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One-pot synthesis of multivalent arrays of mannose mono- and disaccharides

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Abstract—The synthesis of a selection of multivalent arrays of mannose mono- and disaccharides, that are of potential use as anti-infective agents against *enterobacteri*a infections, is described.

1. Introduction

It is now accepted that glycoproteins and glycolipids are widely expressed on cell surfaces and participate in many molecular recognition and binding processes in both healthy and diseased states.[1] In particular, some bacterial surface proteins show specific binding for carbohydrates expressed on human cells, and such interactions form an essential part of the infection pathway. It has been demonstrated that administration of synthetic or natural carbohydrate derivatives can disrupt this infective pathway, so long as the administered derivatives have high affinities for the bacterial lectins.[2] In such cases, the bacteria are no longer able to interact with the host, and therefore pass through the body without initiating infection. These therapeutic agents have been termed anti-infective agents. A number of anti-infective agents occur naturally, for example, human breast milk contains numerous soluble oligosaccharides that provide newborn babies with a mechanism for diverting infection processes.[3] However, there is also considerable interest in the design of synthetic, multivalent carbohydrate based anti-infective agents as alternatives to traditional antiobiotic therapies.[4] It has been postulated that since anti-infective agents rely on disrupting carbohydrate–lectin interactions, any mutations that render the bacteria resistant to the anti-infective carbohydrate agents should also produce bacteria that are incapable of binding to the host's carbohydrates.[5] This is particularly useful given the evolution of multi-drug resistant microbial pathogens.

Since the affinity of individual carbohydrate sequences for the binding sites on the bacteria are typically within the micro- to millimolar range it is essential that multivalent arrays of the disease associated carbohydrates are administered. In particular, flexible multivalent arrays and dendritic[6] arrays of receptor carbohydrates are of current interest, as a result of their enhanced activity resulting from the cluster effect.[7]

2. Results and discussion

As part of a programme directed towards the inhibition of infections caused by enterobacteria (for example some *E. coli* and *S. suis* strains), that naturally adhere via type 1 fimbriae to highly-branched mannose chains,[8] we required access to multivalent arrays of mannose saccharides. Although the natural hosts display complex mannose saccharides, it has already been demonstrated that arrays of mannose monosaccharides,[9] as well as Man α-1,2-Man and Man α-1,3-Man disaccharides,[10] are effective for inhibiting the carbohydrate–lectin interactions. The ultimate aim of this programme was to devise methodologies that would allow efficient entry to multivalent mannose anti-infective agents in a concise manner. Initial studies aimed to assess the suitability of forming these targets by condensation of fully protected mannopyranoside donors with a range of alcohol or thiol linkers. However, it is evident from Scheme 1 and Table 1 that access to relatively simple divalent derivatives via such an approach proved problematic, with the reactions only being synthetically useful when more than two carbon units were incorporated within the linker: when shorter linkers such as ethylene glycol, ethane 1,2-dithiol or mercaptoethanol were utilised it generally proved difficult to access synthetically useful quantities of the divalent targets. (Scheme 1, Table 1). This effect was observed presumably

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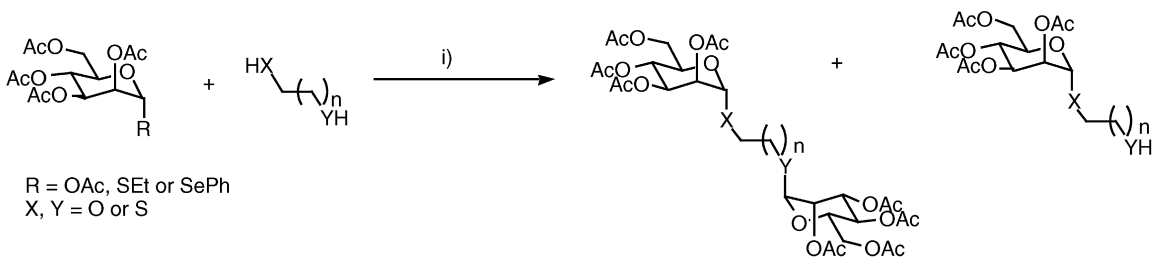
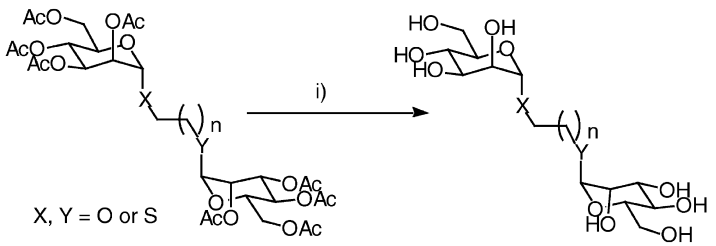


Scheme 1. (i) R=OAc, $BF_3{\cdot}OEt_2$; R=SEt or SePh, NIS, TfOH.

Table 1.

R	Linker	Divalent derivative (%)	Monovalent derivative (%)
OAc	Ethylene glycol	(**1**) 11	(**2**) 15
OAc	Ethane 1,2-dithiol	(**3**) 0	(**4**) 15
OAc	Ethanol mercaptan	(**5**) 39	(**6**) 12
OAc	Butane 1,4-diol	(**7**) 46	–
SEt	Octane 1,8-diol	(**8**) 72	–
SePh	Bis(4-hydroxyphenyl)methane	(**9**) 54	–
SePh	4,4′-Biphenol	(**10**) 49	–
OAc	1,3-Propanedithiol	(**11**) 63	–



Scheme 2. (i) K_2CO_3, MeOH.

Table 2.

Acetylated derivative	Deprotected target	Yield (%)
(**1**) X=O, Y=O, *n*=1	(**12**)	94
(**7**) X=O, Y=O, *n*=3	(**13**)	86
(**9**) X=OPh, Y=OPh, *n*=0	(**14**)	83
(**11**) X=S, Y=S, *n*=2	(**15**)	89

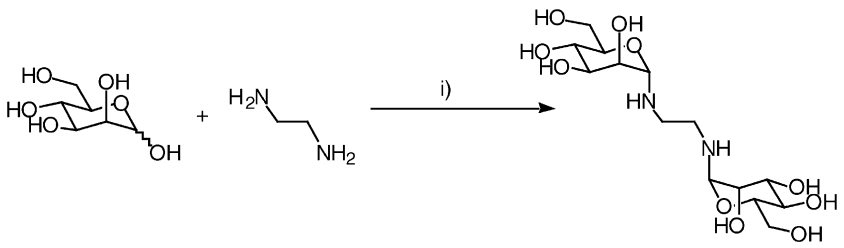
as a result of disfavoured steric interactions that occur between the carbohydrate residues within the short linker targets.

Conversion of the protected intermediates to the deprotected divalent targets proved possible in excellent yield by simple treatment with potassium carbonate and methanol (Scheme 2, Table 2). However, the limited success of the methodology for accessing derivatives derived from short linkers, and the need for conventional carbohydrate protection/deprotection manipulations, sought us to investigate an alternative approach for accessing derivatives of higher valency with greater efficiency.

Preparation of glycosylamines by condensation of amines with reducing sugars is well described in the literature[11] and condensation of a small range of reducing sugars with diamines has also been previously reported to allow efficient access to divalent carbohydrate derivatives in excellent yields.[12] However, this strategy has not been extended to allow synthesis of higher valent derivatives through reaction of more highly functionalised amine clusters with reducing sugars. This strategy was considered particularly attractive for entry to multivalent carbohydrate anti-infective agents since it circumnavigates the need for time consuming protection/deprotection steps and offers equal potential for derivatisation of both mannose mono- and disaccharide units. Initial studies concentrated on the condensation reaction of D-(+)-mannose with ethylene diamine, in methanol, at 50°C. Pleasingly this approach allowed direct access to the target divalent derivative (**16**) in 77% yield, and the target crystallized out of the solution when left at 4°C overnight (Scheme 3).[13]

Moreover, it also proved possible to extend this methodology to allow access to a library of multivalent mannose monosaccharides (**16**–**24**), by incorporation of the multivalent amines illustrated in Figure 1 (Table 3).

Thus linkers of different lengths, flexibility and valency were easily incorporated with each allowing one-pot entry to the desired targets in synthetically useful yields. The anomeric configurations of the glycosylamines were determined by measuring $^1J[^{13}CH(1)]$ coupling constants for representative targets. Comparison of these with values reported in the literature[15] indicated that the glycosylamines were of the α-configuration.



Scheme 3. (i) Anhydrous methanol, room temperature, then 4°C, 77%.

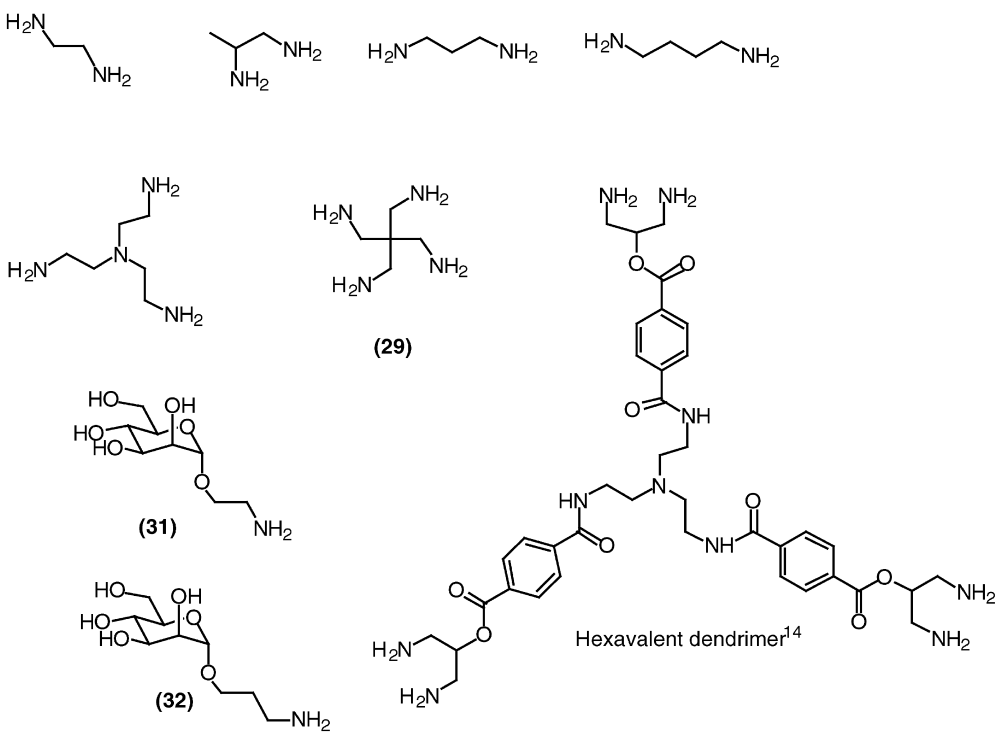


Figure 1.

In some cases the multivalent amines utilised in the reactions were commercially available. However, some amines necessitated synthesis. For example, pentaerythritol tetraamine (**29**) was prepared by reduction of azide (**30**) utilising hydrogen and 10% Pd/C. The azide (**30**) was itself prepared in excellent yield by treatment of pentaerythrityl tetrabromide with sodium azide in DMF at 80°C (Scheme 4).

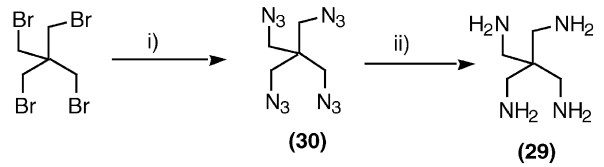
Table 3.

Saccharide	Amine	Yield (%)
D-Mannose	Ethylenediamine	(**16**) 77
D-Mannose	1,2-Propanediamine	(**17**) 64
D-Mannose	1,3-Propanediamine	(**18**) 68
D-Mannose	1,4-Butanediamine	(**19**) 53
D-Mannose	Tris(2-aminoethyl)amine	(**20**) 56
D-Mannose	Pentaerythrityl tetraamine (**29**)	(**21**) 47
D-Mannose	Hexavalent dendrimer[14]	(**22**) 56
D-Mannose	Amine (**31**)	(**23**) 43
D-Mannose	Amine (**32**)	(**24**) 38
Man α-1,3-Man	Ethylenediamine	(**25**) 43
Man α-1,2-Man	Ethylenediamine	(**26**) 39
Man α-1,3-Man	Hexavalent dendrimer[14]	(**27**) 37
Man α-1,2-Man	Hexavalent dendrimer[14]	(**28**) 35

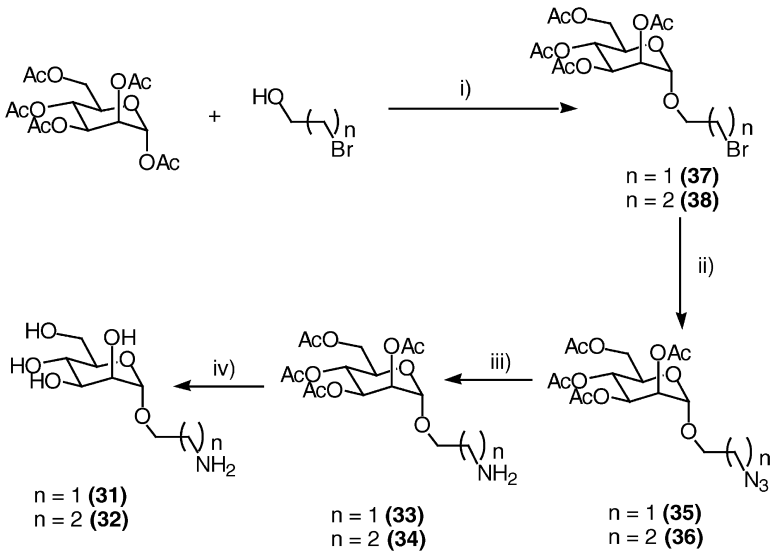
Amines (**31**) and (**32**) were prepared by de-*O*-acetylation of amines (**33**) and (**34**), respectively, with potassium carbonate and methanol with the amines themselves being prepared from azides (**35**) and (**36**) respectively. The azides (**35**) and (**36**) were easily prepared in two steps from 1,2,3,4,6-penta-*O*-acetate mannopyranoside by initial condensation with 2-bromoethanol or 3-bromopropan-1-ol, under Lewis acid mediated conditions (Scheme 5).

