 DOI: 10.1002/masy.200750908

CMC and Phase Separation Studies of RAFT Mediated Amphiphilic Diblock Glycopolymers with Methyl Acrylate and Styrene

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Summary: Interesting new CMC and phase separation data of carbohydrate-based self-assembling core-shell nanoparticles which were synthesized via the Reversible Addition-Fragmentation Transfer (RAFT) process. The macro-RAFT agent, poly(3-O-Methacryloyl-1,2:5,6-di-O-isopropylidene-D-glucofuranose) (PMAIpGlc), was prepared by RAFT polymerization of the glycomonomer with cumyl phenyl dithioacetate as the chain transfer agent. Chain extension with styrene and methyl acrylate afforded the diblock copolymers (PMAIpGlc-b-styrene and PMAIpGlc-b-methyl acrylate) having predetermined molecular weight and narrow molecular weight distributions. Acidolysis of these diblock copolymers were undertaken and confirmed by NMR. Core-shell nanoparticles were observed by TEM.

Keywords: amphiphiles; CMC; glycopolymers; phase separation; RAFT

Introduction

Over the past decade, studies in the field of synthetic carbohydrate based polymers – so called 'glycopolymers' have expanded substantially, as verified by the increasing number of reviews on the subject.[1–3] By displaying complex functionalities, these materials are able to mimic and in some cases surpass the performance of natural bioglycoconjugates. It is for this reason that glycopolymers have enabled unique and specialized applications in the biochemical and biomedical fields, such as drug-delivery systems,[4,5] molecular recognition and separation processes,[6] surfactants,[7] responsive hydrogels,[8] treatment of infectious diseases[9] and treatment of HIV.[10]

In search of novel glycopolymers with tailored applications, finding the appropriate combination of functional groups and macromolecular architecture is an important task. However, many polymerization techniques are limited in their ability to handle both requirements simultaneously. For instance, well-defined glycopolymers have been synthesized by living cationic,[11] anionic,[12] ring-opening methathesis[13] and ring-opening polymerization of N-carboxyanhydrides,[14] but limit the range of monomers as these processes are sensitive to a number of functional groups and require demanding reagent purification procedures. To this end, many groups have researched the preparation of well-defined glycopolymers by living radical polymerization, obtaining polymers with low polydispersities and tailored molecular weights.[15–19] Processes involving living radical polymerization have opened various paths to well defined macromolecules both in academia and industry. These processes include nitroxide-mediated polymerization[20] and atom transfer radical polymerization.[21–23] In these processes, either reversible termination of the propagating radicals to form dormant species occurs, or there is a transfer of the radical to a

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different chain, as found in the reversible addition-fragmentation chain transfer (RAFT) process.[17,24–26]

In comparison to most controlled polymerization techniques, the RAFT process is a robust and versatile method of obtaining polymeric materials of narrow molecular weight distributions.[27] Advantages include it being applicable to a wide range of monomers, increased tolerance to small amounts of impurities, compatibility with various solvents, being amenable to a wide range of working temperatures[28–30] and the synthesis of a variety of molecular architectures.[31–33]

Aqueous RAFT mediated polymerizations of glycomonomers have been successfully carried out,[17,24–26,32,34] using water miscible RAFT agents and hydrophilic monomers, for chain extension studies. The preparation of polymers with self-assembly properties, which are important for many biological applications, requires the introduction of amphiphilic character to provide a driving force for assembly. The chain extension of water soluble polymers with water insoluble monomer units provides the very real scenario in which assembly occurs during polymerization, potentially affecting the nature of the polymer produced. Acetal protection chemistry is a route that has been used in the literature to simplify the preparation of hydrophobic glycopolymers which can then be chain extended in homogeneous organic media prior to being converted to their natural hydrophilic state.[16]

This paper investigates the controlled RAFT mediated polymerization of the protected monomer 3-O-methacryloyl-1, 2:5,6-di-O-isopropylidene-D-glucofuranose (MAlpGlc) utilizing cumyl phenyl dithioacetate (CPDA) as the RAFT agent. CPDA has previously been used for the controlled polymerization of methacrylates.[35] Block copolymers of these glycopolymers with vinyl monomers (methyl acrylate and styrene) were synthesized and characterized. Thereafter, chain extension and their amphiphilic self-assembling character were evaluated.

