cm^{-1}. ^1H NMR spectra were recorded at 400 MHz and GATED-^{13}C spectra at 100 MHz respectively using a Bruker AVIII400 spectrometer. ^1H NMR signals were assigned with the aid of gDQCOSY. ^{13}C NMR signals were assigned with the aid of gHSQCAD. Coupling constants are reported in Hertz. Chemical shifts (δ, in ppm) are standardised against the deuterated solvent peak. NMR data were analysed using Nucleomatica iNMR software. ^1H NMR splitting patterns were assigned as follows: br s (broad singlet), s (singlet), d (doublet), app. t (apparent triplet), t (triplet), dd (doublet of doublets), ddd (doublet of doublet of doublets), or m (multiplet and/or multiple resonances). Reactions were followed by thin layer chromatography (TLC) using Merck silica gel 60F254 analytical plates (aluminium support) and were developed using standard visualising agents: short wave UV radiation (245 nm) and 5% sulfuric acid in methanol/Δ. Purification *via* flash column chromatography was conducted using silica gel 60 (0.043–0.063 mm). Melting points were recorded using open glass capillaries on a Gallenkamp melting point apparatus and are uncorrected. Optical activities were recorded on automatic polarimeter Rudolph autopol I or Bellingham and Stanley ADP430 (concentration in g per 100 mL). MS and HRMS (ESI) were obtained on Waters (Xevo, G2-XS TOF) or Waters Micromass LCT spectrometers using a methanol mobile phase. High resolution (ESI) spectra were obtained on a Xevo, G2-XS TOF mass spectrometer. HRMS was obtained using a lock-mass to adjust the calibrated mass.

***O*-Benzyl (phenyl 2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside) hydroxamate.** To a mixture of **3**[12] (700 mg, 1.50 mmol, 1.0 equiv.) and *O*-benzylhydroxylamine hydrochloride (260 mg, 1.65 mmol, 1.1 equiv.) in CH_2Cl_2 (5 mL) was added successively under N_2 atmosphere, PyBOP (860 mg, 1.65 mmol, 1.1 equiv.) and DIPEA (653 μL, *d* = 0.742, 3.75 mmol, 2.5 equiv.). The reaction mixture was left stirring at room temperature for 3 h. Upon completion of the reaction, the solvent was removed under reduced pressure and the crude was purified using silica gel flash column chromatography, eluting with EtOAc/hexane (30/70, 40/60, 50/50, 90/10) to afford the title compound as a colourless oil (770 mg, 1.35 mmol, 90%). R_f 0.30 (EtOAc/hexane, 1/2); $[\alpha]_D^{22}$ +120.0 (*c*. 1.0, $CHCl_3$); **^1H NMR** (400 MHz; $CDCl_3$) δ 8.84 (1 H, br. s, C(O)N*H*OBn), 7.39–7.21 (20H, m, Ar–H), 5.38 (1 H, d, *J* = 1.4 Hz, H_1), 4.87 (1 H, d, *J* = 11.1 Hz, CH_2Ph-attached to C3), 4.84 (1 H, d, *J* = 10.7 Hz, C(O)NHOCH_2Ph), 4.83 (1 H, d, *J* = 11.2 Hz, CH_2Ph-attached to C3), 4.66 (1 H, d, *J* = 12.0 Hz,

CH_2Ph-attached to C2), 4.64 (1 H, d, J = 12.0 Hz, C(O)NHOCH_2Ph), 4.58 (1 H, d, J = 12.0 Hz, CH_2Ph-attached to C2), 4.54 (1 H, d, J = 9.7 Hz, H_5), 4.30 (1 H, app. t, J = 9.5 Hz, H_4), 3.90 (1 H, dd, J = 2.8, 1.8 Hz, H_2), 3.72 (1 H, dd, J = 9.2, 3.0 Hz, H_3); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 168.4 (*C*(O)NHOBn), 138.5, 137.9, 134.9, 133.1, 132.2, 129.5, 129.4, 128.9, 128.7, 128.5, 128.5, 128.5, 128.2, 128.1, 128.0, 127.95, 127.9, 127.8 (18 C, Ar–C), 86.7 (C1), 78.4 (C(O)NHOCH_2Ph), 77.9 (C3), 76.7 (C2), 73.2 (*C*H_2Ph-attached to C3), 73.0 (*C*H_2Ph-attached to C2), 71.2 (C5), 69.8 (C4); **HRMS** (ES^+) m/z [found: $(M + H)^+$ 572.2111 $C_{33}H_{33}NO_6S$ requires $(MH)^+$, 572.2107]; **IR** ν_{max}/cm^{-1} 3313 (m, N–H), 1659 (s, C=O), 1071 (s, C–O_{ether}).

***O*-Benzyl, *N*-benzyl (phenyl-2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside) hydroxamate 4.** To a stirred solution of *O*-benzyl (phenyl 2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside) hydroxamate (180 mg, 0.31 mmol, 1.0 equiv.) and K_2CO_3 (65.3 mg, 0.47 mmol, 1.5 equiv.) in DMF (3.5 mL) was added benzyl bromide (41.2 μL, d = 1.438, 0.35 mmol, 1.1 equiv.) at room temperature. The reaction mixture stirred for 4 h, diluted with EtOAc (60 mL), washed with H_2O (50 mL) and brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by Reveleris® automated silica gel flash column chromatography (liquid injection onto column), eluting with EtOAc/hexane (0/100, 5/95, 20/80 and 90/10) afforded **4** as a colourless oil (90 mg, 0.13 mmol, 44%). R_f 0.75 (EtOAc/hexane, 1/2); $[\alpha]_D^{22}$ +55.7 (c. 0.22, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.40–7.14 (25 H, m, Ar–H), 5.59 (1 H, d, J = 1.3 Hz, H_1), 5.22 (1 H, d, J = 12.2 Hz, C(O)N(CH_2Ph)OBn), 5.16 (1 H, d, J = 12.2 Hz, C(O)N(CH_2Ph)OBn), 5.06 (1 H, d, J = 12.3 Hz, C(O)N(Bn)OCH_2Ph), 5.00 (1 H, d, J = 12.3 Hz, C(O)N(Bn)OCH_2Ph), 4.71 (1 H, d, J = 11.9 Hz, CH_2Ph), 4.69 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.64 (1 H, d, J = 10.7 Hz, CH_2Ph), 4.62 (2 H, d, J = 8.8 Hz, H_5), 4.59 (1 H, d, J = 11.6 Hz, CH_2Ph), 4.43 (1 H, td, J = 9.6, 2.9 Hz, H_4), 3.96 (1 H, dd, J = 2.9, 1.6 Hz, H_2), 3.66 (1 H, dd, J = 9.8, 3.0 Hz, H_3), 2.57 (1 H, d, J = 2.9 Hz, C4-*OH*); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 151.8 (*C*(O)N(Bn)OBn), 138.2, 137.9, 137.7, 136.7, 134.0, 130.8, 129.2, 128.5, 128.4, 128.4, 128.2, 128.0, 127.94, 127.9, 127.8, 127.7, 127.4, 86.3 (C1), 78.2 (C3), 77.2 (C2), 76.5 (C(O)N(Bn)O*C*H_2Ph), 72.8 (*C*H_2Ph), 72.6 (*C*H_2Ph), 72.3 (C(O)N(*C*H_2Ph)OBn), 71.8 (C5), 67.8 (C4); **^{13}C-GATED** (101 MHz; $CDCl_3$): 86.3 ($^1J_{C1-H1}$ = 168 Hz, C1); **HRMS** (ES^+) m/z [found: $(M + H)^+$ 662.2589 $C_{40}H_{39}NO_6S$ requires $(MH)^+$, 662.2571]; **IR** ν_{max}/cm^{-1} 1640 (m, C=O_{amide}), 1454 (m, C=$C_{aromatic}$), 1223 (s, C–O_{ester}), 1024 (s, C–O_{ether}).

***O*-Benzyl, *N*-benzyl (phenyl 4-*O*-levulinoyl-2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside) hydroxamate 5.** To a mixture of **4** (90 mg, 0.13 mmol, 1.0 equiv.) and levulinoyl anhydride (43 mL, 0.27 mmol, 2.0 equiv.) in CH_2Cl_2 (1 mL) was added pyridine (44 mL, 0.54 mmol, 4.0 equiv.) under N_2 atmosphere. The reaction mixture was left stirring at room temperature for 18 h. Upon completion of the reaction, the mixture was diluted with CH_2Cl_2 (15 mL), and the organic layer was washed successively with 1 M HCl (2 × 10 mL) and sat. aq. $NaHCO_3$ solution (2 × 10 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure furnishing a colourless oil. The crude was purified using silica gel flash column chromatography, eluting with a gradient of diethyl ether/petroleum ether (30%–90% diethyl ether) to afford **5** as a colourless oil (90 mg, 0.12 mmol, 91%). R_f 0.58 (EtOAc/hexane, 1/2); $[\alpha]_D^{22}$ +51.50 (c. 1.00, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.38–7.22 (25 H, m, Ar–H), 5.74 (1 H, app. t, J = 9.6 Hz, H_4), 5.54 (1 H, d, J = 2.0 Hz, H_1), 5.39 (1 H, d, J = 12.0 Hz, C(O)N(CH_2Ph)OBn), 5.32 (1 H, d, J = 12.0 Hz, C(O)N(CH_2Ph)OBn), 4.99 (2 H, s, C(O)N(Bn)OCH_2Ph), 4.67 (1 H, d, J = 12.5 Hz, CH_2Ph-attached to C2), 4.64 (1 H, d, J = 12.9 Hz, CH_2Ph-attached to C2), 4.64 (1 H, d, J = 9.8 Hz, H_5), 4.58 (1 H, d, J = 12.2 Hz, CH_2Ph-attached to C3), 4.53 (1 H, d, J = 12.2 Hz, CH_2Ph-attached to C3), 3.98–3.94 (1 H, m, H_2), 3.75 (1 H, dd, J = 9.4, 2.9 Hz, H_3), 2.66–2.38 (3 H, m, CH_2 Lev), 2.31–2.19 (1 H, m, CH_2 Lev), 2.12 (3 H, s, CH_3 Lev); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 206.2 (C=O Lev ketone), 171.1 (C=O Lev), 150.6 (*C*(O)N(Bn)OBn), 137.9, 137.9, 137.8, 137.1, 131.6, 129.1, 128.4, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 86.1 (C1), 77.2 (C3), 76.4 (C(O)N(Bn)O*C*H_2Ph), 76.1 (C2), 73.1 (C(O)N(*C*H_2Ph)OBn), 72.4 (*C*H_2Ph-attached to C2), 72.1 (*C*H_2Ph-attached to C3), 71.1 (C5), 68.6 (C4), 38.0 (*C*H_2 Lev), 29.8 (*C*H_3 Lev), 28.0 (*C*H_2 Lev); **^{13}C-GATED** (101 MHz; $CDCl_3$): 86.1 ($^1J_{C1-H1}$ = 168 Hz, C1); **HRMS** (ES^+) m/z [found: $(M + H)^+$ 760.2955 $C_{45}H_{45}NO_8S$ requires $(MH)^+$, 760.2939].