Extension of the methodology to allow condensation of multivalent amines with the disaccharides Man-α-1,2-Man[16] and Man-α-1,3-Man[17] also proved straightforward. The disaccharides were prepared via chemical or enzymatic pathways according to literature methods[16,17] and were then reacted in their deprotected forms with ethylene diamine or the hexavalent dendrimer[14] under the one-pot reaction conditions outlined above. Pleasingly this approach allowed entry to the multivalent disaccharide targets (**25**–**28**) in good to excellent yields.

In order to gain preliminary data concerning the stability of the multivalent derivatives in aqueous solutions, divalent



Scheme 4. (i) NaN_3, DMF, 80°C, 81%; ii) Pd/C, H_2, MeOH, 91%.



Scheme 5. (i) CH_2Cl_2, $BF_3{\cdot}OEt_2$; (ii) NaN_3, DMF; (iii) H_2, Pd/C; (iv) K_2CO_3, MeOH.

derivative (**16**) was stirred under aqueous conditions at 23°C for 4 h and the solution analysed by TLC and ^{1}H NMR for evidence of decomposition. Pleasingly no hydrolysis products were detected during this time suggesting that the targets have suitable half lives to be of interest as potential anti-infective agents.

3. Conclusions

A range of multivalent mannose mono- and disaccharides have been prepared in an efficient manner using a range of different methodologies. Of particular interest is the development of a one-pot methodology that allows entry to multivalent derivatives without any need for protecting group strategies. The utility of the derivatives as anti-infective agents against infections caused by *enterobacteri*a is currently being evaluated in our laboratories.

4. Experimental

4.1. General

NMR spectra were recorded on a Bruker AC250 (250 MHz), a Bruker DPX250 (250 MHz), and a Bruker AMX400 (400 MHz) spectrometer. All spectra were recorded in either chloroform-*d*, methanol-*d*, or in deuterated water and are referenced to residual solvent peaks or to an internal standard, tetramethylsilane. Peak positions were recorded in δ ppm with the abbreviations s, d, t, m, denoting singlet, doublet, triplet and multiplet, respectively. All coupling constants (J) are quoted in Hertz.

Infra red spectra were recorded on either a Perkin–Elmer Paragon 1000 FT-IR spectrometer, or a Perkin–Elmer 1720-X spectrometer. Spectra were analysed as either a thin oil film between sodium chloride plates or as a potassium bromide disc. All absorptions are quoted in cm^{-1}.

High-resolution mass-spectrometric data, both low-resolution mass spectra (m/z) and accurate mass spectra (HRMS), were recorded on a Fisons VG Autospec mass spectrometer. All spectra were recorded using either chemical ionisation, with either methane or ammonia gas as the ionising source, fast-atom bombardment using caesium ions as the ion source and glycerol as the matrix, or electrospray ionisation.

All melting points were recorded using a Koffler heated stage microscope and are uncorrected.

Specific optical rotations ($[\alpha]_D^{20}$) were recorded at the sodium D line (589.3 nm) in chloroform, methanol or water and are quoted in units of 10^{-1} deg cm^2 g^{-1}. Solution concentrations (c) are given in units of 10^{-2} g cm^{-3}. Measurements were obtained using a Perkin–Elmer 341 polarimeter.

Elemental analyses were performed by Medac Ltd, Brunel Science Centre, Surrey.

All reactions were monitored by thin layer chromatography (TLC) using Merck aluminium backed plates coated with 0.2 mm silica 60 F_{254}. Product spots were visualised using UV irradiation (254 nm) and by staining the plate with an ethanol/sulfuric acid (25:1, v/v) dip.

Flash column chromatography was performed using Merck 60 silica gel (particle size 0.040–0.063 nm, 230–400 mesh ASTM) using head pressure by means of hand bellows.

Anhydrous solvents were supplied in 'sure seal' bottles by Aldrich. All reactions were performed under an inert atmosphere of argon or nitrogen unless otherwise stated. Solvents were evaporated under aspirator vacuum (ca. 20 mmHg) at approximately 35°C, unless otherwise stated or when coevaporating using toluene.

4.1.1. 1,2-Bis[*O*-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl]ethane-1,2-diol (1) and 2′-hydroxyethyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (2). 1,2,3,4,6-Penta-*O*-acetyl-α-D-mannopyranoside (0.965 g, 2.47 mmol) was dissolved in distilled CH_2Cl_2 (10 cm^3) and ethylene glycol (0.41 cm^3, 7.41 mmol) was added followed, after 30 min, by the addition of boron trifluoride etherate (0.91 cm^3, 7.41 mmol) at 0°C. The reaction mixture was warmed up to room temperature and stirred under an argon atmosphere. The reaction was followed by TLC analysis, using ethyl acetate/hexane (1:1, v/v) as the solvent system. After 14 h saturated sodium bicarbonate solution was added (20 cm^3) and the organic layer extracted with CH_2Cl_2 (3×30 cm^3). The combined organic layers were dried over magnesium sulfate, filtered and concentrated to dryness under reduced pressure. The resulting yellow oil was purified using column chromatography on silica gel (ethyl acetate/hexane, 1:1, v/v). The relevant fractions were collected and combined to give *2,3,4,6-tetra-O-acetyl-α-D-mannose* as a yellow oil (0.16 g, 19%), *2′-hydroxyethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**2**) as a colourless oil (0.45 g, 15%), and *1,2-bis[O-2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl]ethane-1,2-diol* (**1**) as a colourless oil (0.19 g, 11%). Data for (**1**): $[\alpha]_D^{20}$=+7.42 (*c* 1.20, $CHCl_3$); ν_{max} (NaCl, cm^{-1}) 1747 (s, C=O str), 1436 (s, as CH_3), 1373 (s, s CH_3), 1232 (s, CC(=O)–O str); δ_H (400 MHz, $CDCl_3$) 5.28 (2H, dd, *J*=10.0, 3.5 Hz, H-3, H-3′), 5.19–5.21 (4H, m, H-2, H-2′, H-4, H-4′), 4.80 (2H, d, *J*=1.5 Hz, H-1, H-1′), 4.17–4.24 (2H, m, H-6), 4.02–4.08 (2H, m, H-6′), 3.94–3.98 (2H, m, H-5, H-5′), 3.64–3.83 (4H, m, 2×H_a, 2×H_b), 2.09 (6H, s, 2×OAc), 2.03 (6H, s, 2×OAc), 1.98 (6H, s, 2×OAc), 1.93 (6H, s, 2×OAc); δ_C (100 MHz, $CDCl_3$) 170.5 (2×C=O), 169.9 (2×C=O), 169.8 (2×C=O), 169.6 (2×C=O), 97.5 (2×CH), 69.3 (2×CH), 68.8 (2×CH), 68.5 (2×CH), 66.0 (2×CH), 65.9 (2×CH_2), 62.3 (2×CH_2), 20.7 (2×CH_3), 20.6 (6×CH_3); *m/z* (CI) 740 ($M+NH_4^+$, 5%), 331 (43), 229 (11), 168 (26), 87 (100); Found 740.2640, $C_{30}H_{46}O_{20}N$ requires 740.2613.

Data for (**2**): $[\alpha]_D^{20}$=+36.83 (*c* 0.52, $CHCl_3$); ν_{max} (NaCl, cm^{-1}) 3521 (m, OH str), 2940 (m, OH str), 1746 (s, C=O str), 1439 (m, as CH_3), 1372 (s, s CH_3), 1228 (s, CC(=O)–O str), 1138 (s, C–O–C str), 1047 (s, C–O–C str), 980 (s, C–O–C str); δ_H (250 MHz, $CDCl_3$) 5.16–5.25 (3H, m, H-2, H-3, H-4), 4.82 (1H, d, *J*=1.5 Hz, H-1), 4.20 (1H, dd, *J*=5.5 Hz, 12.5, H-6), 4.00–4.08 (2H, m, H-5, H-6), 3.69–3.75 (3H, m, 2×H_b, H_a), 3.56–3.60 (1H, m, H_a), 3.14 (1H, br s, OH), 2.09 (3H, s, OAc), 2.03 (3H, s, OAc), 1.98 (3H, s, OAc), 1.92 (3H, s, OAc); δ_C (62.5 MHz, $CDCl_3$) 171.0 (C=O), 170.3 (2×C=O), 170.0 (C=O), 98.1 (CH), 70.3 (CH_2OH), 69.7 (CH), 69.4 (CH), 68.8 (CH), 66.3 (CH), 62.7 (CH_2), 61.6 (CH_2O), 21.1 (CH_3), 21.0 (2×CH_3), 20.9 (CH_3); *m/z* (CI) 410 ($M+NH_4^+$, 57%), 331 (98), 169 (38), 73 (100); Found 410.1642, $C_{16}H_{28}O_{11}N$ requires 410.1662.

4.1.2. 2′-Thioethyl 2,3,4,6-tetra-*O*-acetyl-1-α-D-mannopyranoside (4). 1,2,3,4,6-Penta-*O*-acetyl-α-D-mannopyranoside (1.700 g, 4.36 mmol) was dissolved in distilled CH_2Cl_2 (20 cm^3) and 1,2-ethane dithiol (1.10 cm^3, 13.08 mmol) was added followed after 30 min by the addition of boron trifluoride etherate (1.60 cm^3, 13.08 mmol) at 0°C. The reaction mixture was warmed up to room temperature and stirred under an argon atmosphere. The reaction was followed by TLC analysis, using ethyl acetate/hexane (1:1, v/v) as the solvent system. After 12 h saturated sodium bicarbonate solution was added (20 cm^3) and the organic layer extracted with dichloromethane (3×30 cm^3). The combined organic layers were dried over magnesium sulfate, filtered and concentrated to dryness under reduced pressure. The resulting yellow oil was purified using column chromatography on silica gel (ethyl acetate/hexane, 1:1, v/v). The relevant fractions were collected and combined to give *2′-thioethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**4**) as a colourless solid (0.46 g, 15%). Mp 39.4–41.2°C; $[\alpha]_D^{20}$=+42.06 (*c* 0.68, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 5.23–5.29 (4H, m, H-1, H-2, H-3, H-4), 4.27 (1H, m, H-5), 4.20–4.23 (1H, m, H-6), 4.03–4.08 (1H, m, H-6), 2.70–2.85 (4H, m, 2×H_a, 2×H_b), 2.11 (3H, s, OAc), 2.06 (3H, s, OAc), 2.01 (3H, s, OAc), 1.94 (3H, s, OAc), 1.63 (1H, t, *J*=8.0 Hz, SH); δ_C (62.5 MHz, $CDCl_3$) 170.9 (C=O), 170.2 (C=O), 170.1 (C=O), 170.0 (C=O), 83.3 (CH), 71.3 (CH), 69.6 (2×CH), 66.6 (CH), 62.8 (CH_2), 36.1 (CH_2SH), 25.0 (CH_2S), 21.2 (CH_3), 21.1 (CH_3), 21.0 (2×CH_3); *m/z* (CI) 442 ($M+NH_4^+$, 18%), 331 (12), 245 (21), 213 (100), 153 (47), 97 (40); Found 442.1209, $C_{16}H_{28}O_9NS$ requires 442.1206.

4.1.3. 1,2-Bis[*O*-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl] ethane-1-hydroxy-2′-thiol (5) and 2′-hydroxythioethyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (6). 1,2,3,4,6-Penta-*O*-acetyl-α-D-mannopyranoside (2.73 g, 7.01 mmol) was dissolved in anhydrous CH_2Cl_2 (20 cm^3) and 2-mercaptoethanol (1.37 cm^3, 21.02 mmol) was added. The reaction mixture was cooled to 0°C and treated with boron trifluoride etherate (2.58 cm^3, 21.02 mmol). The reaction mixture was warmed up to room temperature and stirred under a nitrogen atmosphere for 5 h. An ice-cold solution of saturated sodium bicarbonate (30 cm^3) was added to the reaction mixture and then this mixture was diluted with CH_2Cl_2 (40 cm^3). The organic layer was washed with a saturated solution of sodium bicarbonate (3×40 cm^3) and dried over magnesium sulfate. The resulting solution was filtered and concentrated to dryness in vacuo and then purified using column chromatography on silica gel (ethyl acetate/hexane (2:1, v/v)). The relevant fractions were collected, combined and concentrated to dryness under reduced pressure to yield *1,2-bis[O-2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl] ethane-1-hydroxy-2′-thiol* (**5**) as a colourless solid (0.20 g, 39%) and *2′-hydroxythioethyl*

2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (**6**) as a colourless solid (0.33 g, 12%). Data for (**5**). Mp 68.5–70.2°C; $[\alpha]_D^{20}$=+57.65 (*c* 0.52, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 5.17–5.27 (7H, m, H-2, H-3, H-4, H-1′, H-2′, H-3′, H-4′), 4.78 (1H, d, *J*=1.5 Hz, H-1), 4.19–4.31 (3H, m, H-5, H-6), 3.98–4.07 (3H, m, H-5′, H-6′), 3.58–3.92 (2H, m, CH_2O), 2.66–2.90 (2H, m, CH_2S), 2.09 (3H, s, 2×OAc), 2.04 (3H, s, 2×OAc), 2.00 (3H, s, 2×OAc), 1.93 (3H, s, 2×OAc); δ_C (62.5 MHz, $CDCl_3$) 169.6 (2×C=O), 169.0 (2×C=O), 168.8 (4×C=O), 96.7 (CH), 91.2 (CH), 69.8 (CH), 68.4 (CH), 68.2 (CH), 67.9 (CH), 67.8 (CH), 66.3 (CH_2O), 65.2 (CH), 65.0 (CH), 61.4 (CH_2), 29.2 (CH_2S), 19.9 (2×CH_3), 19.7 (3×CH_3), 19.6 (3×CH_3); *m/z* (CI) 756 ($M+NH_4^+$, 79%), 331 (100), 169 (34); Found 756.2352, $C_{30}H_{46}O_{18}NS$ requires 756.2385.

