

# Influence of preparation procedure on polymer composition: synthesis and characterisation of polymethacrylates bearing $\beta$ -D-glucopyranoside and $\beta$ -D-galactopyranoside residues

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Methacrylate derivatives bearing  $\beta$ -D-glucopyranoside and  $\beta$ -D-galactopyranoside residues are synthesised by glycosylation of 2-hydroxyethyl methacrylate (HEMA) with 2,3,4,6-tetra-*O*-acetyl- $\alpha$ -D-glucopyranosyl bromide and 2,3,4,6-tetra-*O*-acetyl- $\alpha$ -D-galactopyranosyl bromide, respectively.  $\beta$ -Selectivity in the glycosylation reactions is ensured by neighbouring-group participation of acetyl groups at O-2 in the glycosyl donors. 2-(2',3',4',6'-tetra-*O*-acetyl- $\beta$ -D-glucosyloxy)ethyl methacrylate (AcGlcEMA, **1a**) was obtained as a crystalline solid and its crystal structure was determined by single-crystal X-ray diffraction. Deprotected polymers are synthesised in two parallel ways; either polymerisation of the protected monomers and subsequent deacetylation of the resulting polymers, or polymerisation of the previously deprotected monomers. The number- and weight-average relative molecular masses of both the protected and deprotected polymers are determined by size exclusion chromatography (SEC). Absolute molecular masses are obtained using the previously estimated refractive-index increments,  $dn/dc$ . It is found that polymerisation of deprotected monomers leads to polymers of well-defined composition, in contrast to the deacetylation of protected polymers.

## Introduction

Polymers consisting of a chemically and biologically stable C–C backbone and a hydrophilic saccharide moiety in the side chain are called ‘glycopolymers’.<sup>1</sup> Owing to their application in basic biochemical and biomedical research such as molecular-recognition processes, drug-delivery systems, affinity chromatography and cell-culture systems, glycopolymers have attracted increasing attention since they were first developed by Horejši *et al.* in 1978.<sup>2</sup>

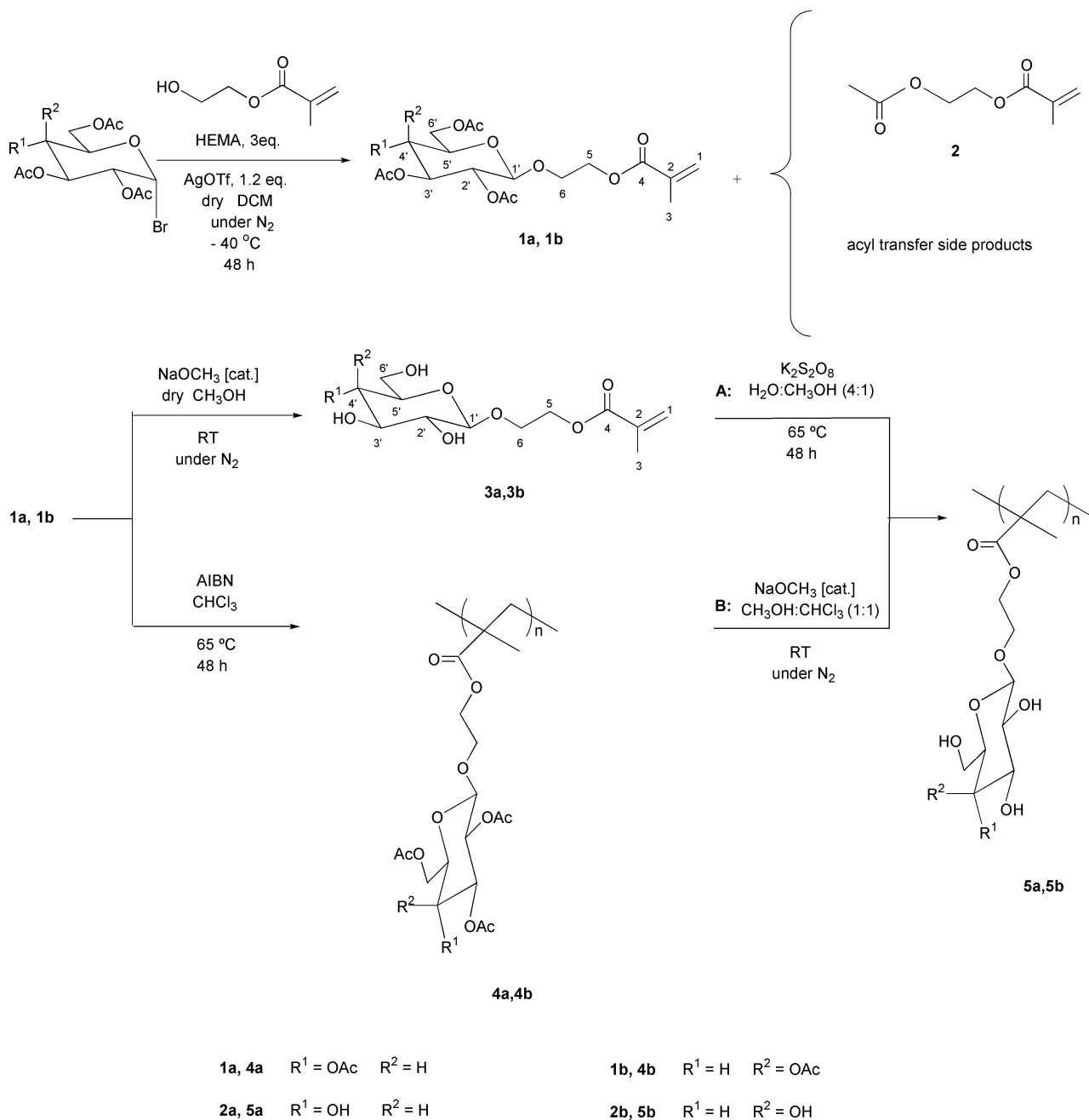
The synthesis of carbohydrate-based polymers usually requires the preparation of polymerisable sugar derivatives,<sup>3–22</sup> although the less frequently employed glycosylation of polymers is also possible.<sup>23,24</sup> Different types of glycopolymers have been synthesised, mainly polyacrylamides,<sup>9,12</sup> polystyrenes,<sup>11,13–15</sup> polyacrylates<sup>3,19–21</sup> and polymethacrylates.<sup>3–6</sup> Kobayashi *et al.*<sup>7</sup> have synthesised a variety of carbohydrate-containing polystyrene derivatives, which have been used as cell-specific biomedical materials. In particular, lactose-carrying polystyrene (PVLA) has been shown to be a useful *substratum* for the culture of hepatocytes. The synthesis of another type of polystyrene derivative bearing lactose or *N,N'*-diacetylchitobiose residues and the investigation of their interaction with lectins by means of a two-dimensional immunodiffusion test in agar and inhibition of haemoagglutinating activity was reported by Kobayashi *et al.*<sup>11</sup> It was found that the lectin-poly(*p*-vinylbenzamido)- $\beta$ -diacetylchitobiose binding was increased 10<sup>3</sup>-times compared with that of the oligosaccharide itself. The attachment of different kinds of cells to tissue culture polystyrene plates coated with polyacrylamide containing glucose residues has been investigated by Bahulekar *et al.*<sup>12</sup> Ohno *et al.*<sup>13</sup> reported the synthesis of PVLA obtained by means of a different route. The deprotected polymer, DODA-PVLA, was then used to prepare sugar-carrying liposomes, the galactose residues of which were specific-

ally and effectively recognised by the galactose-specific lectin *Ricinus communis* agglutinin (RCA).

Due to the polyfunctionality of sugars, multistep reactions including protecting-group chemistry are typically required for their manipulation. Indeed, selective reactions of non-protected sugars to form polymerisable monomers have only been achieved by enzymatic catalysis.<sup>25,26</sup> The removal of protecting groups can be carried out either before or after the polymerisation. When considering the point at which to deprotect, the lability of the monomer and, to a lesser extent, the polymer, together with the possibility of a non-quantitative deprotection of the polymer, all have to be taken in account. Usually, deprotection of the polymers is not quantitative; therefore the removal of protecting groups is, if possible, preferably carried out at the monomer stage.<sup>10</sup> Nevertheless, to our knowledge, only two examples of deprotection at the monomer stage have been reported so far.<sup>6,9</sup> Despite the importance of this strategy, no systematic comparison has been made between deprotection pre- or post-polymerisation.

