

Tailored Glycopolymers

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Declaration

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Abstract

The synthesis of glycopolymers with various comonomers as prepared via the RAFT process is investigated.

The macro-RAFT agent poly(3-O-methacryloyl-1,2:5,6-di-O-isopropylidene-D-glucofuranose) (PMAIpGlc) was prepared by polymerization of the glycomonomer with cumyl phenyl dithioacetate as the chain transfer agent. Chain extension with styrene or methyl acrylate or acrylic acid afforded novel diblock copolymers, (PMAIpGlc-b-poly[styrene] or PMAGlc-b-poly[methyl acrylate] or PMAIpGlc-b-poly[acrylic acid]), with predetermined molecular weights and narrow molecular weight distributions.

The poly(acrylic acid) based glycopolymer was used to modify the surface of CaCO_3 , forming what will be referred to as a ‘sugar-coated CaCO_3 ’ particle. This surface modifying effect was evaluated in depth; a schematic study of the effect of reaction temperature, pH, reaction time and glycopolymer concentration on CaCO_3 crystallization was carried out. The analytical techniques Thermal Gravimetric Analysis (TGA) and Scanning Electron Microscopy (SEM) were used to verify that these ‘sugar-coated CaCO_3 ’ particles have an increased adherence to cellulose compared to ‘non sugar-coated’ particles.

A series of polymer configurations comprising various ratios of glycomoiety to poly(acrylic acid) was prepared. The effect of this polymer series on CaCO_3 crystallization was evaluated and the ideal polymer configuration and its optimum synthesis conditions (i.e. reaction pH, temperature, time and polymer concentration) that gave maximum adherence of the ‘sugar-coated CaCO_3 ’ particle onto cellulose were identified.

The ability of these poly(acrylic acid) based glycopolymers to increase the interaction between CaCO_3 and cellulose was then evaluated. This was done by simply mixing all three substrates, i.e. glycopolymer, cellulose and CaCO_3 together. Analysis by TGA, SEM and Thin Layer Chromatography (TLC) revealed both the ideal polymer configuration that favoured increased

adherence of the CaCO_3 to cellulose and the optimum reaction conditions required for application and testing.

In addition to studying the interaction between cellulose and CaCO_3 , the amphiphilic nature of the glycopolymers was determined. Transmission Electron Microscopy (TEM) confirmed that core-shell particles were prepared and that these particles are solvent exchangeable (in the case of styrene and methyl acrylate glyco-blocks) or pH exchangeable (in the case of acrylic acid glyco-blocks).

Keywords: Glycopolymers, RAFT, cellulose, calcium carbonate, amphiphilic core-shell particles.

Opsomming

Die bereiding van glukopolimere met 'n verskeidenheid komonomere deur van die RAFT-proses gebruik te maak, is ondersoek.

Die makro-RAFT-verbinding, poli(3-O-metakrieloel-1,5:5,6-di-O-isopropielidien-D-glukofuranose) (PMAIpGlc), is berei deur middel van polimerisasie van die glukopolimeer met kumielfeniellitioasetaat as die kettingoordragverbinding. Kettingverlenging van die makro-RAFT-verbinding met stireen of metielakrielaat of akrielsuur het die vorming van 'n nuwe tipe blokpolieer tot gevolg gehad, naamlik PMAIpGlc-b-polistireen of PMAIpGlc-b-poli[metielakrielaat] of PMAIpGlc-b-poliakrielsuur. Hierdie blokpolimere is gevorm met voorafbepaalde molekulêre massas en nou molekulêre massaverspreidings.

Die poliakrielsuur-gebaseerde glukopolimeer is verder gebruik om die oppervlakte van CaCO_3 te wysig om sogenaamde 'suiker-bedekte CaCO_3 ' partikels te vorm. Die oppervlakwysiging is in diepte bestudeer en 'n skematiese studie van die effek van reaksietemperatuur, pH, reaksietyd en glukopolimeerkonsentrasie op die kristallasie van CaCO_3 is uitgevoer. Analitiese metodes soos Termiese gravimetriele analise (TGA) en Skandeerelektronmikroskopie (SEM) is gebruik om te bewys dat die 'suiker-bedekte CaCO_3 ' beter vaskleef aan sellulose as onveranderde CaCO_3 partikels.

'n Reeks polimeerkonfigurasies bestaande uit verskeie glukose tot poliakrielsuur verhoudings, is berei. Die effek van die polimeerreks op die kristallasie van CaCO_3 is beoordeel en die ideale konfigurasie sowel as die optimale bereidingskondisies (i.e. reaksie pH, temperatuur, reaksietyd en polimeerkonsentrasie) wat die maksimum vasklewing van die 'suiker-bedekte CaCO_3 ' partikels aan die sellulose gee, is bepaal.

Die vermoë van hierdie poliakrielsuur-gebaseerde glukopolimere om die interaksie tussen CaCO_3 en sellulose te verbeter, is gevolglik ondersoek. Dit is uitgevoer deur eenvoudig die drie grondstowwe, i.e. glukopolimeer, sellulose en CaCO_3 , bymekaar te voeg. Deur gebruik te maak van analitiese tegnieke soos TGA, SEM en Dunlaagchromatografie (DLC) is beide die ideale polimeerkonfigurasie

wat vasklewing aan CaCO_3 verbeter, sowel as die optimale reaksiekondisies benodig vir toepassing en toetsing, bepaal.

Ter aanvulling van die studie op die interaksie tussen sellulose en CaCO_3 , is die amfifiliese karakter van die glukopolimere bepaal. Transmissie-elektronmikroskopie (TEM) het beslis dat kernskilpartikels gemaak is en dat hierdie partikels oplosmiddeluitruilbaar is (in die geval van stireen en metielakrylaat glukoblokpolimere) of pH-uitruilbaar is (in die geval van akrielsuur blokpolimere).

Sleutelwoorde: Glukopolimere, RAFT, sellulose, kalsiumkarbonaat, amfifiliese kernskilpartikels

To Kamini Ramiah

“When angels visit us, we do not hear the rustle of wings, nor feel the feathery touch of the breast of a dove; but we know their presence by the love they create in our hearts.”

Thank you for being my *true gaurdian angel*....

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List of Publications

During the course of this study the following papers have been published (or accepted/ submitted/ in preparation):

- Ramiah, V., Mathawa, H., Weber, W., McLeary, J. B. and Sanderson, R. D. “CMC and phase separation studies of RAFT mediated amphiphilic diblock glycopolymers with methyl acrylate and styrene” *Macromolecular Symposia*, 2007, 255, 70-80.
- Ramiah, V. Mathawa, H., Terblanche, J. C., Le Grange, M. S. and Sanderson, R. D. “Crystallization of calcium carbonate in presence of acrylic acid based glycopolymers” Submitted to the *Journal of Crystal Growth*, 2008.
- Ramiah, V. Mathawa, H., Terblanche, J. C., Le Grange, M. S. and Sanderson, R. D. “Part 2: Crystallization of calcium carbonate in presence of acrylic acid based glycopolymers” Submitted to the *Journal of Crystal Growth*, 2008.
- Ramiah, V. Mathawa, H., Terblanche, J. C. and Sanderson, R. D. “Novel retention aids” *TAPPI*. (In preparation)
- Mathawa, H., Ramiah, V., Jarrett, W. L., McLeary, J. B. and Sanderson, R. D. “Microwave assisted graft copolymerization of N-isopropyl acrylamide and methyl acrylate on cellulose: solid state NMR analysis and CaCO₃ crystallization” *Macromolecular Symposia*, 2007, 255, 50-56.

- Mathawa, H., Ramiah, V., McLeary, J. B. and Sanderson, R. D. “Calcium carbonate crystallization in the presence of modified polysaccharides and linear polymeric additives” Article in press: *Journal of Crystal Growth and Design*, August 2008
- Weber, W., van den Dungen, E. T. A., Ramiah, V., Rinqest, J., Pretorious, N. O., Klumperman, B. L. and Sanderson, R. D. “Efficient trithiocarbonates bearing tertiary leaving group radicals for RAFT-mediated polymerization.” Submitted to *Polymer*, 2007.

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List of Acronyms

AIBN	2,2-azobis(isobutyronitrile)
AA	Acrylic acid
CaCO ₃	Calcium carbonate
CELL	Cellulose
cmc	Critical micelle concentration
CPDA	Cumyl phenyl dithioacetate
EEA	1-Ethoxyethyl acrylate
KPS	Potassium persulfate
MALLS	Multi angle laser light scattering
MAIpGlc	3- <i>O</i> -methacryloyl-1,2:5,6-di- <i>O</i> -isopropylidene-D-glucofuranose
MAIGlc	Unprotected glucosyl methacrylate
PCC	Precipitated calcium carbonate
PMAIGlc	Poly(unprotected glucosyl methacrylate)
PMAIpGlc	Poly(3- <i>O</i> -methacryloyl-1,2:5,6-di- <i>O</i> -isopropylidene-D-glucofuranose)
Poly(AA)	Poly(acrylic acid)
Poly(MA)	Poly(methyl acrylate)
Poly(STY)	Poly(styrene)
RAFT	Reversible addition fragmentation chain transfer
XRD	X-ray Diffraction

List of Symbols

\overline{M}_n (theor)	Calculated number average molar mass
\overline{M}_n (exp)	Experimental number average molar mass
$[I]_0$	Initial concentration of the initiator
$[M]_0$	Initial concentration of the monomer
$[RAFT]_0$	Initial concentration of the RAFT agent
μs	Microsiemens
\overline{M}_n ($^1\text{H-NMR}$)	Number average molar mass determined by $^1\text{H NMR}$
\overline{M}_n (MALLS)	Number average molar mass determined by MALLS
\overline{M}_n (SEC)	Number average molar mass determined by SEC

Chapter 1

Introduction

1.1 General introduction

The scientific unravelling of carbohydrate chemistry began nearly 100 years ago when scientists attempted to explore the structure of these ubiquitous molecules in relation to their functions. These molecules have a remarkable ability of encoding diverse functions by small changes in their molecular structure. For example, heparin, a sulphated polysaccharide, plays an essential role in blood coagulation whilst chondroitin, another sulphated polysaccharide, exhibits anti-inflammatory activity.¹ As a result carbohydrates form key components in a variety of biological processes and structural materials and serve as a valuable source of energy in nature. Basic understanding of these biological processes was facilitated by the advent of glycopolymers, which can be defined as synthetic polymers containing carbohydrate moieties as terminal groups. It was recognized that synthetic polymers displaying complex functionalities similar to those of natural glycoconjugates might be able to mimic their performance in specific applications. Consequently, the use of glycopolymers in a variety of biological and biomedical applications (such as drug-delivery systems,^{2,3} molecular recognition and separation processes,⁴ surfactants,⁵ responsive hydrogels,⁶ treatment of infectious diseases⁷ and treatment of HIV⁸) has attracted considerable interest.

In this study glycopolymers were studied for another purpose: It was hypothesized that well defined glycopolymers will contribute to understanding the interaction between inorganic particles and cellulose fibers, which is particularly relevant to the paper industry.