Experimental Part

Materials

Unless otherwise specified, all chemicals were reagent grade and used as received. Sodium hydroxide [97%; Associated Chemical Enterprises (Pty.), Ltd.], D(+)glucose [Anhydrous; ACE (Pty.), Ltd.], zinc chloride (97%; Saarchem), methacrylic anhydride (92%; Fluka), o-phosphoric acid (85%; Fluka), magnesium sulphate (Anhydrous; Saarchem), 4-methoxyphenol (99%; Aldrich), azobis (isobutyronitrile) (AIBN; Riedel de Haen), acrylic acid (99%; Anhydrous; Fluka), 1,3,5- trioxane (99%; Riedel de Haen), phenyl magnesium chloride (1.0 M in ether; Aldrich), carbon disulfide (99.9%; Aldrich), p-toluene sulfonic acid (98.5%; Sigma-Aldrich), carbon tetrachloride (99.9%; Aldrich), diethyl ether (99.5%; Merck) and HCl [32%; ACE (Pty.), Ltd.] was used as received. Acetone (98%; CP; Saarchem) was distilled and dried [4-Å molecular sieves (Aldrich)]; pyridine (99%; Saarchem) was dried over sodium hydroxide over three days, distilled and stored [4-Å molecular sieves (Aldrich)]; ethyl acetate [99.5%; CP; Saarchem] and methyl acrylate (99%; Aldrich) were distilled. The water used in all reactions was distilled and deionized (DDI) water obtained from a Millipore Milli-Q purification system.

Analysis

NMR spectra were recorded on a 300 MHz Varian VXR spectrometer equipped with a Varian magnet (7.0 T), and a 600 MHz Varian Unity Inova spectrometer equipped with an Oxford magnet (14.09 T). Standard pulse sequences were used for obtaining ^{1}H, ^{13}C spectra. TEM images were obtained using either a LEO 912 Omega (LEO Elektronmikroskopie, GmbH, Oberkochen) or a JEM 1200 EX II (JEOL Ltd, Tokyo, Japan) Transmission Electron Microscope (TEM) operated at 120 kV. Molecular weights and molecular weight distributions were determined by a SEC system comprising of a Waters 410 Differential Refractometer, Waters 717plus Autosampler, Waters 600E System Contoller and

Wyatt DAWN DSP Multiangle Laser Light Scattering (MALLS) detector. The molecular weights and polydispersity data were calculated using the Wyatt ASTRA4.50 software package. Samples were prepared for analysis by drying the polymer in vacuo and redissolving in THF (HPLC-grade). The flow rate was 1 mL/min. The *dn/dc* values, determined by a ScanRef Monocolor Interferometric Refractometer (LabView 4 Runtime, vers. 4.0.1 software), of the resulting polymers were calculated in duplicate at various concentrations (0.5, 1, 2, 3, 4, 5 mg/L) and were used for molecular weight calculations. Conductivity measurements were done at 295K using a Eurotech cell combined with a Cyberscan 500 device. Data was analyzed via ORIGINLAB v7.5 software which has the statistical feature that estimates the onset of slope change in a curve at four different points.

Synthesis of the Glycomonomer: 3-O-Methacryloyl-1,2:5,6-di-O-isopropylidene-D-glucofuranose (MAlpGlc) (3)

D(+)Glucose (1) was converted into 1,2:5, 6-di-O-isopropylidene-alpha-D-glucofuranose (pGlc) (2) according to the method proposed by Schmidt.[36] (MAlpGlc) was synthesized from (pGlc) by a slight modification of the method proposed by Black et al.[37] The modification involved the use of (a) pentane as an extracting solvent, (b) 4-methoxy phenol as a polymerization inhibitor and product purification was carried out by the method proposed by Ohno et al.[16] A yield of 72% with respect to reacted D(+)Glucose was obtained. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 1.25–1.50 (m, 12H, $4CH_3$); 1.95 (s, 3H, CH_3–C=CH_2); 5.70 (m, 1H, CH_2=C–, E form H); 6.00 (m, 1H, anomeric proton of sugar moiety); 6.15 (m, 1H, CH_2=C, Z form H); 3.90–4.70 (6H, sugar moiety).