Data for (**6**). Mp 101.3–102.8°C; $[\alpha]_D^{20}$=+75.00 (*c* 1.31, $CHCl_3$); ν_{max} (NaCl, cm^{-1}) 3484 (m, O–H str), 2944 (m, O–H str), 1746 (s, C=O str), 1433 (m, as CH_3), 1373 (s, s CH_3), 1229 (s, CC(=O)–O str), 1052 (s, C–O–C str), 976 (m, C–O–C str); δ_H (250 MHz, $CDCl_3$) 5.31 (1H, d, *J*=1.5 Hz, H-2), 5.15–5.26 (3H, m, H-1, H-3, H-4), 4.34–4.39 (1H, m, H-5), 4.21 (1H, dd, *J*=6.0, 12.0 Hz, H-6), 4.04–4.09 (1H, m, H-6), 3.69–3.76 (2H, m, CH_2OH), 2.72–2.92 (2H, m, CH_2S), 2.44 (1H, br s, OH), 2.10 (3H, s, OAc), 2.04 (3H, s, OAc), 1.95 (3H, s, OAc), 1.93 (3H, s, OAc); δ_C (62.5 MHz, $CDCl_3$) 171.0 (C=O), 170.4 (C=O), 170.2 (C=O), 170.1 (C=O), 83.5 (CH), 71.5 (CH), 69.7 (CH), 69.6 (CH), 66.7 (CH), 62.9 (CH_2), 62.1 (CH_2OH), 35.6 (SCH_2), 21.3 (CH_3), 21.1 (CH_3), 21.0 (2×CH_3); *m/z* (CI) 426 ($M+NH_4^+$, 67%), 331 (100), 289 (70), 229 (72), 169 (89), 109 (47).

4.1.4. 1,4-Bis[*O*-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl]butane-1,4-diol (7). 1,2,3,4,6-Penta-*O*-acetyl-α-D-mannopyranoside (0.503 g, 1.28 mmol) was dissolved in distilled CH_2Cl_2 (15 cm^3) and 1,4-butanediol (56.8 μL, 0.64 mmol) was added at 0°C, followed by the addition of boron trifluoride etherate (0.40 cm^3, 3.84 mmol). The reaction was warmed up to room temperature under an argon atmosphere. The reaction was followed by TLC analysis, using diethyl ether as the solvent system. After 16 h saturated sodium bicarbonate solution was added (30 cm^3) and the organic layer extracted with dichloromethane (3×40 cm^3). The combined organic layers were dried over magnesium sulfate, filtered and concentrated to dryness under reduced pressure. The resulting brown oil was purified using column chromatography on silica gel eluting with diethyl ether/hexane (3:1, v/v). The relevant fractions were collected and combined to give *1,4-bis[O-2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl]butane-1,4-diol* (**7**) as a yellow oil (0.23 g, 46%). $[\alpha]_D^{20}$=+55.00 (*c* 0.07, $CHCl_3$); ν_{max} (NaCl, cm^{-1}) 1750 (s, C=O str), 1436 (w, as CH_3), 1370 (s, s CH_3), 1230 (s, CC(=O)–O str), 1135 (m, C–O–C str), 1084 (s, C–O–C str), 1049 (s, C–O–C str), 979 (w, C–O–C str); δ_H (250 MHz, $CDCl_3$) 5.21–5.26 (4H, m, H-3, H-3′, H-4, H-4′), 5.16–5.18 (2H, dd, *J*=2.0, 3.0 Hz, H-2, H-2′), 4.74 (2H, d, *J*=1.5 Hz, H-1, H-1′), 4.22 (2H, dd, *J*=5.5, 12.0 Hz, 2×H-6), 4.04 (2H, dd, *J*=3.0, 12.0 Hz, 2×H-6′), 3.87–3.91 (2H, m, H-5, H-5′), 3.37–3.68 (4H, m, 4×H_a), 2.09 (6H, s, OAc), 2.04 (6H, s, 2×OAc), 1.98 (6H, s, 2×OAc), 1.93 (6H, s, 2×OAc), 1.60–1.67 (4H, m, 4×H_b); δ_C (62.5 MHz, $CDCl_3$) 171.0 (2×C=O), 170.5 (2×C=O), 170.3 (2×C=O), 170.1 (2×C=O), 98.0 (2×CH), 70.0 (2×CH), 69.4 (2×CH), 68.9 (2×CH), 68.3 (2×CH_2), 66.6 (2×CH), 62.9 (2×O*C*$H_2$$CH_2$), 25.8 (2×OC$H_2$*C*$H_2$), 21.4 (2×$CH_3$), 21.3 (4×$CH_3$), 21.1 (2×$CH_3$); *m/z* (CI) 768 ($M+NH_4^+$, 6%), 577 (13), 438 (80), 331 (80), 289 (100), 229 (64), 169 (16), 115 (28); Found 768.2936, $C_{32}H_{50}O_{20}N$ requires 768.2930.

4.1.5. 1,8-Bis[*O*-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl]octane-1,8-diol (8). Ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-mannopyranoside (0.615 g, 1.57 mmol) and 1,8-octanediol (0.274 g, 1.89 mmol) were dissolved in anhydrous acetonitrile (15 cm^3), added to activated molecular sieves (4 Å) and stirred at 0°C for 30 min under a nitrogen atmosphere. To this solution were added *N*-iodosuccinimide (0.705 g, 3.14 mmol) and triflic acid (catalytic amount), the reaction mixture was then allowed to warm to room temperature and stirred for 10 min. TLC analysis of the reaction was performed, using ethyl acetate/hexane (3:1, v/v) as the solvent system, and showed that the reaction had gone to completion (starting material R_f 0.73, product R_f 0.57). The reaction mixture was diluted with CH_2Cl_2 (40 cm^3) and filtered through a pad of Celite® with the aid of CH_2Cl_2 (20 cm^3). The filtrate was then washed with an aqueous 10% sodium thiosulfate solution (2×20 cm^3) to quench any unreacted *N*-iodosuccinimide. The combined organic layers were then washed with a saturated aqueous sodium bicarbonate solution (2×20 cm^3) and then dried over magnesium sulfate, filtered and concentrated to dryness in vacuo to produce a brown oil. The resulting oil was then purified using column chromatography on silica gel (ethyl acetate/hexane (3:1, v/v)). The relevant fractions were collected, combined and concentrated to dryness under reduced pressure to yield *1,8-bis[O-2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl]octane-1,8-diol* (**8**) as a yellow oil (0.91 g, 72%). $[\alpha]_D^{20}$=+28.55 (*c* 0.42, $CHCl_3$); ν_{max} (NaCl, cm^{-1}) 1748 (s, C=O str), 1433 (w, as CH_3), 1374 (s, s CH_3), 1198 (s, CC(=O)–O str), 1135 (m, C–O–C str), 1074 (s, C–O–C str), 1056 (s, C–O–C str), 980 (w, C–O–C str); δ_H (400 MHz, $CDCl_3$) 5.35 (2H, dd, *J*=3.5, 10.0 Hz, H-3, H-3′), 5.27 (2H, t, *J*=10.0 Hz, H-4, H-4′), 5.23 (2H, dd, *J*=1.5, 3.5 Hz, H-2, H-2′), 4.81 (2H, d, *J*=1.5 Hz, H-1, H-1′), 4.28 (2H, dd, *J*=5.5, 12.0 Hz, H-6, H-6′), 4.11 (2H, dd, *J*=2.5, 12.0 Hz, H-6, H-6′), 3.95–4.01 (2H, m, H-5, H-5′), 3.44–3.72 (4H, m, 4×H_a), 2.16 (6H, s, 2×OAc), 2.11 (6H, s, 2×OAc), 2.06 (6H, s, OAc), 2.00 (6H, s, OAc), 1.51–1.63 (2H, m, 2×H_b), 1.28–1.40 (10H, m, 2×H_b, 4×H_c, 4×H_d); δ_C (100 MHz, $CDCl_3$) 170.8 (2×C=O), 170.2 (2×C=O), 170.1 (2×C=O), 169.8 (2×C=O), 97.5 (2×CH), 69.7 (2×CH), 69.2 (2×CH), 68.5 ((O$CH_2CH_2CH_2$-CH_2)$_2$), 68.4 (2×CH), 66.2 (2×CH), 62.5 (2×CH_2), 29.2 ((OCH$_2$*C*H$_2$CH$_2$CH$_2$)$_2$), 26.0 ((OCH$_2$CH$_2$*C*H$_2$CH$_2$)$_2$), 25.7 ((OCH$_2$CH$_2$CH$_2$*C*H$_2$)$_2$), 20.9 (2×OAc), 20.7 (6×OAc); *m/z* (CI) 824 ($M+NH_4^+$, 10%), 331 (100), 229 (17), 169 (15); Found 824.3577, $C_{36}H_{58}O_{20}N$ requires 824.3209.

4.1.6. Bis(4-hydroxyphenyl)methane bis(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside) (9). Bis(4-hydroxyphenyl)-methane (0.309 g, 1.55 mmol) and phenyl 2,3,4,6-tetra-*O*-acetyl-1-seleno-α-D-mannopyranoside (1.832 g, 3.76 mmol) were dissolved in anhydrous DCM (40 cm^3), added to activated molecular sieves (4 Å) and stirred at 0°C for 30 min under a nitrogen atmosphere. To this solution were

added *N*-iodosuccinimide (0.696 g, 3.09 mmol) and triflic acid (catalytic amount), the reaction mixture was allowed to warm to room temperature and stirred for 20 min. TLC analysis of the reaction was performed, using ethyl acetate/hexane (1:1, v/v) as the solvent system, and showed that the reaction had gone to completion (starting material R_f 0.61, product R_f 0.32). The reaction mixture was diluted with CH_2Cl_2 (40 cm^3) and filtered through a pad of Celite® with the aid of CH_2Cl_2 (20 cm^3). The filtrate was then washed with an aqueous 10% sodium thiosulfate solution (2×40 cm^3) to quench any unreacted *N*-iodosuccinimide. The combined organic layers were then washed with a saturated aqueous sodium bicarbonate solution (2×40 cm^3) and then dried over magnesium sulfate, filtered and concentrated to dryness in vacuo to produce a brown oil. The resulting oil was then purified using column chromatography on silica gel (ethyl acetate/hexane (1:1, v/v)). The relevant fractions were collected, combined and concentrated to dryness under reduced pressure to yield *bis(4-hydroxyphenyl)methane bis(2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside)* (**9**) as a colourless foam (0.72 g, 54%). $[\alpha]_D^{20}$=+66.30 (*c* 1.13, $CHCl_3$); ν_{max} (NaCl, cm^{-1}) 3026 (m, ArCH str), 2961 (m, ArCH str), 1746 (s, C=O str), 1609 (m, ArC=C–C–O–C str), 1589 (w, ArC=C–C–O–C str), 1505 (s, ArC=C str), 1433 (s, as CH_3), 1371 (s, s CH_3), 1319 (w, CC(=O)–O str), 1215 (s, CC(=O)–O str), 1176 (m, CC(=O)–O str), 1127 (m, C–O–C str), 1036 (m, C–O–C str), 983 (m, C–O–C str); δ_H (250 MHz, $CDCl_3$) 7.06 (4H, d, *J*=8.5 Hz, 4×*o*-ArH), 6.97 (4H, d, *J*=8.5 Hz, 4×*m*-ArH), 5.55 (2H, dd, *J*=10.0, 3.0 Hz, H-2, H-2′), 5.48 (2H, s, H-1, H-1′), 5.43 (2H, br s, H-4, H-4′), 5.36 (2H, t, *J*=10.0 Hz, H-3, H-3′), 4.28 (2H, dd, *J*=12.0, 5.0 Hz, H-6, H-6′), 4.03–4.12 (4H, m, H-5, H-5′, H-6, H-6′), 3.84 (2H, s, $ArCH_2$), 2.19 (6H, s, 2×OAc), 2.05 (6H, s, 2×OAc), 2.03 (6H, s, 2×OAc), 2.02 (6H, s, 2×OAc); δ_C (62.5 MHz, $CDCl_3$) 170.9 (2×C=O), 170.3 (4×C=O), 170.1 (2×C=O), 154.6 (2×ArCOSug), 136.2 (2×Ar*C*(CH_2)*C*Ar), 130.2 (4×*o*-ArC), 116.9 (4×*m*-ArC), 96.3 (2×CH), 69.8 (2×CH), 69.4 (2×CH), 69.3 (2×CH), 66.3 (2×CH), 62.4 (2×CH_2), 40.6 (CH_2Ar), 21.3 (2×CH_3), 21.2 (2×CH_3), 21.0 (4×CH_3); *m/z* (CI) 878 (M+NH_4^+, 49%), 331 (100), 169 (86), 109 (78); Found 878.3101, $C_{41}H_{52}O_{20}N$ requires 878.3082.