1.2 The importance of fillers

The incorporation of inorganic particles (fillers) in paper has been common practice for many years. Though the term ‘filler’ is somewhat uncomplimentary, this group of predominantly inorganic materials has become a very essential component of many grades of paper. The original purpose of adding filler to the paper matrix was to lower furnish costs, with the amount of filler limited only by strength considerations. Today the principal need for fillers is to impart specific quality improvements to the sheet. Depending on the performance characteristics of the fillers and the amount added to the paper, these fillers can improve the optical, physical and aesthetic properties of the finished sheet. Today the practice of utilizing fillers is based on choosing materials that will provide both cost and quality improvements. The conversion to alkaline papermaking in North America has emphasized this approach, where fillers designed to add value to the paper are routinely used. This trend is confirmed by the rapid growth in the tonnage of value-added specialty fillers purchased by paper mills.

Fillers are added to paper in various percentages, typically 10 to 20%, to perform many different functions. The choice of which filler or blend of fillers to use depends upon the specific properties desired. While fillers are used in many different grades of paper they find their greatest use in printing and writing grade papers. Fillers can contribute to the following properties of paper:

- Improve sheet formation by filling in the void areas around fiber crossings
- Provide a smoother surface
- Increase opacity and brightness
- Provide enhanced printability, for a number of reasons, such as
 - a smoother, more uniform surface,
 - less ‘show through’ caused by increased opacity, and
 - better ink receptivity, reducing ink penetration, wicking, and strike through
- Improve dimensional stability (most fillers are not hydroscopic-like fibers)
- Provide cost savings by replacing higher cost natural fibers with lower cost fillers.

1.3 The paper-makers’ tools and some associated problems

Over the decades, paper-makers have made use of retention aids as a tool to improve the retention of filler particles during paper formation. These retention aids have often been high molecular weight

cationic and anionic polyacrylamides, high molecular weight polyethylene oxides and a most recent invention, microparticles.

Some examples of retention aids are now described. Cationic polyacrylamides (CPs) promote absorption of the fillers to the fibers either by heteroflocculation or heterocoagulation. The former results in a bridge being formed between fibers and fillers and the latter causes a reduction in the electrical charges, resulting in high deposits of filler on the fibers. The disadvantage of this system, however, is that if anionically soluble and colloidal substances are to be introduced then preferential interaction would take place between CPs and anionic particles rather than between CPs and the filler.⁹

A more complex retention aid system, which takes into account the high-speed paper-making processes, the complexity of wet-end paper-making due to the extensive use of additives, and the high degree of water recirculation, has been developed. Dual-component retention aid systems employ a microparticle component (colloidal silica, modified bentonite clay) in conjunction with a cationic polyelectrolyte. The polyelectrolyte absorbs onto the fiber and filler, resulting in the formation of aggregates that may provide anchoring spots for the microparticles. These microparticles reflocculate the entire system and act as a bridge between all the components, thereby increasing the attachment of filler to fiber. It has been shown that at the optimum concentrations bentonite increases the bond strength of cationic polyacrylamide, precipitated CaCO_3 and fibers.¹⁰ However, studies have shown that different microparticle components are efficient for different pulp types and hence for use in different paper mills. Taking into consideration that pulp types change with season and climate, additional costs are incurred by paper mills when they are required, to optimize conditions for various types of microparticles contained within the various pulps.

A third example includes modifying the charge of the filler. Nystrom et al.¹¹ showed that by pretreating CaCO_3 with anionic sodium polyacrylate (NaPA) one is able to anionically modify the particles and reverse the charge character of the originally cationic CaCO_3 . This resulting anionic particle will then subsequently adhere onto cationic starch, which is commonly used as a strength additive in the wet-end of the paper-making process.

Although these synthetic polymers, discussed above, successfully increase filler retention by 30% there are some inherent drawbacks. Polyacrylamides, for instance, are not easily biodegradable and are highly toxic due to the associated high levels of monomers present in the acrylamide copolymers.

Microparticles can often over-flocculate the stock in the process of attaining acceptable filler retention, resulting in sheet web-formation and print quality problems. The use of polyethylenimines has been dismissed mainly because of the discoloration that it brings to cellulose.¹² For most other retention aids the following have shown to be major drawbacks: cost, non-biodegradability, difficulty in controlling/operating processes during manufacture, the low stability of operation, and the production of paper with low quality.

1.4 Novel approach to increase absorption between CaCO_3 and cellulose fibers

In the light of the above-mentioned, the preparation and use of a novel AB block copolymeric dispersant is proposed (see Figure 1.1). Moiety A is a carbohydrate (a so-called ‘glycopolymer’), which is hypothesized to adhere to cellulose via hydrogen bonding, whilst moiety B is a poly(acrylic acid) [poly(AA)] moiety. Poly(AA) is currently used as a dispersant of CaCO_3 by a mechanism shown to rely on the electrostatically driven adsorption of the negatively charged poly(AA) onto the cationic surface of CaCO_3 in the paper coating industry.¹³⁻¹⁶ This concept is illustrated in Figure 1.1.

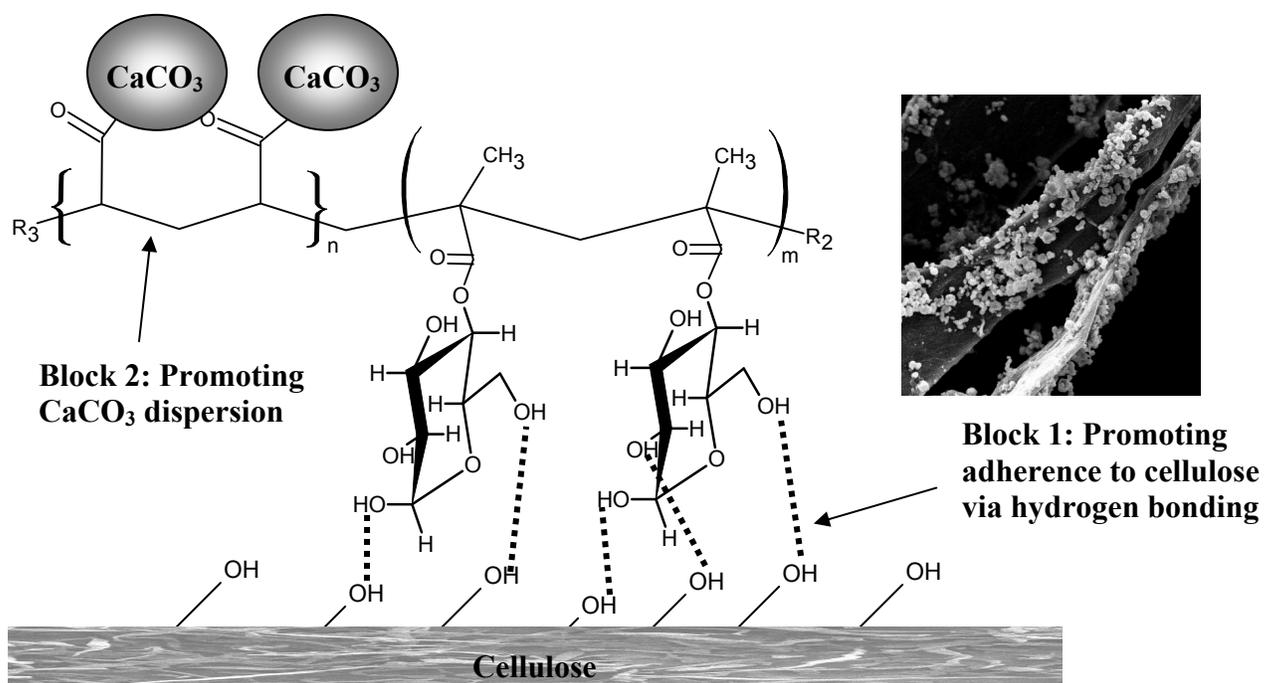


Figure 1.1 Polymer structure and configuration, proposed for this research project, to improve the adsorption of an inorganic particle (CaCO_3) onto cellulose. (Insert: SEM illustration of CaCO_3 particles adhering to cellulose fibers)

1.5 Objectives

The overall aim of this study was to attach as much CaCO_3 to cellulose as possible. The objectives hence emanate from the proposal described in Section 1.4.

The first objective is to determine whether the AB block glycopolymer could indeed be synthesized and, if so, whether the architecture could be controlled by, for example, the RAFT process.

Should it be possible to successfully synthesize the above glycopolymer then the next objective will be to determine whether the glycopolymer dispersant can bind to inorganic CaCO_3 , and thereby determine whether this glycopolymer-modified inorganic material has any positive effect on the adherence capabilities of the filler to the cellulose fibers.

The third objective is to determine the ideal diblock configuration (ratio of the glycopolymer and poly(AA) components of the diblock) that promotes maximum binding of the inorganic particle to the cellulose fiber. This will be determined by Gel Permeation Chromatography (GPC) and TGA.

The final objective is to determine the ability to increase the binding of inorganic particles to cellulose fibers by adjusting the method of addition of the three components (particles and glycopolymer, CaCO_3 particles, and fiber). The following specific questions are addressed: (a) should the glycopolymer be premixed with the particles prior to addition to the fiber, (b) should the glycopolymer be premixed with the fiber prior to its addition of the particles, or (c) should all three components (fiber, particles and glycopolymer) be added simultaneously during a paper-making process. Determination of the best reaction conditions to achieve the optimum ratio of components is very important.

1.6 Thesis layout

This thesis comprises six chapters, three of which describe the experimental work carried out. Chapter 2 presents an important overview of the existing literature on various methods of synthesizing glycopolymers as well as on their self-assembling and binding capabilities. It serves to highlight the need for the research undertaken in this study.

Chapter 3 describes investigations carried out into the synthesis of the glycopolymers, via the RAFT process, with the aim of achieving products with predetermined molecular weight and narrow molecular weight distributions. This chapter is in part reproduced from the following published paper: *CMC and phase separation studies of RAFT mediated amphiphilic diblock glycopolymers with methyl acrylate and styrene, Macromolecular Symposia, 2007.*

Chapter 4 describes the RAFT mediated synthesis of an acrylic acid based glycopolymer and its subsequent role in the crystallization of CaCO₃. Optical microscopy and X-ray diffraction (XRD) analyses confirmed that novel ‘sugar-coated’ CaCO₃ microparticles were indeed synthesized and that the acrylic acid moiety of the polymer modified CaCO₃ crystal growth and resulted in an array of randomly structured round-edged arrangements. Qualitative and quantitative analyses confirmed that these glyco-coated particles adhere to cellulose fibers.

Chapter 5 describes the synthesis of the ‘ideal copolymer configuration’. Specifically, various ratios of glyco to poly(AA) molecular weights were synthesized and the optimum ratio that promotes maximum absorption of the inorganic particle to fiber, utilizing various methods of application, was identified. A study on the effect that these polymers have on CaCO₃ crystallization, under various conditions of reaction pH, temperature and time, was also carried out.

Conclusions are presented in Chapter 6, followed by some recommendations for future research.

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Chapter 2

Tailored Glycopolymers

Abstract

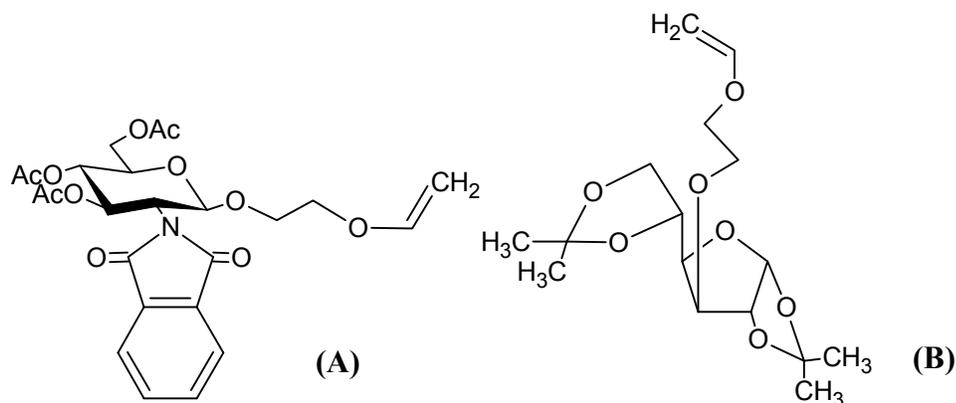
Aspects of the numerous synthetic routes for the preparation of well-defined glycopolymers are discussed. The self-assembling, surface modifying and binding capabilities of glycopolymers in relation to their structures are also discussed. The latter illustrates the importance of this study.