In this paper we report the synthesis of methacrylate derivatives of glucose and galactose by glycosylation of 2-hydroxyethyl methacrylate (HEMA) following the procedure reported in Scheme 1. The protected monomers were polymerised with 2,2'-azoisobutyronitrile (AIBN) in chloroform at 65 °C and the resulting polymers, were subsequently deprotected with sodium methoxide in a 1 : 1 mixture of chloroform and methanol. Alternatively, the protected monomers were first deacetylated with sodium methoxide in methanol and then polymerised in a mixture 4 : 1 of water and methanol at 65 °C using potassium persulfate as initiator.

Methacrylate and acrylate derivatives containing glucose and galactose have been synthesised previously. Kitazawa *et al.*<sup>3</sup> reported the glycosylation of HEMA and 2-hydroxyethyl acrylate (HEA) using several methyl glycosides as glycosyl donors,



**Scheme 1** Monomer and polymer syntheses.

including methyl glucoside and methyl galactoside, in the presence of phosphomolybdic acid as catalyst and 2,4-dinitrochlorobenzene as an inhibitor. However, the stereoselectivity of this method is low and an  $\alpha,\beta$  anomeric mixture is obtained. Nakaya *et al.*<sup>5</sup> synthesised 2-(2',3',4',6'-tetra-*O*-acetyl- $\beta$ -D-glucopyranosyloxy)ethyl methacrylate by reaction of HEMA with 2,3,4,6-tetra-*O*-acetyl- $\alpha$ -D-glucopyranosyl bromide by the method of Helferich,<sup>27</sup> in the presence of silver oxide or mercury(II) cyanide, with yields of 54 and 58%, respectively. After free-radical polymerisation, the polymer obtained was deacetylated with sodium methoxide and the title polymer was identified by infrared spectroscopy data alone. 2-(2',3',4',6'-Tetra-*O*-acetyl- $\beta$ -D-glucopyranosyloxy)ethyl acrylate (AcGEA) was synthesised by Liang *et al.*<sup>19–21</sup> according to the method of Helferich,<sup>27</sup> by glycosylation of HEA with 2,3,4,6-tetra-*O*-acetyl- $\alpha$ -D-glucopyranosyl bromide using mercury(II) bromide as catalyst. After polymerisation by conventional free-radical and atom-transfer radical polymerisation, the polymer was deprotected with sodium-methoxide. The self-association tendency of poly( $\beta$ -D-glucopyranosyloxy)ethyl acrylate (PGEA) in

water was studied; a dependence of the critical aggregation concentration on the relative molecular mass of the polymer and on the temperature was observed. In order to understand the influence of hydrophobicity on the critical aggregation concentration, AcGEA was copolymerised with stearyl acrylate in different ratios.  $\beta$ -D-Galactopyranosyloxyethyl methacrylate has so far been synthesised exclusively by enzymatic catalysis.<sup>25,26</sup>

In light of these disparate routes, some with low yields or stereoselectivities and/or involving toxic mercury salts, we derived parallel routes to protected (**1a,b**) and deprotected (**3a,b**) carbohydrate glycoside esters. Not only was  $\beta$ -stereoselectivity in the glycosylation reactions ensured by neighbouring-group participation of acetyl groups at O-2 in the glycosyl donors, but also the yields of these monomer syntheses were considerably improved compared with previous syntheses. Moreover, all monomeric and polymeric products have been characterised fully by IR and NMR spectroscopy, optical activity measurements, elemental analysis and, for the monomers, mass spectrometry, leading to a more thorough characterisation

than those reported so far<sup>3,5,19-21</sup> – critical for a proper comparison of the influence of sugar type in biological applications. Absolute molecular masses were obtained for all polymers by size-exclusion chromatography (SEC) using the previously estimated refractive-index increments,  $dn/dc$ , determined using a calibrated light-scattering signal and working at known concentrations. Good characterisation, high purity, and a fully known composition are important requirements for the precise use and application of glycopolymers and for a true understanding of any results obtained. Therefore, in this article we report a detailed characterisation of the monomers and polymers and for the first time we describe how the polymer composition depends on the method of preparation used.

## Results and discussion

### 1. Glycomonomers

The protected monomers AcGlcEMA **1a** and AcGalEMA **1b** were synthesised by coupling the glycosyl donors, 2,3,4,6-tetra-*O*-acetyl- $\alpha$ -D-glucopyranosyl bromide and 2,3,4,6-tetra-*O*-acetyl- $\alpha$ -D-galactopyranosyl bromide, respectively, with the glycosyl acceptor 2-hydroxyethyl methacrylate (HEMA), in dry dichloromethane, using silver trifluoromethanesulfonate as catalyst, in good yields. The synthetic procedure is reported in Scheme 1.  $\beta$ -Stereoselectivity in the glycosylation reactions was ensured by neighbouring-group participation of acetyl groups at O-2 in the glycosyl donors. Acetyl transfer to the nucleophilic alcohol (HEMA) led to the formation of AcEMA **2** as the major side product. Such side reactions have been reported previously<sup>23,28-30</sup> and may be attributed to rearrangements of orthoester intermediates.<sup>23</sup> According to several proposals<sup>31,32</sup> in the literature, the glycosylation reaction proceeds by activation of the glycosyl donor by silver trifluoromethanesulfonate, leading to the irreversible formation of a glycosyl oxocarbenium ion<sup>33</sup> that, due to neighbouring-group participation, is in equilibrium with the corresponding carbocationic species.<sup>23,34</sup> Nucleophilic attack of HEMA on the latter species can then result in the formation of the desired products **1a** and **1b** with AcEMA and monoacetylated compounds as side products. Intramolecular neighbouring-group participation is expected to be kinetically favoured with respect to intermolecular nucleophilic attack so that the oxocarbenium ion is unlikely to have a long lifetime.<sup>35,36</sup>

Products **1a**, **1b**, and **2** were isolated by flash column chromatography. 2-Acetoxyethyl methacrylate (AcEMA, **2**) was characterised by NMR spectroscopy and mass spectrometry. In addition to **2**, unchanged HEMA was also present in each crude product; this was not separable from the desired product by column chromatography. This problem was overcome by acetylation of HEMA at the end of the glycosylation reaction to give **2**, which was removed easily by flash chromatography. In this manner, AcGlcEMA **1a** and AcGalEMA **1b** were obtained in yields of 72 and 80%, respectively – a significant advance on previously reported yields. They were characterised by IR and NMR spectroscopy, optical activity measurements, mass spectrometry and elemental analysis. Both glycomonomers were identified by <sup>1</sup>H-NMR spectroscopy as being the  $\beta$ -anomers. AcGlcEMA was obtained as a colourless crystalline solid and its crystal structure was determined by single-crystal X-ray diffraction (Fig. 1). The heterocycle adopts a normal chair conformation, with all the substituents in equatorial orientations. The olefinic C(10)=C(12) bond and the adjacent ester group are nearly coplanar: the O(9)C(9)C(10)C(12) torsion angle is 3.1(3)°.

AcGalEMA **1b** was obtained as colourless oil that was stored at 4 °C after addition of a radical-polymerisation inhibitor (hydroquinone, 10 ppm). AcGlcEMA and AcGalEMA are soluble in chloroform, methanol, dichloromethane, tetrahydrofuran, acetone, benzene and DMF.

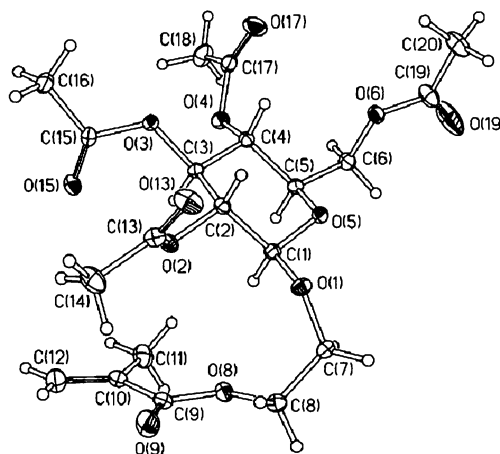


Fig. 1 Crystal structure of **1a**, showing 50% thermal ellipsoids.

