Well-Defined Diblock Glycopolymers from RAFT Polymerization in Homogeneous Aqueous Medium

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ABSTRACT: Reversible addition−fragmentation chain transfer polymerization was applied to the synthesis of well-defined diblock glycopolymers carrying different cyclic carbohydrates on the two blocks. The macroRAFT agents poly(methyl 6-*O*-methacryloyl-α-D-glucoside) dithiobenzoate and poly(2-methacryloxyethyl glucoside) dithiobenzoate were prepared by RAFT polymerization of the corresponding glycomonomers with (4-cyanopentanoic acid)-4-dithiobenzoate as the chain transfer agent. The reactions were stopped around 85% conversion in order to preserve the highest possible end-of-chain-functionality and the glycopolymers were isolated by precipitation in methanol. Chain extension with 2-methacryloxyethyl glucoside and methyl 6-*O*-methacryloyl-α-D-mannoside afforded poly(methyl 6-*O*-methacryloyl-α-D-glucoside-*block*-2-methacryloxyethyl glucoside) and poly(2-methacryloxyethyl glucoside-*block*-methyl 6-*O*-methacryloyl-α-D-mannoside), respectively, having a predetermined molecular weight and narrow polydispersity (PDI ≤ 1.20). The structure of the prepared polymers was confirmed by proton and carbon NMR and their thermal properties investigated via DSC.

Introduction

Glycopolymers are synthetic polymers possessing a non-carbohydrate backbone but carrying carbohydrate moieties as pendant or terminal groups.[1,2] Since the pioneering work of Horejsi et al. on the precipitation of lectins by copolymers of acrylamide and allyl glycosides,[3] glycopolymers have raised an ever increasing interest in their use as artificial materials for a number of biological and biomedical uses. This is mostly due to the expectation that polymers displaying complex functionalities, similar to those found in natural glycoconjugates, might be able to mimic or even exceed their performance in specific applications (biomimetic approach). The presence of appropriate functional groups in a glycopolymer though is usually insufficient to bestow it with the biological and physicochemical properties required for a given application. Indeed, control of the macromolecular architecture has proved essential to enable sophisticated functions[4,5] and to draw a correlation between them and the polymer structure itself. For this reason, an increasing number of polymer chemists, biochemists, and carbohydrate chemists are approaching the synthesis of novel glycopolymers via precise polymerization techniques.[2,6−8]

Among other applications, glycopolymers displaying natural carbohydrates are being investigated as multivalent ligands to probe cell−surface interactions[5,9] and to inhibit viral binding.[10] A prerequisite for the sugar residues to take part in specific molecular recognition and binding events is that they are present in the same cyclic form occurring in natural glycoconjugates.[11] Accordingly, the possibility to prepare diblock glycopolymers carrying different cyclic carbohydrates on the two blocks would add a level of complexity to the design of the glycoligands used in these and other biological studies. The synthesis of AB diblock glycopolymers carrying diverse unprotected carbohydrates on the two blocks via atom transfer radical polymerization has already been reported by S. Armes and co-workers (M_n 18 100 and 21 200 Da, PDI 1.28−1.29).[12] In their study, though, only one of the two sugars was in a cyclic form, and no kinetic data were provided.

The use of reversible addition−fragmentation chain transfer polymerization (RAFT) to prepare diblock and triblock copolymers has already been reported in the literature.[13,14] Also, as part of our ongoing interested in macromolecular design,[15] the successful aqueous RAFT polymerization of a methacryloyl-derived glycomonomer up to quantitative conversion[16] as well as the first synthesis of a narrow polydispersity poly(vinyl ester)-like glycopolymer have been recently described.[17] In this study, we extend our previous findings to the synthesis of dithiobenzoyl-terminated glycopolymers and to their chain extension with vinyl glycomonomers carrying a different carbohydrate. To this aim, only unprotected monomers bearing cyclic sugars were used. The NMR and thermal characterization of the resulting diblock glycopolymers is also reported.

Experimental Section

Materials and Methods. Unless otherwise specified, all chemicals were reagent grade and used as received. 4,4′-Azobis(cyanopentanoic acid) (98%, Fluka), deuterium oxide (99.9%, Cambridge Isotopes), ethanol (spectroscopic grade, Aldrich), ethyl acetate (99.5%, Asia Pacific Specialty Chemicals), methanol-d_4 (99.9% D, Aldrich), and water (HPLC grade, Riedel de Haën) were used as received. The acetone and the acetonitrile (HPLC grade, APS) used for enzymatic synthesis

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Table 1. Summary of Reversible Addition-fragmentation Chain Transfer Polymerization Experiments[a]

run no.	monomer (concn (M))	RAFT agent (concn (mM))	reaction time (min)	convn (%)[b]	M_n (Da) theory[c]	M_n (Da) NMR[d]	M_n (Da) SEC[e]	M_w/M_n SEC[e]	polymer[f]
1	**2** (0.85)	CPADB (12)	300	85	15 600	17 900	21 200	1.12	$\mathbf{6}_{(67)}$
2	**5** (0.87)	CPADB (8.0)	91	83	26 600	34 200	25 600	1.12	$\mathbf{8}_{(116)}$
3	**5** (0.86)	$\mathbf{6}_{(67)}$ (3.9)	80	71	63 100	66 000	52 000	1.20	**7**
4	**4** (0.90)	$\mathbf{8}_{(116)}$ (2.6)	90	52	81 500	76 200	61 300	1.16	**9**

[a] Temperature 70 °C; solvent = water/ethanol ~9:1. Initiator concentration: run 1 and 2, 3.8 mM; run 3, 2.2 mM; run 4, 2.1 mM. M_n is the number-average molecular weight, M_w is the weight-average molecular weight, and CPADB is (4-cyanopentanoic acid)-4-dithiobenzoate. [b] Calculated via size exclusion chromatography from the relative area of monomer and polymer peaks according to eq 1. [c] Calculated using eq 3. [d] ^{1}H NMR, calculated from the ratio between the peak area of the RAFT agent end-of-chain aromatic protons and the peak area(s) of the glycoside anomeric proton. [e] Measured via size exclusion chromatography as polystyrene equivalent. [f] See Scheme 2 for structure; the subscript next to a compound number indicates DP_n as estimated by ^{1}H NMR.

were dried for 48 h on activated 4 Å molecular sieves prior to use. Flash chromatography was carried out with a 76 mm o.d. glass column loaded with 200 g of silica gel (60 Å, ≤ 63 μm, Fluka) and eluted at a flow rate of 5 cm min^{-1}. TLC analysis was performed on glass backed silica gel plates (60 Å, 5−17 μm, Macherey-Nagel); following solvent evaporation, the developed plates were immersed in a 20% H_2SO_4/ethanol solution and heated at 80 °C for 30 min for spots detection. 2-*O*-Methacryloxyethyl glucoside (Polysciences, 50% w/v water solution, anomeric ratio ~3:1) was purified by freeze-drying first (4 days) followed by flash chromatography (ethyl acetate/hexane/ethanol 6.5:2:1.5, R_f 0.20). After spectroscopic characterization, the compound was redissolved in water (HPLC grade, pH 7) to give a 1.00 M solution that was stored in a freezer (−18 °C). ESI-MS: calcd for $C_{12}H_{20}NaO_8$, 315.1; found, 315.1 (M + Na$^+$). ^{1}H NMR (300 MHz, CD_3OD, 30 °C) δ (ppm): 6.12 (s, 1 H, H-11$_Z$), 5.62 (m, 1 H, H-11$_E$), 4.84 (d, J = 3.7 Hz, H-1α), 3.10−4.40 (carbohydrate ring nuclei H-2 to H-5 α/β, plus H-7 and H-8), 1.94 (s, 3 H, H-12). ^{13}C NMR (300 MHz, CD_3OD, 30 °C) δ (ppm): 168.82 and 168.88 (C-9); 137.67 and 137.63 (C-10); 126.46 and 126.40 (C-11); 104.64 (C-1β); 100.44 (C-1α); 78.01, 75.02, 73.76, 73.50, 71.64, 71.60, 68.55, 67.01, 65.24, 65.00 (carbohydrate ring nuclei C-2 to C-5 α/β, plus C-7 and C-8); 62.76, 62.58 (C-6); 18.42 and 18.38 (C-12). Accurate volumes were measured with an automatic pipettor (Eppendorf Research, 200−1000 μL) calibrated with distilled water (22 °C, d_{H_2O} = 0.9878, mean error = 0.05%).