2.1 Glycopolymers – synthesis routes and historical highlights

The synthesis of glycopolymers can be achieved by either polymerizing carbohydrate-based monomers or chemically modifying preformed polymers with carbohydrate-based reagents. Each of these procedures has its own pros and cons. The advantage of the latter is that the reaction procedure is much simpler and convenient, mainly because the synthesis of carbohydrate-based monomers involves tedious, multi-step reactions. However, the disadvantage is that a mixture of structures results from the latter method, mainly due to steric hindrance that affects reaction kinetics. In the light of this, research over the past years has focused on the former technique, mainly due to its superior advantage of allowing the synthesis of glycopolymers with well-defined architectures. This section describes the synthetic work that has been carried out to date, with special emphasis placed on the polymerization techniques used.

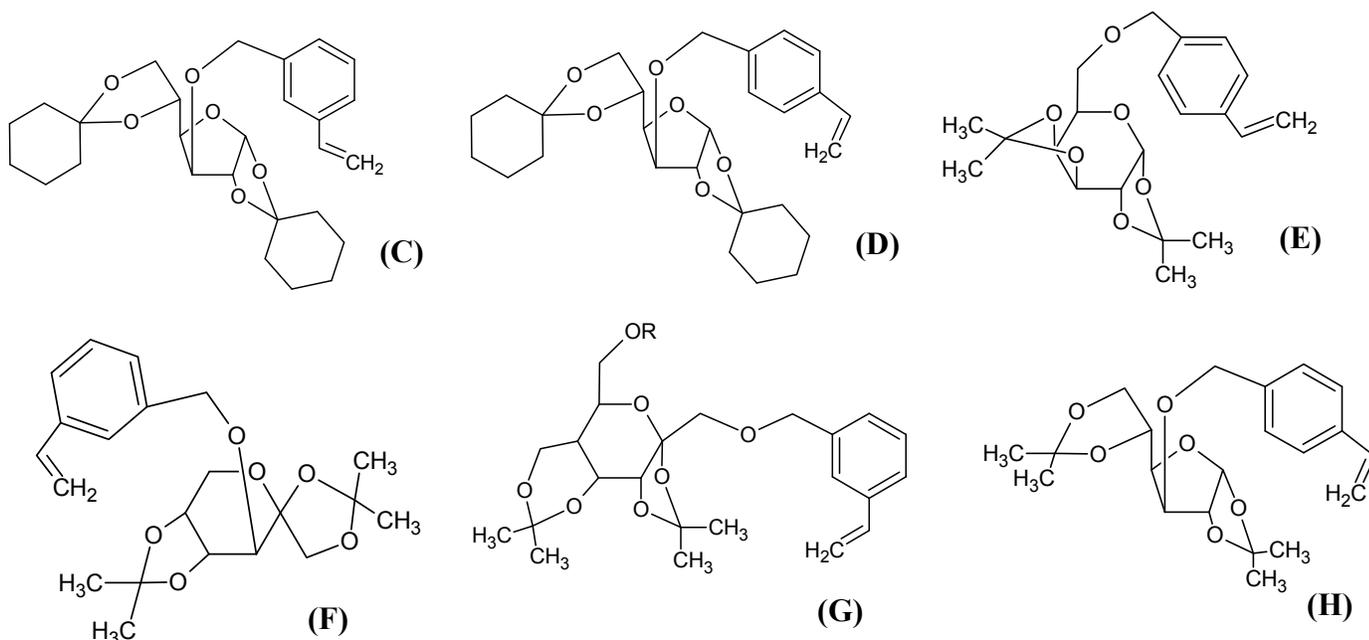
2.1.1 Glycopolymers synthesis by ionic polymerization

Initially, cationic polymerization did not receive much recognition as polymers such as vinyl ethers and styrenes with controlled molecular weights could not be obtained. However, in 1989 Higashimura and Sawamoto¹ showed that by using hydrogen iodide/iodine or hydrogen iodide/weak Lewis acid initiator systems one is able to stabilize the growing end in a polymer, and thereby facilitate controlled polymerizations. This set the groundwork for Yamada et al.²⁻⁴ who used this methodology to successfully synthesize glycopolymers with controlled molecular weights by cationically polymerizing carbohydrate-carrying vinyl ethers. They used a $\text{CF}_3\text{COOH}/\text{EtAlCl}_2$ initiating system in the presence of a base (1,4-dioxane) and cationically polymerized isobutyl vinyl ether (IBVE) and a vinyl ether carrying 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-beta-D-glucose (A). This reaction yielded a living amphiphilic block copolymer with a narrow molecular weight distribution (PDI ~1.1).



Yamada et al.^{2,5} also experimented with another initiating system, $(\text{CH}_3\text{CH}(\text{O}_i\text{Bu})\text{Cl})$, in conjunction with zinc iodide, to synthesize block copolymers of IBVE and 1,2:5,6-diisopropylidene-3-2-(2-vinyloxy ethyl)-D-glucofuranose (**B**). Once again, selective polymers with low polydispersities (< 1.20) and highly specific predetermined molecular weights were obtained.

The synthesis of glycopolymers using living anionic polymerization stemmed from research done by a group led by Hirao et al.,⁶⁻⁸ who initially investigated the use of monomers with protected functional groups using this polymerization technique. Six styrene derivatives *meta*-substituted with (**C**) and (**D**) acetal-protected glucofuranose, galactopyranose (**E**), fructopyranose (**F**), sorbofuranose (**G**) and *para*-substituted with acetal-protected glucofuranose (**H**) were synthesized by Williamson reactions and polymerized with *s*-BuLi in THF at $-78\text{ }^\circ\text{C}$. Results indicated that when monomers (**C**) to (**G**) were used then polymers of predictable molecular weights and narrow molecular weight distributions ($\text{PDI} < 1.13$) were obtained. However, no appreciable polymerization of monomer (**H**) occurred under identical conditions. Ishizone et al.⁹ and Hirao et al.^{10,11} compared this behaviour to anionic polymerizations of styrene derivatives possessing benzyl ether skeletons and explained that there could be a generation of a very reactive *p*-xylene or biradical intermediate, which may readily react with each other, resulting in an uncontrolled insoluble crosslinked polymer.



Anionic and cationic living polymerizations produce polymers of specific architecture and stereochemistry. However, there are some limitations associated with both procedures. The

polymerizations usually require aprotic solvents and all reagents must be of highest purity. Monomers should not contain acidic protons, in order to reduce side reactions. In addition, the reactions are sensitive to oxygen and water, and usually require sub-ambient temperatures. Hence, these techniques are expensive and not well suited for synthesis on an industrial scale.^{2,4-6,12,13}

2.1.2 Glycopolymer synthesis by ring-opening metathesis polymerization (ROMP)

Various well-defined glycopolymers have been synthesized by ROMP¹⁴⁻¹⁹ and lately the use of ROMP in glycopolymer synthesis has become very attractive. This is mainly because of the advent of new ROMP catalysts (for example, ruthenium carbene,¹⁴ molybdenum *tert*-butoxide¹⁵ and ruthenium trichloride,^{17,18} to name a few).

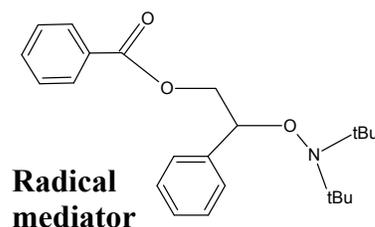
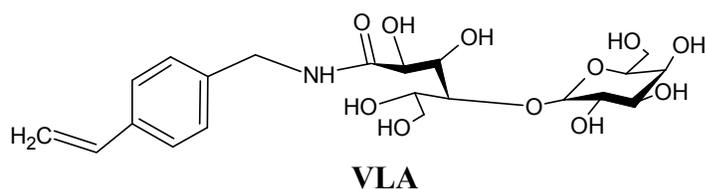
Fraser and Grubbs¹⁴ made use of a ruthenium carbene catalyst to synthesize several sugar-substituted norbornene derivatives with a series of protected glucose functionalities attached via an amide linkage. This catalyst also facilitated living ROMP and block copolymerization in various solvents. According to Fraser and Grubbs,¹⁴ a further benefit of this type of catalyst is that it tolerates monomers with unprotected polar functionalities. This will allow scientists to use many more naturally occurring carbohydrates, especially carbohydrates that contain groups that are not easily masked, such as sulphated groups. This idea was investigated further and proved by Manning et al.¹⁹

However, ROMP does have some disadvantages. In addition to having similar limitations to ionic polymerization,²⁰ although in the case of ROMP they were simply overcome by the use of ruthenium based catalysts,^{14,17} ROMP requires the post-polymerization removal of the heavy metal catalyst residues, which adversely affects industrial costs.

2.1.3. Glycopolymer synthesis by nitroxide mediated polymerization (NMP)

NMP has found some application in glycopolymer syntheses.²¹⁻²⁸ A typical example makes use of [*N*-(*p*-vinylbenzyl)-[*O*-β-D-galactopyranosyl-(1-4)]-D-gluconamide (VLA) and an acetylated VLA monomer, (2-(benzoyloxy)-1-(phenylethyl)-di-*tert*-butyl nitroxide as a radical mediator and dicumyl peroxide as an accelerator, in DMF]. Ohno et al.²⁹ reported the synthesis of the first glycopolymer prepared by NMP. However, conversions were limited and no polymerization resulted when higher degrees of polymerization were targeted. They furthered their study into this phenomenon and claimed

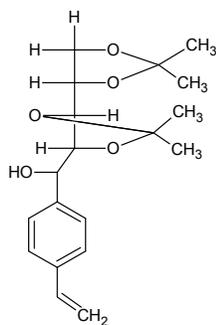
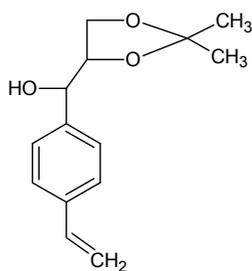
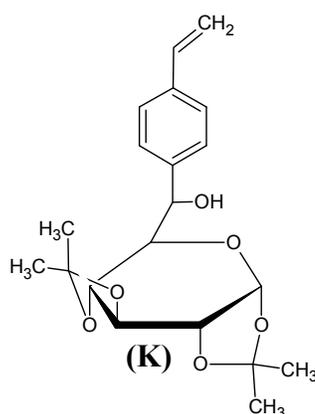
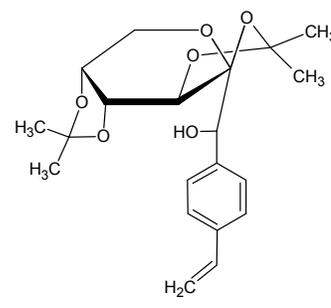
that this retardation (i.e., low conversions) is attributed to the occurrence of side reactions, specifically due to the transfer of the propagating chain to a hydroxyl group of the monomer. This implies that if one desires living glycopolymers to be prepared by NMP then protection of the carbohydrate hydroxyl groups with isopropylidene groups is required.