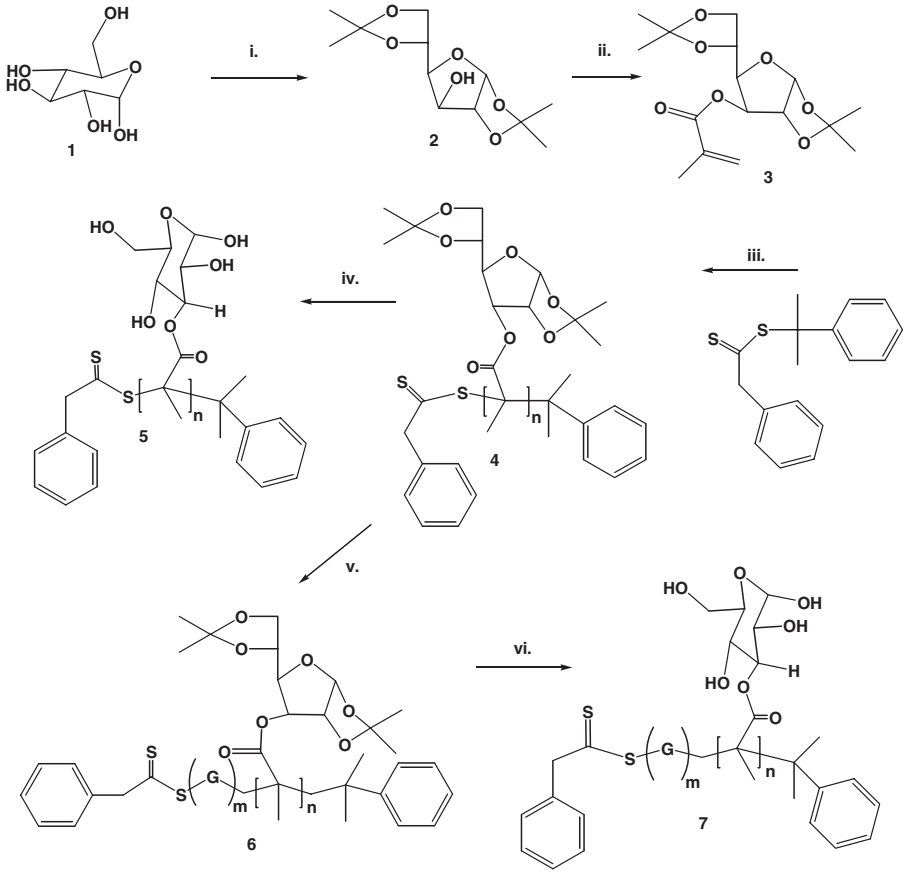
RAFT Agent Synthesis: Cumyl Phenyl Dithioacetate (CPDA)

The synthesis of phenyl dithioacetic acid was made by a modification of the method proposed by Quinn et al.,[38] in that a solution of benzyl magnesium chloride was prepared from benzyl chloride (50.60 g, 0.40 mol), magnesium turnings (10.90 g, 0.45 mol) and catalytic amounts of iodine in 300 ml dry ether. After the dropwise addition of benzyl chloride the solution was refluxed for an hour and cooled to ambient temperature. CS_2 (30.40 g, 0.40 mol) was added within 20 min., while the temperature was kept constant at room temperature with cold water. Thereafter, the orange mixture was stirred for another hour at room temperature, decanted from excess magnesium and poured onto ice. The red aqueous layer was separated, washed with ether, acidified with hydrochloric acid and the dithioacetic acid was extracted with ether (3×100 mL).

Drying over $MgSO_4$ for 30 min. and removing the solvent under reduced pressure afforded the crude phenyl dithioacetic acid as red oil (25.31 g, 37.60% yield). The crude phenyl dithioacetic acid (25.31 g, 0.15 mol) was refluxed for 15 hours with α-methyl styrene (20.01 g, 0.17 mol) and 0.10 g p-toluene sulfonic acid in 100 mL dry CCl_4. After removal of the solvent under reduced pressure the resulting red oil was left overnight in the freezer to crystallize. The formed orange crystals were separated and recrystallized from hexane. (11.30 g, 26.3% yield) ^{1}H NMR, (600 MHz, $CDCl_3$) δ (ppm): 2.00 (s, 6H, $2CH_3$); 4.2 (s, 2H, CH_2); 7.2–7.6 (m, 10H, H_{ar}). ^{13}C NMR, (300 MHz, $CDCl_3$) δ (ppm): 27.6 ($2CH_3$); 56.02 (C); 59.16 (CH_2); 126.6, 126.8, 127.1, 127.9, 128.4, 128.7, 137.1, 144.0 (C_{ar}); 233.59 (C=S).

Macro-RAFT Agent Synthesis: Poly(3-O-Methacryloyl-1,2:5,6-di-O-isopropylidene-D-glucofuranose), (PMAlpGlc) (4)

The reaction procedure involved adding MAlpGlc (91.51 mmol, 30.05 g), CPDA (1.215 mmol, 0.3484 g) and ethyl acetate (25% w/v monomer) into a three necked round bottom flask (Scheme 1, Table 1). The contents were thereafter heated to 75 °C (±1 °C) while being purged with nitrogen for 25 min. After initial purging, the free radical initiator AIBN (0.125 mmol,



Scheme 1.
The synthetic approach to well-defined diblock glycopolymers using methyl acrylate and styrene i. Acetone/$ZnCl_2$/H_3PO_4/NaOH; ii. Pyridine/pentane and methacrylic anhydride; iii. CPDA, ethyl acetate, AIBN, 75 °C; iv. HCl and 100 °C; v. Ethyl acetate, (Toluene in the case of styrene), AIBN, methyl acrylate/styrene, 75 °C; vi. HCl and 100 °C. G = methyl acrylate/styrene moiety.