The monomers were deprotected using a catalytic quantity of sodium methoxide in methanol, as reported in Scheme 1. The reaction, monitored continuously by TLC (acetonitrile–water, 9 : 1), was stopped when the product resulting from the cleavage of the ester bond of the HEMA moiety was observed (as a spot having  $R_f = 0.2$ ). The purification of GlcEMA **3a** and GalEMA **3b** by chromatography (chloroform–methanol, 8 : 2) afforded the products in high purity. GlcEMA and GalEMA were obtained as strongly hygroscopic, amorphous, colourless solids, in yields of 80 and 75%, respectively. They were fully characterised for the first time by IR and NMR spectroscopy, optical activity measurements, mass spectrometry and elemental analysis. ES-mass spectra showed only one signal each, corresponding to the completely deprotected products. IR spectra showed the complete disappearance of the carbonyl absorption bands at  $\approx 1750$   $\text{cm}^{-1}$  corresponding to the *O*-acetyl protecting groups. No signal due to the protecting groups could be seen in the <sup>1</sup>H- and <sup>13</sup>C-NMR spectra. Differences characteristic of acetyl removal in the <sup>1</sup>H-NMR spectra were observed.

GlcEMA and GalEMA are soluble in methanol, DMF, water and, sparingly, in chloroform.

### 2. Glycopolymers

pAcGlcEMA **4a** and pAcGalEMA **4b** were obtained as white solids by polymerising **1a** and **1b**, respectively, with AIBN in chloroform at 65 °C for 48 h. The IR spectra showed that the vinyl absorption bands (1321 and 1299  $\text{cm}^{-1}$ , 1320 and 1295  $\text{cm}^{-1}$ , for AcGlcEMA and AcGalEMA, respectively) had disappeared. Moreover, no signals due to vinyl protons and carbons could be seen in the <sup>1</sup>H- and <sup>13</sup>C-NMR spectra. As for the corresponding monomers, pAcGlcEMA and pAcGalEMA showed optical activity due to the saccharide units (the specific rotations  $[\alpha]_D^{25}$ , measured in chloroform, are reported in the Experimental section). pAcGlcEMA and pAcGalEMA are soluble in chloroform, THF, benzene, DMF and acetone.

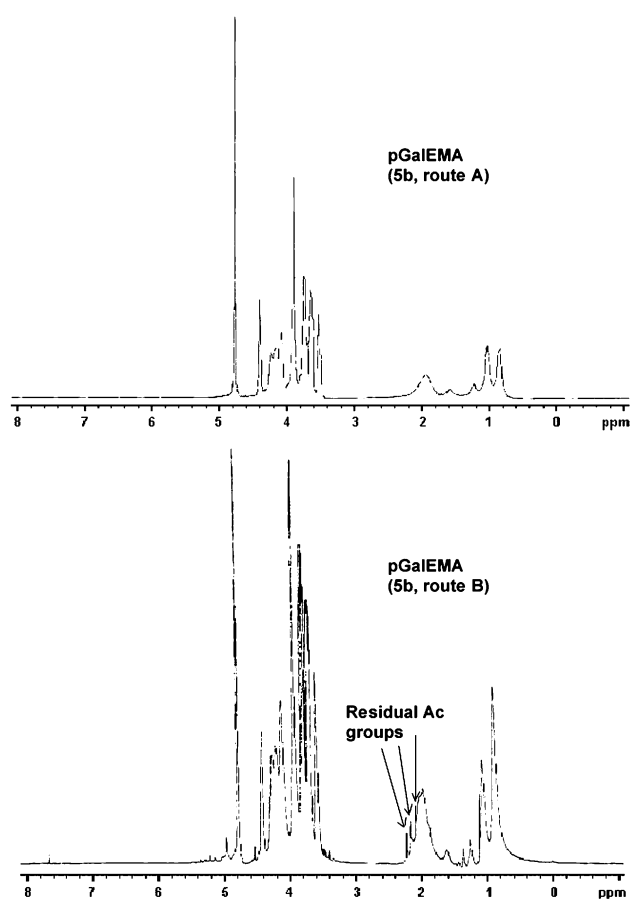
The number- and weight-average relative molecular masses were determined by size-exclusion chromatography (SEC). Absolute molecular mass values were obtained using the previously estimated refractive-index increments,  $dn/dc$ , which were determined in THF at 30 °C using a calibrated light-scattering signal, working at known concentrations and with a He–Ne laser (wavelength 670 nm) as the light source. Values of 0.058  $\text{ml g}^{-1}$  and 0.071  $\text{ml g}^{-1}$  for pAcGlcEMA and pAcGalEMA, respectively, were obtained. These values were consistent for three batches of the same polymer. Since the experimental conditions were the same for both polymer solutions, this interesting difference could possibly be explained by different conformations of the two polymers in solution perhaps induced by the different side-chain stereochemistries. The average relative molecular masses determined using these  $dn/dc$  values are reported in Table 1.

**Table 1** Absolute relative molecular masses as determined by SEC and  $dn/dc$  of polymers

Polymer	$M_n/g\ mol^{-1}$	$M_w/g\ mol^{-1}$	$M_w/M_n$	$(dn/dc)/ml\ g^{-1}$
pAcGlcEMA <b>4a</b>	61 600	135 900	2.21	$0.058 \pm 0.001$
pAcGalEMA <b>4b</b>	63 000	156 870	2.49	$0.071 \pm 0.002$
pGlcEMA <b>5aA</b>	23 000	60 000	2.61	0.131
pGalEMA <b>5bA</b>	461 000	1 019 000	2.21	0.140
pGlcEMA <b>5aB</b>	5 932	10 410	1.75	0.126
pGalEMA <b>5bB</b>	2 984	6 410	2.15	0.146

The deprotected polymers, pGlcEMA **5a** and pGalEMA **5b**, were obtained following the two different procedures reported in Scheme 1. In route A, the deprotected monomers **3a** and **3b** were polymerised with potassium persulfate in a 4 : 1 mixture of water and methanol at 65 °C for 48 h. In route B, the protected polymers **4a** and **4b** were deacetylated with sodium methoxide in a 1 : 1 mixture of chloroform and methanol. In both cases, **5a** and **5b** were obtained as highly hygroscopic white solids. The two polymers synthesised by polymerisation of the deprotected monomers are denoted by (A); polymers obtained by deacetylating the protected polymers are denoted by (B). pGlcEMA and pGalEMA were characterised by IR and NMR spectroscopy, optical activity measurements and elemental analysis. All the four deprotected polymers synthesised were soluble only in water and the resulting aqueous solutions tended to foam on agitation, perhaps indicating surface activity. Measurements of surface tension and critical-aggregation concentration are in progress.

The  $^1H$ -NMR spectra of the polymers prepared by each route showed noticeable differences, as reported in Fig. 2 for

**Fig. 2**  $^1H$ -NMR spectra of pGalEMA(A) and pGalEMA(B).

pGalEMA(A) and pGalEMA(B). It can be seen that, despite exhaustive deprotecting conditions, signals due to methyl protons of the protecting acetyl groups can still be seen in the range

$\delta$  2.0–2.2 in the spectrum of pGalEMA(B), while no trace of these signals is present in the spectrum of pGalEMA(A). The presence in pGalEMA(B) of some residual protecting groups was also shown in the  $^{13}C$ -NMR spectrum by peaks in the range  $\delta_c$  22.0–24.0. Moreover, microanalyses of pGalEMA(B) typically gave a higher carbon percentage than expected (see the Experimental section). In only one case was the result in agreement with the calculated composition. The same results were found for pGlcEMA(A) and pGlcEMA(B). It should be noted that deprotection could not be continued to completion due to precipitation of the partially deprotected polymers from solution. Moreover, cleavage of the methacrylate ester bonds could occur during the deacetylation of pAcGlcEMA and pAcGalEMA, leading to polymers containing methyl ester and/or acid functionalities in the side chains. While there is no clear evidence to support this, the  $^1H$ -NMR spectrum of pGalEMA(B) contains many more weak signals just above the baseline, indicating more impurities than in pGalEMA(A) (Fig. 2). Some of these resonances are in regions where the OMe signals of methyl methacrylate units would be expected ( $\delta \approx 3.5$ ).