This concept was pursued further by Chen and Wulff,²⁴ who carried out the bulk polymerization of four different isopropylidene-protected sugar monomers, namely:

- 2,3:4,5-Di-*O*-isopropylidene-1-(4-vinylphenyl)-D-gluco(D-manno)pentitol (**I**)
- 2,3-isopropylidene-1-(4-vinylphenyl)-D-threo(D-erythro)triol (**J**)
- 1,2:3,4-di-*O*-isopropylidene-1-(4-vinylphenyl)-D-glyero(L-glyero)-alpha-D-galactopyranose (**K**)
- 2,3:4,5-Di-*O*-isopropylidene-1-(4-vinylphenyl)-D-manno(D-gluco)hexulo-2,6-pyranose (**L**)

(in which a C-C bond is used to connect the vinyl groups to the monosaccharide). Using these protected monomers, they reported molecular weight distributions of < 1.5 and confirmed the hypothesis of Ohno et al.,²⁹ namely that in order to produce living glycopolymers via NMP then protection of the carbohydrate hydroxyl groups with isopropylidene groups is required.

**(I)****(J)****(K)****(L)**

2.1.4 Glycopolymer synthesis: Polymerizations mediated by the cyanoxyl radical (NC-O•)

This technique offers some major advantages over NMP in that reaction temperatures are lower (often between ambient and 70 °C), thus reducing problems of thermal instability and leaving

polymerizations unaffected by the presence of functional groups. The latter makes it suitable for polymerizations to be carried out with unprotected sugar monomers.^{30,31}

Grande et al.^{32,33} and Sun et al.³⁴ studied this polymerization technique in detail by utilizing it in homo- and copolymerizations of acrylamide. The cyanoxyl radical was formed in situ by an electron transfer reaction between cyanate anions and *p*-chlorobenzenediazonium cations (the *p*-chlorophenyl radical byproduct acting as an initiating fragment in the presence of an appropriate monomer species, see Figure 2.1). Grande et al.^{32,33} and Sun et al.³⁴ reported that conversions were low, particularly when high glycomonomer feed ratios were used. However, polymers with relatively high molecular weight (> 100 kDa) can be produced when high feed ratios of acrylamide are used. It was however, favourable, that molecular weight distributions were below 1.5.

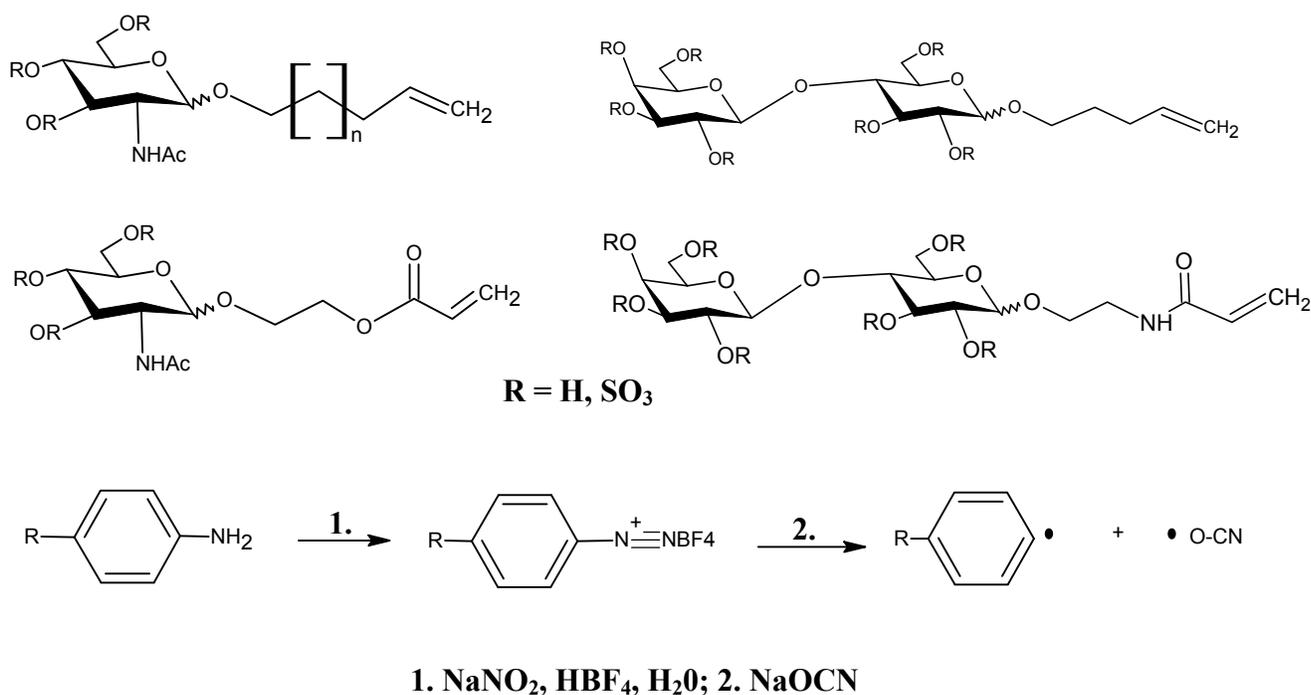


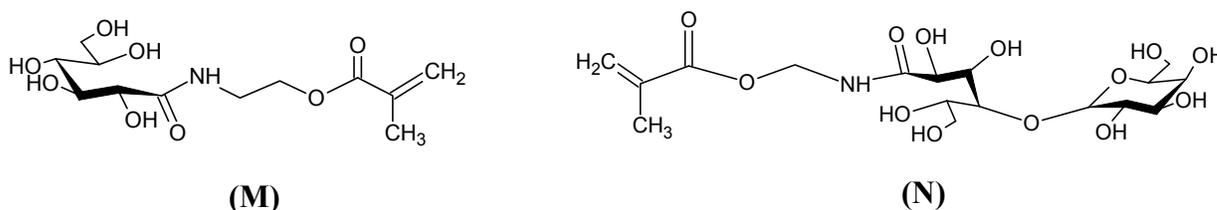
Figure 2.1 Monomers used and the reaction scheme for the in situ formation of cyanoxyl radicals as used by Grande et al.,^{32,33} and Sun et al.³⁴ in the synthesis of glycopolymers.

2.1.5 Glycopolymer synthesis by atom transfer radical polymerization (ATRP)

ATRP is a useful technique for the synthesis of glycopolymers. However, as with NMP, many of the syntheses carried out using ATRP have involved the use of protected sugar monomers.³⁵⁻³⁷ For example, Ohno et al.³⁸ polymerized 3-*O*-methacryloyl-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (MAIpGlc) in veratrole, using 4,4'-di-*n*-heptyl-2,2'-bipyridine as the catalyst. Results showed that the

polymerization was controlled and yielded polymers of narrow molecular weight distributions (PDI 1.2).

To avoid the use of protected sugar monomers, Narian and Armes³⁹⁻⁴¹ synthesized unprotected sugar monomers via ring-opening of either glucono- or lactobiono-lactone (**M** and **N**) with 2-aminoethyl methacrylate. In their polymerization reactions they used a MeOH/H₂O medium, a CuBr/bipy catalyst and an aldehyde-functional initiator. Results showed that when high MeOH/H₂O ratios were used at ambient temperatures, then high conversions were obtained within 15 hours. The resulting polymers were controlled in terms of molecular weight and had narrow molecular weight distributions. With regards to industrial viability, they concluded this work by carrying out the reactions in water alone. Interestingly enough, reaction times were drastically reduced to under an hour, albeit at the expense of some control.



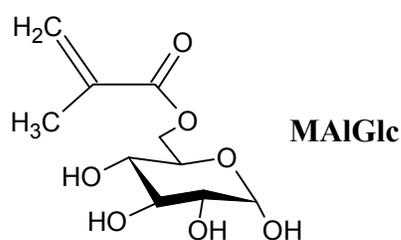
In general, ATRP has a number of advantages and disadvantages. The main advantage is that if the correct initiating species is chosen then the reaction is very fast and it is possible to produce polymers with very low polydispersity.^{42,43} The main disadvantage to this technique is related to the catalyst. First, the removal of the metal catalyst is typically very expensive, but a necessary step. Second, the metal is sensitive to other redox processes and hence several problems are encountered in aqueous or acidic media. Investigations are however, currently being undertaken to overcome these problems, and some success has already been achieved.⁴⁴

2.1.6 Glycopolymer syntheses by reversible addition-fragmentation chain transfer (RAFT)

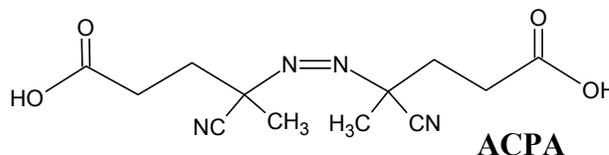
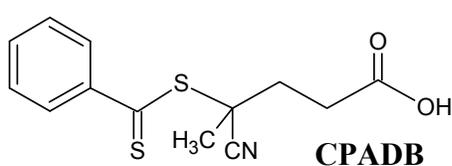
In comparison to most controlled polymerization techniques, the RAFT process is a robust and versatile method of obtaining polymeric materials of narrow molecular weight distributions.⁴⁵ Advantages include it being applicable to a wide range of monomers, having increased tolerance to small amounts of impurities, compatibility with various solvents, being amenable to a wide range of working temperatures,⁴⁶⁻⁴⁸ and the synthesis of a variety of molecular architectures can be achieved.⁴⁹⁻⁵¹

As with ATRP, the RAFT technique has been used for the polymerization of unprotected and protected sugar monomers.

Lowe et al.⁵² used (4-cyano-pentanoic acid)-4-dithiobenzoate (CPADB) as the RAFT agent and 4,4'-azobis(4-cyano-pentanoic acid) (ACPA) as the initiator for a polymerization of unprotected glucosyl methacrylate (MAIGlc). Results indicated that the polymerization was controlled and the polymers had narrow molecular weight distributions ($PDI < 1.07$). Lowe et al.⁵² used the resulting living polymer (\overline{M}_n , 14200) and chain extended it with MAIGlc and 3-sulphopropyl methacrylate (SPMA), separately.



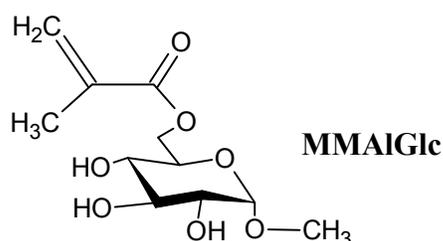
Size exclusion chromatograms indicated that in the case of poly(MAIGlc)-b-poly(MAIGlc) there was no detectable low molecular weight peak, the molecular weight distribution increased to 1.54 and there were some high molecular weight termination products. In the case of poly(MAIGlc)-b-poly(SPMA) block copolymer formation was successful, even though the molecular weight distribution was rather high at 1.63. The experiment was later revisited and it was decided to first synthesize the SPMA homopolymer and thereafter chain extend this resulting polymer with MAIGlc, whilst using the same RAFT agent and initiator as before. Interestingly, they found that they could now obtain copolymers of high molecular weight and narrow molecular weight distributions (PDI 1.18).