0.0199 g) was added to the reaction solution to start the polymerization reaction. 1,3,5-Trioxane was added as an inert internal reference to determine the monomer concentration, by comparison to the signals of the vinyl protons corresponding to the monomer. The amount of 1,3,5-trioxane added was equivalent to 20% of the total

Table 1.
Starting compositions for the synthesis of the glycopolymers: PMAlpGlc-b-poly(methyl acrylate) and PMAlpGlc-b-poly(styrene).

Material used	PMAlpGlc-b-poly(methyl acrylate)	PMAlpGlc-b-poly(styrene)
PMAlpGlc[a)]	0.1254 mmol, 3.010 g	0.2087 mmol, 5.010 g
Monomer (methyl acrylate/styrene)	36.39 mmol, 3.135 g	200.3 mmol, 20.87 g
AIBN	0.0125 mmol, 0.0021 g	0.0208 mmol, 0.0034 g
Reaction temp. (°C)	75	80
% w/v monomer	Ethyl acetate, 25%	Toluene, 25%

[a)] MAlpGlc: 91.51 mmol, 30.05 g; CPDA: 1.215 mmol, 0.3484 g; AIBN: 0.1251 mmol, 0.0199 g; Ethyl acetate (25% w/v monomer); 1,3,5 trioxane: 18.30 mmol, 1.645 g; reaction temp.: 75 °C.

molar amount of monomer. ^{1}H-NMR (600 MHz, acetone-*d8*) spectra were recorded before the start of the reaction and samples were withdrawn at specific time intervals. The samples were dried in vacuo overnight before analysis. The ratio of the integrated signals of the internal reference, before and after the reactions, was used to calculate monomer incorporation. A typical ^{1}H-NMR spectra of a reaction sample (Figure 1) shows the pronounced signal at 5.18 ppm for 1,3,5-trioxane protons and that it is well isolated from the vinyl proton peaks of the glycomononer. The broad peak at 5.7– 6.0 ppm is due to the anomeric proton peak of the sugar moiety in the polymer.

Data obtained via this method were in excellent agreement with the theoretical values, $\overline{M}_n$, calculated from Equation (1):

$$\overline{M}_n = M_{RAFT} + \frac{x[M]_0 M_M}{[RAFT]_0 + 2f[I]_0(1 - e^{-k_d t})} \quad (1)$$

where $\overline{M}_n$ is the predicted number average molar mass; M_M is the monomer molar mass; M_{RAFT} the molar mass of the RAFT agent; $[M]_0$, $[RAFT]_0$, $[I]_0$ are the initial concentrations of the monomer, RAFT agent and initiator respectively; k_d is the initiator dissociation constant; f is the initiator efficiency; and x is the fractional conversion at time t.

Termination of the reaction was carried out by placing the system in an ice-bath. The macro-RAFT agent was precipitated and filtered out in an excess of methanol. 95% conversion occurred within five and a half hours. $\overline{M}_n$(SEC): 12000, $\overline{M}_n$(MALLS): 24500, $\overline{M}_n$(^{1}H-NMR): 24000 and PDI (MALLS): 1.16. ^{1}H-NMR (acetone-*d8*, 600 MHz) (Scheme 1, compound 4): δ (ppm) 0.9–1.8 (m, 12H, CH_3), 4.0–5.2 (4H, sugar moiety), 5.7–6.0 (m, ^{1}H, anomeric proton of sugar moiety) and between 7.2–7.8 (aromatic protons of CPDA).

Synthesis of PMAlpGlc-b-(styrene) and PMAlpGlc-b-(methyl acrylate) (6)

The reaction procedure was very similar to the synthesis of the homopolymer PMAlpGlc except that the (i) monomer (styrene and methyl acrylate) conversion was determined gravimetrically, (ii) PMAlpGlc was used as the macro-RAFT agent and (iii) toluene was used in the case of styrene polymerizations. The starting polymerization compositions are documented in Table 1. In both cases, the produced copolymers were precipitated in excess methanol. In the case of PMAlpGlc-b- (methyl acrylate): at 82% conversion, $\overline{M}_n$(SEC): 22000, $\overline{M}_n$(MALLS): 49000, $\overline{M}_n$(^{1}H-NMR): 52000, $\overline{M}_n$(Theo): 50000 and the PDI (MALLS): 1.56. ^{1}H-NMR (acetone-*d8*, 600 MHz) (Scheme 1, compound 5): δ (ppm) 0.9–1.8 (m, 12H, CH_3), 4.0–5.2 (4H,