***O*-Benzyl, *N*-benzyl (phenyl 4-*O*-acetyl-2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside) hydroxamate 6.** To a stirred solution of **4** (900 mg, 1.47 mmol, 1.0 equiv.) and K_2CO_3 (240 mg, 1.76 mmol, 1.2 equiv.) in DMF (11 mL) was added benzyl bromide (0.2 mL, d = 1.438, mmol, 1.1 equiv.) at room temperature. The reaction mixture stirred for 15 h, diluted with EtOAc (60 mL), washed with H_2O (50 mL) and brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by Reveleris® automated silica gel flash column chromatography (liquid injection onto column), eluting with EtOAc/hexane (0/100, 5/95, 20/80 and 90/10) afforded **6** as a colourless oil (450 mg, 0.64 mmol, 42%). R_f 0.80 (EtOAc/hexane, 1/2); $[\alpha]_D^{22}$ +46.7 (c. 1.17, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.40–7.20 (25 H, m, Ar–H), 5.73 (1 H, t, J = 9.6 Hz, H_4), 5.55 (1 H, d, J = 2.0 Hz, H_1), 5.42 (1 H, d, J = 11.9 Hz, C(O)N(CH_2Ph)OBn), 5.35 (1 H, d, J = 12.0 Hz, C(O)N(CH_2Ph)OBn), 5.00 (1 H, d, J = 12.5 Hz, C(O)N(Bn)OCH_2Ph), 4.97 (1 H, d, J = 12.5 Hz, C(O)N(Bn)OCH_2Ph), 4.65 (2 H, s, CH_2Ph-attached to C2), 4.63 (1 H, d, J = 9.8 Hz, H_5), 4.57 (1 H, d, J = 12.2 Hz, CH_2Ph-attached to C3), 4.49 (1 H, d, J = 12.2 Hz, CH_2Ph-attached to C3), 3.98 (1 H, app. t, J = 2.5 Hz, H_2), 3.74 (1 H, dd, J = 9.4, 2.9 Hz, H_3), 1.80 (3 H, s, C(O)CH_3); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 169.3 (*C*(O)CH_3), 150.7 (*C*(O)N(Bn)OBn), 137.9, 137.9, 137.8, 137.2, 133.7, 131.7, 129.1, 128.4, 128.4, 128.3, 128.2, 128.1, 127.8, 127.7, 127.7, 127.7, 127.7, 127.6, 127.6, 86.2 (C1), 76.8 (C3), 76.4 (C(O)N(Bn)O*C*H_2Ph), 76.0 (C2), 73.2 (C(O)N(*C*H_2Ph)OBn), 72.4 (*C*H_2Ph-attached to C2), 72.0 (*C*H_2Ph-attached to C3), 71.3 (C5), 68.3 (C4), 20.7 (C(O)*C*H_3); **^{13}C-GATED** (101 MHz; $CDCl_3$): 86.2 ($^1J_{C1-H1}$ = 168 Hz, C1); **HRMS** (ES^+) m/z [found: $(M + H)^+$ 704.2681 $C_{42}H_{41}NO_7S$ requires $(MH)^+$, 704.2676]; **IR** ν_{max}/cm^{-1} 1751 (m, C=O_{ester}), 1639 (m, C=O_{amide}), 1496, 1454 (C=$C_{aromatic}$), 1223 (s, C–O_{ester}), 1024 (s, C–O_{ether}).

3-Bromopropyl *O*-benzyl, *N*-benzyl (4-*O*-levulinoyl-2,3-di-*O*-benzyl-β-D-mannopyranoside) hydroxamate 7. A solution of **5** (100 mg, 0.13 mmol, 1.0 equiv.), diphenyl sulphoxide (34 mg, 0.187 mmol, 1.3 equiv.) and tri-*tert*-butylpyrimidine (81 mg, 0.33 mmol, 2.5 equiv.) in CH_2Cl_2 (2.5 mL) was stirred over activated 4ÅMS for 40 min. The mixture was cooled to −60 °C and triflic anhydride (28 μL, d = 1.720, 0.17 mmol, 1.3 equiv.) was then added. The mixture was stirred for 5 min followed by cooling to −90 °C, upon 3-bromopropanol (18 μL, d = 1.537, 0.20 mmol, 1.5 equiv.) was added. The reaction mixture was allowed to warm up to −20 °C, and stirring was continued for 1 h. At that temperature triethylamine was added until pH = 7, the organic layer was washed with H_2O (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification using silica gel flash column chromatography, eluting with diethyl ether/petroleum ether (10/90, 20/80, 30/170) afforded **7** as a colourless oil (80 mg, 0.10 mmol, 78%). R_f 0.46 (EtOAc/hexane, 1/2); $[\alpha]_D^{22}$ +39.5 (*c*. 0.84, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.40–7.24 (20 H, m, Ar–H), 5.65 (1 H, app. t, J = 9.9 Hz, H_4), 5.48 (1 H, d, J = 12.0 Hz, C(O)N(CH_2Ph)OBn), 5.42 (1 H, d, J = 12.0 Hz, C(O)N(CH_2Ph)OBn), 4.98 (1 H, d, J = 12.5 Hz, C(O)N(Bn)OCH_2Ph), 4.95 (1 H, d, J = 12.4 Hz, C(O)N(Bn)OCH_2Ph), 4.88 (1 H, d, J = 12.3 Hz, CH_2Ph-attached to C2), 4.81 (1 H, d, J = 12.3 Hz, CH_2Ph-attached to C2), 4.52 (1 H, d, J = 12.3 Hz, CH_2Ph-attached to C3), 4.43 (1 H, d, J = 12.3 Hz, CH_2Ph-attached to C3), 4.39 (1 H, s, H_1), 3.94–3.88 (1 H, m, OCH_2CH$_2$CH$_2$Br), 3.88 (1 H, d, J = 2.6 Hz, H_2), 3.83 (1 H, d, J = 10.0 Hz, H_5), 3.56 (1 H, ddd, J = 9.8, 7.7, 4.8 Hz, OCH_2CH$_2$CH$_2$Br), 3.44 (1 H, dd, J = 9.8, 2.9 Hz, H_3), 3.46–3.38 (2 H, m, OCH$_2$CH$_2$CH_2Br), 2.64–2.37 (3 H, m, CH_2 Lev), 2.27–2.15 (1 H, m, CH_2 Lev), 2.11 (3 H, s, CH_3 Lev), 2.10–1.97 (2 H, m, OCH$_2$CH_2CH$_2$Br); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 206.3 (C=O Lev ketone), 171.2 (C=O Lev), 150.7 (*C*(O)N(Bn)OBn), 138.5, 137.9 (2 C), 137.3, 128.4, 128.3, 128.2, 128.1, 128.1, 128.1, 127.7, 127.7, 127.6, 127.6, 127.4, 101.7 (C1), 78.8 (C3), 76.3 (C(O)N(Bn)O*C*H$_2$Ph), 74.0, 73.9, 73.8 (3C, C2, C5, *C*H$_2$Ph-attached to C2), 73.1 (C(O)N(*C*H$_2$Ph)OBn), 71.5 (*C*H$_2$Ph-attached to C3), 68.3 (C4), 67.4 (O*C*H$_2$CH$_2$CH$_2$Br), 37.9 (*C*H$_2$ Lev), 32.7 (OCH$_2$*C*H$_2$CH$_2$Br), 30.3 (OCH$_2$CH$_2$*C*H$_2$Br), 29.8 (*C*H$_3$ Lev), 27.8 (*C*H$_2$ Lev); **^{13}C-GATED** (101 MHz; $CDCl_3$): 101.7 ($^1J_{C1-H1}$ = 156 Hz, C1); **HRMS** (ES$^+$) m/z [found: (M + H)$^+$ 788.2465 $C_{42}H_{46}BrNO_9$ requires (MH)$^+$, 788.2429].

3-Azidopropyl *O*-benzyl, *N*-benzyl (4-*O*-levulinoyl-2,3-di-*O*-benzyl-β-D-mannopyranoside) hydroxamate. Compound **7** (90 mg, 1.14 mmol, 1.0 equiv.) and NaN_3 (37 mg, 5.70 mmol, 5.0 equiv.) and tetrabutylammonium iodide (2.11 g, 5.70 mmol, 5.0 equiv.) were dissolved in acetone (12 mL) and the reaction mixture was stirred for 24 h at 55 °C. Upon completion, the reaction mixture was cooled to room temperature and EtOAc (25 mL) was added. The organic layer was washed with H_2O (20 mL), brine (20 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the crude product. Purification using silica gel flash column chromatography, eluting with EtOAc/hexane (20/80, 40/60, 50/50) afforded the title compound as a colourless oil (62 mg, 0.83 mmol, 73%). R_f 0.38 (EtOAc/hexane, 1/2); $[\alpha]_D^{22}$ −41.5 (*c*. 2.00, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) 7.41–7.23 (20 H, m, Ar–H), 5.65 (1 H, app. t, J = 9.9 Hz, H_4), 5.48 (1 H, d, J = 12.0 Hz, C(O)N(CH_2Ph)OBn), 5.42 (1 H, d, J = 12.0 Hz, C(O)N(CH_2Ph)OBn), 4.98 (1 H, d, J = 12.4 Hz, C(O)N(Bn)OCH_2Ph), 4.95 (1 H, d, J = 12.5 Hz, C(O)N(Bn)OCH_2Ph), 4.88 (1 H, d, J = 12.3 Hz, CH_2Ph-attached to C2), 4.81 (1 H, d, J = 12.3 Hz, CH_2Ph-attached to C2), 4.52 (1 H, d, J = 12.3 Hz, CH_2Ph-attached to C3), 4.43 (1 H, d, J = 12.3 Hz, CH_2Ph-attached to C3), 4.37 (1 H, s, H_1), 3.90–3.84 (1H, m, OCH_2CH$_2$CH$_2$N$_3$) 3.88 (1 H, d, J = 3.0 Hz, H_2), 3.82 (1 H, d, J = 10.0 Hz, H_5), 3.48 (1 H, ddd, J = 6.6, 6.0, 3.6 Hz, OCH_2CH$_2$CH$_2$N$_3$), 3.44 (1 H, dd, J = 9.8, 2.8 Hz, H_3), 3.30 (2 H, ddd, J 13.9, 9.9, 4.0 Hz, OCH$_2$CH$_2$CH_2N$_3$), 2.63–2.37 (3 H, m, CH_2 Lev), 2.24 (1 H, ddd, J = 10.8, 8.8, 4.0 Hz, CH_2 Lev), 2.10 (3 H, s, CH_3 Lev), 1.81 (2 H, ddt, J = 24.6, 12.3, 6.3 Hz, OCH$_2$CH$_2$CH$_2$N$_3$); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 206.2 (C=O Lev ketone), 171.2 (C=O Lev), 150.7 (C(O)N(Bn)OBn), 138.5, 137.8 (2 C), 137.3, 128.4, 128.3, 128.1, 128.1, 128.1, 128.0, 127.7, 127.7, 127.6, 127.6, 127.4, 101.7 (C1), 78.7 (C3), 76.3 (C(O)N(Bn)O*C*H$_2$Ph), 74.0, 73.9, 73.9 (3C, C2, C5, *C*H$_2$Ph-attached to C2), 73.1 (C(O)N(*C*H$_2$Ph)OBn), 71.5 (*C*H$_2$Ph-attached to C2), 68.3 (C4), 66.6 (O*C*H$_2$CH$_2$CH$_2$N$_3$), 48.3 (OCH$_2$CH$_2$*C*H$_2$N$_3$), 37.9 (*C*H$_2$ Lev), 29.8 (*C*H$_3$ Lev), 29.1 (OCH$_2$*C*H$_2$CH$_2$N$_3$), 27.8 (*C*H$_2$ Lev); **^{13}C-GATED** (101 MHz; $CDCl_3$): 101.7 ($^1J_{C1-H1}$ = 156 Hz, C1); **HRMS** (ES$^+$) m/z [found: (M + H)$^+$ 751.3342 $C_{42}H_{46}N_4O_9$ requires (MH)$^+$, 751.3338].