Absolute relative molecular masses of the deprotected polymers were determined by SEC in aqueous solution and the obtained values are reported in Table 1. The refractive-index increments,  $dn/dc$ , were determined by means of a differential refractometer, working under the same experimental conditions as used for the SEC measurements. Values of  $0.131\ ml\ g^{-1}$ ,  $0.140\ ml\ g^{-1}$ ,  $0.126\ ml\ g^{-1}$  and  $0.146\ ml\ g^{-1}$  for pGlcEMA(A), pGalEMA(A), pGlcEMA(B) and pGalEMA(B), respectively, were obtained.

The average molar mass values of **5bA** are much higher than those of **5aA**, which may be indicative of a tendency of the former to aggregate more strongly in aqueous solution (it was noticed that aqueous solutions of the deprotected polymers had a tendency to froth). However, more surprising is the difference in average molar mass values of deprotected polymers prepared by route B compared with their parent polymers (compare **5aB** with **4a** and **5bB** with **4b**). While a reduction in relative molecular mass is expected due to removal of four acetyl groups per sugar residue, this alone cannot account for the differences observed in  $M_n$  and  $M_w$  between **5B** and **4**. Scission of polymer chain C–C bonds during deprotection is an unlikely explanation. The average molar mass values for **5B** polymers may in fact be artefacts of the polymer-deprotection procedure. During the deprotection, a white polymeric precipitate is produced, which is collected as the product. Since the chains become less soluble in the reaction medium as the extent of deprotection of each chain increases, precipitation of shorter chains is likely to occur before that of longer chains. Therefore, we may have inadvertently fractionated our polymer samples during deprotection, leaving the longer chains in solution. This serves to highlight the differences between the glycopolymer preparation routes and reinforces our belief in the unreliability of the polymer deprotection route (B).

## Experimental

### General

2,3,4,6-Tetra-*O*-acetyl- $\alpha$ -D-glucopyranosyl bromide (>95%) and 2,3,4,6-tetra-*O*-acetyl- $\alpha$ -D-galactopyranosyl bromide ( $\approx$ 95%)

were purchased from Sigma and Fluka, respectively. 2-Hydroxyethyl methacrylate (HEMA, >99%), silver trifluoromethanesulfonate (>99%), acetic anhydride (>99%), potassium persulfate (>99%), pyridine (99.8%), methanol (99.8%) and cation-exchange resin DOWEX  $\times$  50W  $\times$  2-200 were purchased from Aldrich. 2,2'-Azobisobutyronitrile (AIBN, 97%) was obtained from BDH Laboratory Supplies. HEMA was purified by distillation under vacuum; dichloromethane (DCM) was distilled from calcium hydride under  $N_2$ ; all other chemicals were used without further purification.

NMR spectra were recorded with a Varian Inova 500 spectrometer, operating at 499.78 ( $^1H$ ) and at 125.67 MHz ( $^{13}C$ ). IR spectra were obtained with a Perkin-Elmer 1600 Series FTIR spectrometer. Mass spectra were obtained with a Micromass Platform spectrometer and with a Micromass LCT spectrometer, ionisation modes ES+ or ES-. Size-exclusion chromatography (SEC) of pAcGlcEMA and of pAcGalEMA was performed with a Viscotek 200 + light scattering, in THF, using a Plgel 10  $\mu$  MIXED-B column and working with a flow rate of 1.000 ml  $min^{-1}$  and an injection volume of 100  $\mu$ l. Absolute molecular masses of pGlcEMA(A,B) and pGalEMA(A,B) were determined by aqueous size-exclusion chromatography coupled to a Water 410 RI detector and a Wyatt DAWN DSP MALLS, using a TSK GMPW column (30 cm  $\times$  7.8 mm id). The mobile phase consisted of 80% HPLC-grade water, 20% methanol, 0.05 M  $NaNO_3$  and 2.5 ml  $l^{-1}$  1.0 M NaOH at a flow rate of 0.8 ml  $min^{-1}$ . The MALLS detectors were normalised using 50K pullulan purchased from Gearing Scientific. All polymer samples were prepared as 0.2–0.6 wt% solutions and filtered through 0.2  $\mu$ m filters. Molecular mass averages and polydispersity were calculated using Astra 32 software. The  $dn/dc$  values used were previously determined using a model BP-2000-V Brice-Phoenix Visual Laboratory Type Differential Refractometer, Phoenix Precision Instrument Company, Pennsylvania (USA); four solutions of concentration ranging between ca.  $\approx$ 4% and 15% in 20% methanol, 80% 0.05 M  $NaNO_3$  and 2.5 ml  $l^{-1}$  1.0 M NaOH solution were prepared for each polymer and the measurements carried out at 25  $^\circ$ C. Optical rotations were estimated using a P-1020 Series Polarimeter, JASCO (UK) Ltd.  $[a]_D$ -Values are in units of  $10^{-1}$  deg  $cm^2$   $g^{-1}$ . Elemental analyses were obtained with an Exeter Analytical Inc. CE-440 Elemental Analyzer. Products were freeze-dried using a Christ ALPHA-1-4 freeze-dryer with controller LDC-1M.

#### X-Ray crystallography †

The diffraction experiment (nominally covering the full sphere of reciprocal space) was carried out at  $T = 100$  K on a SMART 3-circle diffractometer with a 1K CCD area detector, ‡ using graphite-monochromated Mo- $K_\alpha$  radiation ( $\lambda = 0.71073$  Å) and a Cryostream (Oxford Cryosystems) open-flow  $N_2$  gas cryostat.

**Crystal data.**  $C_{20}H_{28}O_{12}$ ,  $M$  460.42, orthorhombic, space group  $P2_12_12_1$  (No. 19),  $a = 8.442(2)$ ,  $b = 12.466(4)$ ,  $c = 21.904(7)$  Å,  $V = 2305(1)$  Å $^3$ ,  $Z = 4$ ,  $D_x = 1.33$  g  $ml^{-1}$ ,  $\mu = 0.11$  mm $^{-1}$ . 28 228 Reflections were measured ( $2\theta < 58^\circ$ ; of these 3451 were independent and 2631 were Friedel equivalents thereof [5679 and 2430 respectively with  $I \geq 2\sigma(I)$ ]). The structure was solved by direct methods and refined by full-matrix least squares against  $F^2$  of all data, using SHELXTL software.§ All non-hydrogen atoms were refined in anisotropic approximation, the

H-atoms on C(12) isotropically, methyl groups as rigid bodies (with a common refined  $U$  for three H-atoms); other H-atoms were treated in a 'riding' model. Final  $R = 0.037$  for data with  $I \geq 2\sigma(I)$ ,  $wR(F^2) = 0.097$  for all data. The absolute configuration could not be determined and was assigned from the known one of the starting material. Full data (excluding structure factors) have been deposited at the Cambridge Crystallographic Data Centre.