Analysis. NMR experiments were conducted on Bruker Avance DMX300, DMX500, and DMX600 spectrometers (resonance frequencies of 300.2, 500.1, and 600.1 MHz for ^{1}H nuclei and 75.5, 125.8, and 150.9 MHz for ^{13}C nuclei, respectively). Molecular weights and molecular weight distributions were measured by size exclusion chromatography (SEC) on a Shimadzu modular LC system comprising a DGU-12A solvent degasser, a LC-10AT pump, a SIL-10AD auto injector, a CTO-10A column oven and a RID-10A refractive index detector. The system was equipped with a 50 × 7.8 mm guard column and four 300 × 7.8 mm linear columns (Phenomenex 500, 10^3, 10^4, and 10^5 Å pore size; 5 μm particle size). *N*,*N*-Dimethylacetamide (HPLC, 0.03% w/v LiBr, 0.05% w/v BHT) was used as eluant at a flow rate of 1 mL min^{-1} while the column temperature was maintained at 40 °C. Polymer solutions (3−5 mg mL^{-1}) were injected in 50 μL volumes. Calibration was performed with narrow polydispersity polystyrene standards (Polymer Laboratories) in the range 0.5−1000 kDa, and SEC traces were elaborated with Cirrus 2.0 software (Polymer Laboratories). LC−MS analyses were performed with a ThermoMAT high-pressure liquid chromatography system consisting of a solvent degasser, a quaternary pump, an autoinjector and a dual-wavelength UV-detector and equipped with a C8 Luna reverse phase column (Phenomenex, 150 × 4.6 mm, 100 Å pore size, and 5 μm particle size). The system was interfaced to a Thermo Finnigan LCQ Deca ion-trap mass spectrometer (Thermo Finnigan, San José, CA) equipped with an atmospheric pressure-ionization source operated in nebulizer-assisted electro-spray mode (ESI). The instrument was calibrated with caffeine (Aldrich), MRFA (tetrapeptide, Thermo Finnigan), Ultramark 1621 (Lancaster) and polypropylene glycol (M_n 2700, Aldrich) in the mass range 195−3822 amu. All spectra were acquired in positive ion mode over the *m*/*z* range 100−1000 or 500−4000 with a spray voltage of 5 kV, a capillary voltage of 35 V, a tube lens offset of −30 V, and a capillary temperature of 275 °C. Nitrogen was used as sheath gas at a flow rate of 0.5 L min^{-1} and helium as the dumping gas. DSC measurements were carried out using a Perkin-Elmer DSC 7 attached to a Perkin-Elmer CCA 7 controlled cooling accessory and a TAC 7/DX thermal analysis controller. The temperature, heat flow and furnace control of the instrument were calibrated using cyclohexane and indium standards. Scans were performed under a nitrogen atmosphere using a heating rate of 10 °C min^{-1} and a cooling rate of 20 °C min^{-1}. T_g was calculated from the third heating scan as the temperature at which half the increase in heat capacity had occurred.

Synthesis of the Monomers. Methyl 6-*O*-Methacryloyl-α-D-glucoside (2) (6-*O*-MAMGlc). The title compound was prepared according to the described method (yield 70%) [16] and used as a 1.00 M water (HPLC grade, pH 7) solution.

Methyl 6-*O*-Methacryloyl-α-D-mannoside (4) (6-*O*-MAMMan). Methyl α-D-mannoside **3** (9.2 g, 0.047 mol), Novozym 435 (4.6 g), 2,6-di-*tert*-butyl-4-methylphenol (50 mg, 2.3×10^{-4} mol), and vinyl methacrylate (5.1 g, 0.044 mol) were introduced into a conical flask and suspended in acetonitrile (45 mL). The flask was sealed with a rubber septum and shaken at 200 rpm and 50 °C for 4 days, after which another 1.6 g of enzyme were added. The reaction was then allowed to proceed for 3 further days before stopping it by filtering off the enzyme. The filtrate was washed with methanol (100 mL) and the collected organic phases were rotary evaporated to dryness to yield a yellow-brown syrup. The gross product was then purified by flash chromatography (ethyl acetate/hexane/ethanol 6:3:1) and the collected fractions checked by TLC for the presence of the product (same eluant as for the column, R_f 0.30). The pooled fractions were then rotary evaporated to afford the title product as clear syrup. Yield: 5.6 g (48%). Alternatively, methyl α-D-mannoside (10 g, 0.051 mol), Novozym 435 (3.0 g), 2,6-di-*tert*-butyl-4-methylphenol (50 mg, 2.3 × 10^{-4} mol), and vinyl methacrylate (4.0 g, 0.035 mol) were introduced into a conical flask and suspended in dry acetone (150 mL). The flask was then sealed with a rubber septum and shaken at 200 rpm and 50 °C for 2 days before stopping the reaction by filtering off the enzyme. Workup was performed as above. Yield: 2.7 g (29% with respect to vinyl methacrylate). ^{1}H NMR (300 MHz, CD_3OD, 30 °C), δ (ppm): 1.94 (m, 3 H, H-11), 3.36 (s, 3 H, H-7), 3.65 (m, 3 H, H-3, H-4 and H-5), 3.80 (dd, 1 H, J = 2.9, 1.7 Hz, H-2), 4.27 (dd, 1 H, J = 11.7, 6.3 Hz, H-6), 4.48 (dd, 1 H, J = 11.7, 1.8 Hz, H-6), 4.62 (d, 1 H, J = 1.6 Hz, H-1), 5.62 (m, 1 H, H-10$_E$), 6.13 (m, 1 H, H-10$_Z$). ^{13}C NMR (300 MHz, CD_3OD, 30 °C), δ (ppm): 18.38 (C-11), 55.10 (C-7), 65.49 (C-6), 72.03 (C-5), 68.72 (C-4), 71.89 (C-2), 72.57 (C-3), 102.74 (C-1), 126.28 (C-10), 137.71 (C-9), 168.78 (C-8). After characterization, the monomer was dissolved in water (HPLC grade, pH 7) to give a 1.00 M solution that was stored in a freezer at −18 °C.

Synthesis of the MacroRAFT agents. Poly(methyl 6-*O*-methacryloyl-α-D-glucoside) Dithiobenzoate ($\mathbf{6}_{(67)}$) (Poly(6-*O*-MAMGlc)DB). The experiment is summarized in run 1 in Table 1. The monomer solution (4.00 mL, 4.00 × 10^{-3} mol) was introduced into a Schlenk tube and mixed with ethanol

solutions of 4,4′-azobis(4-cyanopentanoic acid) (5.45×10^{-2} M, 330 μL, 1.80×10^{-5} mol) and (4-cyanopentanoic acid)-4-dithiobenzoate (1.47×10^{-1} M, 390 μL, 5.72×10^{-5} mol). The tube was sealed with a rubber septum, degassed with four freeze−evacuate−thaw cycles and transferred to an oil bath preheated to 70 °C. At regular intervals, an aliquot of solution (150 μL) was drawn and diluted in DMAc (0.05% w/v BHT) for SEC analysis. The reaction was stopped by cooling in ice−water (5 min) and the macroRAFT agent was recovered by precipitation in excess methanol followed by centrifugation and freeze-drying in the dark (48 h, 246 mg). Total reaction time: 300 min. Final conversion: 85%. M_n(NMR) = 17 900; M_n(SEC) = 21 200; PDI(SEC) = 1.12. ^{1}H NMR (500 MHz, D_2O, 40 °C), δ (ppm): 0.98 and 1.09 (H-11), 1.9 (CH_2 chain), 3.39 (H-4), 3.45 (H-7), 3.57 (2-H), 3.67 (3-H), 3.81 (5-H), 4.07 and 4.36 (6-H), 4.80 (H-1), 7.55 (H_{meta} arom), 7.73 (H_{para} arom), 7.97 (H_{ortho} arom). ^{13}C NMR (126 MHz, D_2O, 40 °C), δ (ppm): 17.4 and 19.0 (C-11), 45.4 (C-9), 54.5 (C-10), 55.75 (C-7), 65.29 (C-6), 69.78 (C-5), 70.63 (C-4), 71.89 (C-2), 73.82 (C-3), 99.87 (C-1), 179.6 (C-8). After characterization, the compound was stored in a freezer at −18 °C.