3-Bromopropyl *O*-benzyl, *N*-benzyl (4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-mannopyranoside) hydroxamate 8. A solution of **6** (100 mg, 0.14 mmol, 1.0 equiv.), diphenyl sulphoxide (37 mg, 0.18 mmol, 1.3 equiv.) and tri-*tert*-butylpyrimidine (88 mg, 0.35 mmol, 2.5 equiv.) in CH_2Cl_2 (3 mL) was stirred over activated MS4Å for 40 min. The mixture was cooled to −60 °C and triflic anhydride (30 μL, d = 1.720, 0.18 mmol, 1.3 equiv.) was then added. The mixture was stirred for 5 min followed by cooling to −80 °C, whereupon 3-bromopropanol (19 μL, d = 1.537, 0.21 mmol, 1.5 equiv.) was added. The reaction mixture was allowed to warm up to −20 °C, and stirring was continued for 1 h. At that temperature triethylamine was added until pH = 7, the organic layer was washed with H_2O (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification using silica gel flash column chromatography, eluting with diethyl ether/petroleum ether (10/90, 20/80, 30/170) afforded **8** as a colourless oil (91 mg, 0.12 mmol, 89%). R_f 0.58 (EtOAc/hexane, 1/2); $[\alpha]_D^{22}$ +12.81 (*c*. 0.50, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.42–7.23 (25 H, m, Ar–H), 5.63 (1 H, t, J = 9.9 Hz, H_4), 5.50 (1 H, d, J = 12.0 Hz, C(O)N(CH_2Ph)OBn), 5.45 (1 H, d, J = 12.0 Hz, C(O)N(CH_2Ph)OBn), 4.99 (1 H, d, J = 12.6 Hz, C(O)N(Bn)OCH_2Ph), 4.94 (1 H, d, J = 12.6 Hz, C(O)N(Bn)OCH_2Ph), 4.89 (1 H, d, J = 12.3 Hz, CH_2Ph-attached to C2), 4.81 (1 H, d, J = 12.3 Hz, CH_2Ph-attached to C2), 4.52 (1 H, d, J = 12.3 Hz, CH_2Ph-attached to C3), 4.39 (1 H, s, H_1) 4.38 (1 H, d, J = 11.3 Hz, CH_2Ph-attached to C3), 3.95–3.88 (1 H, m, OCH_2CH$_2$CH$_2$Br), 3.89 (1 H, d, J = 2.6 Hz, H_2), 3.81 (1 H, d, J = 10.0 Hz, H_5), 3.61–3.52 (1 H, m, OCH_2CH$_2$CH$_2$Br), 3.43 (1 H, dd, J = 9.7, 3.1 Hz, H_3), 3.46–3.39 (2 H, m, OCH$_2$CH$_2$CH_2Br), 2.18–2.10 (2 H, m, OCH$_2$CH_2CH$_2$Br), 1.77 (3 H, s, C(O)CH_3); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 169.3 (*C*(O)CH3), 150.9

(*C*(O)N(Bn)OBn), 138.5, 137.9, 137.9, 137.3, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.7, 127.7, 127.7, 127.6, 127.4, 127.4, 101.8 (C1), 78.9 (C3), 76.3 (C(O)N(Bn)O*C*H$_2$Ph), 74.1 (2 C, C5 and *C*H$_2$Ph-attached to C2), 73.9 (C2), 73.1 (C(O)N(*C*H$_2$Ph)OBn), 71.4 (*C*H$_2$Ph-attached to C3), 68.1 (C4), 67.4 (O*C*H$_2$CH$_2$CH$_2$Br), 32.8 (OCH$_2$*C*H$_2$CH$_2$Br), 30.2 (OCH$_2$CH$_2$*C*H$_2$Br), 20.7 (C(O)*C*H$_3$); **^{13}C-GATED** (101 MHz; CDCl$_3$): 101.8 ($^1J_{C1-H1}$ = 152 Hz, C1); **HRMS** (ES$^+$) *m*/*z* [found: (M + H)$^+$ 732.2188 $C_{39}H_{42}BrNO_8$ requires (M + H)$^+$, 732.2167]; **IR** ν_{max}/cm^{-1} 1745 (m, C=O ester), 1637 (w, C=O amide), 1051 (m, C–O ester).

3-Azidopropyl *O*-benzyl, *N*-benzyl (4-*O*-acetyl-2,3-di-*O*-benzyl-1-β-D-mannopyranoside) hydroxamate. Compound **8** (20 mg, 0.03 mmol, 1.0 equiv.) and NaN_3 (10 mg, 0.02 mmol, 6.5 equiv.) were dissolved in acetone (1.5 mL) and the reaction mixture was stirred for 2 days at 55 °C. Upon completion, the reaction mixture was cooled to room temperature and EtOAc (10 mL) was added. The organic layer was washed with H_2O (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the crude product. Purification using silica gel flash column chromatography, eluting with EtOAc/hexane (10/90, 20/80, 40/60) afforded the title compound as a colourless oil (16 mg, 0.02 mmol, 76%). R_f 0.60 (EtOAc/hexane, 1/2); $[\alpha]_D^{22}$ −50.8 (*c*. 0.93, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) 7.43–7.19 (20 H, m), 5.63 (1 H, t, *J* = 9.9 Hz, H_4), 5.50 (1 H, d, *J* = 12.0 Hz, C(O)N(C*H*$_2$Ph)OBn), 5.45 (1 H, d, *J* = 12.0 Hz, C(O)N(C*H*$_2$Ph)OBn), 4.99 (1 H, d, *J* = 12.6 Hz, C(O)N(Bn)OC*H*$_2$Ph), 4.94 (1 H, d, *J* = 12.6 Hz, C(O)N(Bn)OC*H*$_2$Ph), 4.89 (1 H, d, *J* = 12.3 Hz, C*H*$_2$Ph-attached to C2), 4.81 (1 H, d, *J* = 12.3 Hz, C*H*$_2$Ph-attached to C2), 4.52 (1 H, d, *J* = 12.3 Hz, C*H*$_2$Ph-attached to C3), 4.38 (1 H, d, *J* = 12.2 Hz, C*H*$_2$Ph-attached to C3), 4.37 (1 H, s, H_1), 3.94–3.85 (1 H, m, OC*H*$_2$CH$_2$CH$_2$N$_3$), 3.89 (1 H, d, *J* = 2.8 Hz, H_2), 3.81 (1 H, d, *J* = 10.0 Hz, H_5), 3.48 (1 H, ddd, *J* = 9.8, 7.6, 5.1 Hz, OC*H*$_2$CH$_2$CH$_2$N$_3$), 3.43 (1 H, dd, *J* = 9.7, 2.8 Hz, H_3), 3.38–3.25 (2 H, m, OCH$_2$CH$_2$C*H*$_2$N$_3$), 1.85 (2 H, ddd, *J* = 18.1, 11.5, 4.8 Hz, OCH$_2$C*H*$_2$CH$_2$N$_3$), 1.77 (3 H, s, C(O)C*H*$_3$); **^{13}C NMR** (101 MHz; $CDCl_3$) *δ* 169.3 (*C*(O)CH$_3$), 150.8 (*C*(O)N(Bn)OBn), 138.5, 137.9, 137.8, 137.3, 128.4, 128.3, 128.2, 128.1, 128.0, 127.7, 127.7, 127.7, 127.6, 127.5, 127.4, 124.8, 101.7 (C1), 78.8 (C3), 76.3 (C(O)N(Bn)O*C*H$_2$Ph), 74.1 (2 C, C5, *C*H$_2$Ph-attached to C2), 74.0 (C2), 73.1 (C(O)N(*C*H$_2$Ph)OBn), 71.4 (*C*H$_2$Ph-attached to C3), 68.1 (C4), 66.6 (O*C*H$_2$CH$_2$CH$_2$N$_3$), 48.3 (OCH$_2$CH$_2$*C*H$_2$N$_3$), 29.1 (OCH$_2$*C*H$_2$CH$_2$N$_3$), 20.7 (C(O)*C*H$_3$); **^{13}C-GATED** (101 MHz; $CDCl_3$): 101.7 ($^1J_{C1-H1}$ = 152 Hz, C1); **HRMS** (ES$^+$) *m*/*z* [found: (M + H)$^+$ 695.3097 $C_{39}H_{42}N_4O_8$ requires (MH)$^+$, 695.3075]; **IR** ν_{max}/cm^{-1} 2095 (m, N=N=N), 1746 (m, C=O$_{ester}$), 1637 (w, C=O$_{amide}$), 1050 (s, C–O$_{ester}$).

3-Azidopropyl *O*-benzyl, *N*-benzyl (2,3-di-*O*-benzyl-β-D-mannopyranoside) hydroxamate 9. From 3-azidopropyl (*O*-benzyl, *N*-benzyl (phenyl 4-*O*-acetyl-2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside) hydroxamate): to a stirred solution of the starting material (280 g, 0.40 mmol, 1.0 equiv.) in anhydrous MeOH (3.5 mL), Na (0.93 mg, 0.04 mmol, 0.1 equiv.) dissolved in anhydrous MeOH (0.5 mL) was added dropwise at room temperature under a N_2 atmosphere. The mixture was stirred for 24 h, then neutralised with ion exchange Amberlite 120 (H$^+$) resin (approximately 0.2 g, 5 min), filtered, and concentrated under reduced pressure. Flash column chromatography, eluting with EtOAc/hexane (20/80, 50/50, 90/10) afforded **9** as a colourless oil (200 mg, 0.3 mmol, 76%).

From: 3-azidopropyl (*O*-benzyl, *N*-benzyl (phenyl 4-*O*-levulinoyl-2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside) hydroxamate): starting material (1.87 g, 2.49 mmol, 1.0 equiv.) was dissolved in a mixture of pyridine/AcOH (4/1 v/v, 30 mL), after which hydrazine acetate (1.14 g, 12.45 mmol, 5.0 equiv.) was added. The mixture was stirred for 1 h at room temperature and was diluted with EtOAc (150 mL). The organic layer was washed with 1 M HCl (2 × 80 mL), sat. aq. $NaHCO_3$ solution (2 × 80 mL) and brine (80 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to furnish a yellow oil. Purification by silica gel flash column chromatography, eluting with EtOAc/hexane (20/80, 50/50, 90/10) afforded **9** as a colourless oil (1.50 g, 2.29 mmol, 92%).

R_f 0.56 (EtOAc/hexane, 1/2); $[\alpha]_D^{22}$ −31.5 (*c*. 0.65, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) *δ* 7.50–7.25 (20 H, m, Ar–H), 5.41 (1 H, d, *J* = 12.1 Hz, C(O)N(C*H*$_2$Ph)OBn), 5.32 (1 H, d, *J* = 12.2 Hz, C(O)N(C*H*$_2$Ph)OBn), 5.05 (1 H, d, *J* = 12.1 Hz, C(O)N(Bn)OC*H*$_2$Ph), 4.99 (1 H, d, *J* = 12.2 Hz, C(O)N(Bn)OC*H*$_2$Ph), 4.93 (1 H, d, *J* = 12.4 Hz, C*H*$_2$Ph-attached to C2), 4.78 (1 H, d, *J* = 12.4 Hz, C*H*$_2$Ph-attached to C2), 4.58 (1 H, d, *J* = 12.4 Hz, C*H*$_2$Ph-attached to C3), 4.54 (1 H, d, *J* = 12.3 Hz, C*H*$_2$Ph-attached to C3), 4.37 (1 H, s, H_1), 4.32 (1 H, dd, *J* = 9.5, 2.8 Hz, H_4), 3.97–3.88 (1 H, m, OC*H*$_2$CH$_2$CH$_2$N$_3$), 3.86 (1 H, d, *J* = 2.9 Hz, H_2), 3.71 (1 H, dd, *J* = 9.4, 2.1, H_5), 3.52–3.42 (1 H, m, OC*H*$_2$CH$_2$CH$_2$N$_3$), 3.36–3.30 (3 H, m, H_3, OCH$_2$CH$_2$C*H*$_2$N$_3$), 2.53 (1 H, d, *J* = 2.9 Hz, C4-O*H*), 1.93–1.76 (2 H, m, OCH$_2$C*H*$_2$CH$_2$N$_3$); **^{13}C NMR** (101 MHz; $CDCl_3$) *δ* 151.4 (*C*(O)N(Bn)OBn), 138.6, 138.1, 137.5, 136.9, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 127.7, 127.5, 127.4, 102.1 (C1), 80.1 (C3), 76.6 (C(O)N(Bn)O*C*H$_2$Ph), 74.8 (C5), 74.5 (C2), 74.3 (*C*H$_2$Ph-attached to C2), 72.8 (C(O)N(*C*H$_2$Ph)OBn), 72.2 (*C*H$_2$Ph-attached to C3), 67.5 (C4), 66.6 (O*C*H$_2$CH$_2$CH$_2$N$_3$), 48.3 (OCH$_2$CH$_2$*C*H$_2$N$_3$), 29.2 (OCH$_2$*C*H$_2$CH$_2$N$_3$); **^{13}C-GATED** (101 MHz; $CDCl_3$): 102.1 ($^1J_{C1-H1}$ = 152 Hz, C1); **HRMS** (ES$^+$) *m*/*z* [found: (M + H)$^+$ 653.2971 $C_{37}H_{40}N_4O_7$ requires (MH)$^+$, 653.2970].