#### Monomer and polymer syntheses

**2-(2',3',4',6'-Tetra-*O*-acetyl- $\beta$ -D-glucosyloxy)ethyl methacrylate, AcGlcEMA 1a.** To a stirred solution of 2,3,4,6-tetra-*O*-acetyl- $\alpha$ -D-glucopyranosyl bromide (10 g, 24.3 mmol) and an excess of HEMA (9.5 g, 72.8 mmol) in dry DCM at  $-40$   $^\circ$ C under  $N_2$  containing 3 Å powdered molecular sieves (12 g), was added an excess of silver trifluoromethanesulfonate (7.5 g, 29.2 mmol) and the reaction mixture was stirred under the same conditions for 48 h. After this time the mixture was gradually allowed to reach room temperature and was then filtered through Celite. After evaporation of the solvent, the residue (10.9 g) was dissolved in a mixture of pyridine (250 ml) and acetic anhydride (100 ml) and stirred under  $N_2$  overnight in order to acetylate unchanged HEMA and so aid purification. After evaporation of the solvent the residue was dissolved in DCM (250 ml), washed successively with hydrochloric acid (0.25 M, aliquots of 100 ml), saturated aq.  $NaHCO_3$  (aliquots of 100 ml) and brine (100 ml) and dried over  $Na_2SO_4$ . The solvent was removed, and the residue was then purified by flash chromatography (ethyl acetate–hexane, 3 : 7) to afford the product **1a** (8.3 g, 72%) as colourless plate-like crystals suitable for X-ray analysis; mp 77–79  $^\circ$ C (lit.<sup>5</sup> 77.5  $^\circ$ C);  $[a]_D^{28} = -12.8$  ( $c$  0.14 in  $CHCl_3$ ) {lit.<sup>5</sup>  $[a]_D^{15} = -12.7$  (0.015 mol  $l^{-1}$  in  $CHCl_3$ )}. (Found: C, 52.11; H, 6.19.  $C_{20}H_{28}O_{12}$  requires C, 52.17; H, 6.13%); IR (KBr disc)  $\nu/cm^{-1}$  1758 (C=O of *O*-acetyl groups), 1718 (C=O of HEMA moiety), 1635, 1321, 1299 (C=C);  $\delta_H^\parallel$  (500 MHz;  $CDCl_3$ ) 1.99 (3H, s, 3  $\times$  H-3), 2.00, 2.01, 2.03, 2.07 (3H  $\times$  4, 4s Ac  $\times$  4), 3.68 (1H, ddd,  $J_{4',5'}$  10.5 Hz,  $J_{5',6a'}$  2.5 Hz,  $J_{5',6b'}$  4.5 Hz, H-5'), 3.81 (1H, ddd,  $J_{6a,6b}$  11.5 Hz,  $J_{5a,6a}$  7.0 Hz,  $J_{5b,6a}$  3.5 Hz, H-6a), 4.04 (1H, ddd,  $J_{6a,6b}$  11.5 Hz,  $J_{5a,6b} = J_{5b,6b} = 5.0$  Hz, H-6b), 4.12 (1H, dd,  $J_{6a',6b'}$  12.2 Hz,  $J_{5',6a'}$  2.5 Hz, H-6'a), 4.25 (1H, dd,  $J_{6a',6b'}$  12.2 Hz,  $J_{5',6b'}$  4.5 Hz, H-6'b), 4.23–4.32 (2H, m, 2  $\times$  H-5a,b), 4.56 (1H, d,  $J_{1',2'}$  7.9 Hz, H-1'), 4.99 (1H, dd,  $J_{1',2'}$  7.7 Hz,  $J_{2',3'}$  9.7 Hz, H-2'), 5.07 (1H, t,  $J$  9.7 Hz, H-4'), 5.18 (1H, t,  $J$  9.5 Hz, H-3'), 5.57–5.59 (1H, m, H-1 Z to  $CH_3$ –C=C), 6.10–6.12 (1H, m, H-1 E to  $CH_3$ –C=C); NOESY correlation studies allowed the differentiation between H-1(Z) and H-1(E) due to the long range coupling of H-1(Z) with 3  $\times$  H-3; NOESY also allowed the differentiation between 2  $\times$  H-5 and 2  $\times$  H-6 due to the long-range coupling of H-6 with H-1';  $\delta_C$  (125.67 MHz, decoupled  $^1H$  500 MHz;  $CDCl_3$ ) 18.2 (C-3); 20.5, 20.6 ( $H_3CCOO \times 4$ ), 61.8 (C-6'), 63.3 (C-5), 67.4 (C-6), 68.2 (C-4'), 71.0 (C-2'), 71.8 (C-5'), 72.6 (C-3'), 100.7 (C-1'), 125.8 (C-1), 135.9 (C-2), 167.1 (C-4), 169.2, 169.3, 170.2, 170.6 ( $H_3CCOO \times 4$ ); results of HETCOR and COSY correlation studies have been used in order to assign the observed signals to the hydrogen and carbon atoms of the compound; LRMS  $m/z$  (ES+): Found: 483.5 (M + Na) $^+$ , 100%.

**2-(2',3',4',6'-Tetra-*O*-acetyl- $\beta$ -D-galactosyloxy)ethyl methacrylate, AcGalEMA 1b.** 2,3,4,6-Tetra-*O*-acetyl- $\alpha$ -D-galactopyranosyl bromide (10 g, 24.3 mmol) and an excess of HEMA (9.5 g, 72.8 mmol) were allowed to react and the resulting product purified as described for **1a**, to afford product **1b** (8.9 g, 80%) as a viscous, colourless oil;  $[a]_D^{28} = -5.5$  ( $c$  0.25 in  $CHCl_3$ ) (Found: C, 51.94; H, 6.03.  $C_{20}H_{28}O_{12}$  requires C, 52.17; H, 6.13%); IR (Nujol)  $\nu/cm^{-1}$  1756 (C=O of acetate groups), 1724 (C=O of HEMA moiety), 1632, 1320, 1295 (C=C);  $\delta_H^\parallel$

¶ See Scheme 1 for numbering scheme.

† CCDC reference number 171347. See <http://www.rsc.org/suppdata/p1/b1/b108421f/> for crystallographic files in .cif or other electronic format.

‡ SMART and SAINT, Area Detector Control and Integration Software. Version 6.0. Bruker AXS, Madison, Wisconsin, USA, 1999.

§ SHELXTL, An Integrated System for Solving, Refining and Displaying Crystal Structures from Diffraction Data, Version 5.10. Bruker AXS, Madison, Wisconsin, USA, 1997.

(500 MHz; CDCl<sub>3</sub>) 1.96 (3H, s, 3 × H-3), 1.99, 2.02, 2.03, 2.13 (3H × 4, s, Ac × 4), 3.82 (1H, ddd,  $J_{6a,6b}$  11.5 Hz,  $J_{5a,6a}$  7.5 Hz,  $J_{5b,6a}$  4.0 Hz, H-6a), 3.90 (1H, td,  $J_t = J_{5',6a'} = J_{5',6b'} = 6.5$  Hz,  $J_d = J_{4',5'} = 1.1$  Hz, H-5'), 4.04 (1H, ddd,  $J_{6a',6b'}$  11.5 Hz,  $J_{5a,6b} = J_{5b,6b} = 5.0$  Hz, H-6b), 4.10 (1H, dd,  $J_{6a',6b'}$  10.3 Hz,  $J_{5',6a'}$  6.7 Hz, H-6'a), 4.14 (1H, dd,  $J_{6a',6b'}$  10.9 Hz,  $J_{5',6b'}$  6.5 Hz, H-6'b), 4.26 (1H, ddd,  $J_{5a,5b}$  12.0 Hz,  $J_{5a,6a}$  7.5 Hz,  $J_{5a,6b}$  4.5 Hz, H-5a), 4.31 (1H, ddd,  $J_{5a,5b}$  12.5 Hz,  $J_{5b,6a} = J_{5b,6b} = 5.0$  Hz, H-5b), 4.52 (1H, d,  $J_{1',2'}$  8.0 Hz, H-1'), 4.98 (1H, dd,  $J_{2',3'}$  10.5 Hz,  $J_{3',4'}$  3.5 Hz, H-3'), 5.19 (1H, dd,  $J_{1',2'}$  8.0 Hz,  $J_{2',3'}$  10.5 Hz, H-2'), 5.36 (1H, dd,  $J_{3',4'}$  3.5 Hz,  $J_{4',5'}$  1.0 Hz, H-4'), 5.57–5.58 (1H, m, H-1 Z to CH<sub>3</sub>–C=C), 6.10–6.11 (1H, m, H-1 E to CH<sub>3</sub>–C=C);  $\delta_C$  (125.67 MHz, decoupled <sup>1</sup>H 500 MHz; CDCl<sub>3</sub>) 18.2 (C-3), 20.5, 20.6 (H<sub>3</sub>CCOO × 4), 61.2 (C-6'), 63.4 (C-5), 66.9 (C-4'), 67.3 (C-6), 68.5 (C-2'), 70.6 (C-3'), 70.8 (C-5'), 101.2 (C-1'), 125.8 (C-1), 136.0 (C-2), 167.0 (C-4), 169.3, 170.1, 170.2, 170.3 (H<sub>3</sub>CCOO × 4); results of HETCOR and COSY correlation studies have been used in order to assign the observed signals to the hydrogen and carbon atoms of the compound; LRMS  $m/z$  (ES+): Found: 483.3 (M + Na)<sup>+</sup>, 100%.