An issue that arose from the work of Lowe et al.⁵² was the solubility of CPADB, to which they used a base (sodium hydrogen carbonate) to facilitate dissolving the RAFT agent in the reaction medium. The reason for this is the stubborn solubility properties of CPADB. It is virtually insoluble in pure water at room temperature and only sparingly soluble at 60 to 70 °C.⁵³ In fact, the only ways in which CPADB can be used in a homogenous aqueous solution is either using it in its salt form,^{45,54} or adding high

concentrations of an amphiphilic monomer⁵⁵ or, as was done by Lowe together with Somerlin et al.,⁵⁶ increasing the pH of the solution by adding a base. The question arose however: would this base not hydrolyze the RAFT agent and if so, what process/additive would be preferable?

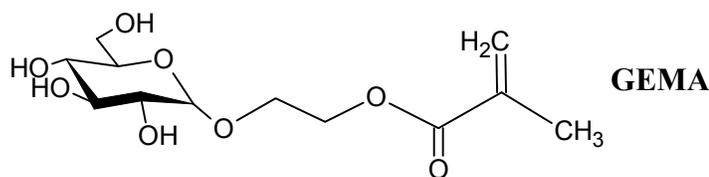
To address this issue, Albertin et al.⁵³ investigated the RAFT polymerization of unprotected methyl 6-*O*-methacryloyl- α -D-glucoside (MMAIGlc) and CPADB in water and a water/ethanol mixture, and determined the influence of the additive (base [sodium carbonate and sodium bicarbonate] or ethanol), used to aid the dissolution of the RAFT agent, on the polymerization kinetics and the molecular weight distributions of the resulting polymers. In all cases the RAFT agent and the initiator were dissolved in the additive prior to carrying out the polymerizations.



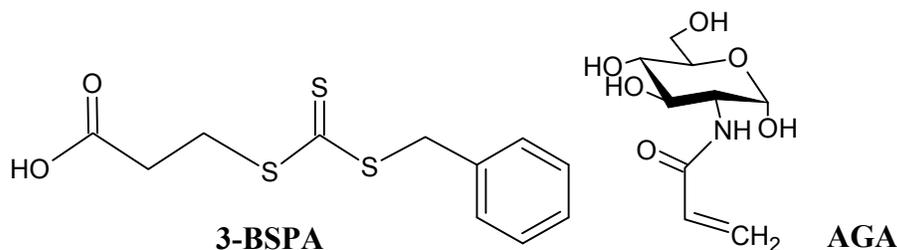
In general, when sodium carbonate or sodium bicarbonate was used to dissolve the RAFT agent in an aqueous solution, together with an inhibition period of 60 to 90 minutes being observed in the initial stages of the polymerization reaction, there was a decrease in the overall polymerization rate. In addition, experimental molecular weights were much higher than the predetermined ones. (Sodium carbonate: \bar{M}_n (theor), 26200; \bar{M}_n (exp), 327150; PDI, 3.67; conversion, 97%; sodium bicarbonate: \bar{M}_n (theor), 26100; \bar{M}_n (exp), 174000; PDI, 1.75; conversion, 99%). However, when ethanol was used in the polymerization mixture then narrow molecular weight distributions (PDI 1.14) were obtained and the experimental molecular weight (\bar{M}_n , 26300) values were close to the predetermined values (\bar{M}_n , 28300) (conversion, 100%). These deviations in results, as Albertin⁵³ concluded, are due to the hydrolysis of the RAFT agent and the terminal end dithiobenzoyl groups under basic conditions. The use of ethanol was therefore recommended.

This issue was pursued further by Spain et al.,⁵⁷ who used CPADB and ACPA, and demonstrated the RAFT polymerization of unprotected 2-(beta-D-galactosyloxy)ethyl methacrylate (GEMA) in the same reaction medium (4:1 H₂O:EtOH) as reported by Albertin et al.⁵³ This allowed for the synthesis of novel glycosylated nanoparticles to be documented. Results showed that the polymerization followed pseudo first-order kinetics and well-defined glycopolymers with predictable molecular weights, narrow

molecular weight distributions ($PDI < 1.09$) and near complete conversion ($> 95\%$) were obtained.



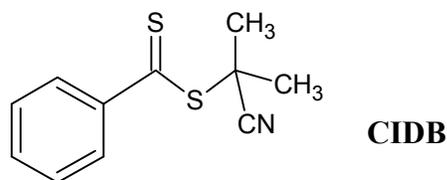
Bernard et al.⁵⁸ took glycopolymers to the next level. In their paper, entitled: Synthesis of various glycopolymers via RAFT polymerization: From block copolymers to stars, they initially made use of 3-benzylsulphonylthiocarbonyl-sulphonylpropionic acid (3-BSPA) and exploited RAFT polymerization for the preparation of a range (\bar{M}_n , 3000 to 120000; PDI , 1.1 to 1.3) of narrow dispersed acryloyl glucosamine (AGA)-based glycopolymers. Subsequently, these resulting polymers were chain extended with *N*-isopropylacrylamide (NIPAAm), affording a well-defined poly(AGA)-*b*-poly(NIPAAm) diblock copolymer (\bar{M}_n (exp), 88400; \bar{M}_n (theor), 82000; PDI , < 1.25 ; conversion, 85%). Finally, a 3-arm star water soluble trifunctional macro-RAFT agent poly(hydroxyethyl acrylate), derived from 3-BSPA, was prepared and polymerized with AGA, to yield well-defined stars (\bar{M}_n (exp), 131000; \bar{M}_n (theor), 117010; PDI , 1.37).



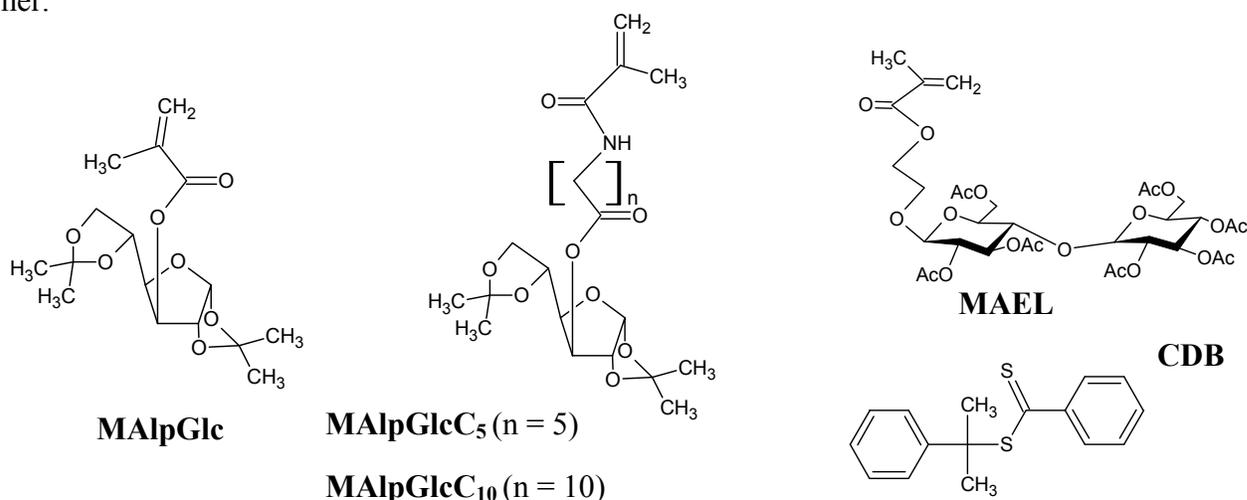
2-cyanoisopropyl dithiobenzoate (CIDB); cumyl dithiobenzoate (CDB) and 1-cyano-1-methylethyl dithiobenzoate (CMED) were used as RAFT agents for the synthesis of the protected sugar monomers.

CIDB was used in the AIBN initiated RAFT mediated polymerization of three isopropylidene group protected glycomonomers, which differed in the length of their hydrophobic spacer units between the polymerizable functional groups and the sugar moiety:

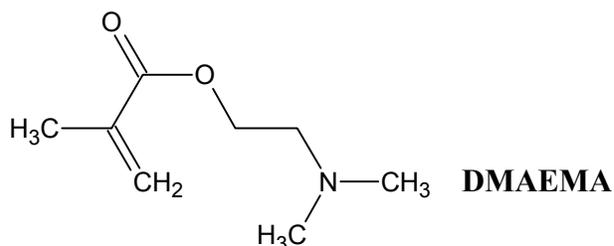
- 3-(1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranosyl)-6-methacrylamido-hexanoate (MAIpGlc₅) [*solvent used in polymerization: dioxane*]
- 3-(1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranosyl)-6-methacrylamido-undecanoate (MAIpGlc₁₀) [*solvent used in polymerization: anisole*]
- 3-*O*-Methacryloyl-(1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranoside (MAIpGlc) [*solvent used in polymerization: anisole*]



Following their block and random copolymerization with NiPAAm, well-defined glycopolymers with narrow molecular weight distributions ($1.1 < \text{PDI} > 1.5$) were obtained. Ozyurek et al.⁵⁹ pointed out that the spacer chain improves the reactivity of the methacrylic glycomonomers. For example, MAIpGlcC₁₀ (70% yield in 48 h), MAIpGlcC₅ (65% yield in 49 h) and MAIpGlc (75% yield in 96 h) were obtained. This study also confirmed research carried out by Black et al.,^{60,61} who demonstrated that under conventional free radical polymerization conditions MAIpGlc behaves as a ‘typical’ methacrylic monomer.



The RAFT mediated polymerization of protected 2-*O*-meth-acryloyloxyethoxyl-(2,3,4,6-tetra-*O*-acetyl-beta-D-galactopyranosyl)-(1-4)-2,3,6-tri-*O*-acetyl-beta-D-glucopyranoside (MAEL) was performed by Guo et al.⁶² using CDB, and resulted in well-defined glycopolymers with pendant lactose residues ($1.07 < \text{PDI} > 1.34$). These living glycopolymer chains were subsequently grafted onto gamma-methacryloxypropyl-trimethoxy modified silica particles. Guo claims that the versatility of the grafting technique, combined with the advantages of the RAFT process and the great biological potential of glycopolymers, provides a route by which ‘intelligent’ silica particles can be obtained.



It has been documented that in the case of CDB and CMED, the stabilizing phenyl Z group and either the cumyl or cyanoisopropyl R group (and simple derivatives thereof) allow these RAFT agents to be highly efficient for mediating methacrylate polymerizations.⁶³ In the light of this, Lowe and Wang⁶⁴ utilized these RAFT agents for the homo- and copolymerization of MAIpGlc and 2-(dimethylamino)ethyl methacrylate (DMAEMA) in DMF. In all cases, well-defined glycopolymers were obtained with narrow molecular weight distributions ($1.17 < \text{PDI} < 1.21$). Deprotection of the resulting polymers was carried out using TFA/H₂O and analytical results (SEC, NMR and FTIR) demonstrated that such deprotection chemistry does not have any adverse effect on the final polymers.

Lowe and Ozyurek concluded their work with a very powerful finding: by using RAFT and protected glycomonomers one can synthesize and analyze (co)polymers, via SEC, in organic media. This allows researchers to avoid problems that are typically encountered in aqueous RAFT mediated processes (such as RAFT agent hydrolysis and consequent side reactions.)

2.2 Properties of glycopolymers

2.2.1 Surface modifier properties

Synthetic polymers such as polyethylene, polystyrene, polypropylene and poly(ethylene terephthalate) have poor reactive properties, mainly because they have hydrophobic surfaces and no polar functional groups. Due to the occurrence of static electric discharge on surfaces they exhibit poor adhesion to a substrate, poor dyability and poor printability. Thus, being able to chemically modify these polymers with a glycopolymer may be potentially interesting.