Methyl (phenyl 4-*O*-*tert*-butyl dimethylsilyl-2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside) uronate 12. To a mixture of methyl (phenyl 2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside) uronate[10] (100 mg, 0.21 mmol, 1.0 equiv.), imidazole (42 mg, 0.62 mmol, 3.0 equiv.) and 4-dimethylaminopyridine (42.5 mg, 0.62 mmol, 0.5 equiv.) in DMF (2 mL) was added *tert*-butyldimethylsilyl trifluoromethanesulphonate (144 μL, *d* = 1.151, 0.62 mmol, 3.0 equiv.). The reaction mixture was left stirring overnight at room temperature and was quenched with H_2O (1 mL). The mixture was concentrated under reduced pressure and the remaining crude was reconstituted in CH_2Cl_2 (25 mL) and H_2O (20 mL). The organic layer was washed with H_2O (2 × 20 mL), separated, dried over $MgSO_4$, filtered and concentrated under reduced pressure to furnish a colourless oil. Purification

by silica gel flash column chromatography, eluting with EtOAc/hexane (0/100, 5/95, 10/90) afforded **12**, as a colourless oil (120 mg, 0.20 mmol, 96%). R_f 0.77 (EtOAc/hexane, 1/2); $[\alpha]_D^{22}$ +22.3 (*c*. 4.65, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.62–7.20 (15 H, m, Ar–H), 5.68 (1 H, d, J = 2.6 Hz, H_1), 4.58 (1 H, d, J = 11.8 Hz, CH_2Ph), 4.55 (1 H, d, J = 11.5 Hz, CH_2Ph), 4.50 (1 H, d, J = 11.9 Hz, CH_2Ph), 4.42 (1 H, d, J = 12.0 Hz, CH_2Ph), 4.40–4.35 (2 H, m, H_4, H_5), 3.81 (1 H, dd, J = 7.5, 2.6 Hz, H_2), 3.60 (3 H, s, CO_2CH_3), 3.54 (1 H, dd, J = 5.6, 2.7 Hz, H_3), 0.80 (9 H, s, SiC(CH_3)$_3$), 0.00 (3 H, s, Si(CH_3)$_2$), −0.08 (3 H, s, Si(CH_3)$_2$); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 169.7 (CO_2CH_3), 138.0, 137.9, 134.0, 131.3, 128.8, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.0, 82.9 (C1), 77.3 (C3), 76.4 (C4), 73.7 (C2), 72.5 (CH_2Ph), 72.5 (CH_2Ph), 69.7 (C5), 52.0 (CO_2CH_3), 25.7 (SiC(CH_3)$_3$), 18.0 (SiC(CH_3)$_3$), −4.7 (Si(CH_3)$_2$), −5.2 (Si(CH_3)$_2$); **^{13}C-GATED** (101 MHz; $CDCl_3$): 82.9 ($^1J_{C1-H1}$ = 168 Hz, C1); **HRMS** (ES^+) *m*/*z* [found: $(M + NH_4)^+$ 612.2832 $C_{33}H_{42}O_6SSiNH_4$ requires $(MNH_4)^+$, 612.2810].

3-Azidopropyl (methyl 2,3-di-*O*-benzyl-4-*O*-(methyl (4-*O*-*tert*-butyl dimethylsilyl-2,3-di-*O*-benzyl-β-D-mannopyranosyl) uronate)-β-D-mannopyranoside) uronate 14. A solution of **12** (110 mg, 0.18 mmol, 1.0 equiv.) and **13**[1] (96 mg, 0.20 mmol, 1.1 equiv.) in CH_2Cl_2 (3.5 mL) was stirred over activated MS4Å for 30 min before *N*-iodosuccinimide (54 mg, 0.24 mmol, 1.3 equiv.) was added. The mixture was cooled to −10 °C before trimethylsilyl trifluoromethanesulfonate (6.7 μL, d = 1.225, 0.04 mmol, 0.2 equiv.) was added. The reaction was left stirring for 30 min at room temperature, and upon completion, triethylamine was added until pH = 7. The reaction mixture was filtered through Celite® and concentrated under reduced pressure. Purification by silica gel flash column chromatography, eluting with EtOAc/toluene (0/100, 5/95, 10/90) afforded **14**, as a colourless oil (105 mg, 0.11 mmol, 61%). R_f 0.76 (EtOAc/toluene, 3/7); $[\alpha]_D^{22}$ +8.0 (*c*. 0.21, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.41–7.15 (20 H, m, Ar–H), 4.82 (1 H, d, J = 12.3 Hz, CH_2Ph), 4.80 (1 H, d, J = 12.5 Hz, CH_2Ph), 4.74 (1 H, d, J = 12.7 Hz, CH_2Ph), 4.71 (1 H, s, H_1'), 4.70 (1 H, d, J = 12.9 Hz, CH_2Ph), 4.67 (1 H, d, J = 12.3 Hz, CH_2Ph), 4.56 (1 H, d, J = 11.8 Hz, CH_2Ph), 4.55 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.47 (1 H, d, J = 11.4 Hz, CH_2Ph), 4.45 (1 H, s, H_1), 4.41 (1 H, app. t, J = 8.6 Hz, H_4), 4.30 (1 H, app. t, J = 9.2 Hz, H_4'), 4.08–3.99 (1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 3.86 (1 H, d, J = 8.6 Hz, H_5), 3.83 (1 H, d, J = 2.5 Hz, H_2'), 3.80 (1 H, d, J = 2.2 Hz, H_2), 3.74 (1 H, d, J = 9.2 Hz, H_5'), 3.62 (6 H, s, CO_2CH_3), 3.62–3.56 (1 H, m, H_3), 3.52 (1 H, ddd, J = 9.6, 7.6, 5.2 Hz, OCH_2CH$_2$CH$_2$N$_3$), 3.35 (2 H, t, J = 6.7 Hz, OCH$_2$CH$_2$CH_2N$_3$), 3.28 (1 H, dd, J = 9.2, 2.7 Hz, H_3'), 1.92–1.82 (2 H, m, OCH$_2$CH_2CH$_2$N$_3$), 0.81 (9 H, s, SiC(CH_3)$_3$), 0.00 (6 H, s, Si(CH_3)$_2$); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 168.7 (CO_2CH_3), 168.7 (CO_2CH_3), 139.2, 138.8, 138.5, 137.9, 128.4, 128.2, 128.1, 128.1, 128.0, 127.6, 127.5, 127.5, 127.5, 127.4, 127.3, 127.2, 102.6 (C1′), 101.7 (C1), 81.8 (C3′), 79.1 (C3), 77.5 (C5′), 77.2 (C4), 75.0 (C2′), 74.6 (C5), 74.5 (CH_2Ph), 74.4 (C2), 73.9 (CH_2Ph), 72.6 (CH_2Ph), 71.4 (CH_2Ph), 68.9 (C4′), 66.8 (OCH_2CH$_2$CH$_2$N$_3$), 52.3 (CO_2CH_3), 52.0 (CO_2CH_3), 48.3 (OCH$_2$CH$_2$CH_2N$_3$), 29.1 (OCH$_2$CH_2CH$_2$N$_3$), 25.8 (SiC(CH_3)$_3$), 18.0 (SiC(CH_3)$_3$), −3.9 (Si(CH_3)$_2$), −5.3 (Si(CH_3)$_2$); **HRMS** (ES^+) *m*/*z* [found: $(M + NH_4)^+$ 973.4639 $C_{51}H_{65}N_3O_{13}SiNH_4$ requires $(MNH_4)^+$, 973.4625].

3-Azidopropyl (methyl 2,3-di-*O*-benzyl-4-*O*-(methyl (4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-mannopyranosyl) uronate)-β-D-mannopyranoside) uronate 15. A solution of **11**[10] (160 mg, 0.30 mmol, 1.0 equiv.) and **13**[10] (220 mg, 0.46 mmol, 1.5 equiv.) in CH_2Cl_2 (5 mL) was stirred over activated MS4Å for 30 min before *N*-iodosuccinimide (90 mg 0.40 mmol, 1.3 equiv.) was added. The mixture was cooled to −60 °C before trimethylsilyl trifluoromethanesulfonate (5.6 μL, d = 1.225, 0.03 mmol, 0.1 equiv.) was added. The reaction was left stirring for 30 min at room temperature, and upon completion, triethylamine was added until pH = 7. The reaction mixture was filtered through Celite® and concentrated under reduced pressure. Purification by Reveleris® automated silica gel flash column chromatography (liquid injection onto column), eluting with EtOAc/toluene (0/100, 5/95 and 10/90) afforded **15** as a colourless oil (150 mg, 0.17 mmol, 56%). R_f 0.42 (EtOAc/toluene, 3/7); $[\alpha]_D^{22}$ −35.3 (*c*. 3.65, $CHCl_3$); **^{1}H NMR** (500 MHz; $CDCl_3$) δ 7.50–7.21 (20 H, m, Ar–H), 5.44 (1 H, app. t, J = 9.8 Hz, H_4'), 4.88 (1H, d, J = 12.3 Hz, CH_2Ph), 4.84 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.79 (1 H, d, J = 12.3 Hz, CH_2Ph), 4.78 (2 H, d, J = 12.1 Hz, CH_2Ph), 4.76 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.72 (1 H, d, J = 11.9 Hz, CH_2Ph), 4.60 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.54 (1 H, d, J = 12.3 Hz, CH_2Ph), 4.52 (1 H, d, J = 0.9 Hz, H_1'), 4.46 (1 H, s, H_1), 4.43 (1 H, app. t, J = 8.8 Hz, H_4), 4.03 (1 H, dt, J = 9.7, 5.7 Hz, OCH_2CH$_2$CH$_2$N$_3$), 3.93 (1 H, d, J = 8.8 Hz, H_5), 3.89–3.88 (2 H, m, H_2', H_2), 3.71 (1 H, d, J = 9.8 Hz, H_5'), 3.67 (3 H, s, CO_2CH_3), 3.66 (1 H, dd, J = 8.8, 3.0 Hz, H_3), 3.58 (3 H, s, CO_2CH_3), 3.55 (1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 3.49 (1 H, dd, J = 9.8, 2.8 Hz, H_3'), 3.37 (2 H, t, J = 6.8 Hz, OCH$_2$CH$_2$CH_2N$_3$), 2.02 (3 H, s, C(O)CH_3), 1.95–1.84 (2 H, m, OCH$_2$CH_2CH$_2$N$_3$); **^{13}C NMR** (126 MHz; $CDCl_3$) δ 169.8 (C(O)CH$_3$), 168.7 (CO_2CH_3), 167.8 (CO_2CH_3), 138.7 (C_q Bn), 138.6 (C_q Bn), 138.4 (C_q Bn), 137.8 (C_q Bn), 128.4, 128.3, 128.2, 128.1, 128.1, 127.9, 127.7, 127.5, 127.5, 127.4, 127.3, 127.2, 102.4 (C1′), 101.9 (C1), 79.4 (C3), 78.5 (C3′), 77.6 (C4), 75.0 (C2′ or C2), 74.5 (C5), 74.4 (CH_2Ph), 74.0 (C2′ or C2, CH_2Ph), 73.4 (C5′), 72.2 (CH_2Ph), 71.7 (CH_2Ph), 68.7 (C4′), 66.9 (OCH_2CH$_2$CH$_2$N$_3$), 52.4 (CO_2CH_3), 52.4 (CO_2CH_3), 48.3 (OCH$_2$CH$_2$CH_2N$_3$), 29.1 (OCH$_2$CH_2CH$_2$N$_3$), 20.8 (C(O)CH_3); **^{13}C-GATED** (126 MHz; $CDCl_3$): 102.4 ($^1J_{C1'-H1'}$ = 155 Hz, C1′), 101.9 ($^1J_{C1-H1}$ = 156 Hz, C1); **HRMS** (ES^+) *m*/*z* [found: $(M + NH_4)^+$ 901.3877 $C_{47}H_{53}N_3O_{14}NH_4$ requires $(MNH_4)^+$, 901.3866].