**2-Acetoxyethyl methacrylate, AcEMA 2.** Colourless oil;  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 1.92–1.93 (3H, m, CH<sub>3</sub>–C=C), 2.05 (3H, s, CH<sub>3</sub>–C=O), 4.26–4.36 (4H, m, CH<sub>2</sub>CH<sub>2</sub>), 5.56–5.58 (1H, m, vinyl proton Z to CH<sub>3</sub>–C=C), 6.10 (1H, m, vinyl proton E to CH<sub>3</sub>–C=C); LRMS  $m/z$  (ES+): Found: 195 (M + Na)<sup>+</sup>, 100%, 211 (M + K)<sup>+</sup>, 10.

**2-(β-D-Glucosyloxy)ethyl methacrylate, GlcEMA 3a.** **1a** (2 g, 4.3 mmol) was dissolved in 10 ml of dry methanol and the obtained solution was stirred for 15 min at room temperature under N<sub>2</sub>. Then, 1 ml of freshly prepared 0.03 M sodium methoxide in methanol was added. The solution was stirred at room temperature and continuously monitored by TLC (acetonitrile–water, 9 : 1). The reaction was stopped after 40 min when the formation of the product resulting from the cleavage of the ester bond of HEMA moiety was observed ( $R_f = 0.2$ ). Cation-exchange resin (DOWEX 50W × 2-200) was added in order to bring the pH to neutral and to remove Na<sup>+</sup> cations. The solution was stirred for 15 min before filtration to remove the resin. After evaporation of the solvent, the residue was purified by flash chromatography (chloroform–methanol, 8 : 2) to afford **3a** as a viscous, colourless oil that gave a strongly hygroscopic amorphous colourless solid after freeze-drying (1 g, 80%);  $[\alpha]_D^{20} = -22.5$  (*c* 0.20 in CH<sub>3</sub>OH) (Found: C, 48.99; H, 7.01. C<sub>12</sub>H<sub>20</sub>O<sub>8</sub> requires C, 49.31; H, 6.90%); IR (KBr disc)  $\nu/cm^{-1}$  3364 (OH), 1715 (C=O of HEMA moiety), 1635, 1320, 1298 (C=C);  $\delta_H$  (500 MHz; CD<sub>3</sub>OD) 1.93 (3H, m, 3 × H-3), 3.17 (1H, dd,  $J_{1',2'}$  8.0 Hz,  $J_{2',3'}$  9.5 Hz, H-2'), 3.25–3.35 (3H, m, H-3', H-4', H-5'), 3.65 (1H, dd,  $J_{6a',6b'}$  12.0 Hz,  $J_{5',6a'}$  5.5 Hz, H-6'a), 3.83 (1H, ddd,  $J_{6a,6b}$  11.5 Hz,  $J_{5a,6a}$  6.0 Hz,  $J_{5b,6a}$  3.5 Hz, H-6a), 3.84 (1H, dd,  $J_{6a',6b'}$  11.7 Hz,  $J_{5',6b'}$  1.7 Hz, H-6'b), 4.09 (1H, ddd,  $J_{6a,6b}$  11.5 Hz,  $J_{5a,6b}$  4.0 Hz,  $J_{5b,6b}$  6.0 Hz, H-6b), 4.29 (1H, ddd,  $J_{5a,5b}$  12.0 Hz,  $J_{5a,6a}$  5.5 Hz,  $J_{5a,6b}$  3.5 Hz, H-5a), 4.30 (1H, d,  $J_{1',2'}$  8.0 Hz, H-1'), 4.34 (1H, ddd,  $J_{5a,5b}$  12.0 Hz,  $J_{5b,6a}$  3.5 Hz,  $J_{5b,6b}$  6.0 Hz, H-5b), 5.61–5.62 (1H, m, H-1 Z to CH<sub>3</sub>–C=C), 6.11–6.12 (1H, m, H-1 E to CH<sub>3</sub>–C=C);  $\delta_C$  (125.67 MHz, decoupled <sup>1</sup>H 500 MHz; CD<sub>3</sub>OD) 18.4 (C-3), 62.7 (C-6'), 65.3 (C-5), 68.6 (C-6), 71.6 (C-3' or C-4' or C-5'), 75.0 (C-2'), 78.0 (2C, C-3' or C-4' or C-5'), 104.6 (C-1'), 126.4 (C-1), 137.6 (C-2), 168.9 (C-4) [HRMS  $m/z$  (ES+): Found: 315.1049 (M + Na)<sup>+</sup>. C<sub>12</sub>H<sub>20</sub>NaO<sub>8</sub> requires  $m/z$ , 315.1056].

**2-(β-D-Galactosyloxy)ethyl methacrylate, GalEMA 3b.** **1b** (2 g, 4.3 mmol) was treated using an identical procedure to that described in the preparation of **3a**, to afford **3b** as a viscous, colourless oil that gave a strongly hygroscopic, amorphous, colourless solid after freeze-drying (0.95 g, 75%);  $[\alpha]_D^{20} = -5.5$  (*c* 0.20 in CH<sub>3</sub>OH) [Found: C, 48.34; H, 6.96. (C<sub>12</sub>H<sub>20</sub>O<sub>8</sub> + 0.3 mol H<sub>2</sub>O) requires C, 48.42; H, 6.97%]; IR (KBr disc)  $\nu/cm^{-1}$  3384

(OH), 1712 (C=O of HEMA moiety), 1636, 1320, 1298 (C=C);  $\delta_H$  (500 MHz; CD<sub>3</sub>OD) 1.93 (3H, m, 3 × H-3), 3.45 (1H, dd,  $J_{2',3'}$  9.7 Hz,  $J_{3',4'}$  3.3 Hz, H-3'), 3.50 (1H, td,  $J_t = J_{5',6a'} = J_{5',6b'} = 5.5$  Hz,  $J_d = J_{4',5'} = 1.0$  Hz, H-5'), 3.52 (1H, dd,  $J_{1',2'}$  7.5 Hz,  $J_{2',3'}$  10.0 Hz, H-2'), 3.71 (1H, dd,  $J_{6a',6b'}$  11.0 Hz,  $J_{5',6a'}$  5.5 Hz, H-6'a), 3.74 (1H, dd,  $J_{6a',6b'}$  11.0 Hz,  $J_{5',6b'}$  7.0 Hz, H-6'b), 3.82 (1H, dd,  $J_{3',4'}$  3.3 Hz,  $J_{4',5'}$  0.7 Hz, H-4'), 3.84 (1H, ddd,  $J_{6a,6b}$  12.0 Hz,  $J_{5a,6a}$  6.0 Hz,  $J_{5b,6a}$  4.0 Hz, H-6a), 4.10 (1H, ddd,  $J_{6a,6b}$  12.0 Hz,  $J_{5a,6b}$  3.7 Hz,  $J_{5b,6b}$  6.0 Hz, H-6b), 4.26 (1H, d,  $J_{1',2'}$  7.5 Hz, H-1'), 4.31 (1H, ddd,  $J_{5a,5b}$  12.0 Hz,  $J_{5a,6a}$  6.0 Hz,  $J_{5a,6b}$  3.5 Hz, H-5a), 4.35 (1H, ddd,  $J_{5a,5b}$  12.0 Hz,  $J_{5b,6a}$  3.5 Hz,  $J_{5b,6b}$  6.0 Hz, H-5b), 5.61–5.62 (1H, m, H-1 Z to CH<sub>3</sub>–C=C), 6.12 (1H, m, H-1 E to CH<sub>3</sub>–C=C);  $\delta_C$  (125.67 MHz; decoupled <sup>1</sup>H 500 MHz; CD<sub>3</sub>OD) 18.4 (C-3), 62.5 (C-6'), 65.3 (C-5), 68.5 (C-6), 70.3 (C-4'), 72.4 (C-2'), 74.9 (C-3'), 76.7 (C-5'), 105.3 (C-1'), 126.4 (C-1), 137.7 (C-2), 168.8 (C-4) [HRMS  $m/z$  (ES+): Found: 315.1065 (M + Na)<sup>+</sup>. C<sub>12</sub>H<sub>20</sub>NaO<sub>8</sub> requires  $m/z$ , 315.1056].