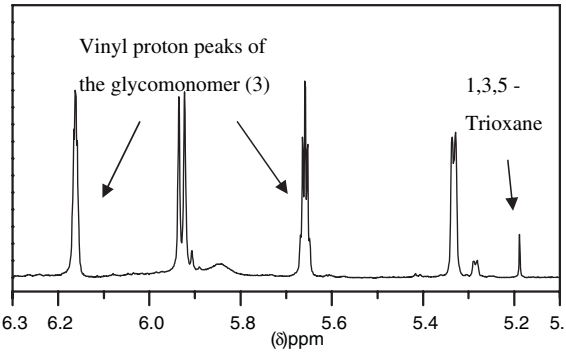


Figure 1.
An expansion of a typical ^{1}H-NMR spectrum of a PMAlpGlc homopolymerization reaction mixture in ($CDCl_3$) showing the region of interest.

sugar moiety), 5.7–6.0 (m, ^{1}H, anomeric proton of sugar moiety), 3.4–3.8 (s, 3H, CH_3) and between 7.2–7.8 (aromatic protons of CPDA). In the case of PMAlpGlc-b-(styrene): at 40% conversion, $\overline{M}_n$(SEC): 36000, $\overline{M}_n$(MALLS): 44000, $\overline{M}_n$(Theo): 45000 and PDI(MALLS): 1.60. ^{1}H-NMR spectroscopy was not used for determining $\overline{M}_n$ values in this system, as there was an overlap of the aromatic protons of CPDA and styrene.

Deprotection by Acidolysis (5 and 7)

The removal of the acetyl protecting groups, after the RAFT mediated polymerization process, was performed by modifying the method proposed by Black et al.[37] The protected polymer (20.00 g) was heated and rapidly stirred with 1N-hydrochloric acid (400 mL) for 2 hours at 100 °C. Water (100 mL) was added and the mixture was neutralized with 4N sodium hydroxide. The solution was dialyzed against distilled water for 3 days, and finally freeze-dried to render the deprotected polymer (verified by ^{1}H NMR) as a white powder with a quantitative yield.

Results and Discussion

Synthesis of the macro-RAFT Agent: Poly(3-O-Methacryloyl-1,2:5,6-di-O-isopropylidene-D-glucofuranose), (PMAlpGlc) (4)

The homopolymerization of MAlpGlc proceeded with 90% conversion being achieved within five and a half hours ($\overline{M}_n$(SEC): 12000, $\overline{M}_n$(MALLS): 24500, $\overline{M}_n$(^{1}H-NMR): 24000, $\overline{M}_n$(Theo): 25000 and PDI(MALLS): (1.16). Due to the inadequacy of polystyrene standards to approximate the hydrodynamic volume of these resulting polymers[20,39], molecular weights of polymers synthesized in this were determined by ^{1}H-NMR and MALLS.

In the case of ^{1}H-NMR, the anomeric proton of the sugar moiety (5.8–6.0 ppm) in the polymer was used in conjunction with the aromatic protons of the RAFT agent (7.2–7.8 ppm) to calculate the molecular weight of the resulting polymer.

Figure 2 shows the plots of (i) $\overline{M}_n$(Exp) and $\overline{M}_n$(Theo) versus time, (ii) % conversion versus time, and (iii) the UV (310 nm) and RI normalized responses for the homopolymerization of MAlpGlc. These results correspond well with studies conducted by Barner-Kowollik et al.,[35] who found that in the early stages of (CPDA) mediated meth(acrylate) polymerization, the transfer agent (CPDA) depletes more slowly resulting in a 'conventional' chain transfer distribution emerging. However, at higher conversion a strictly 'living' character dominates. This effect, a so-called

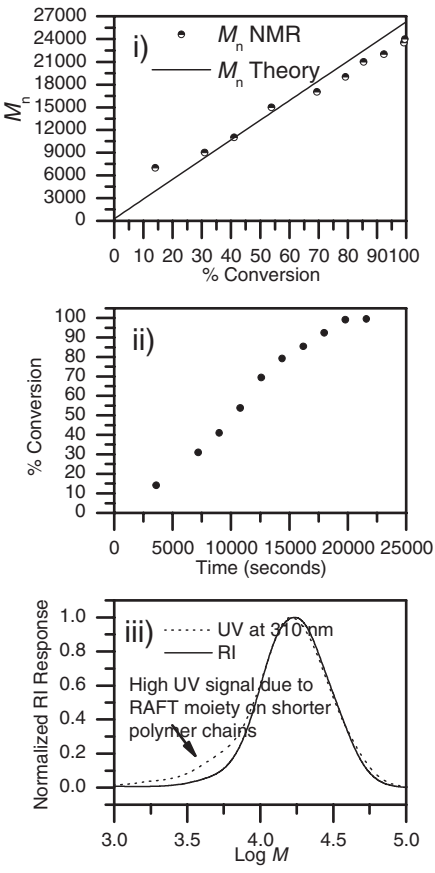


Figure 2.
Plots of i) $\overline{M}_n$ (Exp) and $\overline{M}_n$ (Theo) versus time, ii) % conv. vs time, and iii) the UV (310 nm) and RI normalized responses for the homopolymerization of MAlpGlc in ethyl acetate (25% w/v monomer) at 75 °C.