3-Azidopropyl (methyl 2,3-di-*O*-benzyl-4-*O*-(methyl (2,3-di-*O*-benzyl-β-D-mannopyranosyl) uronate)-β-D-mannopyranoside) uronate 16. To a stirred solution of **14** (70 mg, 0.07 mmol, 1.0 equiv.) in anhydrous MeOH (0.7 mL) at 0 °C, was added AcCl (1.6 μL, d = 1.104, 0.02 mmol, 0.3 equiv.) and the reaction was left stirring at room temperature for 24 h. The mixture was then neutralised and diluted with sat. aq. $NaHCO_3$ (20 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure to furnish a colourless oil. Purification by silica gel flash column chromatography, eluting with diethyl ether/toluene (10/90, 20/80, 25/75)

afforded **16** as a colourless oil (20 mg, 0.02 mmol, 32%). R_f 0.30 (EtOAc/hexane, 1/2); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.38–7.22 (20 H, m), 4.84 (1 H, d, J = 12.3 Hz, CH_2Ph), 4.79 (1 H, d, J = 12.1 Hz, CH_2Ph), 4.76 (1 H, d, J = 12.1 Hz, CH_2Ph), 4.75 (1 H, d, J = 12.3 Hz, CH_2Ph), 4.72 (1 H, s, H_1'), 4.67 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.60 (1 H, d, J = 12.3 Hz, CH_2Ph), 4.57 (1 H, d, J = 12.0 Hz, CH_2Ph), 4.55 (1 H, d, J = 12.3 Hz, CH_2Ph), 4.48 (1 H, d, J = 0.7 Hz, H_1), 4.45 (1 H, app. t, J = 8.6 Hz, H_4), 4.19 (1 H, app. t, J = 9.6 Hz, H_4'), 4.07–3.99 (1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 3.90 (1 H, d, J = 8.7 Hz, H_5), 3.85 (1 H, d, J = 2.3 Hz, H_2), 3.83 (1 H, d, J = 2.5 Hz, H_2'), 3.70 (1 H, dd, J = 9.0, 4.4 Hz, H_3), 3.64 (3 H, s, CO$_2$CH_3), 3.62 (3 H, s, CO$_2$CH_3), 3.59 (1 H, d, J = 9.6 Hz, H_5'), 3.57–3.51(1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 3.36 (2 H, t, J = 6.7 Hz, OCH$_2$CH$_2$CH_2N$_3$), 3.32 (1 H, dd, J = 9.5, 2.8 Hz, H_3'), 2.93 (1 H, br. s, C4-*OH*), 1.94–1.81 (2 H, m, OCH$_2$CH_2CH$_2$N$_3$); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 169.9 (*C*O$_2$CH$_3$), 168.6 (*C*O$_2$CH$_3$), 138.8, 138.7, 138.4, 138.0, 128.5, 128.3, 128.2, 128.1, 128.1, 127.8, 127.8, 127.7, 127.5, 127.4, 127.4, 127.1, 102.5 (C1′), 101.8 (C1), 80.4 (C3′), 79.4 (C5′), 77.2 (C4), 75.2 (C2′), 74.8 (C3), 74.6 (*C*H$_2$Ph), 74.5 (C5), 73.9 (C2, *C*H$_2$Ph), 72.1 (*C*H$_2$Ph), 71.9 (*C*H$_2$Ph), 68.2 (C4′), 66.9 (O*C*H$_2$CH$_2$CH$_2$N$_3$), 52.5 (CO$_2$*C*H$_3$), 52.4 (CO$_2$*C*H$_3$), 48.3 (OCH$_2$*C*H$_2$CH$_2$N$_3$), 29.1 (OCH$_2$*C*H$_2$CH$_2$N$_3$); **^{13}C-GATED** (101 MHz; $CDCl_3$): 102.5 ($^1J_{C1-H1}$ = 156 Hz, C1′), 101.8 ($^1J_{C1'-H1'}$ = 156 Hz, C1); **HRMS** (ES$^+$) m/z [found: (M + NH$_4$)$^+$ 859.3781 C$_{45}$H$_{51}$N$_3$O$_{13}$NH$_4$ requires (MNH$_4$)$^+$, 859.3760]; these data were consistent with literature values.[10]

3-Azidopropyl (methyl 2,3-di-*O*-benzyl-4-*O*-(methyl (2,3-di-*O*-benzyl-β-D-mannopyranosyl) uronate)-α-D-mannopyranoside) uronate 17. To a stirred solution of **15** (50 mg, 0.06 mmol, 1.0 equiv.) in anhydrous MeOH (1 mL), Na (0.06 mg, 0.003 mmol, 0.05 equiv.) dissolved in anhydrous MeOH (30 μL) was added at room temperature under a N_2 atmosphere. The mixture was stirred for 2 h, then neutralised with ion exchange Amberlite 120 (H^+) resin (approximately 0.1 g, 5 min), filtered, and concentrated under reduced pressure. Flash column chromatography, eluting with EtOAc/hexane (20/80, 50/50, 70/30, 90/10) afforded **17** as a colourless oil (15 mg, 0.02 mmol, 46% based on recovered starting material, 16 mg). R_f 0.42 (EtOAc/toluene, 3/7); $[\alpha]_D^{22}$ −17.8 (*c*. 0.74, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.65–6.80 (20 H, m, Ar–H), 5.42 (1 H, s, H_1'), 4.94 (1 H, d, J = 12.5 Hz, CH_2Ph), 4.73 (1 H, d, J = 12.5 Hz, CH_2Ph), 4.63 (1 H, d, J = 11.9 Hz, CH_2Ph), 4.55 (1 H, d, J = 11.9 Hz, CH_2Ph), 4.45 (1 H, app. t, J = 9.3, H_4), 4.43 (1 H, s, H_1), 4.40 (1 H, d, J = 11.6 Hz, CH_2Ph), 4.32 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.23 (1 H, d, J = 12.3 Hz, CH_2Ph), 4.22 (1 H, d, J = 9.3 Hz, H_4'), 4.19 (1 H, d, J = 11.9 Hz, CH_2Ph), 4.07–3.98 (1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 4.01 (1 H, d, J = 9.7 Hz, H_5'), 3.91 (1 H, d, J = 2.6 Hz, H_2), 3.84 (1 H, d, J = 9.4 Hz, H_5), 3.80 (3 H, s, CO$_2$CH_3), 3.76 (3 H, s, CO$_2$CH_3), 3.67–3.62 (2 H, m, H_2', H_3'), 3.57–3.49 (1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 3.43–3.36 (2 H, m, OCH$_2$CH$_2$CH_2N$_3$), 3.40 (1 H, dd, J = 9.3, 2.7 Hz, H_3), 2.95 (1 H, s, C4-*OH*), 2.01–1.78 (2 H, m, OCH$_2$CH_2CH$_2$N$_3$); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 170.9 (*C*O$_2$CH$_3$), 168.3 (*C*O$_2$CH$_3$), 138.5 (C$_q$ Bn), 138.3 (C$_q$ Bn), 138.3 (C$_q$ Bn), 137.4 (C$_q$ Bn), 128.5, 128.4, 128.2, 128.1, 128.0, 127.6, 127.6, 127.5, 127.4, 127.4, 102.0 (C1), 99.8 (C1′), 81.5 (C3), 78.2 (C2′), 75.8 (C5), 75.0 (C3′), 74.7 (C4), 74.1 (*C*H$_2$Ph), 72.9 (C2), 72.4 (2 C, *C*H$_2$Ph), 72.4 (C5′), 71.0 (*C*H$_2$Ph), 68.4 (C4′), 67.0 (O*C*H$_2$CH$_2$CH$_2$N$_3$), 52.6 (CO$_2$*C*H$_3$), 52.5 (CO$_2$*C*H$_3$), 48.3 (OCH$_2$*C*H$_2$CH$_2$N$_3$), 29.1 (OCH$_2$*C*H$_2$CH$_2$N$_3$); **^{13}C-GATED** (101 MHz; $CDCl_3$): 102.0 ($^1J_{C1-H1}$ = 156 Hz, C1), 99.8 ($^1J_{C1'-H1'}$ = 176 Hz, C1′); **HRMS** (ES$^+$) m/z [found: (M + Na)$^+$ 864.3343 C$_{47}$H$_{53}$N$_3$O$_{14}$Na requires (MNa)$^+$, 864.3314].

***O*-Benzyl, *N*-benzyl (phenyl 4-*O*-levulinoyl-2,3-di-*O*-benzyl-1-hydroxyl-α/β-D-mannopyranoside) hydroxamate.** A solution of **5** (100 mg, 0.13 mmol, 1.0 equiv.) in CH_2Cl_2/H_2O (10/1 v/v, 1.4 mL in total) was cooled to 0 °C followed by the addition of *N*-iodosuccinimide (30 mg 0.13 mmol, 1.0 equiv.) and a catalytic amount of silver trifluoromethanesulfonate (6.8 mg 0.03 mmol, 0.2 equiv.). The reaction was left stirring at 0 °C for 4 h before it was quenched by the addition of 10% aq. $Na_2S_2O_3$ solution (5 mL) and diluted with CH_2Cl_2 (15 mL). The organic layer was subsequently washed with sat. aq. $NaHCO_3$ solution (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified using silica gel flash column chromatography, eluting with diethyl ether/toluene (5/95, 10/90, 20/80) to furnish the title compound as a yellow oil (0.056 mg, 0.10 mmol, 78%). R_f 0.50 (EtOAc/tolene, 3/7); the NMR data reported refer to the major α-anomer (α/β = 87/13): **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.41–7.20 (20 H, m, Ar–H), 5.70 (1 H, app. t, J = 9.7 Hz, H_4), 5.46 (1 H, d, J = 12.0 Hz, C(O)N(CH_2Ph)OBn), 5.42 (1 H, d, J = 12.0 Hz, C(O)N(CH_2Ph)OBn), 5.20 (1 H, dd, J = 3.5, 2.2 Hz, H_1), 4.97 (1 H, d, J = 12.7 Hz, C(O)N(Bn)OCH_2Ph), 4.93 (2 H, d, J = 13.1 Hz, C(O)N(Bn)OCH_2Ph), 4.76 (1 H, d, J = 12.2 Hz, CH_2Ph-attached to C2), 4.64 (1 H, d, J = 12.1 Hz, CH_2Ph-attached to C2), 4.59 (1 H, d, J = 12.1 Hz, CH_2Ph-attached to C3), 4.54 (1 H, d, J = 12.2 Hz, CH_2Ph-attached to C3), 4.33 (1 H, d, J = 9.9 Hz, H_5), 3.90 (1 H, dd, J = 9.5, 2.9 Hz, H_3), 3.77–3.74 (1 H, app. t, J = 2.6 Hz, H_2), 3.38 (1 H, d, J = 3.7 Hz, O*H*), 2.63–2.35 (3 H, m, CH_2 Lev), 2.30–2.21 (1 H, m, CH_2 Lev), 2.09 (3 H, s, CH_3 Lev); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 206.4 (C═O Lev ketone), 171.4 (C═O Lev), 151.5 (*C*(O)N(Bn)OBn), 138.2, 137.7, 137.2, 128.3, 128.3, 128.3, 128.2, 128.1, 127.7, 127.7, 127.6, 127.5, 127.5, 93.0 (C1), 76.2 (2C, C3, (C(O)N(Bn)O*C*H$_2$Ph)), 74.8 (C2), 73.3 (C(O)N(*C*H$_2$Ph)OBn), 72.9 (*C*H$_2$Ph-attached to C2), 72.2 (*C*H$_2$Ph-attached to C3), 70.5 (C5), 68.7 (C4), 37.9 (*C*H$_2$ Lev), 29.8 (*C*H$_3$ Lev), 27.9 (*C*H$_2$ Lev); **^{13}C-GATED** (101 MHz; $CDCl_3$): **α-anomer**: 93.0 ($^1J_{C1-H1}$ = 176 Hz, C1), **β-anomer**: 93.7 ($^1J_{C1-H1}$ = 164 Hz, C1); **HRMS** (ES$^+$) m/z [found: (M + H)$^+$ 668.2860 C$_{39}$H$_{41}$NO$_9$ requires (MH)$^+$, 668.2854].