Poly(2-methacryloxyethyl glucoside) Dithiobenzoate ($8_{(116)}$) (Poly(2-MAOEGlc)DB). This experiment is summarized in run 2 in Table 1. The monomer solution (4.00 mL, 4.00×10^{-3} mol) was introduced into a Schlenk tube and mixed with ethanol solutions of 4,4′-azobis(4-cyanopentanoic acid) (7.52×10^{-2} M, 235 μL, 1.17×10^{-5} mol) and (4-cyanopentanoic acid)-4-dithiobenzoate (8.47×10^{-2} M, 440 μL, 3.73×10^{-5} mol). The tube was sealed with a greased glass stopper, degassed with 4 freeze−evacuate−thaw cycles and transferred to an oil bath preheated to 70 °C. The reaction was stopped by cooling in ice−water (5 min) and an aliquot of solution (100 μL) was drawn for SEC analysis. The sampled solution was freeze-dried for 43 h, redissolved in DMAc (0.03% LiBr w/v, 0.05% w/v BHT) and injected to the SEC. The macroRAFT agent was recovered by precipitation in excess methanol followed by centrifugation, washing with fresh methanol, and freeze-drying in the dark (43 h, 542 mg). Total reaction time: 91 min. Final conversion: 83%. M_n(NMR) = 34 200; M_n(SEC) = 25 600; PDI(SEC) = 1.12. ^{1}H NMR (600 MHz, D_2O, 50 °C), δ (ppm): 0.92 and 1.02 (H-12), 1.92 (CH_2 chain), 3.37−4.37 (carbohydrate ring nuclei H-2 to H-6 α/β, plus H-7 and H-8), 4.95 (1-Hα), 7.52 (H_{meta} arom), 7.69 (H_{para} arom), 7.95 (H_{ortho} arom). ^{13}C NMR (151 MHz, D_2O, 50 °C), δ (ppm): 17.9 and 19.6 (C-12), 45.8 (C-10), 54.5 (C-11), 61.31 and 61.77 (C-6); 65.8, 67.76, 70.22, 70.53, 72.09, 72.67, 73.89, 74.00, 76.62, 76.72 (carbohydrate ring nuclei C-2 to C-5 α/β, plus C-7 and C-8); 69.78 (C-5), 70.62 (C-4), 71.89 (C-2), 73.82 (C-3), 99.12 (C-1α), 103.26 (C-1β), 179.2, 180.0 (C-9). After characterization, the compound was stored in a freezer at −18 °C.

Synthesis of the *block*-Glycopolymers. Chain Extension of Poly(6-*O*-MMAGlc)DB with 2-Methacryloxyethyl Glucoside. This experiment is summarized in run 3 in Table 1. Poly(methyl 6-*O*-methacryloyl-α-D-glucoside) dithiobenzoate $\mathbf{6}_{(67)}$ (246 mg, 1.37×10^{-5} mol) was added to a Schlenk tube containing a water solution of 2-methacryloxyethyl glucoside **5** (3.00 mL, 1.00 M, 3.00×10^{-3} mol). Once the macroRAFT agent had completely dissolved, 4,4′-azobis(4-cyanopentanoic acid) was added as ethanol solution (1.50×10^{-2} M, 500 μL, 7.52×10^{-6} mol) and a 100 μL sample was drawn for SEC analysis of the initial reaction mixture. The tube was then sealed with a rubber septum, degassed with four cycles of freeze−evacuate−thaw and transferred to a water bath preheated to 70 °C. At regular intervals, aliquots of solution (200 μL) were drawn from the reaction mixture using a gastight syringe pre-purged with nitrogen and fitted with a 0.72 mm OD needle. The sampled solution was split in two, quenched in ice−water and stored in a refrigerator. At the end of the polymerization, all collected samples were freeze-dried for 3 h and redissolved in DMAc (0.05% BHT) for SEC analysis. The remaining polymer was recovered by precipitation in excess methanol followed by centrifugation and freeze-drying (4 days, 391 mg). Final conversion: 71%. M_n(NMR) = 66 000; M_n(SEC) = 52 000; PDI(SEC) = 1.20. ^{1}H NMR (600 MHz, D_2O, 50 °C), δ (ppm): 0.9 and 1.1 (CH_3), 1.92 (CH_2 chain), 3.35−4.45 (carbohydrate ring nuclei H-2 to H-6 and H-2′ to H-6′, plus H-7, H-8 and H-7′), 4.80 (H-1′), 4.95 (H-1α), 7.51 (H_{meta} arom), 7.68 (H_{para} arom), 7.95 (H_{ortho} arom). ^{13}C NMR (151 MHz, D_2O, 50 °C), δ (ppm): 17.85 and 19.54 (C-11′, C-12), 45.49 and 45.80 (C-9′, C-10), 54.3 (C-10′, C-11), 55.87 (C-7′), 61.31 and 61.76 (C-6), 65.4 and 65.8 (C-6′); 65.79, 67.76, 67.88, 69.91, 70.21, 70.52, 70.80, 72.09, 72.66, 73.88, 73.99, 76.61, and 76.71 (carbohydrate ring nuclei C-2′ to C-6′ and C-2 to C-6, plus C-7 and C-8); 99.12 (C-1α), 100.00 (C-1′), 103.26 (C-1β), 179.87 (C-9, C-8′).

Chain Extension of poly(2-MAOEGlc)DB with Methyl 6-*O*-Methacryloyl-α-D-mannoside. Run 4 in Table 1. Poly(2-methacryloxyethyl glucoside) dithiobenzoate $\mathbf{8}_{(116)}$ (295 mg, 8.63×10^{-6} mol) was added to a Schlenk tube containing a water solution of 6-*O*-methacryloyl-α-D-mannoside **4** (3.00 mL, 1.00 M, 3.01×10^{-1} mol). Once the macroRAFT agent had completely dissolved, 4,4′-azobis(4-cyanopentanoic acid) was added as ethanol solution (2.10×10^{-2} M, 340 μL, 7.13×10^{-6} mol) and a 100 μL sample was drawn for SEC analysis of the initial reaction mixture. The tube was then sealed with a rubber septum, degassed with four cycles of freeze−evacuate−thaw and transferred to a water bath preheated to 70 °C. At regular intervals, aliquots of solution (100 μL) were drawn from the reaction mixture using a gastight syringe pre-purged with nitrogen and fitted with a 0.72 mm OD needle. The sampled solution was quenched in ice−water and stored in a refrigerator. At the end of the polymerization, all collected samples were freeze-dried for 1 h and redissolved in DMAc (0.03% w/v LiBr, 0.05% w/v BHT) for SEC analysis. The remaining polymer was recovered by precipitation in excess methanol followed by centrifugation and freeze-drying (4 days, 391 mg). Final conversion: 52%. M_n(NMR) = 76 200; M_n(SEC) = 61 300; PDI(SEC) = 1.16. ^{1}H NMR (600 MHz, D_2O, 50 °C), δ (ppm): 0.9 and 1.1 (CH_3), 1.91 (m, CH_2 chain), 3.37−4.37 (carbohydrate ring nuclei H-2 to H-6 and H-2′ to H-6′, plus H-7, H-8 and H-7′), 4.74, 4.77 (H-1′), 4.95 (H-1α), 7.54 (H_{meta} arom), 7.72 (H_{para} arom), 7.96 (H_{ortho} arom). ^{13}C NMR (151 MHz, D_2O, 50 °C), δ (ppm): 17.8 and 19.4 (C-12, C-11′), 45.6 and 45.9 (C-10, C-9′), 52.3 and 54.4 (C-11, C-10′), 55.5 (C-7′), 61.3 and 61.8 (C-6); 65.8, 67.8, 70.2, 70.6, 70.9, 71.4, 72.1, 72.7, 73.9, 74.0, 76.6, and 76.7 (carbohydrate ring nuclei C-2 to C-6 and C-2′ to C-6′, plus C-7 and C-8); 99.12 (C-1α), 101.59 (C-1′), 103.26 (C-1β), 179.5 (C-9, C-8′).

Conversion Calculations. Conversions were estimated directly from the SEC chromatograms of the reaction mixture at increasing reaction time. For runs 1 and 2 (Table 1), the following formula was used: [16]

$$x = \frac{(A_{poly}/\kappa)}{(A_{poly}/\kappa) + A_{mono}} \quad (1a)$$

Here A_{poly} and A_{mono} are the area of the polymer and monomer peaks respectively, and κ is the ratio between the specific refractive index of polymer and monomer.

$$\kappa = \frac{(dn/dc)_{poly}}{(dn/dc)_{mono}} \quad (2)$$

Analogously, for runs 3 and 4 the applied formula was

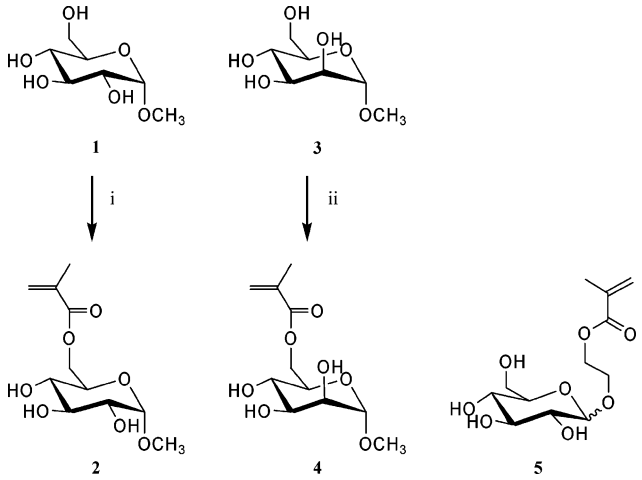
$$x = \frac{(A_{poly}/\kappa)}{(A_{poly}/\kappa) + A_{mono}} - \frac{(A_{macroRAFT,\,0}/\kappa)}{(A_{macroRAFT,\,0}/\kappa) + A_{mono,\,0}} \quad (1b)$$

where $A_{macroRAFT,0}$ and $A_{mono,0}$ are the area of the macroRAFT agent and monomer peaks, respectively, at time zero. A κ value of 1.18 was used that was determined from repeated SEC injections of 6-*O*-MAMGlc and poly(6-*O*-MAMGlc) samples of know concentration (M_n(SEC) = 174 000; PDI(SEC) = 1.75). Detailed calculations are reported in the Supporting Information.