4.1.7. 4,4′-Biphenol bis(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside) (10). 4,4′-Biphenol (0.2878 g, 1.55 mmol) and phenyl 2,3,4,6-tetra-*O*-acetyl-1-seleno-α-D-mannopyranoside (1.810 g, 3.71 mmol) were dissolved in anhydrous CH_2Cl_2 (40 cm^3), added to activated molecular sieves (4 Å) and stirred at 0°C for 30 min under a nitrogen atmosphere. To this solution were added *N*-iodosuccinimide (0.696 g, 3.09 mmol) and triflic acid (catalytic amount), the reaction mixture was allowed to warm to room temperature and stirred for 20 min. TLC analysis of the reaction was performed, using ethyl acetate/hexane (1:1, v/v) as the solvent system, and showed that the reaction had gone to completion (starting material R_f 0.61, product R_f 0.35). The reaction mixture was diluted with CH_2Cl_2 (40 cm^3) and filtered through a pad of Celite® with the aid of CH_2Cl_2 (20 cm^3). The filtrate was then washed with an aqueous 10% sodium thiosulfate solution (2×40 cm^3) to quench any unreacted *N*-iodosuccinimide. The combined organic layers were then washed with a saturated aqueous sodium bicarbonate solution (2×40 cm^3) and then dried over magnesium sulfate, filtered and concentrated to dryness in vacuo to produce a brown oil. The resulting oil was then purified using column chromatography on silica gel (ethyl acetate/hexane (1:1, v/v)). The relevant fractions were collected, combined and reduced to dryness under reduced pressure to yield *4,4′-biphenol bis(2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside)* as two rotamer isomers, both as colourless foams (**10a**: 0.36 g, 28%, **10b**: 0.27 g, 21%). Data for **10a**: $[\alpha]_D^{20}$=+66.64 (*c* 1.44, $CHCl_3$); ν_{max} (NaCl, cm^{-1}) 3456 (s, ArCH str), 3025 (s, ArCH str), 2963 (s, ArCH str), 1741 (s, C=O str), 1607 (m, ArC=C–C–O–C str), 1495 (m, ArC=C str), 1439 (s, as CH_3), 1367 (s, s CH_3), 1239 (s, CC(=O)–O str), 1215 (s, CC(=O)–O str), 1127 (m, C–O–C str), 1037 (s, C–O–C str), 978 (m, C–O–C str); δ_H (400 MHz, $CDCl_3$) 7.41 (4H, d, *J*=8.5 Hz, 4×*o*-ArH), 7.08 (4H, d, *J*=8.5 Hz, 4×*m*-ArH), 5.55 (2H, d, *J*=1.5 Hz, H-1, H-1′), 5.45 (2H, dd, *J*=1.5, 3.5 Hz, H-2, H-2′), 5.41 (2H, dd, *J*=3.5, 10.0 Hz, H-3, H-3′), 5.24 (2H, ddd, *J*=2.0, 3.5, 10.0 Hz, H-4, H-4′, 4.25 (2H, dd, *J*=5.0, 12.0 Hz, H-6, H-6′), 4.09–4.14 (2H, m, H-5, H-5′), 4.03–4.08 (2H, m, H-6, H-6′), 2.15 (6H, s, 2×OAc), 2.09 (6H, s, 2×OAc), 2.04 (6H, s, 2×OAc), 1.99 (6H, s, 2×OAc); δ_C (100 MHz, $CDCl_3$) 170.8 (2×C=O), 170.2 (2×C=O), 170.0 (2×C=O), 169.8 (2×C=O), 154.9 (2×ArCOSug), 135.3 (2×ArCCAr), 127.9 (4×*o*-ArC), 116.8 (4×*m*-ArC), 96.2 (2×CH), 69.8 (2×CH), 69.2 (2×CH), 68.8 (2×CH), 66.5 (2×CH), 63.0 (2×CH_2), 21.3 (4×CH_3), 21.2 (2×CH_3), 21.1 (2×CH_3); *m/z* (CI) 864 (M+NH_4^+, 21%), 331 (100), 169 (47), 109 (28); Found 864.2941, $C_{40}H_{50}O_{20}N$ requires 864.2926.

Data for **10b**. $[\alpha]_D^{20}$=+65.82 (*c* 1.32, $CHCl_3$); ν_{max} (NaCl, cm^{-1}) 3475 (s, ArCH str), 3025 (m, ArCH str), 2956 (m, ArCH str), 1741 (s, C=O str), 1645 (w, ArC=C–C–O–C str), 1604 (w, ArC=C–C–O–C str), 1495 (m, ArC=C str), 1432 (m, as CH_3), 1370 (s, s CH_3), 1224 (s, CC(=O)–O str), 1124 (m, C–O–C str), 1074 (m, C–O–C str), 1043 (s, C–O–C str), 978 (m, C–O–C str); δ_H (400 MHz, $CDCl_3$) 7.41 (4H, dd, *J*=8.5, 19.0 Hz, 4×*o*-ArH), 6.91 (4H, dd, *J*=8.5, 84.5 Hz, 4×*m*-ArH), 5.60 (2H, dd, *J*=3.5, 10.0 Hz, H-3, H-3′), 5.56 (2H, d, *J*=2.0 Hz, H-1, H-1′), 5.48 (2H, dd, *J*=2.0, 3.5 Hz, H-2, H-2′), 5.36–5.42 (2H, m, H-4, H-4′), 4.30 (2H, dd, *J*=5.0, 12.5 Hz, H-6, H-6′), 4.10–4.16 (4H, m, H-5, H-5′, H-6, H-6′), 2.22 (6H, s, 2×OAc), 2.08 (6H, s, 2×OAc), 2.04 (6H, s, 2×OAc); δ_C (100 MHz, $CDCl_3$) 171.2 (2×C=O), 170.6 (4×C=O), 170.3 (2×C=O), 128.4 (ArCOSug), 128.2 (ArCOSug), 117.1 (ArCCAr), 116.1 (ArCCAr), 96.2 (2×CH), 69.9 (2×CH), 69.5 (2×CH), 69.4 (2×CH), 66.4 (2×CH), 62.5 (2×CH_2), 21.3 (4×CH_3), 21.1 (4×CH_3); *m/z* (CI) 864 (M+NH_4^+, 22%), 534 (49), 331 (52), 186 (100); Found 864.2941, $C_{40}H_{50}O_{20}N$ requires 864.2926.

4.1.8. 1,3-Bis[*S*-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl]propane-1,3-dithiol (11). 1,2,3,4,6-Penta-*O*-acetyl-α-D-mannopyranoside (5.790 g, 14.83 mmol) was dissolved in distilled CH_2Cl_2 (40 cm^3) and 1,3-propanedithiol (0.74 cm^3, 7.42 mmol) was added followed by boron trifluoride etherate (1.88 cm^3, 14.83 mmol). The reaction was stirred at room temperature under an argon atmosphere. The reaction was followed by TLC analysis, using diethyl ether/ethyl acetate (1:1, v/v) as the solvent system. After 24 h saturated sodium bicarbonate solution was added (40 cm^3) and the organic layer extracted with CH_2Cl_2 (3×30 cm^3).

The combined organic layers were dried over magnesium sulfate, filtered and concentrated to dryness under reduced pressure. The resulting yellow oil was purified using column chromatography on silica gel eluting with diethyl ether/ethyl acetate (1:1, v/v). The relevant fractions were collected and combined to give *1,3-bis[S-2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl]propane-1,3-dithiol* (**11**) as a colourless solid (3.57 g, 63%). Mp 77.8–79.5°C; $[\alpha]_D^{20}$=+78.06 (*c* 1.47, $CHCl_3$); ν_{max} (NaCl, cm^{-1}) 1742 (s, C=O str), 1432 (w, as CH_3), 1368 (m, s CH_3), 1225 (s, CC(=O)–O str), 1136 (w, C–C–O str), 1048 (s, C–O–C str), 976 (w, C–O–C str); δ_H (250 MHz, $CDCl_3$) 5.23–5.30 (2H, m, 2×H-3, 2×H-4), 5.17–5.21 (2H, m, 2×H-1, 2×H-2), 4.25–4.32 (2H, m, 2×H-5, 2×H-6), 4.18–4.423 (1H, m, 2×H-6′), 2.65–2.78 (4H, m, H_a), 1.89–1.99 (2H, m, $SCH_2CH_2CH_2S$), 2.09 (6H, s, 2×OAc), 2.03 (6H, s, 2×OAc), 1.98 (6H, s, 2×OAc), 1.91 (6H, s, 2×OAc); δ_C (62.5 MHz, $CDCl_3$) 170.4 (2×C=O), 170.0 (2×C=O), 169.8 (2×C=O), 169.6 (2×C=O), 82.4 (2×CH), 70.4 (2×CH), 69.3 (2×CH), 69.1 (2×CH), 66.2 (2×CH), 62.3 (2×CH_2), 29.8 (2×CH_2S), 28.6 ($SCH_2CH_2CH_2S$), 20.7 (2×CH_3), 20.6 (4×CH_3), 20.5 (2×CH_3); *m/z* (CI) 786 ($M+NH_4^+$, 30%), 331 (100), 213 (40), 169 (36); Found 786.2333, $C_{31}H_{48}O_{18}NS_2$ requires 786.2313.

4.1.9. 1,2-Bis[*O*-α-D-mannopyranosyl]ethane-1,2-diol (12). A flask was charged with *1,2-bis[O-2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl]ethane-1,2-diol* (**1**) (0.367 g, 0.51 mmol) dissolved in anhydrous methanol (15 cm^3). To this solution a catalytic amount of anhydrous potassium carbonate (0.007 g, 0.05 mmol) was added and the reaction mixture was stirred at room temperature under a nitrogen atmosphere. TLC analysis using ethyl acetate/hexane (1:1, v/v), showed that after 3 h the reaction had gone to completion (starting material R_f 0.36, product R_f 0.00). Amberlite IR-120 (PLUS) ion-exchange resin was washed with methanol and then added to and stirred with the reaction mixture for 30 min. The resin was then filtered off under gravity and the resulting solution concentrated to dryness in vacuo to yield *1,2-bis[O-α-D-mannopyranosyl]-ethane-1,2-diol* (12) as a colourless oil (0.18 g, 94%) which was purified on a G-15 Sephadex size exclusion column. $[\alpha]_D^{25}$=+18.95 (*c* 0.01, H_2O); ν_{max} (NaCl, cm^{-1}) 3362 (s, O–H str), 2926 (m, O–H str), 1454 (w, as CH_3), 1373 (m, s CH_3), 1132 (m, C–O–C str), 1094 (m, C–O–C str), 1054 (s, C–O–C str), 1033 (s, C–O–C str); δ_H (400 MHz, D_2O) 4.51 (2H, d, *J*=1.5 Hz, H-1, H-1′), 3.57–3.98 (10H, m, H-5, H-5′, 2×H-6, 2×H-6′, 2×CH_2O), 3.37–3.50 (4H, m, H-3, H-3′, H-4, H-4′), 3.30 (2H, t, *J*=1.5 Hz, H-2, H-2′); δ_C (100 MHz, D_2O) 84.6 (2×CH), 72.2 (2×CH), 70.0 (2×CH), 69.5 (2×CH), 68.0 (2×CH_2), 66.2 (2×CH), 60.0 (2×CH_2O).

4.1.10. 1,4-Bis[*O*-α-D-mannopyranosyl]butane-1,4-diol (13). A flask was charged with *1,4-bis[O-2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl]butane-1,4-diol* (**7**) (0.147 g, 0.20 mmol) dissolved in anhydrous methanol (15 cm^3). To this solution a catalytic amount of anhydrous potassium carbonate (0.002 g, 0.02 mmol) was added and the reaction mixture was stirred at room temperature under a nitrogen atmosphere. TLC analysis using ethyl acetate/hexane (1:1, v/v), showed that after 3 h the reaction had gone to completion (starting material R_f 0.36, product R_f 0.00). Amberlite IR-120 (PLUS) ion-exchange resin was washed with methanol and then added to and stirred with the reaction mixture for 30 min. The resin was then filtered off under gravity and the resulting solution concentrated to dryness in vacuo to yield *1,2-bis[O-α-D-mannopyranosyl]-ethane-1,2-diol* (**13**) as a colourless oil (0.07 g, 86%) which was purified on a G-15 Sephadex size exclusion column. $[\alpha]_D^{20}$=+27.08 (*c* 0.07, H_2O), (lit.[18] $[\alpha]_D^{22}$=+76.00 (*c* 1.00, H_2O); ν_{max} (NaCl, cm^{-1}) 3328 (s, O–H str), 2954 (m, O–H str), 1134 (m, C–O–C str), 1107 (m, C–O–C str), 1056 (s, C–O–C str); δ_H (400 MHz, D_2O) 4.82 (2H, d, *J*=1.5 Hz, H-1, H-1′), 3.89 (2H, dd, *J*=1.5, 3.5 Hz, H-2, H-2′), 3.84 (2H, dd, *J*=1.5, 12.0 Hz, H-6, H-6′), 3.68–3.77 (6H, m, H-3, H-3′, H-6, H-6′, H_a, $H_{a'}$), 3.57–3.61 (4H, m, H-4, H-4′, H-5, H-5′), 3.49–3.55 (2H, m, H_a, $H_{a'}$), 1.53–1.65 (4H, m, 2×H_b, 2×$H_{b'}$); δ_C (100 MHz, D_2O) 100.0 (2×CH), 73.1 (2×CH), 70.9 (2×CH), 70.4 (2×CH), 67.9 (2×CH_2O), 67.1 (2×CH), 61.2 (2×CH_2), 28.5 (OCH_2CH_2), 25.4 (OCH_2CH_2).

4.1.11. Bis(4-hydroxyphenyl)methane bis(α-D-mannopyranoside) (14). A flask was charged with *bis(4-hydroxyphenyl)methane bis(2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside)* (**9**) (0.50 g, 0.58 mmol) dissolved in anhydrous methanol (20 cm^3). To this solution a catalytic amount of anhydrous potassium carbonate (0.006 g, 0.06 mmol) was added and the reaction mixture was stirred at room temperature under a nitrogen atmosphere. TLC analysis using ethyl acetate/hexane (1:1, v/v), showed that after 4 h the reaction had gone to completion (starting material R_f 0.32, product R_f 0.00). Amberlite IR-120 (PLUS) ion-exchange resin was washed with methanol and then added to and stirred with the reaction mixture for 30 min. The resin was then filtered off under gravity and the resulting solution concentrated to dryness in vacuo to yield *bis(4-hydroxyphenyl)methane bis(α-D-mannopyranoside)* (**14**) as a colourless foam (0.25 g, 83%) which was not purified further. ν_{max} (KBr, cm^{-1}) 3256 (s, ArCH str), 2920 (m, ArCH str), 2835 (m, O–H str), 1545 (m, ArC=C–O–C str), 1056 (s, C–O–C str), 1022 (s, C–O–C str), 970 (s, C–O–C str); δ_H (400 MHz, D_2O) 7.18 (4H, d, *J*=8.5 Hz, 4×*o*-ArH), 7.08 (4H, d, *J*=8.5 Hz, 4×*m*-ArH), 5.52 (2H, s, H-1, H-1′), 4.08 (2H, br s, H-2, H-2′), 3.89 (2H, dd, *J*=5.0, 12.0 Hz, H-6, H-6′), 3.67–3.85 (6H, m, H-3, H-3′, H-4, H-4′, H-6, H-6′), 3.58–3.65 (2H, m, H-5, H-5′), 2.71–2.76 (2H, m, $ArCH_2Ar$); δ_C (100 MHz, D_2O) 154.5 (2×ArCOSug), 135.0 (2×Ar*C*(CH_2)*C*Ar), 129.7 (4×*o*-ArCH), 116.8 (4×*m*-ArCH), 99.8 (2×CH), 74.2 (2×CH), 72.2 (2×CH), 71.2 (2×CH), 66.8 (2×CH), 60.5 (2×CH_2), 38.7 (Ar*C*H_2Ar).