**Poly[2-(2',3',4',6'-tetra-O-acetyl-β-D-glucosyloxy)ethyl methacrylate], pAcGlcEMA 4a.** A solution of **1a** (2 g, 4.3 mmol) and AIBN (20 mg, 1 wt%) in chloroform was degassed by bubbling N<sub>2</sub> through for 15 min at room temperature. Then, the flask was sealed and the polymerisation carried out at 65 °C for 48 h. The resulting viscous solution was poured into 10 times excess of diethyl ether in order to precipitate the polymer. The product was then purified by re-precipitation from chloroform in diethyl ether to obtain **4a** (1.9 g, 95%) as a white solid;  $[\alpha]_D^{22} = -11.7$  (*c* 0.11 in CHCl<sub>3</sub>) [lit.,<sup>10</sup> –10.3 (0.015 mol l<sup>-1</sup> in benzene)] [Found: C, 52.03; H, 6.17. (C<sub>20</sub>H<sub>28</sub>O<sub>12</sub>)<sub>m</sub> requires C, 52.17; H, 6.13%]; IR (KBr disc)  $\nu/cm^{-1}$  2960 (CH<sub>2</sub>), 1756 (C=O of acetate groups);  $\delta_H$  (500 MHz; CDCl<sub>3</sub>) 0.75–1.15 (3H, br m, CH<sub>3</sub>–C), 1.60–2.27 (2H, br, CH<sub>2</sub>), 2.01, 2.03, 2.06, 2.10 (12H, 4 s, Ac × 4), 3.70–3.88, 3.95–4.07, 4.10–4.25, 4.99–5.03, 5.08–5.18, 5.20–5.28 (10H, protons of the carbohydrate residue and the methylene groups of the side chains), 4.66 (1H, br, anomeric proton);  $\delta_C$  (125.67 MHz, decoupled <sup>1</sup>H 500 MHz; CDCl<sub>3</sub>) 6.5, 18.2 (1C, br, CH<sub>3</sub>–C, racemic–racemic (rr) and *meso*–racemic (mr) triads, respectively), 20.6, 20.7, 20.8 (4C, H<sub>3</sub>CCOO × 4), 45.2 (1C, CH<sub>2</sub>), 52.2–55.6 (1C, br, CH<sub>3</sub>–C), 61.1 (1C, carbohydrate residue of the side chains), 63.6 (1C, CH<sub>2</sub>O-carbohydrate residue), 66.6 (1C, CH<sub>2</sub>OCO), 67.3, 69.1, 70.6, 70.8 (4C, carbohydrate residue of the side chain), 100.5 (1C, anomeric carbon), 169.3, 170.0, 170.3 (4C, H<sub>3</sub>CCOO × 4), 176.5, 176.9–177.8 (1C, br, CCOO, *meso*–racemic (mr) and racemic–racemic (rr) triads, respectively); results of HETCOR correlation studies have been used in order to assign the observed signals to hydrogen and carbon atoms of the compound.

**Poly[2-(2',3',4',6'-tetra-O-acetyl-β-D-galactosyloxy)ethyl methacrylate], pAcGalEMA 4b.** **1b** (2 g, 4.3 mmol) was polymerised in an identical procedure to that described for **4a**, to obtain **4b** (1.86 g, 93%) as a white solid;  $[\alpha]_D^{22} = -12.2$  (*c* 0.11 in CHCl<sub>3</sub>) [Found: C, 51.92; H, 6.26. (C<sub>20</sub>H<sub>28</sub>O<sub>12</sub>)<sub>m</sub> requires C, 52.17; H, 6.13%]; IR (KBr disc)  $\nu/cm^{-1}$  2960 (CH<sub>2</sub>), 1752 (C=O of acetate groups);  $\delta_H$  (500 MHz; CDCl<sub>3</sub>) 0.78–1.16 (3H, br m, CH<sub>3</sub>–C), 1.63–2.20 (2H, br, CH<sub>2</sub>), 1.98, 2.05, 2.06, 2.16 (12H, 4 s, Ac × 4), 3.71–3.83, 3.95–4.09, 4.10–4.24, 5.05–5.21, 5.37–5.43 (10H, protons of the carbohydrate residue and the methylene groups of the side chains), 4.62 (1H, br, anomeric proton);  $\delta_C$  (125.67 MHz; decoupled <sup>1</sup>H 500 MHz; CDCl<sub>3</sub>) 17.4, 18.9 (1C, br, CH<sub>3</sub>–C, racemic–racemic (rr) and *meso*–racemic (mr) triads, respectively), 20.8, 20.9, 21.0 (4C, H<sub>3</sub>CCOO × 4), 45.2 (1C, CH<sub>2</sub>), 52.5–56.1 (1C, br, CH<sub>3</sub>–C), 61.3 (1C, carbohydrate residue of the side chains), 63.6 (1C, CH<sub>2</sub>O-carbohydrate residue), 66.6 (1C, CH<sub>2</sub>OCO), 67.3, 68.9, 70.9, 71.0 (4C, carbohydrate residue of the side chain), 101.1 (1C, anomeric carbon), 169.5, 170.2, 170.5 (4C, H<sub>3</sub>CCOO × 4), 176.5, 177.1–177.8 (1C, br, CCOO, racemic–racemic (rr) and

*meso*-racemic (mr) triads, respectively); results of HETCOR correlation studies have been used in order to assign the observed signals to hydrogen and carbon atoms of the compound.

#### Poly[2-( $\beta$ -D-glucosyloxy)ethyl methacrylate], pGlcEMA **5a**.

**Synthesis A.** A solution of **3a** (1 g, 3.4 mmol) and  $K_2S_2O_8$  (25 mg, 2.5 wt%) in a mixture of high-purity water-methanol (4 : 1) was degassed by bubbling  $N_2$  through for 15 min at room temperature. Then, the flask was sealed and the polymerisation was carried out at 65 °C for 48 h. The resulting solution was freeze-dried and the recovered polymer was then purified by dialysis against water (Dialysis Tubing-Visking, Size 20 Inf. Dia. 18/32" (14.3 mm): 30 M, MWCO-12-14 000 Daltons) for 1 week. The solution was freeze-dried to afford **5a** (0.82 g, 82%) as a white hygroscopic solid;  $[\alpha]_D^{22} -14.8$  (*c* 0.12 in water); {Found: C, 48.82; H, 6.92.  $[(C_{12}H_{20}O_8)_m + 0.1 \text{ mol } H_2O]$  requires C, 49.01; H, 6.92%}; IR (KBr disc)  $\nu/cm^{-1}$  3446 (OH), 1718 (C=O of HEMA moiety);  $\delta_H$  (500 MHz;  $D_2O$ ) 0.73-1.22 (3H, br m,  $CH_3-C$ ), 1.78-2.22 (2H, br,  $CH_2$ ), 3.25-3.53, 3.67-3.76, 3.86-3.98, 4.08-4.32 (10H, protons of the carbohydrate residue and of the methylene groups of the side chains), 4.47 (1H, d, *J* 7.5 Hz, anomeric proton);  $\delta_C$  (125.67 MHz; decoupled  $^1H$  500 MHz;  $D_2O$ ) 17.2, 18.8, 21.2 (1C, br,  $CH_3-C$ , racemic-racemic (rr), *meso*-racemic (mr) and *meso*-*meso* (mm) triads, respectively), 45.0 (1C,  $CH_2$ ), 51.0-53.7 (1C, br,  $CH_3-C$ ), 61.1 (1C, carbohydrate residue of the side chains), 65.1 (1C,  $CH_2O$ -carbohydrate residue), 67.3 (1C,  $CH_2OCO$ ), 69.9, 73.3, 76.0, 76.1 (4C, carbohydrate residue of the side chain), 102.7 (1C, anomeric carbon), 178.9, 179.7-180.0 (1C, br,  $CCOO$ , *meso*-racemic (mr) and racemic-racemic (rr) triads, respectively).