Results and Discussion

Synthesis of the Glycomonomers. Methacrylate ester-type glycomonomers methyl 6-*O*-methacryloyl-α-

Scheme 1. Glycomonomers Used in This Study and Their Preparation: 6-*O*-Methacryloyl-α-D-glucoside (2) (6-*O*-MAMGlc), 6-*O*-Methacryloyl-α-D-mannoside (4) (6-*O*-MAMMan), and 2-Methacryloxyethyl Glucoside (5) (MAOEGlc)[a]



[a] Conditions: vinyl methacrylate, 2,6-di-*tert*-butyl-4-methylphenol, Novozym 435, acetonitrile, and 50 °C. Key: (i) 5 days; (ii) 4 days.

D-glucoside (**2**) and 6-*O*-methacryloyl-α-D-mannoside (**4**) (Scheme 1) were prepared by direct acylation of methyl α-D-glucoside (**1**) and methyl α-D-mannoside **3**, respectively, with vinyl methacrylate (**2**) (an activated acyl donor) in dry organic solvent (acetonitrile or acetone). Novozym 435, an immobilized Lipase B from *Candida antarctica*, was used as the catalyst. Following flash chromatographic purification [silica gel, ethyl acetate/hexane/ethanol 7:2:1 (**2**, R_f 0.39) and 6:3:1 (**4**, R_f 0.30)], both monomers were recovered in fair to good yield (29−70%) as viscous liquids and their structure and purity were confirmed by nuclear magnetic resonance and electrospray ionization−mass spectrometry. In the following polymerization experiments, all monomers were used as in the form of a 1.00 M water (HPLC grade, pH 7) solution.

Synthesis of the MacroRAFT Agents. The RAFT polymerization of methyl 6-*O*-methacryloyl-α-D-glucoside **2** (6-*O*-MAMGlc) and 2-methacryloxyethyl glucoside **5** (MAOEGlc) was performed in aqueous solution with (4-cyanopentanoic acid)-4-dithiobenzoate (CPADB) as the chain transfer agent (Scheme 2). In line with the protocol developed by our laboratory,[16,18] about 10% v/v of ethanol was added to the polymerization mixture to allow complete RAFT agent dissolution without altering the pH. An initial attempt to use MAOEGlc as received (∼50% w/w monomer solution in water; ∼1.7 M) resulted in the formation of a gel within the first hour of reaction. Subsequently, the remaining monomer stock was first freeze-dried and then purified by flash chromatography (ethyl acetate/hexane/ethanol 6.5:2:1.5, R_f 0.20). After LC−MS and NMR analysis had confirmed that the isolated compound was pure MAOEGlc (anomeric ratio α/β 61:39), the same was redissolved in HPLC grade water to give a 1.00 M solution and was used in this form in all following experiments.

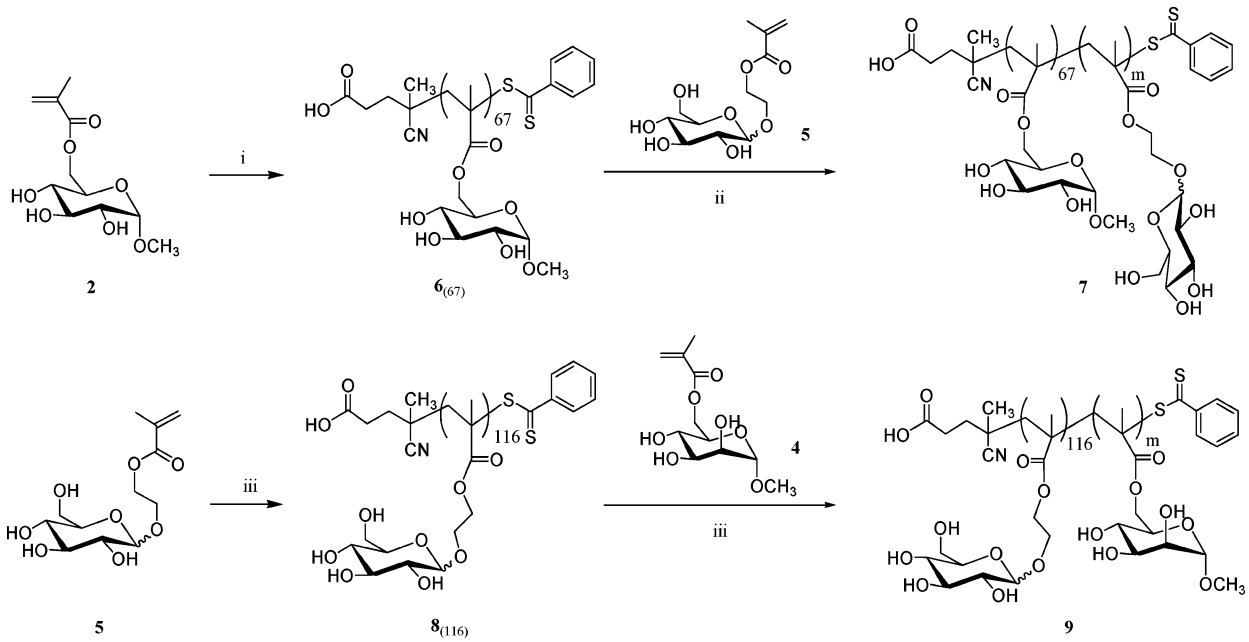
The details of all polymerization experiments are summarized in Table 1. For the syntheses of the macroRAFT agents (runs 1 and 2), the reactions were stopped around 85% monomer consumption to minimize the loss of end-of-chain dithiobezoyl groups and to ensure that all macromolecules could be chain extended.[19,20] Although the same monomer and initiator concentrations were used in both experiments, the RAFT polymerization of 6-*O*-MAMGlc took a considerably longer time to achieve the same conversion (300 min vs the 91 min of MAOEGlc). This was most probably due to the higher RAFT agent concentration employed (12 vs 8.0 mM), and is consistent with that previously observed for the influence of CPADB concentration on polymerization kinetics.[16] Also, the greater steric hindrance around the propagating radical of 6-*O*-MAMGlc with respect to MAOEGlc could result in a lower value of k_p.

SEC analysis of the final reaction mixtures indicates that narrow polydispersity had been attained in both cases (PDI 1.12) together with M_n values of 21 200 and 25 600 Da for poly(methyl 6-*O*-methacryloyl-α-D-glucoside) dithiobenzoate and poly(2-methacryloxyethyl glucoside) dithiobenzoate, respectively (polystyrene equivalent). Following reprecipitation in methanol and freeze-drying, pure poly(6-*O*-MAMGlc)DB (**6**) and poly(MAOEGlc)DB (**8**) were obtained as pink brittle solids and their structures confirmed by ^{1}H and ^{13}C NMR. The nucleus numbering used for NMR spectral assignment can be found in Scheme 3. Please note that the same numbering was used for the starting macroRAFT agent and for the corresponding block in the final block copolymer.

In the proton NMR spectrum of poly(MAOEGlc)DB (**8**) (Figure 1), backbone methyl groups are responsible for the two peaks at 0.92 and 1.02 ppm, as expected for an atactic poly(methacrylate) obtained from radical polymerization.[21,22] Chain methylene protons give rise to one broad signal around 1.92 ppm (H-12), while all carbohydrate ring protons (H-2 to H-6) and the side chain oxyethylene protons (H-7, H-8) resonate between 3.37 and 4.37 ppm. In the reported spectrum, only the signal from the α anomeric proton can be seen at 4.95 ppm (1-Hα), while the corresponding signal from the β anomer is covered by the residual water peak. Indeed, when a second spectrum was acquired at 30 °C (thus shifting the water signal to lower fields) peaks from both anomeric protons were observed (See Supporting Information).[23] Finally, enlargement of the aromatic region reveals three signals from the end-of-chain dithiobenzoyl group (7.52 H_{meta}, 7.69 H_{para} 7.95 H_{ortho}): The ratio between the area under these peaks and the area under the anomeric proton peak(s) was used to calculate the average degree of polymerization of both macroRAFT agents. A value of 67 and 116 was estimated for poly(6-*O*-MAMGlc)DB and poly(MAOEGlc)DB, respectively, and it is reported in subscript next to the relevant compound number in Table 1 and in Table 2.