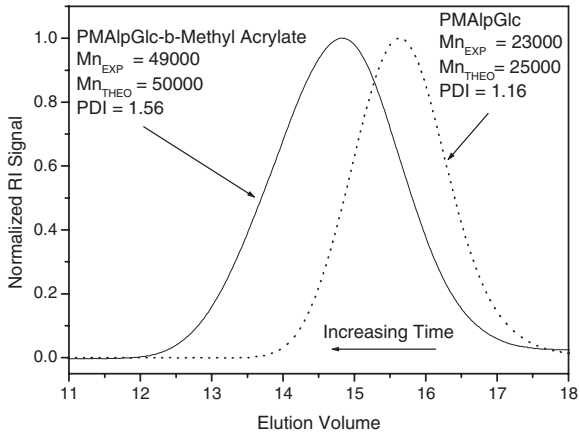


Figure 3.
SEC traces for the RAFT mediated copolymerization of PMAlpGlc and methyl acrylate in ethyl acetate (25% w/v monomer) at 75 °C. Starting compositions are tabulated in Table 1.

'hybrid' behaviour of conventional chain transfer and living free-radical polymerization, results in a subsequent decrease in the initial PDI of the system.[35] In this study, the PDI value decreased from a value of 1.5 to 1.16.

Styrene and Methyl Acrylate Chain Extension Polymerization Systems

To synthesize sugar-based block copolymers, the PMAlpGlc homopolymer was employed as a macro-RAFT agent for the block copolymerization of methyl acrylate and styrene. Figure 3 and 4 illustrate the evolution of molecular weight over time for the chain extension of PMAlpGlc with methyl acrylate and styrene. The observed blocking efficiency confirms the retention of the 'living' character of the resulting polymer, with RAFT chain-end functionality. The apparent absence of lower molecular weight elutions indicated that there was minimal unreactivated macro-RAFT agent (PMAlpGlc) present in the system. Although the $\overline{M}_n$(Exp) corresponded well with the $\overline{M}_n$(Theo), the final polydispersities were relatively large 1.56 and 1.60 for PMAlpGlc-b-(methyl acrylate)

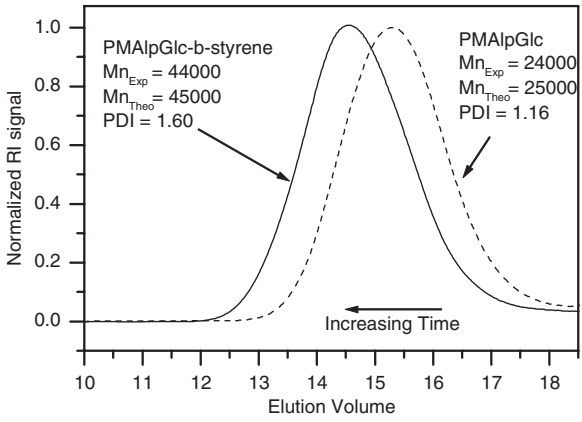


Figure 4.
SEC traces for the RAFT mediated copolymerization of PMAlpGlc and styrene in toluene (25% w/v monomer) at 80 °C. Starting compositions included are tabulated in Table 1.

and PMAlpGlc-b-(styrene) respectively. The *dn/dc* value for the MALLS measurement was calculated in duplicate for the final precipitated polymers to be 0.1946 (±0.0002) mL/g with a correlation coefficient of 0.9991 (±0.0050) and 0.1069 (±0.0004) mL/g with a correlation coefficient of 0.9989 (±0.0020) for PMAlpGlc-b-(methyl acrylate) and PMAlpGlc-b-(styrene), respectively. In ^{1}H-NMR spectroscopy, the methyl substituent in methyl acrylate, the anomeric proton of the sugar moiety in the polymer and the aromatic protons of CPDA were used in determining the $\overline{M}_n$(Exp) value. However, this approach could not be used for PMAlpGlc-b-(styrene) as there was an overlap of the aromatic protons of CPDA and styrene.