4.1.12. 1,3-Bis[*S*-α-D-mannopyranosyl]propane-1,3-dithiol (15). A flask was charged with *1,3-bis[S-2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl]propane-1,3-dithiol* (**11**) (0.411 g, 0.53 mmol) dissolved in anhydrous methanol (15 cm^3). To this solution a catalytic amount of anhydrous potassium carbonate (0.007 g, 0.05 mmol) was added and the reaction mixture was stirred at room temperature under a nitrogen atmosphere. TLC analysis using ethyl acetate/hexane (1:1, v/v), showed that after 3 h the reaction had gone to completion (starting material R_f 0.41, product R_f 0.00). Amberlite IR-120 (PLUS) ion-exchange resin was washed with methanol and then added to and stirred with the reaction mixture for 30 min. The resin was then filtered off

under gravity and the resulting solution concentrated to dryness in vacuo to yield *1,3-bis[S-α-D-mannopyranosyl]-propane-1,3-dithiol* (**15**) as a colourless oil (0.21 g, 89%) which was purified on a G-15 Sephadex size exclusion column. $[\alpha]_D^{20}=+38.25$ (*c* 1.47, H_2O); ν_{max} (NaCl, cm^{-1}) 3334 (s, O–H str), 2928 (m, O–H str), 1137 (m, C–O–C str), 1093 (m, C–O–C str), 1052 (s, C–O–C str); δ_H (400 MHz, D_2O) 4.97 (2H, d, *J*=1.0 Hz, H-1, H-1′), 3.72 (2H, dd, *J*=1.5, 3.0 Hz, H-2, H-2′), 3.63–3.67 (2H, m, H-5, H-5′), 3.54 (2H, dd, *J*=2.5 Hz, 12.5 Hz, H-6, H-6′), 3.43–3.49 (4H, m, H-4, H-4′, H-6, H-6′), 3.34 (2H, t, *J*=10.0 Hz, H-3, H-3′), 2.38–2.54 (4H, m, SCH_2), 1.65 (2H, q, *J*=7.0 Hz, $SCH_2CH_2CH_2S$); δ_C (100 MHz, D_2O) 85.1 (2×CH), 73.5 (2×CH), 72.6 (2×CH), 72.1 (2×CH), 71.4 (2×CH), 67.3 (2×CH), 61.1 (2×CH_2), 29.9 (2×SCH_2), 28.8 ($SCH_2CH_2CH_2S$).

4.1.13. *N,N′*-Di-α-D-mannopyranosyl ethylenediamine (16). Ethylenediamine (0.39 cm^3, 6.48 mmol), was dissolved in anhydrous methanol (7 cm^3) and the mixture heated to 50°C. To this was added D-(+)-mannose (2.10 g, 11.66 mmol) and the resulting solution stirred under a nitrogen atmosphere at 50°C. After 5 min the D-(+)-mannose dissolved and after 1 h a colourless solid precipitated from the solution. Another aliquot of anhydrous methanol (7 cm^3) was added in order to ensure complete dissolution of the reaction mixture. After 3 h a colourless precipitate had formed in the reaction mixture. The reaction mixture was stored for 24 h at 4°C, and then the precipitate was filtered off, washed with ice-cold methanol and then dried in vacuo (using a drying piston) for 48 h at 40°C. This yielded *N,N′-di-α-D-mannopyranosyl ethylenediamine* (**16**) as a colourless powder (1.77 g, 77%). Mp 152.8–153.4°C; $[\alpha]_D^{20}=-10.74$ (*c* 3.55, H_2O); ν_{max} (KBr, cm^{-1}) 3510 (s, as N–H str), 3311 (s, s N–H str), 2931 (s, O–H str), 2885 (s, O–H str), 2841 (s, O–H str), 1618 (m, N–H bend), 1136 (s, C–O–C str), 995 (s, C–O–C str), 696 (s, N–H wagging); δ_H (400 MHz, D_2O) 4.03 (2H, s, H-1, H-1′), 3.71 (2H, dd, *J*=2.5, 12.0 Hz, H-6, H-6′), 3.68 (2H, d, *J*=3.5 Hz, H-2, H-2′), 3.49 (2H, dd, *J*=6.5, 12.0 Hz, H-6, H-6′), 3.42 (2H, dd, *J*=3.5, 9.5 Hz, H-3, H-3′), 3.32 (2H, t, *J*=9.5 Hz, H-4, H-4′), 3.10–3.14 (2H, m, H-5, H-5′), 2.61–2.81 (4H, m, 2×H_a, 2×H_b); δ_C (100 MHz, D_2O) 89.5 (2×CH), 80.0 (2×CH), 76.6 (2×CH), 73.6 (2×CH), 69.9 (2×CH), 64.0 (2×CH_2), 47.1 (2×CH_2); $^1J[^{13}CH(1)]=166$ Hz; *m/z* (FAB) 385 ($M+H^+$, 22%); Found 385.1832, $C_{14}H_{29}O_{10}N_2$ requires 385.1822.

4.1.14. *N,N′*-Di-α-D-mannopyranosyl 1,2-propanediamine (17). 1,2-Propanediamine (0.54 cm^3, 6.48 mmol), was dissolved in anhydrous methanol (10 cm^3) and the mixture stirred at room temperature. To this was added D-(+)-mannose (2.10 g, 11.66 mmol) and the resulting solution stirred under a nitrogen atmosphere. After 5 min the D-(+)-mannose dissolved and after 4.5 h a colourless solid precipitated from the solution. After 7 h a colourless precipitate had formed in the reaction mixture. The reaction mixture was stored for 24 h at 4°C, and then the precipitate was filtered off, washed with ice-cold methanol and then dried in vacuo (using a drying piston) for 48 h at 40 °C. This yielded *N,N′-di-α-D-mannopyranosyl 1,2-propanediamine* (**17**) as a colourless powder (1.66 g, 64%). Mp 138.1–139.3°C; $[\alpha]_D^{20}=-21.06$ (*c* 0.93, H_2O); ν_{max} (KBr, cm^{-1}) 3331 (s, s N–H str), 2952 (s, O–H str), 2921 (s, O–H str), 2895 (s, O–H str), 1664 (m, N–H bend), 1466 (s, as CH_3), 1248 (s, s CH_3), 1162 (s, C–O–C str), 967 (s, C–O–C str), 700 (m, N–H wagging); δ_H (400 MHz, D_2O) 4.09 (1H, s, H-1), 4.00 (1H, s, H-1′), 3.61–3.69 (4H, m, H-2, H-2′, H-6, H-6′), 3.46 (2H, dd, *J*=6.5, 11.5 Hz, H-6, H-6′), 3.38 (2H, dd, *J*=3.5, 10.0 Hz, H-3, H-3′), 3.29 (2H, t, *J*=10.0 Hz, H-4, H-4′), 3.07–3.10 (2H, m, H-5, H-5′), 2.78 (1H, q, *J*=4.5, 12.5 Hz, H_b or C*H*MeN), 2.60 (1H, dd, *J*=4.5, 12.5 Hz, H_a or CH_2N), 2.49 (1H, dd, *J*=9.0, 12.5 Hz, H_a or CH_2N), 0.81 (3H, dd, *J*=6.5, 9.0 Hz, CH_3); δ_C (100 MHz, D_2O) 89.3 (CH), 86.6 (CH), 79.9 (2×CH), 76.6 (2×CH), 74.0 (2×CH), 69.9 (2×CH), 63.9 (2×CH_2), 55.2 (CH_2N), 48.8 (*C*HMeN), 20.4 (CH_3); $^1J[^{13}CH(1)]=165$ Hz; *m/z* (ES^+) 399 ($M+H^+$, 100%); Found 399.1970, $C_{15}H_{31}O_{10}N_2$ requires 399.1980.

4.1.15. *N,N′*-Di-α-D-mannopyranosyl 1,3-propanediamine (18). 1,3-Propanediamine (0.57 cm^3, 6.48 mmol), was dissolved in anhydrous methanol (10 cm^3) and the mixture stirred at room temperature. To this was added D-(+)-mannose (2.10 g, 11.66 mmol) and the resulting solution stirred under a nitrogen atmosphere. After 5 min the D-(+)-mannose dissolved and after 4 h a colourless solid precipitated from the solution. After 6 h a colourless precipitate had formed in the reaction mixture. The reaction mixture was stored for 24 h at 4°C, and then the precipitate was filtered off, washed with ice-cold methanol and then dried in vacuo (using a drying piston) for 48 h at 40 °C. This yielded *N,N′-di-α-D-mannopyranosyl 1,3-propanediamine* (**18**) as a colourless powder (1.76 g, 68%). Mp 134.7–135.6°C; $[\alpha]_D^{20}=-29.39$ (*c* 0.40, H_2O); ν_{max} (KBr, cm^{-1}) 3374 (s, s N–H str), 2929 (s, O–H str), 1654 (w, N–H bend), 697 (m, N–H wagging); δ_H (400 MHz, D_2O) 3.87 (2H, s, H-1, H-1′), 3.56 (2H, dd, *J*=2.0, 12.0 Hz, H-6, H-6′), 3.49–3.52 (2H, m, H-2, H-2′), 3.33–3.42 (2H, m, H-6, H-6′), 3.28 (2H, dd, *J*=3.5, 10.0 Hz, H-3, H-3′), 3.18 (2H, t, *J*=10.0 Hz, H-4, H-4′), 2.97–2.99 (2H, m, H-5, H-5′), 2.77–2.81 (2H, m, 2×H_a or CH_2N), 2.39–2.47 (2H, m, 2×H_a or CH_2N), 1.15–1.19 (2H, m, 2×H_b or $NCH_2CH_2CH_2N$); δ_C (100 MHz, D_2O) 89.2 (2×CH), 79.9 (2×CH), 76.6 (2×CH), 73.8 (2×CH), 69.9 (2×CH), 63.9 (2×CH_2), 46.9 (2×CH_2N), 28.5 ($NCH_2CH_2CH_2N$); $^1J[^{13}CH(1)]=166$ Hz; *m/z* (ES^+) 399 ($M+H^+$, 100%); Found 399.1971, $C_{15}H_{31}O_{10}N_2$ requires 399.1980; Found: C, 43.58; H, 7.69; N, 6.46. Calc. for $C_{15}H_{30}O_{10}N_2$ (M_r 398.19): C, 43.27; H, 7.70; N, 6.73%.

4.1.16. *N,N′*-Di-α-D-mannopyranosyl 1,4-butanediamine (19). 1,4-Butanediamine (0.65 cm^3, 6.48 mmol), was dissolved in anhydrous methanol (20 cm^3) and the mixture stirred at room temperature. To this was added D-(+)-mannose (2.10 g, 11.66 mmol) and the resulting solution stirred under a nitrogen atmosphere. After 30 min the D-(+)-mannose dissolved e and after 5 h a colourless solid precipitated from the solution. After 8 h a colourless precipitate had formed in the reaction mixture. The reaction mixture was stored for 24 h at 4°C, and then the precipitate was filtered off, washed with ice-cold methanol and then dried in vacuo (using a drying piston) for 48 h at 40°C. This yielded *N,N′-di-α-D-mannopyranosyl 1,4-butanediamine* (**19**) as an off-white powder (1.30 g, 53%). Mp 125.7–127.2°C; $[\alpha]_D^{20}=-29.97$ (*c* 1.00, H_2O); ν_{max} (KBr, cm^{-1}) 3303 (s, s N–H str), 2918 (m, O–H str), 2864 (m, O–H str), 1650 (w, N–H bend), 687 (m, N–H wagging); δ_H (400 MHz, D_2O) 4.24 (2H, s, H-1, H-1′), 3.94 (2H, dd,

J=2.0, 12.0 Hz, H-6, H-6′), 3.89 (2H, d, J=3.0 Hz, H-2, H-2′), 3.73 (2H, dd, J=6.5, 12.0 Hz, H-6, H-6′), 3.66 (2H, dd, J=3.0, 10.0 Hz, H-3, H-3′), 3.55 (2H, t, J=10.0 Hz, H-4, H-4′), 3.34–3.38 (2H, m, H-5, H-5′), 2.95–2.97 (2H, m, CH_2N or H_a), 2.68–2.71 (2H, m, CH_2N or H_a), 1.54–1.55 (4H, m, 2×CH_2CH$_2$N or NCH$_2$CH_2CH_2CH$_2$N or 4×H_b); δ_C (100 MHz, D_2O) 89.3 (2×CH), 80.0 (2×CH), 76.6 (2×CH), 73.7 (2×CH), 69.7 (2×CH), 63.9 (2×CH$_2$), 47.2 (2×*C*H$_2$N), 29.3 (2×*C*H$_2$CH$_2$N); ^{1}J[^{13}CH(1)]=165 Hz; *m/z* (FAB) 413 (M+H$^+$, 87%); Found 413.2134, $C_{16}H_{33}O_{10}N_2$ requires 413.2135; Found: C, 46.56; H, 7.98; N, 6.55. Calc. for $C_{16}H_{32}O_{10}N_2$ (M_r 412.21): C, 46.60; H, 7.82; N, 6.79%.