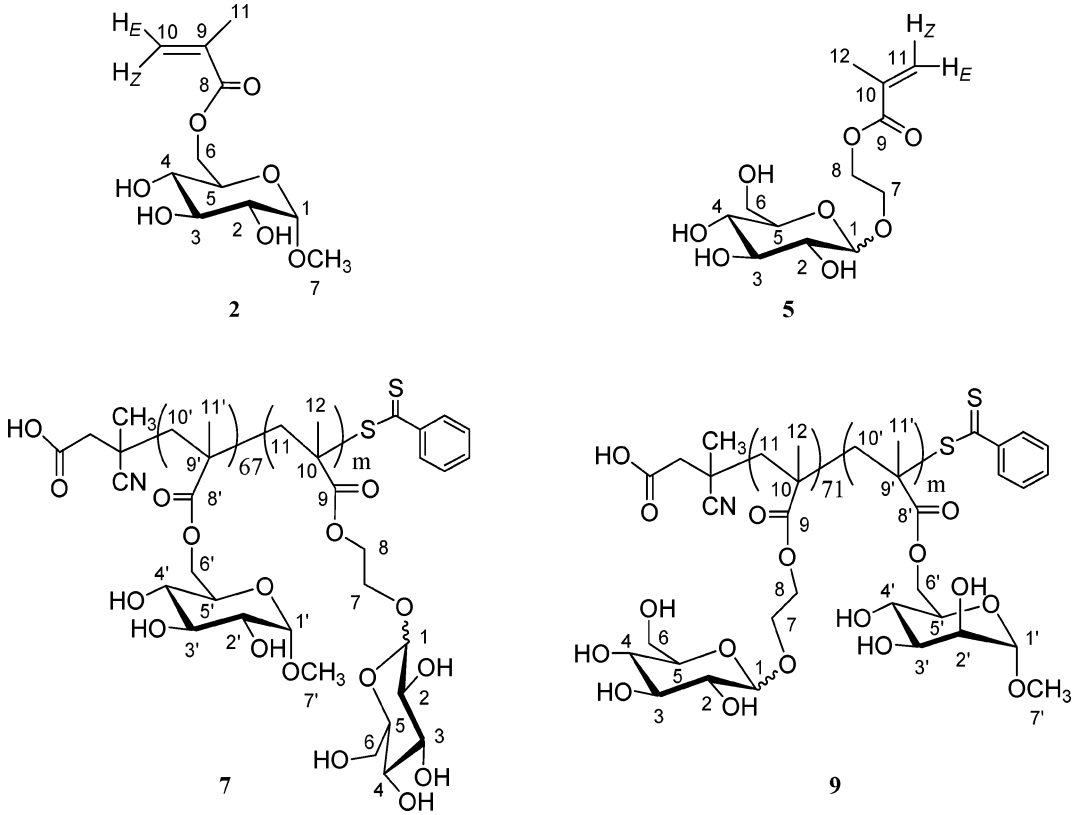
Block Glycopolymers. Poly(methyl 6-*O*-methacryloyl-α-D-glucoside) dithiobenzoate ($\mathbf{6}_{(67)}$) and poly(2-methacryloxyethyl glucoside) dithiobenzoate ($\mathbf{8}_{(116)}$) were chain extended with 2-methacryloxyethyl glucoside and methyl 6-*O*-methacryloyl-α-D-mannoside (6-*O*-MAMMan) respectively, to afford well-defined block glycopolymers **7** and **9** (Scheme 2). Both reactions were carried out in water/ethanol mixtures (∼9:1 v/v), and after an induction period of about 10 min proceeded with pseudo-first-order kinetics up to 51% (run 3, Table 1) and 43% (run 4) monomer conversion (Figure 2). In both cases, in the last stage of polymerization the overall reaction rate decreased, which cannot be explained at this stage. Also, despite the lower macroRAFT agent concentration used for the polymer-

Scheme 2. Two-Step Synthesis of the Diblock Glycopolymers Poly(methyl 6-*O*-methacryloyl-α-D-glucoside-*block*-2-methacryloxyethyl Glucoside) (7) and Poly(2-methacryloxyethyl glucoside-*block*-methyl 6-*O*-methacryloyl-α-D-mannoside) (9)[a]



[a] Conditions: 4,4′-azobis(cyanopentanoic acid), 70 °C, and water/ethanol ~ 9:1. Key: (i) 300 min; (ii) 80 min; (iii) 90 min.

Scheme 3. Position Numbering Used for NMR Spectral Assignment[a]



[a] Note that the same numbering was used for compounds **2** and **4** and for the starting macroRAFT agent and the corresponding block in the final block copolymer.

ization of 6-*O*-MAMMan, this reaction was fairly slower than the counterpart with MAOEGlc, all other parameters being identical. Again, this might be due to the greater steric hindrance around the propagating radical of 6-*O*-MAMMan with respect to MAOEGlc, yet the observed kinetics is also significantly slower than what was previously obtained for the homopolymerization of 6-*O*-MAMGlc (an epimer of 6-*O*-MAMMan) with a comparable RAFT agent concentration.[16]

The results of all polymerization experiments are summarized in Table 1. Similarly to what described for the synthesis of the macroRAFT agents, the average degree of polymerization of the diblock glycopolymers was calculated from the ratio between the peak area of

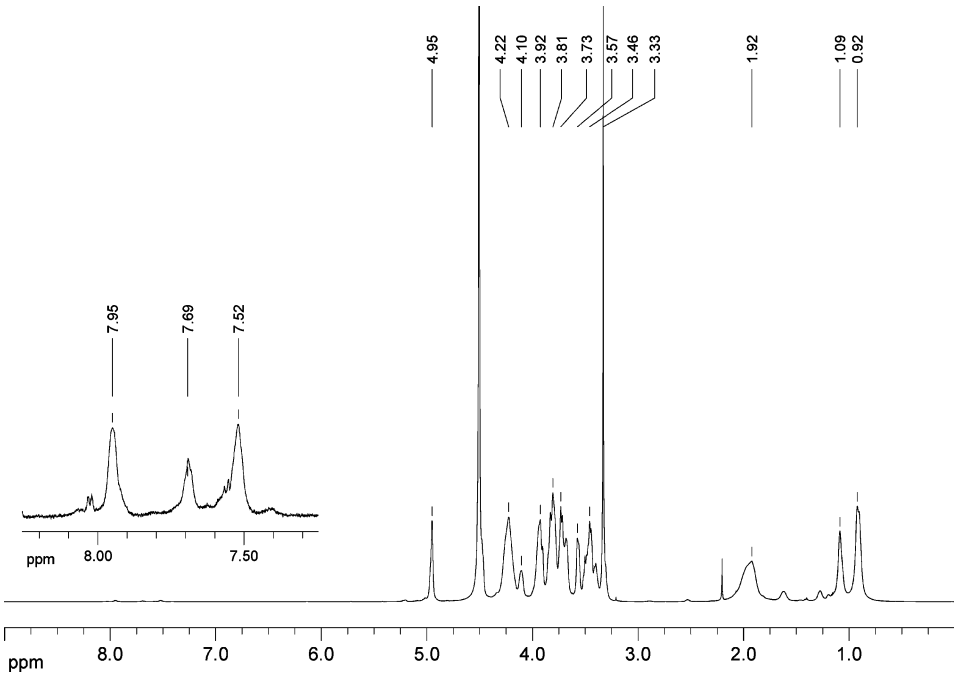


Figure 1. ^{1}H NMR spectrum of poly(2-methacryloxyethyl glucoside) dithiobenzoate (**8**$_{(116)}$) (600 MHz, D_2O, 50 °C).