Wulff et al.⁶⁵⁻⁶⁷ investigated this approach by copolymerizing several isopropylidene-protected vinyl sugars with not only styrene but also with methyl methacrylate and acrylonitrile. After acidolyzing the hydrophobic protecting groups from the copolymer surfaces, they used X-ray photoelectron spectroscopy (XPS) and verified that there was a change in the chemical composition of the surface. By creating OH groups on the surface of these polymers there was an improvement in the dyability and surface conductivity of the polymers. Wulff⁶⁵⁻⁶⁷ pointed out that it was the sugar monomer that determined the degree to which the hydrophilicity of the copolymer surface improved. Vinyl sugars with an open chain structure were much more efficient than those with cyclic structures.

Polymer colloids modified with immobilized sugar residues were also investigated. Davies et al.^{68,69}

used TOF-SIMS and XPS and proved that by increasing the amount of sugar residue he could decrease the particle size and electrophoretic mobility of a polystyrene-based colloid. The presence of a steric stabilizing water-soluble polymer layer at the colloid surface was also determined.

Nakamae et al.⁷⁰ also prepared copolymers of 2-(glucosyloxy)ethyl methacrylate (GEMA) and styrene and/or methyl methacrylate (MMA). Using XPS and contact angle measurements, they initially found that when the GEMA content is between 10 and 60 mol%, the surface characteristics of the resulting copolymers were insignificantly influenced. However, after pretreating these copolymers with hot water the surface characteristics, after the addition of GEMA, were significantly altered (the polystyrene copolymer more so than the MMA copolymer). They ascribed this difference to structural differences: the polystyrene copolymer is block-like, whilst the MMA copolymer is random-like.

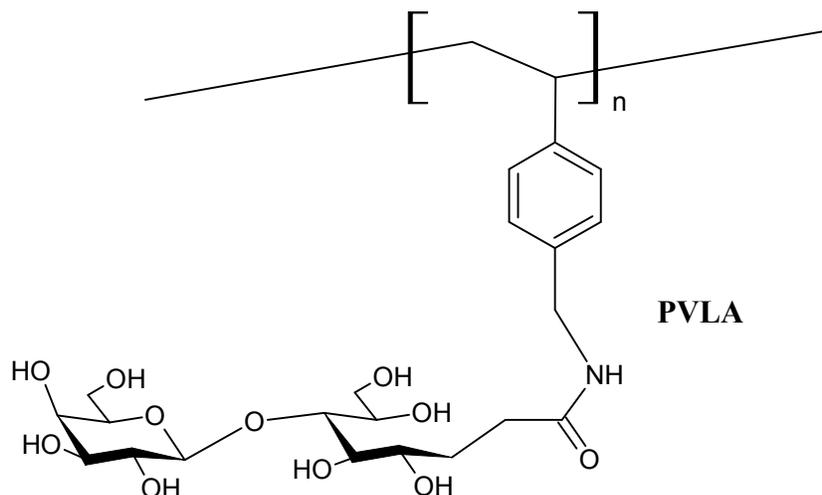
A block copolymer of the type polystyrene-*b*-poly(3-*O*-methacryloyl-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose) was prepared by an ATRP technique.³⁸ The resulting copolymer exhibited a microdomian surface morphology with spherical polystyrene domains in a sugar matrix. This introduces the following section (2.2.2.)

2.2.2 Self-assembling properties

Intelligently designed glycopolymers have been exploited mainly because of their ability, when combined with a hydrophobic moiety, to self assemble and form aggregates of micellar structure. This phenomenon occurs *above* the critical concentration of a polymer, well known as the critical micelle concentration (cmc). (This micelle forming ability has been clearly identified by the biomedical/pharmacological fields, and consequently has been developed for applications such as drug-delivery systems,^{71,72} molecular recognition and separation processes,⁷³ surfactants,⁷⁴ responsive hydrogels,⁷⁰ treatment of infectious diseases⁷⁵ and treatment of HIV.⁷⁶

Goto et al.⁷⁷ investigated the micellar behaviour of a poly[*N*-*p*-vinylbenzyl-*O*-beta-D-galactopyranosyl-(1 - 4)-D-gluconamide] (PVLA) homopolymer in aqueous solution. PVLA is composed of polystyrene as the hydrophobic backbone and an oligo-sugar residue in the pendant side chain, forming the hydrophilic moiety. In aqueous solution this amphiphilic polymer forms a micellar structure with an inner hydrophobic region, which was claimed to serve as an ideal binding pocket for the protection of water sensitive drugs. Thus, is a potential inclusion carrier of drugs in a target-specific drug delivery

system. Furthermore, results indicated that by increasing reacting time, larger micelles can be formed (45 nm particles initially, increasing to 110 nm particles after 100 h).



In a separate study carried out by Li et al.,⁷⁸ TEM results confirmed the formation of multiple morphologies when well-defined block copolymers were prepared with polystyrene (as the hydrophobic block) and poly(2-beta-D-glucopyranosyloxyethyl acrylate) as the hydrophilic block. Their objective was to evaluate the effect of solvent and glycopolymers concentration on self-assembly. Results indicated that in the presence of DMF, at low copolymer concentrations, small spheres with an average diameter of 25 nm and low dispersity were observed, whilst above a certain concentration, large compounded micelles coexisting with crew-cut micelles were observed.⁷⁹ However, in the presence of dioxane, polydisperse vesicles were observed, with sizes ranging from 100 nm (low polymer concentration) to 200 nm (high polymer concentration).

Aoudia and Zana⁸⁰ went one step further and evaluated the effect of temperature (range 12 to 60 °C) and nonionic polymers on the cmc values of glycopolymers. They chose three representative sugar surfactants: dodecyl-beta-D-maltoside (DM), octylglucoside (OG) and 6-*O*-(*N*-heptylcarbamoyl)methyl-alpha-D-glucopyranoside (6OG). In 6OG the junction between the alkyl chain and the sugar ring is more complex than in the other two surfactants. He also chose three nonionic water-soluble polymers: poly(oxyethylene) (POE), poly(oxypropylene) (POP) and poly(vinylpyrrolidone) (PVP) to complete his study. Results indicated that in the cases of DM and 6OG the cmc value increased with temperature. However, in the case of OG the cmc value increased with temperature to 30 °C, and thereafter remained constant, irrespective of increasing temperature. This is because of the large isotropic range that DM and 6OG exhibits over a wide range of temperatures (up to 100 °C), whilst OG has a much smaller range. None of these sugars interacted with POE and PVP upon addition of either of these two nonionic polymers over the entire temperature range. However, there was

some interaction with POP, which resulted in a decrease in the cmc value at low temperatures (< 16 °C). The reason for this is that POP is the most hydrophobic of the three nonionic polymers. It is known that if one increases the degree of hydrophobicity of a system, then the cmc will decrease.⁸¹

In addition to changing the above-mentioned parameters (i.e. temperature, addition of a water-soluble nonionic polymer, solvent and concentration of the test sample) the size and association number* of the micelles can also be systematically controlled by pH. Butun et al.⁸² investigated the effect of pH by making use of a PDMA-b-PDEA system. Diblocks of this type dissolve molecularly at low pH and, according to static and dynamic light scattering results and surface tension measurement, the copolymers can be considered to be double hydrophilic. However, as the pH is increased deprotonation occurs and the PDEA block becomes hydrophobic, leading to micellization.

In another study, Gohy et al.⁸³ prepared a P2VP-b-PDMA copolymer and evaluated the occurrence of micelles at various pH values. At low pH, polydisperse loose aggregates were formed, while micelles with a protonated PDMA corona were observed at intermediate pH. However, at higher pH values, the PDMA corona becomes deprotonated, leading to micellar aggregation.

The question that arose here was therefore: would one be able to achieve self-assembly for a poly(AA) based glycopolymer by simply adjusting the pH of the solution? This will be investigated in this study.

2.2.3 The binding ability of glycopolymers

The binding ability of glycopolymers is their most advanced property. As a result, great interest in the molecular design of glycopolymers has been directed toward endowing the sophisticated biological functions of sugars to synthetic polymer backbones.⁸⁴⁻⁸⁷ Some examples include work carried out by Yamada et al.⁴ and Hasegawa et al.⁸⁸

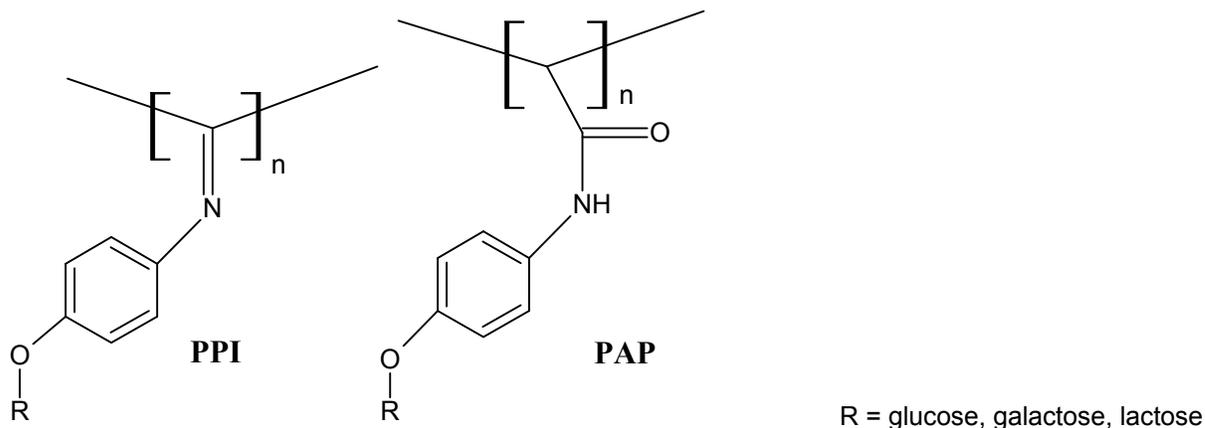
Yamada et al.⁴ investigated the interaction between a GlcNAc-carrying polyvinyl ether-poly(isobutyl vinyl ether) block copolymer and a wheat germ agglutinin lectin[♦]. This lectin is known to

* The number of molecules needed to form a closed micelle

♦ Lectins are carbohydrate-binding proteins.

specifically recognize GlcNAc and its oligomers. Results showed that the GlcNAc-carrying block copolymers exhibit a higher binding affinity towards lectin compared to when using the GlcNAc-homopolymer (control sample 1), which showed a stronger affinity than the oligosaccharide (control sample 2) itself. In view of the fact that the GlcNAc-carrying block copolymer has the ability of forming micellar aggregates in aqueous media, they came to the conclusion that this increased binding affinity is related to the dissolution state of the block copolymer in aqueous media in the presence of a lectin.