4.1.17. Tris{*N,N*-α-D-mannopyranosyl-2-aminoethyl}-amine (20). Tris(2-aminoethyl)amine (2.69 cm^3, 17.97 mmol), was dissolved in anhydrous methanol (20 cm^3) and the mixture stirred at room temperature. To this was added D-(+)-mannose (2.160 g, 11.99 mmol) and the resulting solution stirred under a nitrogen atmosphere. After 30 min the D-(+)-mannose dissolved and after 16 h the reaction mixture was stored for 24 h at 4°C, the reaction mixture was concentrated in vacuo to dryness, and then the resulting oil was dried in vacuo (using a drying piston) for 48 h at 40°C. This yielded *tris{N,N-α-D-mannopyranosyl-2-aminoethyl}amine* (**20**) as a yellow oil (6.37 g, 56%). $[\alpha]_D^{20}$=−21.88 (*c* 0.16, H_2O); ν_{max} (KBr, cm^{-1}) 3248 (m, s N–H str), 3034 (m, O–H str), 2951 (w, O–H str), 1661 (w, N–H bend), 695 (s, N–H wagging); δ_H (400 MHz, D_2O) 3.96 (3H, s, H-1, H-1′, H-1″), 3.66 (3H, d, J=12.0 Hz, H-6, H-6′, H-6″), 3.60 (3H, d, J=3.0 Hz, H-2, H-2′, H-2″), 3.44 (3H, dd, J=3.0, 10.0 Hz, H-3, H-3′, H-3″), 3.26 (3H, t, J=10.0 Hz, H-4, H-4′, H-4″), 3.04–3.09 (3H, m, H-5, H-5′, H-5″), 2.46 (6H, t, J=6.5 Hz, 3×CH$_2$N), 2.30 (6H, t, J=6.5 Hz, N(CH_2)$_3$); δ_C (100 MHz, D_2O) 88.1 (CH), 78.9 (CH), 75.4 (CH), 72.6 (CH), 68.7 (CH), 62.7 (CH), 57.7 (3×*C*H$_2$N), 39.3 (N(*C*H$_2$)$_3$).

4.1.18. Pentaerythrityl tetra{*N,N*-α-D-manno-pyranosyl}amine (21). Pentaerythrityl tetraamine (**29**) (0.087 g, 0.66 mmol), was dissolved in anhydrous methanol (10 cm^3) and the mixture stirred at room temperature. To this was added D-(+)-mannose (0.472 g, 2.62 mmol) and the resulting solution stirred under a nitrogen atmosphere. After 30 min the D-(+)-mannose dissolved and after 3.5 h a colourless solid precipitated from the solution. After 6 h a colourless precipitate had formed in the reaction mixture. The reaction mixture was stored for 24 h at 4°C, and then the precipitate was filtered off, washed with ice-cold methanol and then dried in vacuo (using a drying piston) for 48 h at 40°C. This yielded *pentaerythrityl tetra{N,N-α-D-manno-pyranosyl}amine* (**21**) as a colourless solid (0.24 g, 47%). Mp 60.3–61.8°C; ν_{max} (KBr, cm^{-1}) 3254 (m, s N–H str), 2934 (w, O–H str), 2851 (w, O–H str), 1665 (w, N–H bend), 702 (s, N–H wagging); δ_H (400 MHz, D_2O) 3.59–3.76 (8H, m, H-1, H-1′, H-1″, H-1‴, H-2, H-2′, H-2″, H-2‴), 3.44–3.56 (20H, m, H-3, H-3′, H-3″, H-3‴, H-4, H-4′, H-4″, H-4‴, H-5, H-5′, H-5″, H-5‴, 2×(H-6, H-6′, H-6″, H-6‴)), 2.37–2.55 (8H, m, 4×CH$_2$); δ_C (100 MHz, D_2O) 71.4 (4×CH), 71.0 (4×CH), 69.9 (4×CH), 69.5 (4×CH), 69.2 (4×CH), 63.6 (4×CH$_2$), 51.9 (C*C*H$_2$), 51.8 (C*C*H$_2$), 49.2 (*C*(CH$_2$)$_4$), 47.4 (2×C*C*H$_2$).

4.1.19. Mannopyranoside based hexavalent glyco-dendrimer (22). The hexafunctional dendrimer core[14] (0.071 g, 47.6 μmol) was dissolved in anhydrous methanol (10 cm^3) and the mixture stirred at room temperature. To this was added freshly distilled triethylamine (0.08 cm^3, 0.57 mmol) and the resulting solution stirred under a nitrogen atmosphere for 30 min. D-(+)-Mannose (0.103 g, 0.57 mmol) was added to the reaction mixture. After 30 min the D-(+)-mannose dissolved and after 8 h a colourless solid precipitated from the solution. After 16 h a white precipitate had formed in the reaction mixture. The reaction mixture was stored for 24 h at 4°C, and then the precipitate was filtered off, washed with ice-cold methanol and then dried in vacuo (using a drying piston) for 48 h at 40°C. This yielded the desired mannose-based dendrimer (**22**) as an off-white powder (0.05 g, 56%). Mp 179.0–181.1°C; $[\alpha]_D^{20}$=−50.00 (*c* 0.01, H_2O); ν_{max} (KBr, cm^{-1}) 3323 (s, s N–H str), 3238 (s, ArCH str), 2955 (m, ArCH str), 2854 (m, O–H str), 1650 (m, N–H bend), 1640 (s, C=O str), 1558 (m, N–H bend and C–N str), 1543 (m, ArC=C–O–C str), 1199 (w, N–H bend, C–N str), 1054 (s, C–O–C str), 1023 (s, C–O–C str), 970 (s, C–O–C str), 798 (s, N–H wagging); δ_H (400 MHz, D_2O) 7.48–7.65 (12H, m, ArCH), 5.27 (3H, s, C*H*(CH$_2$)$_2$), 4.03 (6H, dd, J=1.5, 3.5 Hz, 6×H-2), 3.98 (6H, d, J=1.5 Hz, 6×H-1,), 3.94 (6H, dd, J=3.5, 10.0 Hz, 6×H-3), 3.73–3.92 (18H, m, 3×CH(CH_2NH)$_2$,6×H-6), 3.83 (6H, dd, J=6.0, 11.5 Hz, 6×H-6), 3.67 (6H, t, J=10.0 Hz, 6×H-4), 3.56–3.61 (6H, m, C(O)NHCH_2), 3.45–3.50 (6H, m, 6×H-5), 2.84–2.93 (6H, m, C(O)NHCH$_2$CH_2N); δ_C (100 MHz, D_2O) 169.6 (3×C=O), 169.3 (3×C=O), 136.4 (3×ArC), 136.2 (3×ArC), 127.5 (12×ArCH), 94.3 (3×*C*H(CH$_2$NH)$_2$), 77.5 (6×CH), 73.3 (6×CH), 71.5 (6×CH), 71.0 (6×CH), 67.1 (3×(CH(*C*H$_2$NH)$_2$), 66.9 (6×CH), 61.3 (6×CH$_2$), 54.2 (3×C(O)NH*C*H$_2$), 38.0 (3×C(O)NHCH$_2$*C*H$_2$N).

4.1.20. 1,2-Bis[*O*-α-D-mannopyranosyl] ethane-1-hydroxy-2′-amine (23). 2′-Aminoethyl-*O*-α-D-manno-pyranoside (**31**) (0.17 g, 0.81 mmol), was dissolved in anhydrous methanol (10 cm^3) and the mixture stirred at room temperature. To this was added D-(+)-mannose (0.29 g, 1.62 mmol) and the resulting solution stirred under a nitrogen atmosphere. After 30 min the D-(+)-mannose dissolved and after 4 h the reaction mixture was stored for 24 h at 4°C, the reaction mixture was concentrated in vacuo to dryness, and then the resulting foam was dried in vacuo (using a drying piston) for 48 h at 40°C. This yielded *1,2-bis[O-α-D-mannopyranosyl] ethane-1-hydroxy-2′-amine* (**23**) as a colourless foam (0.13 g, 43%). $[\alpha]_D^{20}$=+35.95 (*c* 0.19, H_2O); ν_{max} (KBr, cm^{-1}) 3328 (s, s N–H str), 3258 (s, O–H str), 2928 (s, O–H str), 1657 (m, N–H bend), 702 (m, N–H wagging); δ_H (400 MHz, D_2O) 4.94 (1H, s, H-1), 4.04 (1H, d, J=1.5 Hz, H-2′), 3.80–3.98 (7H, m, H-1′, H-2, H-3′, CH$_2$O, H-4′, H-5, H-6′), 3.61–3.73 (7H, m, H-3, CH$_2$O, H-4, H-5′, H-6′, 2×H-6), 2.90–3.01 (2H, m, CH$_2$N); δ_C (100 MHz, D_2O) 100.2 (CH), 74.2 (CH), 73.1 (CH), 71.4 (CH), 70.9 (CH), 70.8 (CH), 70.3 (CH), 68.0 (CH$_2$O), 67.5 (CH), 67.4 (CH), 67.1 (CH), 61.3 (2×CH$_2$), 47.6 (CH$_2$N); Found: C, 40.08; H, 7.51; N, 3.30. Calc. for $C_{14}H_{27}O_{11}N.2\,H_2O$ (M_r 421.18): C, 39.90; H, 7.41; N, 3.32%; *m/z* (ES$^+$) 386.2 (M+H$^+$, 100%).

4.1.21. 1,3-Bis[*O*-α-D-mannopyranosyl] propane-1-hydroxy-3′-amine (24). 3′-Aminopropyl-*O*-α-D-manno-pyranoside (**32**) (0.42 g, 1.77 mmol), was dissolved in

anhydrous methanol (20 cm^3) and the mixture stirred at room temperature. To this was added D-(+)-mannose (0.64 g, 3.54 mmol) and the resulting solution stirred under a nitrogen atmosphere. After 30 min the D-(+)-mannose dissolved and after 4 h the reaction mixture was stored for 24 h at 4°C, the reaction mixture was then concentrated in vacuo to dryness, and then the resulting foam was dried in vacuo (using a drying piston) for 48 h at 40°C. This yielded *1,3-bis[O-α-D-mannopyranosyl] propane-1-hydroxy-3′-amine* (**24**) as a colourless foam (0.27 g, 38%). $[\alpha]_D^{20}$=+6.53 (*c* 0.38, H_2O); ν_{max} (KBr, cm^{-1}) 3320 (s, s N–H str), 3264 (s, O–H str), 2954 (s, O–H str), 1653 (m, N–H bend), 699 (m, N–H wagging); δ_H (400 MHz, D_2O) 4.93 (1H, s, H-1), 3.49–3.95 (11H, m, H-2, H-3, H-4, H-5, 2×H-6, H-1′, H-2′, H-3′, H-4′, CH_2O), 3.26–3.43 (4H, m, H-5′, 2×H-6′, CH_2O), 2.50–2.60 (2H, m, CH_2N), 1.58–1.62 (2H, m, $OCH_2CH_2CH_2N$); δ_C (100 MHz, D_2O) 94.3 (CH), 94.0 (CH), 76.4 (CH), 73.3 (CH), 72.6 (CH), 71.5 (CH), 71.0 (CH), 70.5 (CH), 67.1 (CH), 66.9 (CH), 65.8 (CH_2O), 61.3 (2×CH_2), 46.0 (CH_2N), 27.7 ($OCH_2CH_2CH_2N$); *m/z* (ES^+) 400.2 ($M+H^+$, 20%).

4.1.22. *N,N′*-Di-[3-*O*-α-D-mannopyranosyl-D-mannose] ethylenediamine (25). Ethylenediamine (0.02 cm^3, 0.32 mmol), was dissolved in anhydrous methanol (10 cm^3) and the mixture stirred at room temperature. To this was added 3-*O*-α-D-mannopyranosyl-D-mannose (0.198 g, 0.52 mmol) and the resulting solution stirred under a nitrogen atmosphere. After 5 min the 3-*O*-α-D-mannopyranosyl-D-mannose dissolved and after 3 h a colourless solid precipitated from the solution. After 8 h a colourless precipitate had formed in the reaction mixture. The reaction mixture was stored for 24 h at 4°C, and then the precipitate was filtered off, washed with ice-cold methanol and then dried in vacuo (using a drying piston) for 48 h at 40°C. This yielded *N,N′-di-[3-O-α-D-mannopyranosyl-D-mannose]ethylenediamine* (**25**) as a colourless powder (0.09 g, 43%). $[\alpha]_D^{20}$=+16.78 (*c* 0.10, H_2O), m.p. 99.0–101.1 °C; ν_{max} (KBr, cm^{-1}) 3318 (s, s N–H str), 3198 (s, O–H str), 2918 (s, O–H str), 1655 (m, N–H bend), 698 (m, N–H wagging); δ_H (400 MHz, D_2O) 4.95 (2H, 2×H-1), 4.03–4.06 (2H, m, 2×H-1′), 3.83–3.89 (4H, m, 2×H-2, 2×H-2′), 3.65–3.73 (6H, m, 2×H-3, 2×H-4′, 2×H-6), 3.55–3.61 (6H, m, 2×H-3′, 2×H-4, 2×H-6′), 3.34–3.50 (4H, m, 2×H-5, 2×H-5′), 2.47–2.90 (4H, m, 2×NCH_2); δ_C (100 MHz, D_2O) 102.5 (2×CH), 87.3 (2×CH), 81.5 (2×CH), 77.4 (2×CH), 73.6 (2×CH), 71.1 (2×CH), 70.7 (2×CH), 70.3 (2×CH), 67.0 (2×CH), 66.9 (2×CH), 61.2 (4×CH_2), 41.1 (2×NCH_2).

4.1.23. *N,N′*-Di-[2-O-α-D-mannopyranosyl-D-mannose] ethylenediamine (26). Ethylenediamine (0.01 cm^3, 0.20 mmol), was dissolved in anhydrous methanol (10 cm^3) and the mixture stirred at room temperature. To this was added 2-*O*-α-D-mannopyranosyl-D-mannose (0.125 g, 0.36 mmol) and the resulting solution stirred under a nitrogen atmosphere. After 5 min the 2-*O*-α-D-mannopyranosyl-D-mannose dissolved and after 3 h a colourless solid precipitated from the solution. After 8 h a colourless precipitate had formed in the reaction mixture. The reaction mixture was stored for 24 h at 4°C, and then the precipitate was filtered off, washed with ice-cold methanol and then dried in vacuo (using a drying piston) for 48 h at 40 °C. This yielded *N,N′-di-[2-O-α-D-mannopyranosyl-D-mannose]ethylenediamine* (**26**) as a colourless powder (0.06 g, 39%). Mp 91.2–92.8°C; $[\alpha]_D^{20}$=+26.40 (*c* 0.12, H_2O); ν_{max} (KBr, cm^{-1}) 3324 (s, s N–H str), 3198 (s, O–H str), 2856 (s, O–H str), 1655 (m, N–H bend), 701 (m, N–H wagging); δ_H (400 MHz, D_2O) 5.13 (2H, d, *J*=1.5 Hz, 2×H-1′), 4.16 (2H, dd, *J*=2.0, 3.0 Hz, 2×H-2′), 4.04–4.07 (2H, m, 2×H-3′), 4.03 (2H, s, 2×H-1), 3.71–4.01 (18H, m, 2×H-2, 2×H-3, 2×H-4, 4×H-6, 2×H-4′, 2×H-5′, 4×H-6′), 3.60–3.70 (2H, m, 2×H-5), 2.52–2.64 (2×$(NCH_2)_2$); δ_C (100 MHz, D_2O) 93.2 (2×CH), 79.6 (2×CH), 73.6 (2×CH), 72.8 (2×CH), 71.6 (2×CH), 70.7 (2×CH), 70.4 (2×CH), 70.0 (2×CH), 67.4 (2×CH), 67.1 (2×CH), 61.3 (2×CH_2), 61.1 (2×CH_2), 33.0 (NCH_2), 32.4 (NCH_2).