Table 2. Comparison between the Theoretical and the Experimental Degree of Polymerization (DP_n) of the Prepared Homo and Block Glycopolymers[e]

	DP_n (NMR)[a]		DP_n (theory)[c]		
polymer	6-*O*-MAMx[b]	MAOEGlc	6-*O*-MAMx	MAOEGlc	T_g[d]
6$_{(67)}$	67		60		
6$_{(222)}$	222		206		180
8$_{(116)}$		116		89	105
7	70	163	67	155	127
9	193	93	181	116	151

[a] Calculated from the ratio between the peak area of the RAFT agent end-of-chain aromatic protons and the peak(s) area of the glycoside anomeric proton; in the case of block copolymers, the molar fraction of each repeating unit was estimated from the ratio between the peak area of the respective glycosides anomeric protons. [b] 6-*O*-MAMx indicates methyl 6-*O*-methacryloyl-α-D-glucoside or methyl 6-*O*-methacryloyl-α-D-mannoside; MAOEGlc is 2-methacryloxyethyl glucoside. [c] Values calculated from the formula: $DP_n = x[M]_0/[RAFT]_0$, where x is conversion and $[M]_0$ and $[RAFT]_0$ are the initial concentrations of monomer and RAFT agent, respectively. [d] Differential scanning calorimetry, calculated from the third heating scan as the temperature at which half the increase in heat capacity has occurred. [e] The corresponding glass transition temperatures (T_g) are also reported.

the end-of-chain dithiobenzoyl groups and the peak area of the glycosides anomeric protons (see full NMR spectra in the Supporting Information). Since only the H-1α signal of the MAOEGlc units is visible, the anomeric ratio for this monomer (α/β 61:39) was taken into account in the calculation (Table 2). For both block glycopolymers, the experimental DP_n of each block and the corresponding theoretical value agree well. The same holds for macroRAFT agent **6**$_{(67)}$, while the bigger deviation observed for **8**$_{(116)}$ (~30%) might be due to inaccurate determination of the degree of polymerization for this polymer via proton NMR. In fact, the estimated DP_n for the same block in the derived block copolymer **9** is much closer to its theoretical value (93 vs 89).

Accordingly, for the chain extension experiments (runs 3 and 4 in Table 1), the final molecular weights as determined by ^{1}H NMR are close to the theoretical

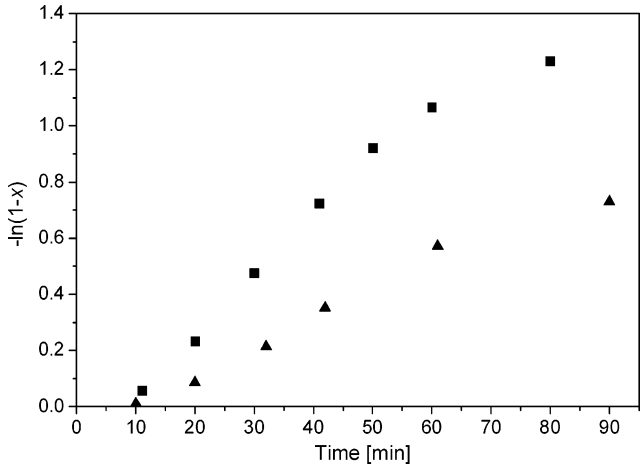


Figure 2. First-order kinetic plot for the chain extension of poly(methyl 6-*O*-methacryloyl-α-D-glucoside) dithiobenzoate (**6**$_{(67)}$) with 2-methacryloxyethyl glucoside (**5**) (■) and of poly-(2-methacryloxyethyl glucoside) dithiobenzoate (**8**$_{(116)}$) with methyl 6-*O*-methacryloyl-α-D-mannoside (**4**) (▲). x is conversion. See Scheme 2 for compound structures. Conditions: water/ethanol ~9:1, 4,4′-azobis(cyanopentanoic acid), 70 °C; [macroRAFT] (mM) = 3.9 (■) and 4.2 (▲); [initiator] (mM) = 2.2 (■) and 2.1 (▲).

values obtained from the formula[24]

$$M_n = M_M x \frac{[M]_0}{[RAFT]_0} + M_{RAFT} \qquad (3)$$

where M_M and M_{RAFT} are the molecular weights of monomer and macroRAFT agent (the latter from ^{1}H NMR) respectively, x is conversion, and $[M]_0$ and $[RAFT]_0$ are the initial concentrations of monomer and macroRAFT agent. Average molecular weights measured by size exclusion chromatography (SEC) are instead considerably lower than the calculated values, as already observed in the case of poly(6-*O*-MAMGlc). This is most probably due to the inadequacy of polystyrene standards to approximate the hydrodynamic volume of **7** and **9** in *N*,*N*-dimethylacetamide,[25] and similar

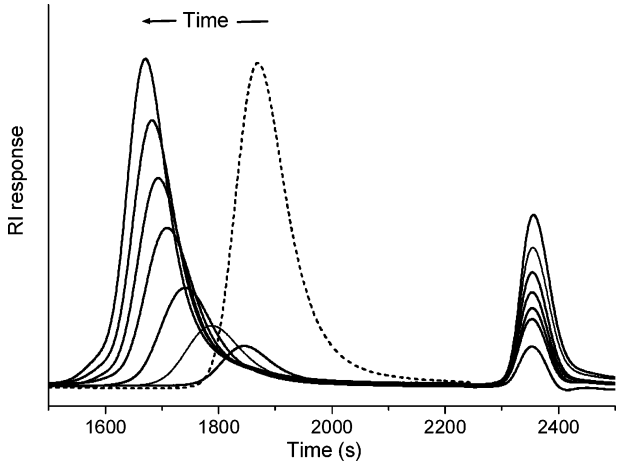


Figure 3. Evolution of the size exclusion chromatography traces with time for the chain extension of poly(methyl 6-*O*-methacryloyl-α-D-glucoside) dithiobenzoate $\mathbf{6}_{(67)}$ with 2-methacryloxyethyl glucoside **5**. For reference, the chromatogram of the initial macroRAFT agent is also shown (dotted line, not to scale).

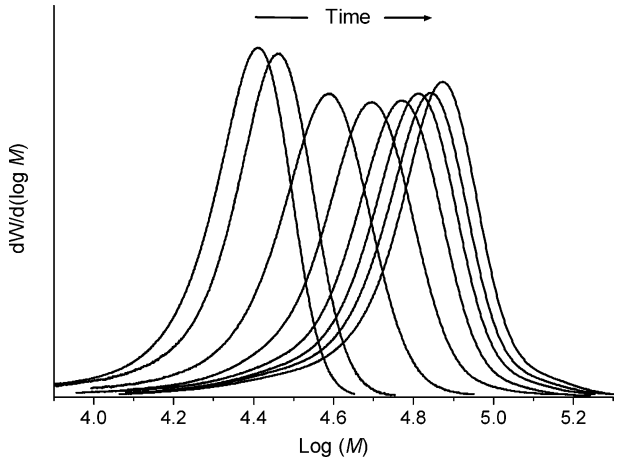


Figure 4. Evolution of the molecular weight distribution with conversion for the chain extension of poly(methyl 6-*O*-methacryloyl-α-D-glucoside) dithiobenzoate ($\mathbf{6}_{(67)}$) with 2-methacryloxyethyl glucoside (**5**) (run 3 in Table 1). From left to right, each curve corresponds to 0%, 3%, 18%, 37%, 51%, 58%, 64%, and 71% conversion, respectively, with normalized areas. Size exclusion chromatography was used with polystyrene equivalents.

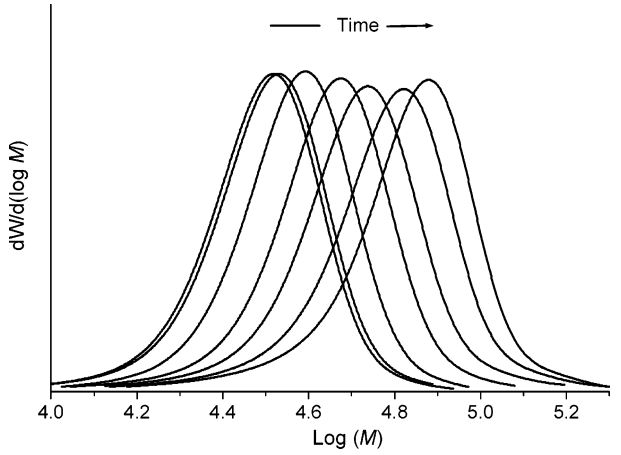


Figure 5. Evolution of the molecular weight distribution with conversion for the chain extension of poly(2-methacryloxyethyl glucoside) dithiobenzoate ($\mathbf{8}_{(116)}$) with methyl 6-*O*-methacryloyl-α-D-mannoside (**4**) (run 4 in Table 1). From left to right, each curve corresponds to 0%, 1%, 8%, 19%, 30%, 44%, and 52% conversion, respectively, with normalized areas. Size exclusion chromatography was used with polystyrene equivalents.