Deprotection of MAlpGlc Units into MAlGlc Units

All polymer samples were treated with hydrochloric acid. Figure 5 shows typical ^{1}H NMR spectra taken before and after acidolysis. Acidolysis allowed for the complete disappearance of the isopropylidene protons [1.2–1.4 ppm in Figure 5(a)] and instead, a broad signal assignable to the anomeric hydroxyl groups of the sugar moiety [6.4–7.0 ppm in Figure 5(b)] appeared. The spectrum obtained conforms to existing literature and verifies the quantitative deprotection of the isopropylidene groups.[16,23]

Self-assembly/Aggregation Studies

The Critical Micelle Concentration (CMC) of the diblock glycopolymers was investigated by conductivity, whereby conductivity was measured (μS) at various polymer concentrations in water. Figure 6 and 7 show that self assembly/CMC occurs at 0.12 (±0.01) and 0.13 (±0.01) g/L for PMAlGlc-b-poly(styrene) and PMAlGlc-b-poly(methyl acrylate) respectively. These results are an average of triplicate measurements carried out at 295K. Due to the fact that the hydrophobicity of poly(methyl acrylate) and poly(styrene) are similar, relative to that of the glycol-moiety, the CMC values obtained from Figure 6 and 7 in this study are similar.

Micellar behaviour of sugar containing polymers in aqueous solutions has been reported previously.[40] However, a direct comparison between their results and ours

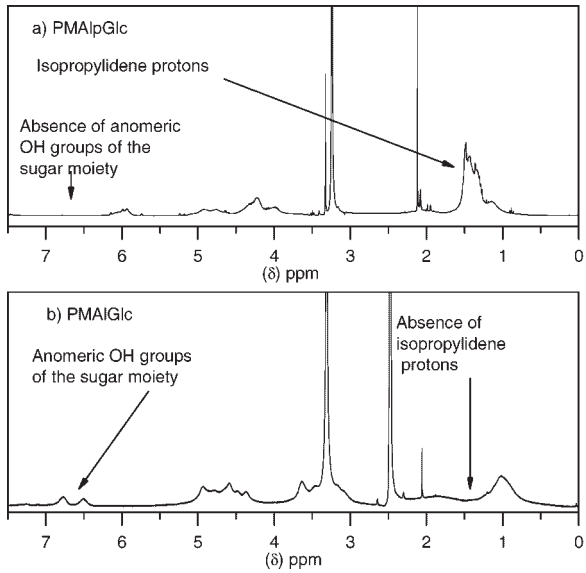


Figure 5.
Typical ^{1}H NMR spectra taken a) before and b) after the acidolysis of PMAlpGlc. The solvents were a) $CDCl_3$ and b) DMSO-*d6*.

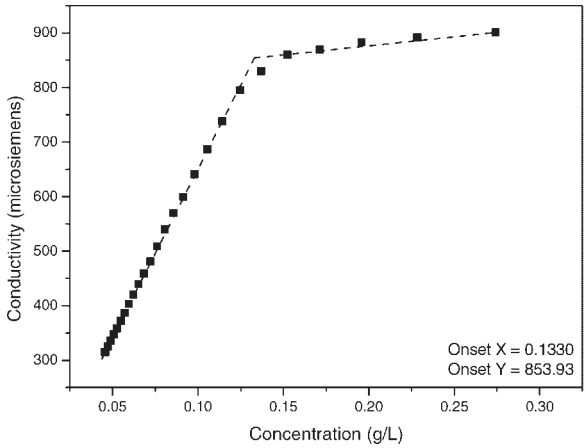


Figure 6.
Variation of conductivity with concentration of PMAlGlc-b-poly(styrene) in an aqueous solution at 295K.

can not be drawn, due primarily to the novel glycopolymers (i.e. monomer compositions and molecular weights and architectural design) produced in this study. For instance, Goto et al.[41] documented the CMC value of poly[N-p-vinyl-benzyl-O-β-D-galactopyranosyl-(1$\sim$4)-D-gluconamide] to be about 4 g/L. In their study, an amphiphilic homopolymer was used, whereby the hydrophilic head group is part of the monomer itself and thus homogeneously distributed along the main polymer backbone whereas in our case we have a diblock copolymer, thus behaving as a giant classical surfactant.

In other cases, isometrically pure sugar surfactants of β-D-alkylmaltoside and β-D-alkylglucoside types have been studied, with molecular weights of 510 and 292 g/mol, in the case of dodecyl-β-D-maltoside and 1-O-n-octyl-β-D-glucopyranoside respectively.[40] Once again the CMC values of 0.1 and 7.0 g/L, obtained in their study, are not comparable due to the polymers molecular weight, monomer compositions and architectural design.

Particle Morphologies at their CMC Value

Sample preparation for self-assembly studies involved vapor staining of the diblock

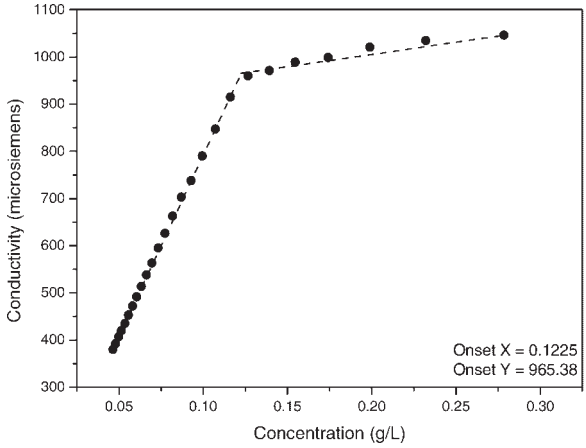


Figure 7.
Variation of conductivity with concentration of PMAlGlc-b-poly(methyl acrylate) in an aqueous solution at 295K.