4.1.24. General method for the preparation of α-1,3- and α-1,2-mannobioside based hexavalent glycodendrimers (27 and 28). The hexavalent dendrimer core[14] (1 equiv.) was dissolved in anhydrous methanol (5 cm^3) and the mixture stirred at room temperature. To this was added freshly distilled triethylamine (12 equiv.) and the resulting solution stirred under a nitrogen atmosphere for 30 min. α-1,3- or α-1,2-Mannobioside (12 equiv.) was added to the reaction mixture, after 2 h the mannobiosides dissolved and after 8 h a colourless solid precipitated out of the solution. After 16 h a colourless precipitate had formed in the reaction mixture. The reaction mixture was stored for 24 h at 4°C, and then the precipitate was filtered off, washed with ice-cold methanol and then dried in vacuo (using a drying piston) for 48 h at 40°C. This yielded both the α-1,2- and α-1,3-mannobioside-based dendrimers (**27** and **28**) as off-white powders.

According to the above procedure the hexavalent dendrimer core[14] (0.090 g, 60.10 μmol) was treated with triethylamine (0.10 cm^3, 0.72 mmol), and then 3-*O*-α-D-mannopyranosyl-D-mannose was added (0.247 g, 0.72 mmol) to yield compound (**27**) as a colourless solid (0.06 g, 37%). Mp 166.8–168.0 °C; $[\alpha]_D^{20}$=+16.75 (*c* 0.21, H_2O); ν_{max} (KBr, cm^{-1}) 3310 (s, s N–H str), 3254 (s, ArCH str), 2938 (m, ArCH str), 2849 (m, O–H str), 1652 (s, N–H bend), 1642 (s, C=O str), 1553 (m, N–H bend and C–N str), 1541 (m, ArC=C–O–C str), 1204 (w, N–H bend, C–N str), 1053 (s, C–O–C str), 1017 (s, C–O–C str), 980 (s, C–O–C str), 799 (s, N–H wagging); δ_H (400 MHz, D_2O) 7.15–7.26 (12H, m, ArCH), 4.85 (3H, s, $CH(CH_2)_2$), 4.84 (6H, d, *J*=1.5 Hz, 6×H-1′), 3.77 (6H, dd, *J*=1.5, 3.5 Hz, 6×H-2′), 3.65 (6H, dd, *J*=3.5, 10.0 Hz, 6×H-3′), 3.31–3.62 (72H, m, 6×H-1, 6×H-2, 6×H-3, 6×H-4, 12×H-6, 6×H-4′, 6×H-5′, 12×H-6′, 3×$CH(CH_2NH)_2$), 3.22–3.29 (6H, m, $C(O)NHCH_2$), 3.08–3.14 (6H, m, 6×H-5), 2.52–2.57 (6H, m, $C(O)NHCH_2CH_2N$); δ_C (100 MHz, D_2O) 170.1 (6×C=O), 138.0 (3×ArC), 136.5 (3×ArC), 127.6 (12×ArCH), 102.7 (6×CH), 94.5 (3×$CH(CH_2NH)_2$), 78.3 (6×CH), 76.3 (6×CH), 73.7 (6×CH), 72.8 (6×CH), 70.8 (6×CH), 70.7 (6×CH), 70.4 (6×CH), 67.1 (3×$CH(CH_2NH)_2$), 66.6 (6×CH), 66.4 (6×CH), 61.3 (6×CH_2), 61.2 (6×CH_2), 53.5 (3×$C(O)NHCH_2$), 37.1 (3×$C(O)NHCH_2CH_2N$).

According to the above procedure the hexavalent dendrimer core[14] (0.029 g, 36.20 μmol) was treated with triethylamine (0.10 cm^3, 0.43 mmol), and then 2-*O*-α-D-mannopyranosyl-D-mannose was added (0.149 g, 0.43 mmol) to yield

compound (**28**) as a colourless solid (0.06 g, 35%). Mp 159.5–161.0°C; $[\alpha]_D^{20}$=+20.45 (*c* 0.11, H_2O); ν_{max} (KBr, cm^{-1}) 3313 (s, s N–H str), 3240 (s, ArCH str), 2925 (m, ArCH str), 2850 (m, O–H str), 1654 (s, N–H bend), 1638 (s, C═O str), 1561 (m, N–H bend and C–N str), 1545 (m, ArC═C–O–C str), 1204 (w, N–H bend, C–N str), 1052 (s, C–O–C str), 1022 (s, C–O–C str), 973 (s, C–O–C str), 802 (s, N–H wagging); δ_H (400 MHz, D_2O) 7.18–7.32 (12H, m, ArCH), 5.17 (3H, s, C*H*$(CH_2)_2$), 4.84 (6H, d, *J*=1.5 Hz, 6×H-1′), 3.87 (6H, dd, *J*=1.5, 3.0 Hz, 6×H-2′), 3.42–3.75 (78H, m, 6×H-1, 6×H-2, 6×H-3, 6×H-4, 12×H-6, 6×H-3′, 6×H-4′, 6×H-5′, 12×H-6′, 3×CH(C*H*$_2$NH)$_2$), 3.32–3.41 (6H, m, C(O)NHC*H*$_2$), 3.21–3.31 (6H, m, 6×H-5), 2.53–2.61 (6H, m, C(O)NHCH$_2$C*H*$_2$N); δ_C (100 MHz, D_2O) 171.0 (3×C═O), 168.1 (3×C═O), 136.4 (3×ArC), 136.1 (3×ArC), 127.5 (12×ArCH), 102.5 (6×CH), 93.0 (3×*C*H(CH$_2$NH)$_2$), 79.5 (6×CH), 73.5 (6×CH), 72.8 (6×CH), 71.6 (6×CH), 70.6 (12×CH), 70.5 (6×CH), 70.3 (6×CH), 67.3 (3×CH(*C*H$_2$NH)$_2$), 67.1 (6×CH), 61.3 (6×CH$_2$), 61.2 (6×CH$_2$), 52.5 (3×C(O)NH*C*H$_2$), 45.0 (3×C(O)NHCH$_2$*C*H$_2$N).

4.1.25. Pentaerythrityl tetraazide (30). Pentaerythrityl tetrabromide (2.747 g, 7.08 mmol) and sodium azide (5.615 g, 86.40 mmol) were dissolved in anhydrous DMF (50 cm^3) and stirred at 80°C for 4 h under a nitrogen atmosphere. TLC analysis of the reaction mixture was performed, using hexane/ethyl acetate (3:1, v/v) as the solvent system, and this showed that the reaction had gone to completion (starting material R_f 0.88, product R_f 0.80). The reaction mixture was concentrated to dryness under reduced pressure, dissolved in CH_2Cl_2 (50 cm^3) and then washed with deionised water (4×50 cm^3). The combined organic layers were then dried over magnesium sulfate, filtered azeotroped with toluene (3×50 cm^3) and then concentrated to dryness in vacuo. The resulting oil was then purified using column chromatography on silica gel (hexane/ethyl acetate, 3:1, v/v). The relevant fractions were collected and combined to give *pentaerythrityl tetraazide* (**30**) as a colourless solid (1.36 g, 81%). Mp 50.2–51.6°C; ν_{max} (NaCl, cm^{-1}) 2100 (s, CN═N$^+$═N$^-$ str), 1445 (m, as CH_3), 1348 (s, s CH_3), 1256 (s, CC(═O)–O str), 1149 (m, as C–C–O str); δ_H (250 MHz, $CDCl_3$) 3.27 (8H, s, 4×CH_2); δ_C (63 MHz, $CDCl_3$) 51.8 (4×CH_2), 44.3 (C); *m*/*z* (CI) 296 (M+NH_4^+, 91%), 169 (46); Found 236.1972, $C_5H_{12}N_{13}$ requires 236.1979.

4.1.26. Pentaerythrityl tetraamine (29). A solution of *pentaerythrityl tetraazide* (**30**) (0.470 g, 1.99 mmol) in dry methanol (15 cm^3) containing 10% palladium-on-charcoal (0.50 g) was exposed to hydrogen at room temperature for 10 h. TLC analysis of the reaction mixture was performed, using hexane/ethyl acetate (3:1, v/v) as the solvent system, and this showed that the reaction had gone to completion. The catalyst was filtered off through Celite® and washed with methanol. The filterate was concentrated in vacuo to yield *pentaerythrityl tetraamine* (**29**) as a colourless oil (0.24 g, 91%) which was not purified further. ν_{max} (NaCl, cm^{-1}) 3489 (s, as N–H str), 3362 (s, s N–H str), 1648 (m, N–H bend), 1576 (s, N–H bend), 1484 (m, as CH_3), 1324 (s, s CH_3), 682 (m, N–H wagging); δ_H (250 MHz, $CDCl_3$) 4.26 (8H, s, 4×NH_2), 2.45 (8H, s, 4CH_2); δ_C (62.5 MHz, $CDCl_3$) 44.6 (C), 43.6 (4×CH_2).

4.1.27. 2′-Bromoethyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (37). Boron trifluoride etherate (11.60 cm^3, 94.32 mmol) was added to a solution of 1,2,3,4,6-penta-*O*-acetyl-α-D-mannopyranoside (10.834 g, 27.76 mmol) and 2-bromoethanol (1.96 cm^3, 27.65 mmol) in dry CH_2Cl_2 (100 cm^3). The reaction mixture was stirred in the dark under a nitrogen atmosphere for 3 h. TLC analysis, using ethyl acetate/hexane (1:1, v/v), showed that the reaction had gone to completion (starting material R_f 0.53, product R_f 0.63). CH_2Cl_2 (200 cm^3) was added, the reaction mixture was neutralised by adding saturated sodium bicarbonate solution (200 cm^3) and the resulting solution was washed with deionised water (2×200 cm^3). The combined organic layers were dried over magnesium sulfate, filtered and concentrated to dryness under reduced pressure. The resulting oil was then purified using column chromatography on silica gel (ethyl acetate/hexane (1:1, v/v)). The relevant fractions were collected, combined and concentrated to dryness under reduced pressure to yield *2′-bromoethyl-2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**37**) as a colourless powder (5.17 g, 41%). Mp 115.1–117.2°C, (lit.[19] 118–119°C); $[\alpha]_D^{20}$=+42.09 (*c* 0.53, $CHCl_3$), (lit.[19] $[\alpha]_D^{23}$=+45.00 (*c* 0.60, $CDCl_3$)); ν_{max} (NaCl, cm^{-1}) 1745 (s, C═O str), 1733 (s, C═O str), 1435 (w, as CH_3), 1381 (m, s CH_3), 1367 (m, s CH_3), 1291 (w, s CH_3), 1230 (s, CC(═O)–O str), 1137 (m, C–O–C str), 1086 (m, C–O–C str), 1051 (s, C–O–C str), 1006 (m, C–O–C str), 979 (m, C–O–C str), 683 (m, C-Br str); δ_H (250 MHz, $CDCl_3$) 5.25–5.33 (3H, m, H-2, H-3, H-4), 4.87 (1H, s, H-1), 4.27 (1H, dd, *J*=11.5, 5.5 Hz, H-6), 4.10–4.15 (2H, m, H-5, H-6), 3.87–3.96 (2H, m, CH_2O), 3.52 (2H, app t, *J*=5.5 Hz, CH_2Br), 2.15 (3H, s, OAc), 2.10 (3H, s, OAc), 2.00 (3H, s, OAc), 1.99 (3H, s, OAc); δ_C (62.5 MHz, $CDCl_3$) 171.0 (C═O), 170.4 (C═O), 170.2 (C═O), 170.1 (C═O), 98.1 (CH), 69.8 (CH), 69.4 (CH), 69.3 (CH), 68.9 (CH_2O), 66.4 (CH), 62.8 (CH_2), 30.0 (CH_2Br), 21.3 (CH_3), 21.1 (3×CH_3); *m*/*z* (CI) 472 (M+NH_4^+, 50%), 331 (100), 169 (23), 81 (18); Found 472.0806, $C_{16}H_{27}O_{10}$ $N^{79}Br$ requires 472.0818.