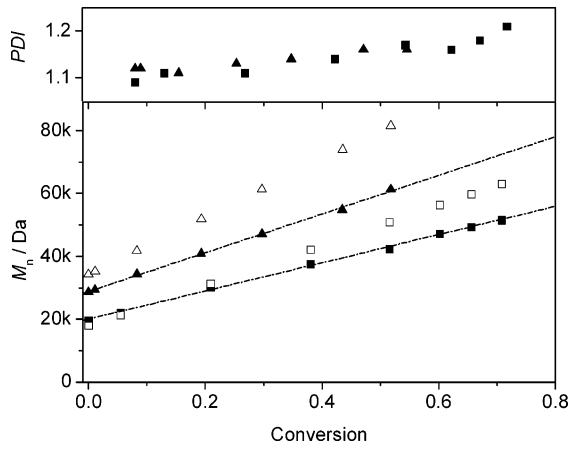


Figure 6. Evolution of the molecular weight and polydispersity with conversion for the chain extension of poly(methyl 6-*O*-methacryloyl-α-D-glucoside) dithiobenzoate ($\mathbf{6}_{(67)}$) with 2-methacryloxyethyl glucoside (**5**) (■) and of poly(2-methacryloxyethyl glucoside) dithiobenzoate ($\mathbf{8}_{(116)}$) with methyl 6-*O*-methacryloyl-α-D-mannoside (**4**) (▲). Molecular weights from size exclusion chromatography as polystyrene equivalents; hollow symbols indicate theoretical values. See runs 3 and 4 in Table 1 for details. Dotted line: linear regression of experimental data.

problems with polystyrene-equivalent molecular weights of glycopolymers have been previously reported in the literature.[26−29]

Intermediate molecular weight distributions and conversions were obtained from SEC analysis of samples collected at increasing reaction times by using eq 1b. The evolution of the SEC traces with time for the chain extension of poly(6-*O*-MAMGlc)DB $\mathbf{6}_{(67)}$ with 2-methacryloxyethyl glucoside (**5**) is shown in Figure 3. As the reaction proceeds, the monomer peak around 2350 s disappears while the polymer peak grows in intensity and shifts toward higher molecular weight values. As a reference, the chromatogram of the initial macroRAFT agent is shown in dotted line. The evolution of the molecular weight distributions with time for runs 3 and 4 are reproduced in Figure 4 and in Figure 5. In both cases, the distribution shifts to higher molecular weights as the polymerization proceeds, while no high molecular weight shoulder can be seen up to 71% and 52% conversion, respectively. Also, little or no trace of the initial macroRAFT agents seems to be present in the final block glycopolymer samples and nearly quantitative chain extension appears to have taken place.

When the M_n values obtained from SEC are plotted against conversion, they increase linearly as expected for a well controlled living process (Figure 6, bottom panel). However, the experimental trend lines are systematically lower than the theoretical lines as previously observed in the case of poly(6-*O*-MAMGlc),[16] and the deviation becomes more pronounced with increasing molecular weights. As mentioned above, this is most probably due to the use of a polystyrene calibration for the SEC system. The polydispersity index remained low throughout the polymerization in all cases, with a final value of 1.20 for poly(6-*O*-MAMGlc-*b*-MAOEGlc) (**7**) and of 1.16 for poly(MAOEGlc-*b*-6-*O*-MAMMan) (**9**) (Figure 6, top panel).

To corroborate the structure and composition of the prepared block glycopolymers, high field NMR spectra were acquired at 50 °C in order to reduce sample

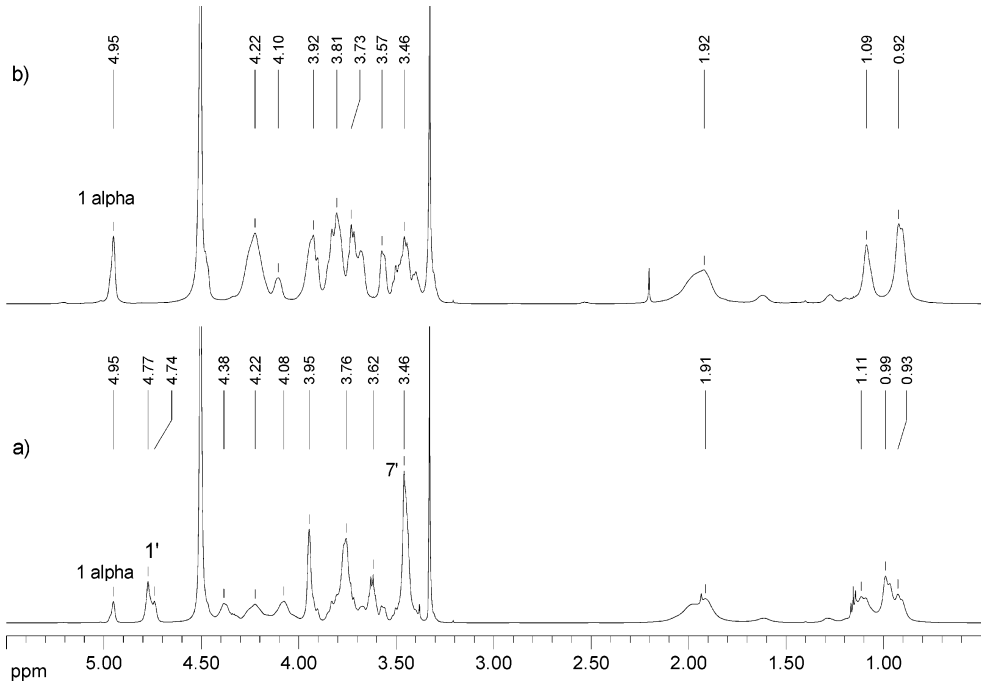


Figure 7. ^{1}H NMR spectrum of poly(2-methacryloxyethyl glucoside) dithiobenzoate ($\mathbf{8}_{(116)}$) (b) and poly(2-methacryloxyethyl glucoside-*block*-methyl 6-*O*-methacryloyl-α-D-mannoside) (**9**) (a) (600 MHz, D_2O, 50 °C). See Scheme 3 for nucleus numbering.

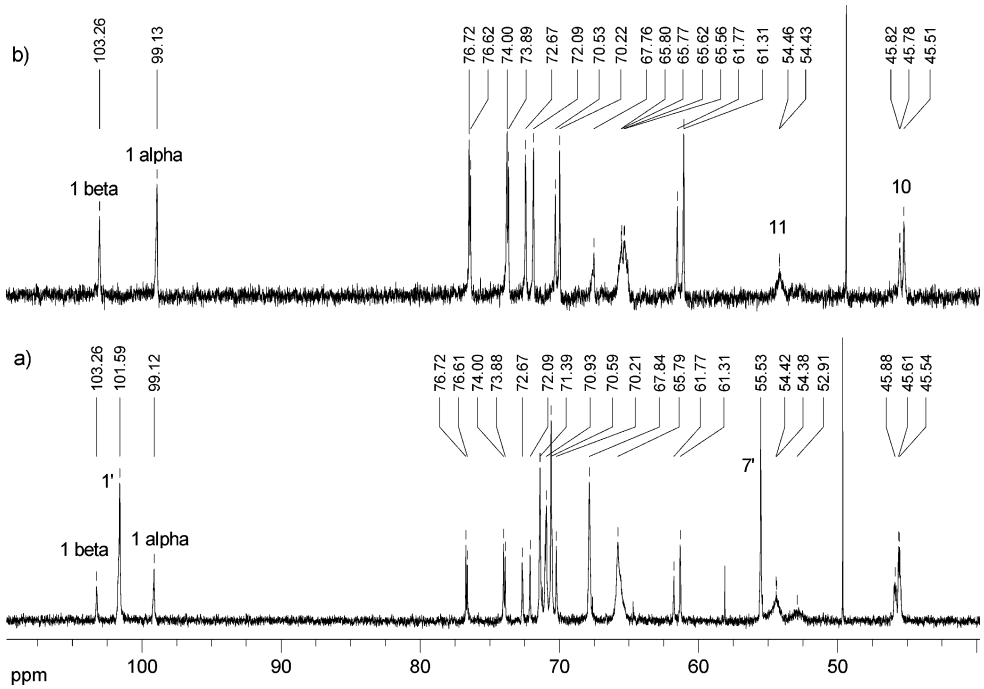


Figure 8. ^{13}C NMR spectrum of poly(2-methacryloxyethyl glucoside) dithiobenzoate ($\mathbf{8}_{(116)}$) (b) and poly(2-methacryloxyethyl glucoside-*block*-methyl 6-*O*-methacryloyl-α-D-mannoside) (**9**) (a) (151 MHz, D_2O, 50 °C). See Scheme 3 for nucleus numbering.

viscosity and improve resolution. Figure 7a shows the ^{1}H NMR spectrum of poly(2-methacryloxyethyl glucoside-*block*-methyl 6-*O*-methacryloyl-α-D-mannoside) (**9**) isolated by precipitation in methanol followed by centrifugation and freeze-drying. With respect to that of the starting macroRAFT agent (Figure 7b), the spectrum of **9** shows a new strong singlet at 3.46 ppm and two partially superimposed peaks around 4.75 ppm due to the methoxy-group 7′ and to the α anomeric proton 1′ of the mannoside unit, respectively. Together with the evolution of the MWD curves with conversion, this spectroscopic evidence confirms that both glycomonomers were indeed incorporated into the final block copolymer. This conclusion is further supported by inspection of the relevant ^{13}C spectra (Figure 8). The spectrum of **9** in fact, shows an anomeric carbon signal (101.59 ppm, C-1′) and a methoxide carbon signal (55.5 ppm, C-7′) not present in the initial block. Similar remarks can be made for poly(methyl 6-*O*-methacryloyl-α-D-glucoside-*block*-2-methacryloxyethyl glucoside) (**7**), and the full proton and carbon spectra of both diblock glycopolymers can be found in the Supporting Information.