**Synthesis B.** A solution of **4a** (0.20 g) in  $CHCl_3-CH_3OH$  (1 : 1, 8 ml) was stirred at room temperature under  $N_2$  for 15 min. Then, 1 ml of a freshly prepared 1 M solution of sodium methoxide in methanol was added and the formation of a white precipitate was observed after around 30 s. After stirring at room temperature under  $N_2$  for 1 h, the solid was filtered off, dissolved in water, and a cation-exchange resin (DOWEX 50W  $\times$  2-200) was added in order to remove  $Na^+$  cations. The solution was stirred for 15 min before filtration to remove the resin. After purification by dialysis against water, the solution was freeze-dried to afford **5a** (0.80 g, 63%) as a white hygroscopic solid [Found: C, 51.26; H, 6.69.  $(C_{12}H_{20}O_8)_m$  requires C, 49.31; H, 6.90%. Assuming that two *O*-acetyl groups were still present after the deprotection:  $(C_{16}H_{24}O_{10})_m$  would require C, 51.06; H, 6.43%]; IR (KBr disc)  $\nu/cm^{-1}$  3423 (OH), 1718 (C=O of HEMA moiety);  $\delta_H$  (500 MHz;  $D_2O$ ) 0.75-1.18 (3H, br m,  $CH_3-C$ ), 1.72-2.22 (2H, br,  $CH_2$ ), 2.06, 2.17, 2.20 (methyl protons of *O*-acetyl groups still present after the deprotection), 3.31-3.52, 3.72, 3.92, 4.05-4.36 (10H, protons of the carbohydrate residue and of the methylene groups of the side chains), 4.48 (1H, d, *J* 7 Hz, anomeric proton);  $\delta_C$  (125.67 MHz; decoupled  $^1H$  500 MHz;  $D_2O$ ) 17.3, 18.9 (1C, br,  $CH_3-C$ , racemic-racemic (rr) and *meso*-racemic (mr) triads, respectively), 45.0 (1C,  $CH_2$ ), 51.0-53.8 (1C, br,  $CH_3-C$ ), 61.1 (1C, carbohydrate residue of the side chains), 65.1 (1C,  $CH_2O$ -carbohydrate residue), 67.3 (1C,  $CH_2OCO$ ), 69.9, 73.3, 76.0, 76.1 (4C, carbohydrate residue of the side chain), 102.7 (1C, anomeric carbon), 178.8, 179.8-180.0 (1C, br,  $CCOO$ , *meso*-racemic (mr) and racemic-racemic (rr) triads, respectively).

#### Poly[2-( $\beta$ -D-galactosyloxy)ethyl methacrylate], pGalEMA **5b**.

**Synthesis A.** **3b** (1 g, 3.4 mmol) was polymerised and the resulting polymer was purified according to the procedure described in the synthesis of **5a** to afford **5b** (0.86 g, 86%) as a white hygroscopic solid;  $[\alpha]_D^{22} +8.0$  (*c* 0.10 in water) {Found: C, 48.82; H, 6.92.  $[(C_{12}H_{20}O_8)_m + 0.1 \text{ mol } H_2O]$  requires C, 49.03; H 6.91%}; IR (KBr disc)  $\nu/cm^{-1}$  3447 (OH), 1718 (C=O of HEMA moiety);  $\delta_H$  (500 MHz;  $D_2O$ ) 0.82-1.20 (3H, br m,  $CH_3-C$ ), 1.78-2.35 (2H, br,  $CH_2$ ), 3.52-3.59, 3.62-3.72, 3.72-

3.85, 3.89-4.02 4.06-4.35 (10H, protons of the carbohydrate residue and of the methylene groups of the side chains), 4.43 (1H, d, *J* 6.5 Hz, anomeric proton);  $\delta_C$  (125.67 MHz; decoupled  $^1H$  500 MHz;  $D_2O$ ) 17.2, 18.9 (1C, br,  $CH_3-C$ , racemic-racemic (rr) and *meso*-racemic (mr) triads, respectively), 45.0 (1C,  $CH_2$ ), 52.0-53.8 (1C, br,  $CH_3-C$ ), 61.1 (1C, carbohydrate residue of the side chains), 65.0 (1C,  $CH_2O$ -carbohydrate residue), 67.1 (1C,  $CH_2OCO$ ), 68.8, 70.9, 73.0, 75.3 (4C, carbohydrate residue of the side chain), 103.2 (1C, anomeric carbon), 178.9, 179.8-180.0 (1C, br,  $CCOO$ , *meso*-racemic (mr) and racemic-racemic (rr) triads, respectively), 182.1 (COOH due to cleavage of the ester bond of the side chains).

**Synthesis B.** **4b** (0.20 g) was deprotected and the resulting polymer purified as for **4a** to afford **5b** (0.83 g, 65%) as a white hygroscopic solid [Found: C, 51.20; H, 6.75.  $(C_{12}H_{20}O_8)_m$  requires C, 49.31; H, 6.90%. Assuming that two *O*-acetyl groups were still present after the deprotection  $(C_{16}H_{24}O_{10})_m$  would require C, 51.06; H, 6.43%. IR (KBr disc)  $\nu/cm^{-1}$  3445 (OH), 1718 (C=O of HEMA moiety);  $\delta_H$  (500 MHz;  $D_2O$ ) 0.76-1.16 (3H, br m,  $CH_3-C$ ), 1.76-2.24 (2H, br,  $CH_2$ ), 2.07, 2.14, 2.20 (methyl protons of *O*-acetyl groups still present after the deprotection), 3.56, 3.61-4.00, 4.12-4.32 (10H, protons of the carbohydrate residue and of the methylene groups of the side chains), 4.43 (1H, d, *J* 6.5 Hz, anomeric proton);  $\delta_C$  (125.67 MHz; decoupled  $^1H$  500 MHz;  $D_2O$ ) 17.2, 18.8, 20.3 (1C, br,  $CH_3-C$ , racemic-racemic (rr), *meso*-racemic (mr) and *meso*-*meso* (mm) triads, respectively), 23.8 (methyl carbon of *O*-acetyl groups still present after the deprotection), 45.0 (1C,  $CH_2$ ), 51.4-53.7 (1C, br,  $CH_3-C$ ), 61.1 (1C, carbohydrate residue of the side chains), 65.1 (1C,  $CH_2O$ -carbohydrate residue), 67.1 (1C,  $CH_2-OCO$ ), 68.7, 70.9, 73.0, 75.3 (4C, carbohydrate residue of the side chain), 103.2 (1C, anomeric carbon), 178.9, 179.7-180.0 (1C, br,  $CCOO$ , *meso*-racemic (mr) and racemic-racemic (rr) triads, respectively).

## Conclusions

Monomeric and polymeric methacrylate derivatives bearing  $\beta$ -D-glucopyranoside and  $\beta$ -D-galactopyranoside residues have been successfully synthesised in high yield and in an efficient stereocontrolled manner and have been fully characterised. Critically, it has been shown that deprotection of the polymers according to the methods used for all previous syntheses of poly(glyco-acrylates) and -methacrylates<sup>5,19-21</sup> results in an incomplete deacetylation and yields products of ill-defined composition. Instead, fully deacetylated, well-defined and pure materials could be obtained by the *novel* method of polymerisation of the deprotected monomers. Absolute number- and weight-average relative molecular masses have been determined for all the polymers synthesised.

A thorough comparison of all functional properties of these glycopolymers, including binding of the deprotected glycopolymers to specific receptor proteins (lectins) to assess their feasibility for the targeted delivery of bioactive species, is underway. Differences between the fully deprotected polymers obtained by route A and the partially acetylated polymers obtained by route B are expected.

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