4.1.28. 3′-Bromopropyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (38). Boron trifluoride etherate (4.06 cm^3, 33.01 mmol) was added to a solution of 1,2,3,4,6-penta-*O*-acetyl-α-D-mannopyranoside (3.338 g, 8.55 mmol) and 3-bromo-1-propanol (0.85 cm^3, 9.40 mmol) in dry CH_2Cl_2 (40 cm^3). The reaction mixture was stirred in the dark under a nitrogen atmosphere for 4 h. TLC analysis, using ethyl acetate/hexane (1:1, v/v), showed that the reaction had gone to completion (starting material R_f 0.43, product R_f 0.57). CH_2Cl_2 (80 cm^3) was added, the reaction mixture was neutralised by adding saturated sodium bicarbonate solution (80 cm^3) and the resulting solution was washed with deionised water (2×80 cm^3). The combined organic layers were dried over magnesium sulfate, filtered and concentrated to dryness under reduced pressure. The resulting oil was then purified using column chromatography on silica gel (ethyl acetate/hexane (1:1, v/v)). The relevant fractions were collected, combined and concentrated to dryness under reduced pressure to yield *3′-bromopropyl-2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**38**) as a pale yellow oil (1.60 g, 39%). $[\alpha]_D^{20}$=+39.10 (*c* 1.95, $CHCl_3$); ν_{max} (NaCl, cm^{-1}) 1746 (s, C═O str), 1435 (m, as CH_3), 1370 (s, s CH_3), 1224 (s, CC(═O)–O str), 1137 (s, C–O–C str), 1088

(s, C–O–C str), 1050 (s, C–O–C str), 981 (m, C–O–C str), 688 (m, C-Br str); δ_H (400 MHz, $CDCl_3$) 5.27–5.29 (2H, m, H-3, H-4), 5.23–5.24 (1H, m, H-2), 4.84 (1H, d, J=1.5 Hz, H-1) 4.28 (1H, dd, J=5.5, 12.5 Hz, H-6), 4.13 (1H, dd, J=2.5, 12.5 Hz, H-6), 4.00–4.04 (1H, m, H-5), 3.88–3.94 (1H, m, CH_2O), 3.53–3.62 (3H, m, CH_2O, CH_2Br), 2.06–2.19 (2H, m, $OCH_2CH_2CH_2Br$) 2.16 (3H, s, OAc), 2.11 (3H, s, OAc), 2.06 (3H, s, OAc), 2.00 (3H, s, OAc); δ_C (62.5 MHz, $CDCl_3$) 170.8 (C=O), 170.2 (C=O), 170.1 (C=O), 170.0 (C=O), 97.9 (CH), 69.7 (CH), 69.3 (CH), 68.9 (CH), 66.3 (CH), 65.8 (CH_2O), 62.7 (CH_2), 32.3 ($OCH_2CH_2CH_2Br$), 30.5 (CH_2Br), 21.1 (CH_3), 21.0 (2×CH_3), 20.9 (CH_3); *m/z* (CI) 488 ($M+NH_4^+$, 22%), 331 (100); Found 488.0973, $C_{17}H_{29}O_{10}N^{81}Br$ requires 488.0955.

4.1.29. 2′-Azidoethyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (35). A solution of *2′-bromoethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**37**) (0.228 g, 0.50 mmol) in anhydrous DMF (20 cm^3) was treated with sodium azide (0.198 g, 3.05 mmol) and the reaction mixture stirred at 60°C for 1 h. TLC analysis, using ethyl acetate/hexane (2:1, v/v), showed that the reaction had gone to completion (starting material R_f 0.69, product R_f 0.60). The reaction mixture was concentrated to dryness under reduced pressure, dissolved in CH_2Cl_2 (50 cm^3) and then washed with deionised water (4×50 cm^3). The combined organic layers were dried over magnesium sulfate, filtered and concentrated to dryness under reduced pressure. The resulting oil was then purified using column chromatography on silica gel (ethyl acetate/hexane (2:1, v/v)). The relevant fractions were collected, combined and concentrated to dryness under reduced pressure to yield *2′-azidoethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**35**) as colourless crystals (0.15 g, 73%). Mp 81.8–82.1°C; $[\alpha]_D^{20}$=+37.39 (*c* 0.55, $CHCl_3$), (lit.[18] $[\alpha]_D^{20}$=+50.2 (*c* 0.75, $CHCl_3$)); ν_{max} (NaCl, cm^{-1}) 2106 (s, CN=N^+=N^- str), 1745 (s, C=O str), 1732 (s, C=O str), 1435 (w, as CH_3), 1379 (m, s CH_3), 1365 (m, s CH_3), 1228 (s, CC(=O)–O str), 1135 (m, C–O–C str), 1108 (w, C–O–C str), 1074 (m, C–O–C str), 1050 (s, C–O–C str), 979 (s, C–O–C str); δ_H (400 MHz, $CDCl_3$) 5.37 (1H, dd, J=10.0, 3.5 Hz, H-3), 5.33 (1H, app t, J=10.0 Hz, H-4), 5.28 (1H, dd, J=3.5, 2.0 Hz, H-2), 4.88 (1H, d, J=2.0 Hz, H-1), 4.30 (1H, dd, J=12.5, 5.5 Hz, H-6), 4.13 (1H, dd, J=12.5, 2.5 Hz, H-6), 4.05 (1H, m, H-5), 3.65–3.91 (2H, m, CH_2O), 3.42–3.54 (2H, m, CH_2N_3), 2.17 (3H, s, OAc), 2.11 (3H, s, OAc), 2.06 (3H, s, OAc), 2.00 (3H, s, OAc); δ_C (62.5 MHz, $CDCl_3$) 171.0 (C=O), 170.4 (C=O), 170.2 (2×C=O), 98.1 (CH), 69.8 (CH), 69.2 (2×CH), 67.4 (CH_2O), 66.4 (CH), 62.8 (CH_2), 50.7 (CH_2N_3), 21.3 (CH_3), 21.1 (3×CH_3); *m/z* (CI) 435 ($M+NH_4^+$, 96%), 390 (35), 331 (100); Found 435.1717, $C_{16}H_{27}O_{10}N_4$ requires 435.1727. Found: C, 46.47; H, 5.54; N, 9.52. Calc. for $C_{16}H_{23}O_{10}N_3$ (M_r 417.14): C, 46.04; H, 5.55; N, 10.07%.

4.1.30. 3′-Azidopropyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (36). A solution of *3′-bromopropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**38**) (1.311 g, 2.72 mmol) in anhydrous DMF (40 cm^3) was treated with sodium azide (1.077 g, 16.56 mmol) and the reaction mixture stirred at 60°C for 1.5 h. TLC analysis, using ethyl acetate/hexane (1:1, v/v), showed that the reaction had gone to completion (starting material R_f 0.57, product R_f 0.47). The reaction mixture was concentrated to dryness under reduced pressure, dissolved in CH_2Cl_2 (50 cm^3) and then washed with deionised water (4×50 cm^3). The combined organic layers were dried over magnesium sulfate, filtered, azeotroped with toluene (3×50 cm^3) and then concentrated to dryness under reduced pressure. The resulting oil was then purified using column chromatography on silica gel (ethyl acetate/hexane (1:1, v/v)). The relevant fractions were collected, combined and concentrated to dryness under reduced pressure to yield *3′-azidopropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**36**) as a colourless solid (0.85 g, 71%). Mp 50.2–51.9°C; $[\alpha]_D^{20}$=+46.02 (*c* 1.08, $CHCl_3$); ν_{max} (NaCl, cm^{-1}) 2101 (s, CN=N^+=N^- str), 1745 (s, C=O str), 1444 (w, as CH_3), 1366 (m, s CH_3), 1232 (s, CC(=O)–O str), 1136 (m, C–O–C str), 1052 (m, C–O–C str); δ_H (400 MHz, $CDCl_3$) 5.25–5.34 (2H, m, H-3, H-4), 5.24 (1H, d, J=2.0, 3.0 Hz, H-2), 4.82 (1H, d, J=1.5 Hz, H-1),4.29 (1H, dd, J=5.5, 12.0 Hz, H-6), 4.12 (1H, dd, J=2.5, 12.0 Hz, H-6), 3.95–3.99 (1H, m, H-5), 3.79–3.85 (1H, m, CH_2O), 3.51–3.56 (1H, m, CH_2O), 3.44 (2H, t, J=6.5 Hz, CH_2N_3), 2.16 (3H, s, OAc), 2.11 (3H, s, OAc), 2.05 (3H, s, OAc), 2.00 (3H, s, OAc), 1.87–1.94 (2H, m, $OCH_2CH_2CH_2N_3$); δ_C (62.5 MHz, $CDCl_3$) 171.0 (C=O), 170.4 (C=O), 170.3 (C=O), 170.1 (C=O), 98.0 (CH), 69.8 (CH), 69.4 (CH), 69.0, (CH), 66.5 (CH), 65.2 (CH_2O), 62.9 (CH_2), 48.5 (CH_2N_3), 29.0 ($OCH_2CH_2CH_2N_3$), 21.3 (2×CH_3), 21.1 (2×CH_3); *m/z* (CI) 449 ($M+NH_4^+$, 20%), 331 (100); Found 449.1904, $C_{17}H_{25}O_{10}N_3$ requires 449.1884; Found: C, 47.49; H, 5.88; N, 9.66. Calc. for $C_{17}H_{29}O_{10}N_4$ (M_r 431.16): C, 47.33; H, 5.84; N, 9.74%.

4.1.31. 2′-Aminoethyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (33). A solution of *2′-azidoethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**35**) (0.772 g, 1.85 mmol) in dry methanol (30 cm^3) containing 10% palladium-on-charcoal (0.235 g) was exposed to hydrogen at room temperature for 16 h. TLC analysis of the reaction mixture was performed, using ethyl acetate/hexane (1:1, v/v) as the solvent system, and showed that the reaction had gone to completion (starting material R_f 0.60, product R_f 0.00). The catalyst was filtered off through Celite® and washed with methanol. The filtrate was concentrated in vacuo to yield *2′-aminoethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**33**) as a yellow oil (0.62 g, 85%) which was not purified further. ν_{max} (NaCl, cm^{-1}) 3509 (s, as N–H str), 3373 (s, s N–H str), 1749 (s, C=O str), 1734 (s, C=O str), 1653 (s, N–H bend), 680 (s, N–H wagging); δ_H (400 MHz, $CDCl_3$) 5.26–5.36 (3H, m, H-2, H-3, H-4), 4.87 (1H, d, J=1.5 Hz, H-1), 4.31 (1H, dd, J=5.0, 12.0 Hz, H-6), 4.11 (1H, dd, J=2.5, 12.0 Hz, H-6), 4.00–4.05 (1H, m, H-5), 3.80–3.85 (1H, m, CH_2O), 3.57–3.62 (1H, m, CH_2O), 2.89 (2H, t, J=5.5 Hz, CH_2NH_2), 2.16 (3H, s, OAc), 2.11 (3H, s, OAc), 2.05 (3H, s, OAc), 1.99 (3H, s, OAc); δ_C (100 MHz, $CDCl_3$) 170.7 (C=O), 170.1 (C=O), 169.9 (C=O), 97.8 (CH), 69.5 (CH), 69.1 (CH), 68.5 (CH), 67.9 (CH_2O), 66.1 (CH), 62.4 (CH_2), 48.6 (CH_2NH_2), 20.9 (2×CH_3), 20.7 (2×CH_3); *m/z* (FAB) 392 ($M+H^+$, 100%), 350 (20), 72 (22); Found 392.1572, $C_{16}H_{26}O_{10}N$ requires 392.1557.

4.1.32. 3′-Aminopropyl-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (34). A solution of *3′-azidopropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**36**) (1.991 g,

4.62 mmol) in dry methanol (20 cm^3) containing 10% palladium-on-charcoal (0.425 g, wet weight) was exposed to hydrogen at room temperature for 12 h. TLC analysis of the reaction mixture was performed, using ethyl acetate/hexane (1:1, v/v) as the solvent system, and showed that the reaction had gone to completion (starting material R_f 0.47, product R_f 0.00). The catalyst was filtered off through Celite® and washed with methanol. The filtrate was concentrated in vacuo to yield *3′-aminopropyl-2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**34**) as a colourless foam (0.67 g, 61%) which was not purified further. ν_{max} (NaCl, cm^{-1}) 3509 (s, as N–H str), 3373 (s, s N–H str), 3341 (s, O–H str), 3324 (s, O–H str), 2897 (s, O–H str), 1653 (s, N–H bend), 1228 (w, as C–C–O str), 1094 (m, C–O–C str), 680 (s, N–H wagging); δ_H (250 MHz, CD_3OD) 4.77 (1H, d, J=1.5 Hz, H-1), 3.46–3.83 (8H, m, H-2, H-3, H-4, H-5, 2×H-6, $OCH_2CH_2CH_2NH_2$), 2.70–2.84 (2H, m, $OCH_2CH_2CH_2NH_2$), 1.79–1.86 (2H, m, $OCH_2CH_2CH_2NH_2$); δ_C (62.5 MHz, CD_3OD) 101.9 (CH), 75.1 (CH), 73.0 (CH), 72.5 (CH), 69.0 (CH), 67.3 ($OCH_2CH_2CH_2NH_2$ or $OCH_2CH_2CH_2NH_2$), 63.3 (CH_2), 48.3 ($OCH_2CH_2CH_2NH_2$ or $OCH_2CH_2CH_2NH_2$), 30.6 ($OCH_2CH_2CH_2NH_2$); *m/z* (ES^+) 238.1 ($M+H^+$, 47%).

4.1.33. 2′-Aminoethyl-*O*-α-D-mannopyranoside (31). A flask was charged with *2′-aminoethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**33**) (0.51 g, 1.30 mmol) dissolved in anhydrous methanol (15 cm^3). To this solution a catalytic amount of anhydrous potassium carbonate (0.005 g, 0.05 mmol) was added and the reaction mixture was stirred at room temperature under a nitrogen atmosphere. TLC analysis using methanol: CH_2Cl_2 (5:95, v/v), showed that after 1.5 h the reaction had gone to completion (starting material R_f 0.98, product R_f 0.32). Amberlite IR-120 (PLUS) ion-exchange resin was washed with methanol and then added to and stirred with the reaction mixture for 30 min. The resin was then filtered off under gravity and the resulting solution concentrated to dryness in vacuo to yield *2′-aminoethyl-O-α-D-mannopyranoside* (**31**) as a colourless foam (0.24 g, 87%) which was used directly in the next reaction.

4.1.34. 3′-Aminopropyl-*O*-α-D-mannopyranoside (32). A flask was charged with *3′-aminopropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside* (**34**) (1.2 g, 2.4 mmol) dissolved in anhydrous methanol (30 cm^3). To this solution a catalytic amount of anhydrous potassium carbonate (0.005 g, 0.05 mmol) was added and the reaction mixture was stirred at room temperature under a nitrogen atmosphere. TLC analysis using methanol: CH_2Cl_2 (5:95, v/v), showed that after 1.5 h the reaction had gone to completion (starting material R_f 0.8, product R_f 0.32). Amberlite IR-120 (PLUS) ion-exchange resin was washed with methanol and then added to and stirred with the reaction mixture for 30 min. The resin was then filtered off under gravity and the resulting solution concentrated to dryness in vacuo to yield *3′-aminopropyl-O-α-D-mannopyranoside* (**32**) as a colourless foam (0.42 g, 86%) which was used directly in the next reaction.

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