Thermal Analysis. Both the reprecipitated block glycopolymers and the initial macroRAFT agents were characterized by differential scanning calorimetry (DSC).

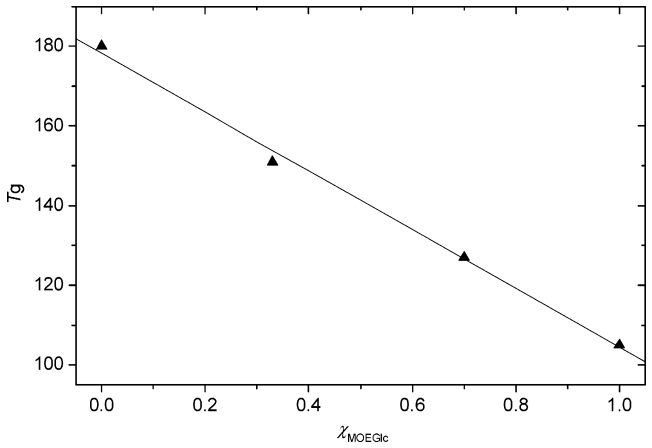


Figure 9. Variation of the glass transition temperature with composition for the block glycopolymers **7** and **9** (Scheme 2). The molar fraction of 2-methacryloxyethyl glucoside is reported in abscissa. Solid line: linear regression of experimental data.

A previously conducted TGA analysis of $\mathbf{8}_{(116)}$ indicated that the onset of the decomposition in nitrogen atmosphere is around 250 °C.[30] Consequently, for DSC analysis, all samples were cycled between 40 and 250 °C. Since all of the $\mathbf{6}_{(67)}$ had been used for chain extension experiments, a higher molecular weight analogue was analyzed in its place ($\mathbf{6}_{(222)}$).

Thermal characterization results are summarized in Table 2. For all samples, a single glass transition was observed, while no melting phenomena were detected even after repeated cycling. The glass transition temperature was calculated from the third scan as the temperature at which half the increase in heat capacity has occurred.[1] Poly(6-*O*-MAMGlc)DB $\mathbf{6}_{(222)}$ displays the highest T_g value at 180 °C, 75 °C higher than poly(methyl methacrylate). A higher T_g is consistent with the presence of a bulky and polar side group which hinders rotation about the backbone,[32] while hydrogen bonding might play a role as well. Interestingly, poly(MAOEGlc)DB has the same glass transition temperature of PMMA (105 °C). The different behavior might result from the presence of a flexible oxyethylene spacer and from the mixed anomeric configuration of the pendant glucoside. The latter could in fact influence the chain flexibility of the polymer in a similar way to what reported for PMMA tacticity.[32] A single glass transition was observed for the block glycopolymers, to indicate that in both cases the two blocks are miscible in bulk and that no phase separation is present. Furthermore, their T_g was intermediate between that of each block: thus where poly(methyl 6-*O*-methacryloyl-α-D-glucoside)DB and poly(2-methacryloxyethyl glucoside)DB have T_g values of 180 and 105 °C respectively, poly(methyl 6-*O*-methacryloyl-α-D-glucoside-*block*-2-methacryloxyethyl glucoside) (**7**) has a T_g of 127 °C. Finally, a direct correlation can be drawn between the molar fraction χ of each repeating unit in the copolymer and the value of T_g (Figure 9), with a higher content of 6-*O*-MAMx (x = Glc, Man) resulting in higher T_g values. This is to say that the glass transition of the prepared block glycopolymers obeys the equation

$$T_g = \chi_1 T_{g,1} + \chi_2 T_{g,2} \quad (4)$$

where the subscript number indicates one of the two blocks in the copolymer. Equation 4 is a simplified version of the relationship derived by Couchman[33] for the glass transition temperature of homogeneous polymer blends based on thermodynamic considerations. For it to hold, the comonomers must have the same molar mass and both pure-component heat capacity increments at T_g must have the same value.[31] The first condition is nearly met in our case (M_r(6-*O*-MAMx) = 262.26; M_r(6-*O*-MAMx) = 292.28), and the second one ($\Delta C_{p,1} \cong \Delta C_{p,2}$) is consistent with the similar chemical natures and steric hindrances of the glycomonomers used.

Conclusion

Reversible addition−fragmentation chain transfer polymerization was applied to the synthesis of well-defined diblock glycopolymers carrying different cyclic carbohydrates on the two blocks. To avoid pH induced degradation of the dithiobenzoyl moiety, all experiments were carried out in aqueous solutions containing ∼10% v/v of ethanol and without the addition of bases, according to the protocol developed by our laboratory.[16,18] The macroRAFT agents poly(methyl 6-*O*-methacryloyl-α-D-glucoside) dithiobenzoate and poly(2-methacryloxyethyl glucoside) dithiobenzoate were prepared by RAFT polymerization of the corresponding glycomonomers with (4-cyanopentanoic acid)-4-dithiobenzoate as the chain transfer agent. The reactions were stopped around 85% conversion in order to preserve the highest possible end-of-chain-functionality and the glycopolymers were isolated by precipitation in methanol. Chain extension with 2-methacryloxyethyl glucoside and methyl 6-*O*-methacryloyl-α-D-mannoside afforded poly(methyl 6-*O*-methacryloyl-α-D-glucoside-*block*-2-methacryloxyethyl glucoside) and poly(2-methacryloxyethyl glucoside-*block*-methyl 6-*O*-methacryloyl-α-D-mannoside), respectively, having a predetermined molecular weight and narrow polydispersity (PDI ≤ 1.20). Also, from the evolution of the MWD traces with conversion, it appears that virtually all the initial macroRAFT chains were incorporated in the final block glycopolymers.

The structure of the prepared polymers was confirmed by proton and carbon NMR and their thermal properties investigated via DSC. Both the diblock glycopolymers and the starting macroRAFT agents displayed a single glass transition in the range 105−180 °C, whereas no melting phenomena were observed. This indicates that the two blocks of the copolymers are miscible in bulk and that no phase separation is present. Also, T_g of the diblock copolymers was found to depend on the relative length of the two blocks, with a higher content of 6-*O*-MAMx units (x = Glc, Man) resulting in a higher glass transition temperature.

To conclude, RAFT polymerization proves to be a viable method for the direct synthesis of well-defined block glycopolymers in aqueous media without the need to resort to protective group chemistry. Indeed, diblock copolymers carrying different cyclic sugars on the two blocks were prepared in good yield and in a controlled fashion. Although chain extension experiments via RAFT invariably lead to the formation of homopolymer chains as well, their proportion in the final material can be kept small by maximizing the ratio between the number of macroRAFT agent molecules used and the number of primary radicals generated by the initiator decay.[13,34] In this sense, the rapid polymerization kinetics observed for the studied glycomonomers are a clear advantage. Hence we anticipate that this approach may

be the base for a higher level of sophistication in the design of macromolecular ligands for lectin binding and drug delivery systems.

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Supporting Information Available: Tables with conversion and theoretical molecular weight calculations for chain extension experiments and figures showing ^{1}H and ^{13}C NMR spectra of methyl 6-*O*-methacryloyl-α-D-mannoside (**4**), 2-methacryloxyethyl glucoside (**5**), poly(methyl 6-*O*-methacryloyl-α-D-glucoside) (**6**$_{(67)}$), poly(2-methacryloxyethyl glucoside) dithiobenzoate (**8**$_{(116)}$), poly(methyl 6-*O*-methacryloyl-α-D-glucoside-*block*-2-methacryloxyethyl glucoside) (**7**), and poly(2-methacryloxyethyl glucoside-*block*-methyl 6-*O*-methacryloyl-α-D-mannoside) (**9**), LC−MS spectrum of 2-methacryloxyethyl glucoside (**5**) and DSC thermograms of the homo and block copolymers. This material is available free of charge via the Internet at http://pubs.acs.org.

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