The binding abilities between polystyrene-type glycopolymers (with *N*-linked beta-anomeric oligosaccharides [*N*-acetyllactosamine, *N*-acetylisolactosamine and 4'-galactosyllactose]) and some lectins were also investigated by using hemagglutination experiments.^{89,90} Results indicated that the glyco-based block copolymers exhibited a strong affinity for the lectins compared to the glyco-based homopolymer, which showed a stronger binding affinity than the oligosaccharide itself. This result complimented results of Yamada et al.⁴ However, these researchers mentioned that in addition to micelle formation (as discussed above) the glycopolymers structure also plays a major role in increasing binding. The interaction of lectins with glycopolymers is more effective when the oligosaccharide units are located at a suitable distance from each other. This concept was verified by comparing the binding affinity of a lectin to a *N*-acetyllactosamine-carrying glycopolymers, it showed a 3×10^3 times weaker affinity than a *N*-acetyllactosamine-carrying glycopolymers that had an *O*-linked beta-anomeric- phenyl-alpha-glycon repeating unit along a polyacrylamide backbone.⁹¹



This concept of glycopolymers structures playing a major role in increasing binding was pursued by Hasegawa et al.,⁸⁸ who prepared a poly(phenyl isocyanide) copolymer substituted with a α -D-glucose, β -D-glucose, β -D-galactose and β -D-lactose. It was found that the rigid cylindrical

phenyl isocyanide glycopolymers (PPI) exhibited poor binding with lectins, which is in sharp contrast to the highly specific binding of the multivalent glycoclusters along flexible phenylacrylamide glycopolymers (PAP). This example indicates that the orientation and spacing of clustered glyco-chains is essential if a high binding affinity is required.

2.3 Conclusions

These results indicate that it is possible for a glycopolymer to bind to a carbohydrate. The question now arises: What if this carbohydrate is cellulose? This, to the best of my knowledge, has not been determined before. Considering the overwhelming molecular size of cellulose when compared to that of a synthetic glycopolymer, would micelle formation be necessary for binding or would hydrogen bonding between the glycopolymer and cellulose be sufficient? If so, how would one quantify and qualify this binding efficiency? Would the structure of the glycopolymer play a role on binding efficiencies?

More importantly, how would one use glycopolymers to promote binding between inorganic particles (e.g. calcium carbonate) and cellulose?

In the following chapters the synthesis of glycopolymers with various comonomers via the RAFT process is investigated. Furthermore, the self assembling properties, the surface modifying and binding capabilities of these resulting glycopolymers with cellulose are considered.

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Chapter 3

Critical micelle concentration and phase separation studies of RAFT mediated amphiphilic diblock glycopolymers containing methyl acrylate and styrene

Abstract

Interesting new critical micelle concentration (cmc) and phase separation data of carbohydrate-based self-assembling core-shell nanoparticles that were synthesized via the RAFT process are reported. The macro-RAFT agent poly(3-O-methacryloyl-1,2:5,6-di-O-isopropylidene-D-glucopyranose) (PMAIpGlc) was prepared by RAFT polymerization of the glycomonomer with cumyl phenyl dithioacetate as the chain transfer agent. Chain extension with styrene and with methyl acrylate afforded the diblock copolymers PMAIpGlc-b-styrene and PMAIpGlc-b-methyl acrylate, which had predetermined molecular weights and narrow molecular weight distributions. Acidolysis of these diblock copolymers were undertaken and the products were confirmed by NMR. Core-shell nanoparticles were observed by TEM.

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

Vernon Ramiah, Howard Matahwa, Wolfgang Weber, James B. McLeary and Ron D. Sanderson, **Macromolecular Symposia**, 2007, 255, 70-80 (See Appendix B).

3.1 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 As they displayed 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 been used for unique and specialized applications in the biochemical and biomedical fields, as mentioned previously.⁴⁻¹⁰

In the search for 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 address both requirements simultaneously. For instance, well-defined glycopolymers have been synthesized by living cationic,¹¹ anionic,¹² ring-opening metathesis¹³ and ring-opening polymerization of N-carboxyanhydrides,¹⁴ but the range of monomers that can be used is limited 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, and obtained polymers with low polydispersities and tailored molecular weights.¹⁵⁻¹⁹ Processes involving living radical polymerization have opened various paths to obtaining well-defined macromolecules both in academia and industry. These processes include NMP¹⁶ and ATRP.^{20,21} 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 different chain, as found in the RAFT process.^{17,22,23}

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.²⁴ Advantages include 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,²⁵⁻²⁷ and the synthesis of a variety of molecular architectures.^{23,28,29}

Aqueous RAFT mediated polymerizations of glycomonomers have been successfully carried out using water miscible RAFT agents and hydrophilic monomers.^{17,22,23,30} The preparation of polymers with self-assembly properties, which is 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 described 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 chapter describes the controlled RAFT mediated polymerization of the protected monomer 3-O-methacryloyl-1,2:5,6-di-O-isopropylidene-D-glucofuranose (MAIpGlc) utilizing cumyl phenyl dithioacetate (CPDA) as the RAFT agent. CPDA has previously been used for the controlled polymerization of methacrylates.³¹ 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.

3.2 Experimental

3.2.1 Materials

Unless otherwise specified, all chemicals were reagent grade and used as received. Sodium hydroxide [97%; ACE (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 disulphide (99.9%; Aldrich), p-toluene sulphonic acid (98.5%; Sigma-Aldrich), carbon tetrachloride (99.9%; Aldrich), diethyl ether (99.5%; Merck) and HCl [32%; ACE (Pty.), Ltd.] were 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.

3.2.2 Analyses

NMR spectra were recorded on a 300 MHz Varian VXR spectrometer equipped with a Varian magnet (7.0 T), or a 600 MHz Varian Unity Inova spectrometer equipped with an Oxford magnet (14.09 T). Standard pulse sequences were used for obtaining ^1H and ^{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) TEM, operated at 120 kV. Molecular weights and molecular weight distributions were determined by a SEC system comprising a Waters 410 Differential Refractometer, Waters 717plus Autosampler, Waters 600E System Controller and Wyatt DAWN DSP 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 it in THF (HPLC grade). The flow rate was 1 mL/min. The dn/dc values of the resulting polymers, determined by a ScanRef Monocolor Interferometric Refractometer (LabView 4 Runtime, vers. 4.0.1 software), were calculated in duplicate at various concentrations (0.5, 1, 2, 3, 4, 5 mg/L) and used for molecular weight calculations. Conductivity measurements were carried out at 295 K using a Eurotech cell combined with a Cyberscan 500 device. Data were 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.

3.2.3 Glycomonomer synthesis: 3-*O*-methacryloyl-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (MAIpGlc)

D(+)-Glucose (1) was converted into 1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranose (pGlc) (2) according to the method proposed by Schmidt.³² MAIpGlc was synthesized from pGlc according to slight modifications of the method proposed by Black et al.³³ The modification involved the use of pentane as an extracting solvent and 4-methoxy phenol as a polymerization inhibitor. 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. ^1H NMR (600 MHz, CDCl_3) δ (ppm): 1.25-1.50 (m, 12H, 4 CH_3); 1.95 (s, 3H, $\text{CH}_3\text{-C}=\text{CH}_2$); 5.70 (m, 1H, $\text{CH}_2=\text{C}$ -, E form H); 6.00 (m, 1H, anomeric proton of sugar moiety); 6.15 (m, 1H, $\text{CH}_2=\text{C}$, Z form H); 3.90-4.70 (6H, sugar moiety).

3.2.4 RAFT agent synthesis: cumyl phenyl dithioacetate (CPDA)

The synthesis of phenyl dithioacetic acid was carried out using a modification of the method proposed by Quinn et al.³⁴ 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 then cooled to ambient temperature. CS₂ (30.40 g, 0.40 mol) was added over 20 min, while the temperature was kept constant at room temperature using 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 MgSO₄ for 30 min and removing the solvent under reduced pressure afforded the crude phenyl dithioacetic acid as a red oil (25.31 g, 37.6% yield). The crude phenyl dithioacetic acid (25.31 g, 0.15 mol) was refluxed for 15 h with α -methyl styrene (20.01 g, 0.17 mol) and 0.10 g *p*-toluene sulphonic acid in 100 mL dry CCl₄. After removal of the solvent under reduced pressure the resulting red oil was left overnight in the freezer at -4 °C to crystallize. The formed orange crystals were separated and recrystallized from hexane. (11.30 g, 26.3% yield). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 2.00 (s, 6H, 2CH₃); 4.2 (s, 2H, CH₂); 7.2-7.6 (m, 10H, H_{ar}). ¹³C NMR (300 MHz, CDCl₃) δ (ppm): 27.6 (2CH₃); 56.02 (C); 59.16 (CH₂); 126.6, 126.8, 127.1, 127.9, 128.4, 128.7, 137.1, 144.0 (C_{ar}); 233.59 (C=S).

3.2.5 Macro-RAFT agent synthesis: Poly(3-*O*-Methacryloyl-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose) (PMAIpGlc)

The reaction procedure involved charging a three-neck round bottom flask with MAIpGlc (91.51 mmol, 30.05 g), CPDA (1.215 mmol, 0.3484 g) and ethyl acetate (25% w/v monomer) (Scheme 3.1, Table 3.1) and heating the contents to 75 (\pm 1) °C for 25 min while purging with nitrogen. Free radical initiator AIBN (0.125 mmol, 0.0199 g) was then added to the reaction mixture to start the polymerization reaction. 1,3,5-Trioxane was added as an inert internal NMR reference in order to later 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 molar amount of monomer.

^1H NMR (600 MHz, acetone- d_8) spectra were recorded before the start of the reaction and then during the course of the reaction. Samples were withdrawn at specific time intervals and dried in vacuo overnight before analysis. The ratios of integrated signals of the internal reference, before and after the reactions, were used to calculate monomer incorporation. A typical ^1H NMR spectrum of a reaction sample (Figure 3.1) 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 glycomonomer. The broad peak at 5.7–6.0 ppm is due to the anomeric proton peak of the sugar moiety in the polymer.

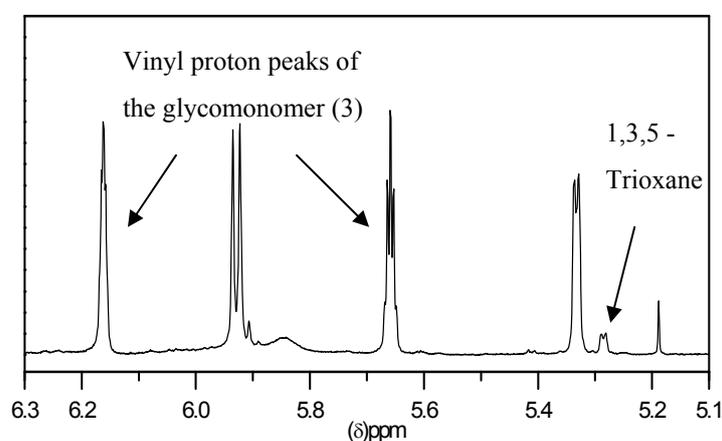


Figure 3.1 A typical ^1H NMR spectrum of a PMAIpGlc homopolymerization reaction mixture in CDCl_3 , showing the region of interest.