***O*-Benzyl, *N*-benzyl (phenyl 4-*O*-levulinoyl-2,3-di-*O*-benzyl-1-*O*-phenyl-*N*-trifluoroacetimidate-α-D-mannopyranoside) hydroxamate 19.** *O*-Benzyl, *N*-benzyl (phenyl 4-*O*-levulinoyl-2,3-di-*O*-benzyl-1-hydroxyl-α/β-D-mannopyranoside) hydroxamate (70 mg, 0.10 mmol, 1.0 equiv.) was dissolved in acetone/H_2O (20/1 v/v, 1.1 mL in total) and the solution was cooled to 0 °C. *N*-Phenyl trifluoroacetimidoyl chloride (25 μL, d = 1.31, 0.16 mmol, 1.5 equiv.) and K_2CO_3 (17 mg, 0.12 mmol, 1.2 equiv.) were added and the resulting suspension was stirred for 20 h at room temperature. The reaction mixture was

diluted with EtOAc (10 mL) and H_2O (10 mL), the organic layer was then washed with brine (10 mL), collected dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified using silica gel flash column chromatography, eluting with diethyl ether/toluene (5/95, 10/90, 20/80) to furnish **19** as a colourless oil which was used immediately (0.06 mg, 0.07 mmol, 66%). R_f 0.68 (EtOAc/tolene, 3/7); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.38–7.22 (25 H, m, Ar–H), 7.11 (1 H, t, J = 7.5 Hz, C*H* NPh), 6.69 (2 H, d, J = 7.7 Hz, C*H* NPh), 6.26 (1 H, br. s, H_1), 5.76 (1 H, t, J = 9.7 Hz, H_4), 5.44 (1 H, d, J = 11.9 Hz, C(O)N(CH_2Ph)OBn), 5.38 (1 H, d, J = 11.9 Hz, C(O)N(CH_2Ph)OBn), 5.02 (1 H, d, J = 12.4 Hz, C(O)N(Bn)OCH_2Ph), 4.99 (1 H, d, J = 12.5 Hz, C(O)N(Bn)OCH_2Ph), 4.72 (1 H, d, J = 10.2 Hz, CH_2Ph), 4.63 (1 H, d, J = 10.3 Hz, CH_2Ph), 4.61 (1 H, d, J = 12.1 Hz, CH_2Ph), 4.54 (1 H, d, J = 12.1 Hz, CH_2Ph), 4.27 (1 H, d, J = 9.9 Hz, H_5), 3.82 (1 H, dd, J = 9.5, 2.7 Hz, H_3), 3.77 (1 H, s, H_2), 2.68–2.41 (3 H, m, CH_2 Lev), 2.30–2.20 (1 H, m, CH_2 Lev), 2.13 (3 H, s, CH_3 Lev); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 206.2 (C=O Lev ketone), 171.2 (C=O Lev), 150.2 (*C*(O)N(Bn)OBn), 143.1 (C_q NPh), 142.3 (q, J = 36.0 Hz, C=NPh), 137.7, 137.5, 137.00, 128.7, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 127.9, 127.8, 127.7, 127.7, 127.5, 124.5, 119.4 (*C*H NPh), 115.8 (d, J = 287.3 Hz, *C*F_3), 94.9 (C1), 75.4, 73.5 (C3), 73.0 (*C*H_2Ph), 72.8 (2C, C2, C5), 72.6 (*C*H_2Ph), 67.7 (C4), 37.9 (*C*H_2 Lev), 29.8 (*C*H_3 Lev), 27.8 (*C*H_2 Lev); **^{13}C-GATED** (101 MHz; $CDCl_3$): 94.9 ($^1J_{C1-H1}$ = 172 Hz, C1); **HRMS** (ES^+) m/z [found: $(M + Na)^+$ 861.2972 $C_{47}H_{45}F_3N_2O_9Na$ requires $(MNa)^+$, 861.2969].

3-Azidopropyl (*O*-benzyl-*N*-benzyl-(methyl 2,3-di-*O*-benzyl-4-*O*-(4-*O*-levulinoyl-2,3-di-*O*-benzyl-β-D-mannopyranosyl) uronate)-β-D-mannopyranoside) hydroxamate 20. A solution of donor **10**[10] (120 mg, 0.21 mmol, 1.2 equiv.) and acceptor **9** (110 mg, 0.17 mmol, 1.0 equiv.) and in CH_2Cl_2 (4 mL) was stirred over activated MS4Å for 30 min before *N*-iodosuccinimide (60 mg 0.27 mmol, 1.3 equiv.-based on donor) was added. The mixture was cooled to −40 °C before trimethylsilyl trifluoromethanesulfonate (7.5 μL, d = 1.225, 0.04 mmol, 0.2 equiv.) was added. The reaction was allowed to warm at 0 °C within 45 min, and upon completion, triethylamine was added until pH = 7. The reaction mixture was filtered through Celite® and concentrated under reduced pressure. Flash column chromatography, eluting with diethyl ether/toluene (0/100, 5/95 and 10/90) afforded **20** as a colourless oil (94 mg, 0.09 mmol, 55%). R_f 0.38 (EtOAc/toluene, 3/7); $[\alpha]_D^{22}$ −29.6 (*c*. 0.5, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.44–7.16 (30 H, m), 5.46 (1 H, d, J = 12.2 Hz, CH_2Ph), 5.35 (1 H, app. t, J = 9.8 Hz, H_4'), 5.31 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.92 (1 H, d, J = 11.8 Hz, CH_2Ph), 4.88 (1 H, d, J = 10.0 Hz, CH_2Ph), 4.85 (1 H, s, J = 13.9 Hz, CH_2Ph), 4.85 (2 H, s, CH_2Ph), 4.83 (4 H, d, J = 14.2 Hz, CH_2Ph), 4.67 (1 H, d, J = 12.3 Hz, CH_2Ph), 4.57 (1 H, d, J = 12.4 Hz, CH_2Ph), 4.44 (1 H, s, H_1'), 4.39 (1 H, s, H_1), 4.36 (1 H, d, J = 11.5 Hz, CH_2Ph), 4.35 (1 H, d, J = 9.4 Hz, H_4), 4.23 (1 H, d, J = 12.4 Hz, CH_2Ph), 3.95–3.88 (1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 3.85 (1 H, d, J = 9.7 Hz, H_5), 3.82 (1 H, d, J = 2.9 Hz, H_2), 3.76 (1 H, d, J = 2.6 Hz, H_2'), 3.53 (3 H, s, CO_2CH_3), 3.50 (1 H, d, J = 9.0 Hz, H_5'), 3.46 (1 H, dd, J = 9.2, 2.9 Hz, H_3), 3.48–3.39 (1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 3.31 (2 H, dd, J = 9.9, 3.9 Hz, OCH$_2$CH$_2$CH_2N$_3$), 3.21 (1 H, dd, J = 9.8, 2.8 Hz, H_3'), 2.69–2.64 (2 H, m, CH_2 Lev), 2.55–2.46 (2 H, m, CH_2 Lev), 2.14 (3 H, s, CH_3 Lev), 1.88–1.76 (2 H, m, OCH$_2$CH_2CH$_2$N$_3$); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 206.2 (C=O Lev ketone), 171.5 (C=O Lev), 167.9 (C=O *C*O_2CH$_3$), 151.8 (*C*(O)N(Bn)OBn), 139.0 (C_q), 138.8 (C_q), 138.7 (C_q), 138.0 (C_q), 137.1 (C_q), 128.5, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 127.6, 127.6, 127.4, 127.4, 127.3, 127.2, 102.3 (C1′), 101.8 (C1), 79.9 (C3), 78.4 (C3′), 77.3 (C4), 76.6 (*C*H_2Ph), 75.1 (C2), 74.9 (C2′), 74.6 (C5, *C*H_2Ph), 74.3 (*C*H_2Ph), 73.3 (C5′), 73.3 (*C*H_2Ph), 72.8 (*C*H_2Ph), 71.2 (*C*H_2Ph), 68.9 (C4′), 66.6 (O*C*H_2CH$_2$CH$_2$N$_3$), 52.3 (CO_2CH_3), 48.3 (OCH$_2$CH$_2$*C*H_2N$_3$), 37.9 (*C*H_2 Lev), 29.8 (*C*H_3 Lev), 29.2 (OCH$_2$CH$_2$*C*H_2N$_3$), 27.9 (*C*H_2 Lev); **^{13}C-GATED** (101 MHz; $CDCl_3$): 102.3 ($^1J_{C1-H1}$ = 156 Hz, C1′), 101.8 ($^1J_{C1'-H1'}$ = 156 Hz, C1); **HRMS** (ES^+) m/z [found: $(M + H)^+$ 1121.4755 $C_{63}H_{68}N_4O_{15}$ requires $(MH)^+$, 1121.4754].

3-Azidopropyl (*O*-benzyl-*N*-benzyl-(methyl 2,3-di-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-β-D-mannopyranosyl)uronate)-β-D-mannopyranoside)hydroxamate 21. Disaccharide **20** (40 mg, 0.03 mmol, 1.0 equiv.) was dissolved in a mixture of pyridine/AcOH (4/1 v/v, 0.5 mL in total), after which hydrazine acetate (16 mg, 0.18 mmol, 5.0 equiv.) was added. The mixture was stirred for 30 min and then was diluted with EtOAc (5 mL), washed with 1 M HCl (5 mL), sat. aq. $NaHCO_3$ solution (5 mL) and brine (5 mL). The organic layer was then dried over $MgSO_4$ filtered and concentrated under reduced pressure to furnish a yellow oil. Purification using silica gel flash column chromatography, eluting with diethyl ether/toluene (0/100, 30/70, 40/60, 90/10) afforded **21** as a colourless oil (25 mg, 0.02 mmol, 81%). R_f 0.60 (EtOAc/toluene, 3/7); $[\alpha]_D^{22}$ −44.5 (*c*. 0.25, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.43–7.20 (30 H, m, Ar–H), 5.46 (1 H, d, J = 12.2 Hz, CH_2Ph), 5.33 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.93 (1 H, d, J = 11.8 Hz, CH_2Ph), 4.89 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.88 (1 H, d, J = 10.6 Hz, CH_2Ph), 4.86 (1 H, d, J = 11.0 Hz, CH_2Ph), 4.85 (1 H, d, J = 12.5 Hz, CH_2Ph), 4.81 (1 H, d, J = 12.1 Hz, CH_2Ph), 4.63 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.56 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.52 (1 H, s, H_1'), 4.43 (1 H, d, J = 12.6 Hz, CH_2Ph), 4.42 (1 H, t, J = 9.2 Hz, H_4), 4.41 (1 H, s, H_1), 4.36 (1 H, d, J = 12.0 Hz, CH_2Ph), 4.12 (1 H, t, J = 9.6 Hz, H_4'), 3.96–3.90 (1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 3.88 (1 H, d, J = 9.7 Hz, H_5), 3.84 (1 H, d, J = 2.9 Hz, H_2), 3.76 (1 H, d, J = 2.2 Hz, H_2'), 3.59 (3 H, s, CO_2CH_3), 3.58–3.54 (1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 3.50 (1 H, dd, J = 9.3, 2.7 Hz, H_3), 3.46 (1 H, d, J = 9.6 Hz, H_5'), 3.32 (2 H, td, J = 6.7, 1.5 Hz, OCH$_2$CH$_2$CH_2N$_3$), 3.12 (1 H, dd, J = 9.5, 2.8 Hz, H_3'), 2.85 (1 H, d, J = 1.7 Hz, C4-*OH*), 1.90–1.77 (2 H, m, OCH$_2$CH_2CH$_2$N$_3$); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 170.0 (C=O *C*O_2CH$_3$), 151.8 (*C*(O)N(Bn)OBn), 139.1, 139.0, 138.8, 138.0, 137.1, 137.0, 128.5, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.0, 127.7, 127.6, 127.5, 127.4, 127.3, 127.3, 102.6 (C1′), 101.7 (C1), 80.3 (C3′), 80.2 (C3), 77.2 (C4), 76.6 (*C*H_2Ph), 75.3 (C2), 75.2 (C2′), 74.9 (C5), 74.8 (*C*H_2Ph), 74.7 (C5′), 74.3 (*C*H_2Ph), 73.3 (*C*H_2Ph), 72.6 (*C*H_2Ph), 71.3 (*C*H_2Ph), 68.0 (C4′), 66.6 (O*C*H_2CH$_2$CH$_2$N$_3$), 52.3 (CO_2CH_3), 48.3 (OCH$_2$CH$_2$*C*H_2N$_3$), 32.8, 30.3, 29.2 (OCH$_2$CH$_2$*C*H_2N$_3$); **^{13}C-GATED** (101 MHz; $CDCl_3$): 102.6 ($^1J_{C1-H1}$ = 156 Hz, C1′),

101.7 ($^1J_{C1'-H1'}$ = 156 Hz, C1); **HRMS** (ES$^+$) *m*/*z* [found: (M + H)$^+$ 1023.4412 $C_{58}H_{62}N_4O_{13}$ requires (MH)$^+$, 1023.4386].