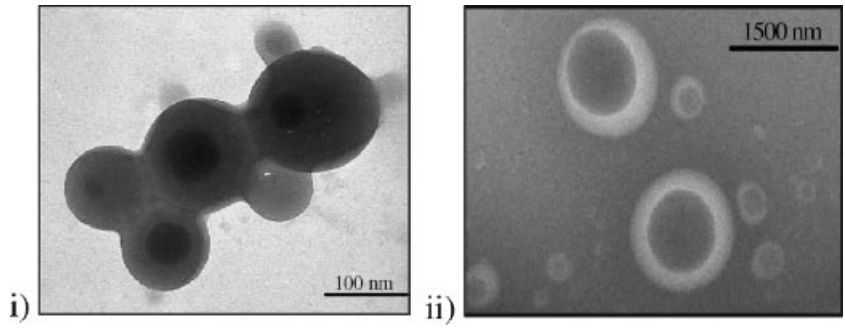


Figure 8.
TEM image illustrating the core-shell self-assembling behaviour of i) PMAlGlc-b-styrene in water (0.12 g/L) after 20 minutes, and ii) PMAlGlc-b-methyl acrylate in water (0.13 g/L) after 20 minutes.

copolymer with OsO_4 for 30 minutes after which a 0.12 and 0.13 g/L solution of the diblock copolymers in water or toluene was stirred at ambient temperature for 20 minutes. The samples were appropriately diluted to a concentration of 2.4×10^{-3} g/L before being applied to a carbon coated copper grid for TEM analysis.[42]

Figure 8 demonstrates the self-assembling spherical core-shell nanoparticles for the amphiphilic diblocks whereby, styrene or methyl acrylate aggregates to form the inner core encapsulated by a hydrophilic carbohydrate-based outer shell.

Inverted core-shell particles were also prepared (Figure 9) in toluene thereby, allowing the hydrophobic moieties (styrene and methyl acrylate) to aggregate on the outer periphery of the particle encapsulating a hydrophilic carbohydrate-based inner core.

These amphiphilic 'smart' polymers, which respond with a considerable change in their properties to small changes in their environment, can serve as a pocket for the protection of water sensitive drugs. Thereby, allowing them to be effectively used in target specific drug delivery systems.[41]

Conclusions

The RAFT mediated synthesis of novel block glycopolymers with well-defined architectures was successfully carried out. Poly(3-O-Methacryloyl-1,2:5,6-di-O-isopropylidene-D-glucofuranose)-b-methyl acrylate and Poly(3-O-Methacryloyl-1,2:5,6-di-O-isopropylidene-D-glucofuranose)-b-styrene were prepared with fairly narrow molar mass distributions. After acidolysis,

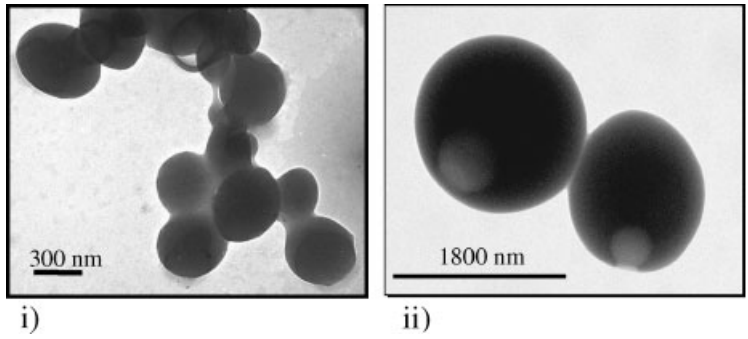


Figure 9.
TEM image illustrating the inverted core-shell self-assembling behaviour of i) PMAlGlc-b-styrene in toluene (0.12 g/L) after 20 minutes and ii) PMAlGlc-b-methyl acrylate in toluene (0.13 g/L) after 20 minutes.

their amphiphilic self-assembling character was measured when these diblock copolymers formed spherical core-shell nanoparticles, where the hydrophobic and hydrophilic moieties were distinguishable. The formation of an encapsulated glycopolymeric core sought for in this project was achieved and was found to be exchangeable by the type of solvent utilized.

Acknowledgements: The authors would like to thank M. A. Jaffer (Electron Microscope Unit, University of Cape Town, Private Bag, Rondebosch, 7701, South Africa) for his continuous support and invaluable contribution throughout the duration of this study.

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