3-Azidopropyl (methyl 2,3-di-*O*-benzyl-4-*O*-(*O*-benzyl-*N*-benzyl-(4-*O*-levulinoy-2,3-di-*O*-benzyl-α-D-mannopyranosyl) hydroxamate)-β-D-mannopyranoside) uronate 22. A solution of acceptor **5** (200 mg, 0.26 mmol, 1.0 equiv.) and donor **13** (140 mg, 0.29 mmol, 1.1 equiv.) and in CH_2Cl_2 (5 mL) was stirred over activated MS4Å for 1 h before *N*-iodosuccinimide (90 mg 0.39 mmol, 1.5 equiv.) was added. The mixture was cooled to −40 °C before trimethylsilyl trifluoromethanesulfonate (4.8 μL, *d* = 1.225, 0.02 mmol, 0.1 equiv.) was added. The reaction was left stirring for 1 h at −40 °C, 2 h at −25 °C, 3 h at −20 °C and 30 min at −10 °C, and quenched with triethylamine until pH = 7. The reaction mixture was filtered through Celite® and concentrated under reduced pressure. Flash column chromatography, eluting with diethyl ether/toluene (0/100, 10/90, 20/80) afforded **22** as a colourless oil (90 mg, 0.08 mmol, 30%, α/β = 90/10). R_f 0.30 (EtOAc/toluene, 3/7); $[\alpha]_D^{22}$ −1.8 (*c*. 1.95, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.39–7.10 (30 H, m, Ar–H), 5.64 (1 H, app. t, *J* = 9.9 Hz, H_4'), 5.43 (1 H, d, *J* = 12.6 Hz, CH_2Ph), 5.40 (1 H, d, *J* = 12.1 Hz, CH_2Ph), 5.38 (1 H, d, *J* = 2.0 Hz, H_1'), 4.97 (1 H, d, *J* = 12.6 Hz, CH_2Ph), 4.94 (1 H, d, *J* = 12.7 Hz, CH_2Ph), 4.92 (1 H, d, *J* = 12.5 Hz, CH_2Ph), 4.73 (1 H, d, *J* = 12.5 Hz, CH_2Ph), 4.56 (1 H, d, *J* = 12.2 Hz, CH_2Ph), 4.52 (1 H, d, *J* = 12.1 Hz, CH_2Ph), 4.52 (1 H, d, *J* = 12.1 Hz, CH_2Ph), 4.42 (1 H, s, H_1), 4.37 (1 H, d, *J* = 11.3 Hz, CH_2Ph), 4.36 (1 H, app. t, *J* = 10.5 Hz, H_4), 4.34 (1 H, d, *J* = 11.9 Hz, CH_2Ph), 4.22 (1 H, d, *J* = 12.0 Hz, CH_2Ph), 4.18 (1 H, d, *J* = 11.6 Hz, CH_2Ph), 4.03 (1 H, dt, *J* = 9.7, 5.6 Hz, OCH_2CH$_2$CH$_2$N$_3$), 3.96 (1 H, d, *J* = 10.0 Hz, H_5'), 3.90 (1 H, d, *J* = 2.7 Hz, H_2), 3.81 (1 H, d, *J* = 9.4 Hz, H_5), 3.79 (1 H, dd, *J* = 10.4, 2.1 Hz, H_3'), 3.64 (1 H, app. t, *J* = 2.1 Hz, H_2'), 3.58 (3 H, s, CO$_2$CH_3), 3.53 (1 H, ddd, *J* = 9.5, 8.0, 5.1 Hz, OCH_2CH$_2$CH$_2$N$_3$), 3.42–3.36 (2 H, m, OCH$_2$CH$_2$CH_2N$_3$), 3.36 (1 H, dd, *J* = 9.3, 2.7 Hz, H_3'), 2.65–2.38 (3 H, m, CH_2 Lev), 2.31–2.20 (1 H, m, CH_2 Lev), 1.99–1.81 (3 H, m, CH_3 Lev), 1.99–1.81 (2 H, m, OCH$_2$CH_2CH$_2$N$_3$); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 206.4 (C═O Lev ketone), 171.5 (C═O Lev), 168.1 (C═O *C*O$_2$CH$_3$), 151.1 (*C*(O)N(Bn)OBn), 138.4 (C_q), 138.2 (C_q), 138.2 (C_q), 138.1 (C_q), 137.3 (C_q), 137.3 (C_q), 128.5, 128.3, 128.2, 128.2, 128.1, 128.1, 1280, 127.9, 127.6, 127.5, 127.5, 127.4, 127.2, 127.2, 101.9 (C1), 99.4 (C1′), 81.5 (C3), 76.1, 76.0 (2 C, C3′ *C*H$_2$Ph), 75.8 (C5), 75.4 (C2′), 74.5 (C4), 74.0 (*C*H$_2$Ph), 73.4 (*C*H$_2$Ph), 72.7 (C2), 72.3 (*C*H$_2$Ph), 72.2 (*C*H$_2$Ph), 71.5 (C5′), 70.9 (*C*H$_2$Ph), 68.7 (C4′), 67.0 (O*C*H$_2$CH$_2$CH$_2$N$_3$), 52.9 (CO$_2$*C*H$_3$), 48.3 (OCH$_2$CH$_2$*C*H$_2$N$_3$), 37.9 (*C*H$_2$ Lev), 29.8 (*C*H$_3$ Lev), 29.0 (OCH$_2$*C*H$_2$CH$_2$N$_3$), 27.9 (*C*H$_2$ Lev); **^{13}C-GATED** (101 MHz; $CDCl_3$): 101.9 ($^1J_{C1-H1}$ = 156 Hz, C1), 99.41 ($^1J_{C1'-H1'}$ = 176 Hz, C1′); **HRMS** (ES$^+$) *m*/*z* [found: (M + H)$^+$ 1121.4770 $C_{63}H_{68}N_4O_{15}$ requires (MH)$^+$, 1121.4754].

3-Azidopropyl (methyl 2,3-di-*O*-benzyl-4-*O*-(*O*-benzyl-*N*-benzyl-(4-*O*-acetyl-2,3-di-*O*-benzyl-α-D-mannopyranosyl) hydroxamate)-β-D-mannopyranoside) uronate 23. A solution of donor **6** (180 mg, 0.26 mmol, 1.1 equiv.) and **13** (110 mg, 0.23 mmol, 1.0 equiv.) and in CH_2Cl_2 (5 mL) was stirred over activated MS4Å for 1 h before *N*-iodosuccinimide (80 mg, 0.35 mmol, 1.5 equiv.) was added. The mixture was cooled to 0 °C before trimethylsilyl trifluoromethanesulfonate (4.2 μL, *d* = 1.225, 0.02 mmol, 0.1 equiv.) was added. The reaction was left stirring for 30 min at 0 °C, and upon completion, triethylamine was added until pH = 7. The reaction mixture was filtered through Celite® and concentrated under reduced pressure. Flash column chromatography, eluting with EtOAc/toluene (0/100, 5/95 and 10/90) afforded **23** as a colourless oil (30 mg, 0.03 mmol, 12%, α/β = 9/1). R_f 0.53 (EtOAc/toluene, 3/7); $[\alpha]_D^{22}$ +0.8 (*c*. 0.63, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.44–7.09 (30 H, m, Ar–H), 5.63 (1 H, app. t, *J* = 9.9 Hz, H_4'), 5.44 (2 H, s, C(O)N(CH_2Ph)OBn), 5.39 (1 H, d, *J* = 1.8 Hz, H_1'), 4.95 (2 H, s, C(O)N(Bn)OCH_2Ph), 4.92 (1 H, d, *J* = 12.6 Hz, CH_2Ph-attached to C2), 4.73 (1 H, d, *J* = 12.5 Hz, CH_2Ph-attached to C2), 4.53 (1 H, d, *J* = 12.7 Hz, CH_2Ph-attached to C3′), 4.50 (1 H, d, *J* = 12.5 Hz, CH_2Ph-attached to C3′) 4.42 (1 H, s, H_1), 4.40 (1 H, d, *J* = 10.3 Hz, H_4), 4.38 (1 H, d, *J* = 11.2 Hz, CH_2Ph-attached to C3), 4.34 (1 H, d, *J* = 12.1 Hz, CH_2Ph-attached to C2′), 4.23 (1 H, d, *J* = 12.0 Hz, CH_2Ph-attached to C2′), 4.18 (1 H, d, *J* = 11.5 Hz, CH_2Ph-attached to C3), 4.06–3.99 (1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 3.95 (1 H, d, *J* = 10.0 Hz, H_5'), 3.90 (1 H, d, *J* = 2.6 Hz, H_2), 3.81 (1 H, d, *J* = 9.4 Hz, H_5), 3.78 (1 H, dd, *J* = 9.9, 2.7 Hz, H_3'), 3.65 (1 H, app. t, *J* = 2.3 Hz, H_2'), 3.59 (3 H, s, CO$_2$CH_3), 3.53 (1 H, ddd, *J* = 9.5, 8.0, 5.1 Hz, OCH_2CH$_2$CH$_2$N$_3$), 3.38 (2 H, ddd, *J* = 11.2, 8.6, 2.2 Hz, OCH$_2$CH$_2$CH_2N$_3$), 3.36 (1 H, dd, *J* = 9.2, 2.3 Hz, H_3) 1.97–1.82 (2 H, m, OCH$_2$CH_2CH$_2$N$_3$), 1.79 (3 H, s C(O)CH_3); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 169.6 (*C*(O)CH$_3$), 168.1 (*C*O$_2$CH$_3$), 151.2 (*C*(O)N(Bn)OBn), 138.4, 138.3, 138.2, 137.4, 137.3, 128.5, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.6, 127.6, 127.5, 127.5, 127.4, 127.4, 127.2, 127.2, 102.0 (C1), 99.4 (C1′), 81.5 (C3), 76.1 (C3′), 76.1 (C(O)N(Bn)OCH_2Ph), 75.8 (C5), 75.4 (C2′), 74.5 (C4), 74.0 (*C*H$_2$Ph-attached to C2), 73.4 (C(O)N(*C*H$_2$Ph)OBn), 72.8 (C2), 72.3 (*C*H$_2$Ph-attached to C2′), 72.1 (*C*H$_2$Ph-attached to C3′), 71.7 (C5′), 71.0 (*C*H$_2$Ph-attached to C3), 68.5 (C4′), 67.0 (O*C*H$_2$CH$_2$CH$_2$N$_3$), 52.9 (CO$_2$*C*H$_3$), 48.3 (OCH$_2$CH$_2$*C*H$_2$N$_3$), 29.1 (OCH$_2$*C*H$_2$CH$_2$N$_3$), 20.7 (C(O)*C*H$_3$); **^{13}C-GATED** (101 MHz; $CDCl_3$): 102.0 ($^1J_{C1-H1}$ = 156 Hz, C1), 99.4 ($^1J_{C1'-H1'}$ = 176 Hz, C1′); **HRMS** (ES$^+$) *m*/*z* [found: (M + H)$^+$ 1065.4525 $C_{60}H_{64}N_4O_{14}$ requires (MH)$^+$, 1065.4492]; **IR** ν_{max}/cm^{-1} 2095 (m, N═N═N), 1746 (m, C═O$_{ester}$), 1638 (w, C═O$_{amide}$), 1229 (m, C–O$_{ester}$), 1084 (s, C–O$_{ether}$), 1024 (C–O$_{ester}$).

3-Azidopropyl (methyl 2,3-di-*O*-benzyl-4-*O*-(*O*-benzyl-*N*-benzyl-(2,3-di-*O*-benzyl-α-D-mannopyranosyl) hydroxamate)-β-D-mannopyranoside) uronate 24

From 23 (OAc). To a stirred solution of **23** (10 mg, 0.009 mmol, 1.0 equiv.) in anhydrous MeOH (0.15 mL), Na (0.01 mg, 0.0004 mmol, 0.05 equiv.) dissolved in anhydrous MeOH (10 μL) was added at room temperature under a N_2 atmosphere. The mixture was stirred for 16 h, then neutralised with ion exchange Amberlite 120 (H^+) resin (approximately 0.05 g, 3 min), filtered through Celite®, and concentrated under reduced pressure. Flash column chromatography, eluting with diethyl ether/petroleum ether (20/80, 50/50, 90/10) afforded **24** as a colourless oil (5 mg, 0.05 mmol, 54%).

From 22 (OLev). **22** (100 mg, 0.09 mmol, 1.0 equiv.) was dissolved in a mixture of pyridine/AcOH (4/1 v/v, 1.5 mL), after

which hydrazine acetate (41 mg, 0.44 mmol, 5.0 equiv.) was added. The mixture was stirred for 1 h at room temperature and was diluted with EtOAc (20 mL). The organic layer was washed with 1 M HCl (2 × 15 mL), sat. aq. $NaHCO_3$ solution (2 × 10 mL) and brine (15 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to furnish a yellow oil. Purification by silica gel flash column chromatography, eluting with EtOAc/hexane (20/80, 50/50, 90/10) afforded **24** as a colourless oil (65 mg, 0.63 mmol, 70%).

R_f 0.58 (EtOAc/toluene, 3/7); $[\alpha]_D^{22}$ −3.2 (*c*. 0.40, $CHCl_3$); **^{1}H NMR** (400 MHz; $CDCl_3$) δ 7.38–7.17 (30 H, m, Ar–H), 5.39 (1 H, s, H_1'), 5.39 (1 H, d, J = 11.7 Hz, CH_2Ph), 5.33 (1 H, d, J = 12.0 Hz, CH_2Ph), 5.05 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.99 (1 H, d, J = 12.2 Hz, CH_2Ph), 4.90 (1 H, d, J = 12.3 Hz, CH_2Ph), 4.71 (1 H, d, J = 12.4 Hz, CH_2Ph), 4.62 (1 H, d, J = 11.7 Hz, CH_2Ph), 4.54 (1 H, d, J = 11.8 Hz, CH_2Ph), 4.43 (1 H, s, H_1), 4.42 (1 H, d, J = 13.7 Hz, CH_2Ph), 4.42 (1 H, app. t, J = 8.9 Hz, H_4) 4.30 (2 H, s, CH_2Ph), 4.23 (1 H, app. t, J = 9.6 Hz, H_4'), 4.23 (1 H, d, J = 11.5 Hz, CH_2Ph), 4.06–4.00 (1 H, m, OCH_2CH$_2$CH$_2$N$_3$), 3.98 (1 H, d, J = 9.6 Hz, H_5'), 3.90 (1 H, d, J = 1.9 Hz, H_2) 3.82 (1 H, d, J = 9.1 Hz, H_5), 3.67 (1 H, d, J = 2.3 Hz, H_2'), 3.66 (1 H, dd, J = 9.6, 2.3 Hz, H_3'), 3.58 (3 H, s, CO$_2$CH_3), 3.53 (1 H, dd, J = 13.7, 8.6 Hz, OCH_2CH$_2$CH$_2$N$_3$), 3.43–3.35 (3 H, m, H_3, OCH$_2$CH$_2$CH_2N$_3$), 2.27 (1 H, d, J = 2.2 Hz, C4-*OH*), 1.90 (2 H, ddd, J = 28.6, 14.0, 7.4 Hz, OCH$_2$CH_2CH$_2$N$_3$); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 168.2 (*C*O$_2$CH$_3$), 152.4 (*C*(O)N(Bn)OBn), 138.5, 138.4, 138.3, 137.7, 137.4, 137.1, 128.5, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 127.4, 127.3, 101.9 (C1), 99.4 (C1′), 81.5 (C3), 78.1 (C3′), 76.4 (*C*H$_2$Ph), 75.6 (C5), 75.3 (C2′), 74.0 (*C*H$_2$Ph and C4), 73.3 (*C*H$_2$Ph), 72.9 (C5′), 72.8 (C2), 72.3 (*C*H$_2$Ph), 72.3 (*C*H$_2$Ph), 70.9 (*C*H$_2$Ph), 67.3 (C4′), 66.9 (OCH_2CH$_2$CH$_2$N$_3$), 52.9 (CO$_2$CH_3), 48.3 (OCH$_2$CH$_2$CH_2N$_3$), 29.1 (OCH$_2$CH_2CH$_2$N$_3$); **^{13}C-GATED** (101 MHz; $CDCl_3$): 101.9 ($^1J_{C1-H1}$ = 156 Hz, C1), 99.4 ($^1J_{C1'-H1'}$ = 176 Hz, C1′); **HRMS** (ES$^+$) *m*/*z* [found: (M + H)$^+$ 1023.4412 $C_{58}H_{62}N_4O_{13}$ requires (MH)$^+$, 1023.4386].

***O*-Benzyl (4-*O*-acetyl-2,3-di-*O*-benzyl-1-*N*-manno-D-pyranoside) hydroxamate 26.** A solution of *O*-benzyl (phenyl 4-*O*-acetyl-2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside) hydroxamate (100 mg, 0.16 mmol, 1.0 equiv.) diphenyl sulphoxide (50 mg, 0.26 mmol, 1.6 equiv.) and tri-*tert*-butylpyrimidine (100 mg, 0.41 mmol, 2.5 equiv.) in CH_2Cl_2 (5 mL) was stirred over activated MS4Å for 30 min. The mixture was cooled to −60 °C and triflic anhydride (67 μL, d = 1.720, 0.41 mmol, 2.5 equiv.) was then added to the reaction mixture. The mixture was allowed to warm to −40 °C over 10 min followed by cooling to −90 °C, when 3-bromopropanol (22 μL, d = 1.537, 0.24 mmol, 1.5 equiv.) in CH_2Cl_2 (0.5 mL) was added. The reaction mixture was allowed to warm to room temperature, and stirring was continued for further 1 h. The reaction was quenched with the addition of Et_3N until pH = 7 and the crude mixture was filtered through Celite® and concentrated under reduced pressure. The residue was then purified by Reveleris® automated silica gel flash column chromatography (liquid injection onto column), eluting with EtOAc/hexane (0/100, 30/70, 50/50, 90/10) to afford compound **26** as a colourless oil (50 mg, 0.1 mmol, 62%). R_f 0.28 (EtOAc/hexane, 1/2); $[\alpha]_D^{22}$ +21.0 (*c*. 1.10, $CHCl_3$); **^{1}H NMR** (300 MHz; $CDCl_3$) δ 7.71–7.21 (15 H, m, Ar–H), 5.80 (1 H, app. t, J = 1.2 Hz, H_1), 5.06 (1 H, t, J = 1.9 Hz, H_4), 4.94 (2 H, s, C(O)N(C1)OCH_2Ph), 4.74 (1 H, app. t, J = 2.0 Hz, H_5), 4.71 (1 H, d, J = 12.2 Hz, CH_2Ph-attached to C3), 4.56 (1 H, d, J = 12.2 Hz, CH_2Ph-attached to C3), 4.54 (1 H, d, J = 12.2, Hz, CH_2Ph-attached to C2), 4.39 (1 H, d, J = 12.2, Hz, CH_2Ph-attached to C2), 3.85 (1 H, dd, J = 5.0, 1.6 Hz, H_3), 3.65 (1 H, dd, J = 5.0, 1.6 Hz, H_2), 2.09 (3 H, s, C(O)CH_3); **^{13}C NMR** (101 MHz; $CDCl_3$) δ 169.6 (*C*(O)CH$_3$), 150.4 (*C*(O)N(C1)), 145.7, 137.8 (C_q Bn), 137.5 (C_q Bn), 137.3 (C_q Bn), 131.1, 129.3, 128.5, 128.3, 128.2, 128.2, 128.0, 127.8, 127.7, 127.7, 124.8, 104.6 (C1), 76.4 (C(O)N(C1)O*C*H$_2$Ph), 73.7 (C3), 73.0 (C5), 72.4 (*C*H$_2$Ph-attached to C3), 72.2 (C2), 71.1 (*C*H$_2$Ph-attached to C2), 69.1 (C4), 20.9 (C(O)*C*H$_3$); **HRMS** (ES$^+$) *m*/*z* [found: (M + H)$^+$ 504.2009 $C_{29}H_{29}NO_7$ requires (MH)$^+$, 504.2017]; **IR** ν_{max}/cm^{-1} 1740 (s, C=O$_{ester}$), 1701 (m, C=O$_{amide}$), 1223 (s, C–O$_{ester}$) 1065 (m, C–O$_{ether}$).

Conflicts of interest

There are no conflicts to declare.

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References

1 Z. Li, M. R. Kosorok, P. M. Farrell, A. Laxova, S. E. West, C. G. Green, J. Collins, M. J. Rock and M. L. Splaingard, *J. Am. Med. Assoc.*, 2005, **293**, 581–588.
2 K. Y. Lee and D. J. Mooney, *Prog. Polym. Sci.*, 2012, **37**, 106–126.
3 W. Sabra, A. P. Zeng and W. D. Deckwer, *Appl. Microbiol. Biotechnol.*, 2001, **56**, 315–325.
4 H. Ertesvåg, *Front. Microbiol.*, 2015, **6**, 1–10.
5 J. Jia, D. J. Richards, S. Pollard, Y. Tan, J. Rodriguez, R. Visconti, T. C. Trusk, M. J. Yost, H. Yao, R. R. Markwald and Y. Mei, *Acta Biomater.*, 2014, **10**, 4323–4331.
6 Q. Zhang, E. R. van Rijssel, M. T. C. Walvoort, H. S. Overkleeft, G. A. van der Marel and J. D. C. Codée, *Angew. Chem., Int. Ed.*, 2015, **54**, 7670–7673.
7 J. Dinkelaar, L. J. van den Bos, W. F. J. Hogendorf, G. Lodder, H. S. Overkleeft, J. D. C. Codée and G. A. van der Marel, *Chem. – Eur. J.*, 2008, **14**, 9400–9411.
8 L. J. van den Bos, J. Dinkelaar, H. S. Overkleeft and G. A. van der Marel, *J. Am. Chem. Soc.*, 2006, **128**, 13066–13067.
9 D. Pan, L. Zhang, Q. Hua and Y. Yang, *Org. Biomol. Chem.*, 2019, **17**, 6174–6177.

10 M. T. C. Walvoort, H. van den Elst, O. J. Plante, L. Kröck, P. H. Seeberger, H. S. Overkleeft, G. A. van der Marel and J. D. C. Codée, *Angew. Chem., Int. Ed.*, 2012, **51**, 4393–4396.
11 J. Dinkelaar, A.-R. de Jong, R. van Meer, M. Somers, G. Lodder, H. S. Overkleeft, J. D. C. Codée and G. A. van der Marel, *J. Org. Chem.*, 2009, **74**, 4982–4991.
12 J. D. C. Codée, L. J. van den Bos, A.-R. de Jong, J. Dinkelaar, G. Lodder, H. S. Overkleeft and G. A. van der Marel, *J. Org. Chem.*, 2009, **74**, 38–47.
13 A. Górska, A. Sloderbach and M. P. Marszałł, *Trends Pharmacol. Sci.*, 2014, **35**, 442–449.
14 N. Ferlin, D. Grassi, C. Ojeda, M. J. L. Castro, E. Grand, A. F. Cirelli and J. Kovensky, *Carbohydr. Res.*, 2008, **343**, 839–847.
15 S. U. Hansen, G. J. Miller, C. Cole, G. Rushton, E. Avizienyte, G. C. Jayson and J. M. Gardiner, *Nat. Commun.*, 2013, **4**, 2016.
16 (*a*) L. Guazzelli, O. McCabe and S. Oscarson, *Carbohydr. Res.*, 2016, **433**, 5–13; (*b*) L. Guazzelli, G. Catelani and F. D'Andrea, *Carbohydr. Res.*, 2010, **345**, 369–376.
17 F. Baleux, L. Loureiro-Morais, Y. Hersant, P. Clayette, F. Arenzana-Seisdedos, D. Bonnaffé and H. Lortat-Jacob, *Nat. Chem. Biol.*, 2009, **5**, 743–748.
18 Y. Yu, T. Tyrikos-Ergas, Y. Zhu, G. Fittolani, V. Bordoni, A. Singhal, R. J. Fair, A. Grafmüller, P. H. Seeberger and M. Delbianco, *Angew. Chem., Int. Ed. Engl.*, 2019, **58**, 13127–13132.