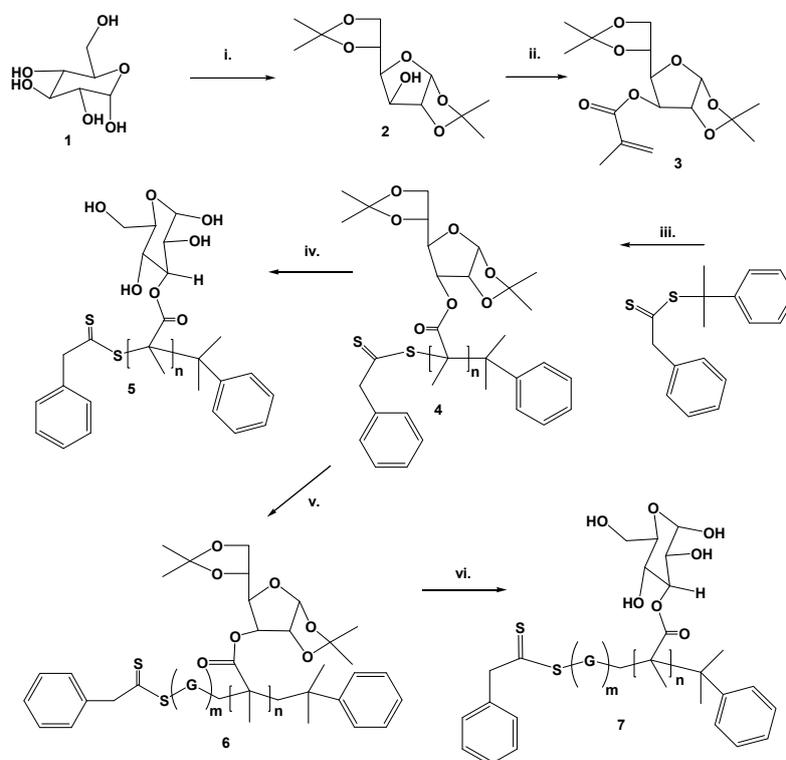
\overline{M}_n Data obtained via this method were in excellent agreement with the theoretical values of \overline{M}_n calculated from equation 3.1:

$$\overline{M}_n = M_{RAFT} + \frac{x[M]_0 M_M}{[RAFT]_0 + 2f[I]_0(1 - e^{-k_d t})} \quad (3.1)$$

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 in an excess of methanol and filtered off. Ninety-five percent

conversion occurred within 5.5 h. \overline{M}_n (SEC): 12000, \overline{M}_n (MALLS): 24500, \overline{M}_n (^1H NMR): 24000 and PDI (MALLS): 1.16. ^1H NMR (acetone- d_8 , 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, 1H, anomeric proton of sugar moiety) and 7.2 - 7.8 (aromatic protons of CPDA).



Scheme 3.1 The synthetic approach used to prepare 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 , NaOH and 100 °C; v. Ethyl acetate for methyl acrylate, and toluene for styrene, AIBN, methyl acrylate/styrene, 75 °C; vi. HCl , NaOH , 100 °C. G = methyl acrylate/styrene moiety.

3.2.6 Synthesis of PMAIpGlc-b-(styrene) and PMAIpGlc-b-(methyl acrylate)

The reaction procedures used to prepare these glycopolymers were very similar to the method of synthesis of the homopolymer PMAIpGlc except that the monomer conversion was determined gravimetrically for styrene and methyl acrylate. PMAIpGlc was used as the macro-RAFT agent and toluene was used in the case of styrene polymerizations. The starting polymerization compositions are tabulated in Table 3.1. In both cases the produced copolymers were precipitated in excess methanol. In the case of PMAIpGlc-b-(methyl acrylate), at 82% conversion, \overline{M}_n (SEC): 22000, \overline{M}_n (MALLS): 49000, \overline{M}_n (^1H NMR): 52000, \overline{M}_n (theor): 50000 and PDI (MALLS):

1.56. ^1H NMR (acetone- d_6 , 600 MHz) (Scheme 1, compound 5): δ (ppm) 0.9-1.8 (m, 12H, CH_3), 4.0-5.2 (4H, sugar moiety), 5.7-6.0 (m, 1H, anomeric proton of sugar moiety), 3.4-3.8 (s, 3H, CH_3) and 7.2-7.8 (aromatic protons of CPDA). In the case of PMAIpGlc-b-(styrene), at 40% conversion, \overline{M}_n (SEC): 36000, \overline{M}_n (MALLS): 44000, \overline{M}_n (theor): 45000 and PDI (MALLS): 1.60. ^1H NMR spectroscopy was not used for determining \overline{M}_n values here as there was an overlap of the aromatic protons of CPDA and styrene.

Table 3.1 Formulations used for the synthesis of the glycopolymers: PMAIpGlc-b-poly(methyl acrylate) and PMAIpGlc-b-poly(styrene).

Reagents and conditions	PMAIpGlc-b-poly(methyl acrylate)	PMAIpGlc-b-poly(styrene)
PMAIpGlc [#]	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. ($^{\circ}\text{C}$)	75	80
% w/v monomer	ethyl acetate, 25%	toluene, 25%

[#] MAIpGlc: 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 $^{\circ}\text{C}$.

3.2.7 Deprotection by acidolysis

The removal of the acetyl protecting groups, after the RAFT mediated polymerization process, was performed using a modification of the method of Black et al.³³ The protected polymer (20 g) was heated and rapidly stirred with 1 N HCl (400 mL) for 2 h at 100 $^{\circ}\text{C}$. Water (100 mL) was added and the mixture was neutralized with 4 N NaOH. The solution was dialyzed against distilled water for 3 days, and finally freeze-dried to yield the deprotected polymer (verified by ^1H NMR) as a white powder, in a quantitative yield.

3.2.8 Particle morphologies above their cmc values

Sample preparation for self-assembly studies involved vapour staining of the diblock copolymers with OsO_4 for 30 min after which a 0.15 g/L solution of the diblock copolymers in water or toluene was stirred at ambient temperature for 20 min. 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.¹⁶

3.3 Results and discussion

3.3.1 Synthesis of the macro-RAFT agent: Poly(3-*O*-methacryloyl-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose) (PMAIpGlc)

The homopolymerization of MAIpGlc proceeded within 5.5 h to 90% conversion (\overline{M}_n (SEC): 12000, \overline{M}_n (MALLS): 24500, \overline{M}_n (¹H NMR): 24000, \overline{M}_n (theor): 25000 and PDI (MALLS): 1.16. Due to the inadequacy of polystyrene standards to approximate the hydrodynamic volume of these resulting polymers,^{16,35} molecular weights of polymers synthesized in this study were determined by ¹H NMR and MALLS. When using ¹H NMR the anomeric proton of the sugar moiety in the polymer (5.8 - 6.0 ppm) 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 3.2 shows the plots of (i) \overline{M}_n (exp) and \overline{M}_n (theor) versus time and (ii) percentage conversion versus time for the homopolymerization of MAIpGlc. These results correspond well with results of studies conducted by Barner-Kowollik et al.,³¹ who found that in the early stages of CPDA mediated meth(acrylate) polymerization the concentration of the transfer agent (CPDA) decreases more slowly, resulting in a ‘conventional’ chain transfer distribution emerging. However, at higher conversion a strictly ‘living’ character dominates. This effect, a so-called ‘hybrid’ behaviour of conventional chain transfer and living free radical polymerization, results in a subsequent decrease in the initial PDI of the system.³¹ In this study the PDI values decreased from 1.5 to 1.16.

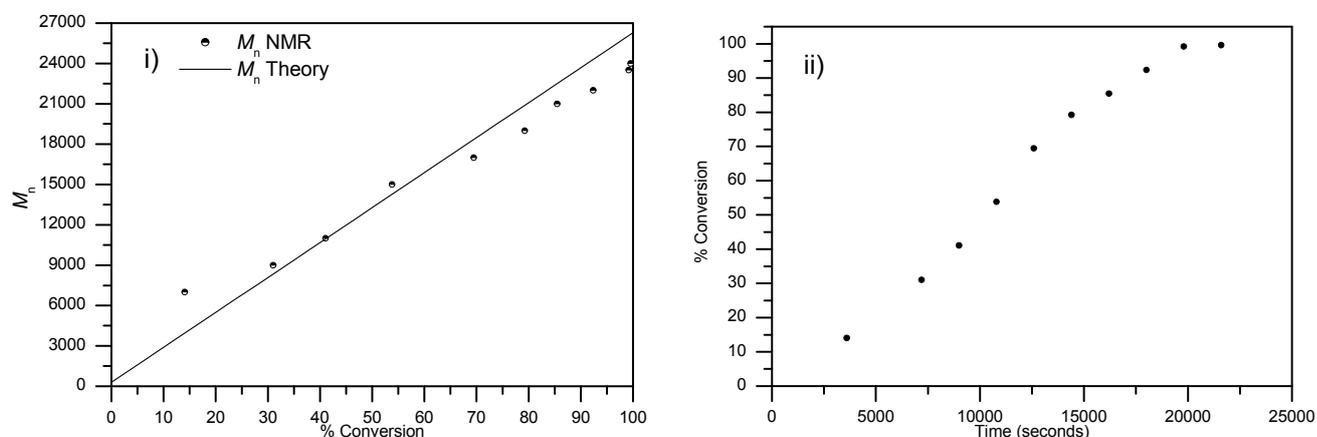


Figure 3.2 Plots of (i) \overline{M}_n (exp) and \overline{M}_n (theor) versus time and (ii) percentage conversion vs. time for the homopolymerization of MAIpGlc in ethyl acetate (25% w/v monomer) at 75 °C.

3.3.2 Styrene and methyl acrylate chain extension polymerization systems

To synthesize sugar-based block copolymers, the PMAIpGlc homopolymer was used as a macro-RAFT agent for the block copolymerization of methyl acrylate and of styrene. Figures 3.3 and 3.4 illustrate the evolution of molecular weight over time for the chain extension of PMAIpGlc with methyl acrylate and styrene, respectively. The observed blocking efficiency confirmed 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 unreacted macro-RAFT agent (PMAIpGlc) present in the system. Although the \overline{M}_n (exp) corresponded well with the \overline{M}_n (theor), the final polydispersities were relatively large. PDI values were 1.56 and 1.60 for PMAIpGlc-b-(methyl acrylate) and PMAIpGlc-b-(styrene), respectively. The dn/dc values for the MALLS measurements were calculated in duplicate for the final precipitated polymers. Values were 0.1946 (\pm 0.0002) mL/g with a correlation coefficient of 0.999 (\pm 0.0050) and 0.1069 (\pm 0.0004) mL/g with a correlation coefficient of 0.999 (\pm 0.0020) for PMAIpGlc-b-(methyl acrylate) and PMAIpGlc-b-(styrene), respectively. From ^1H 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. This approach could however not be used for PMAIpGlc-b-(styrene) as there was an overlap of the aromatic protons of CPDA and styrene.

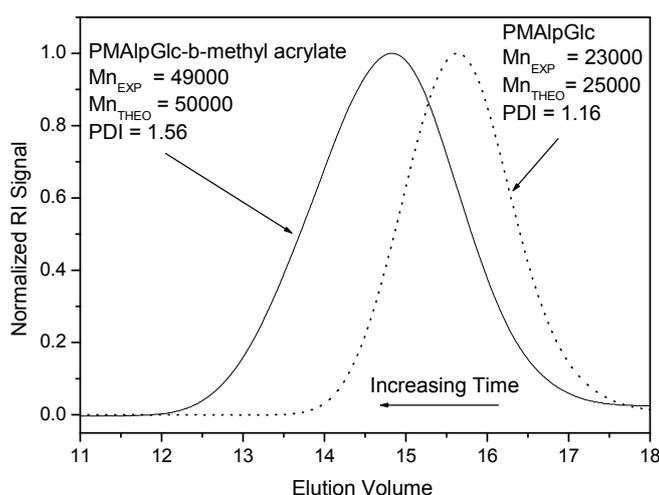


Figure 3.3 SEC traces for the RAFT mediated copolymerization of PMAIpGlc and methyl acrylate in ethyl acetate (25% w/v monomer) at 75 °C. (Starting compositions are tabulated in Table 3.1)

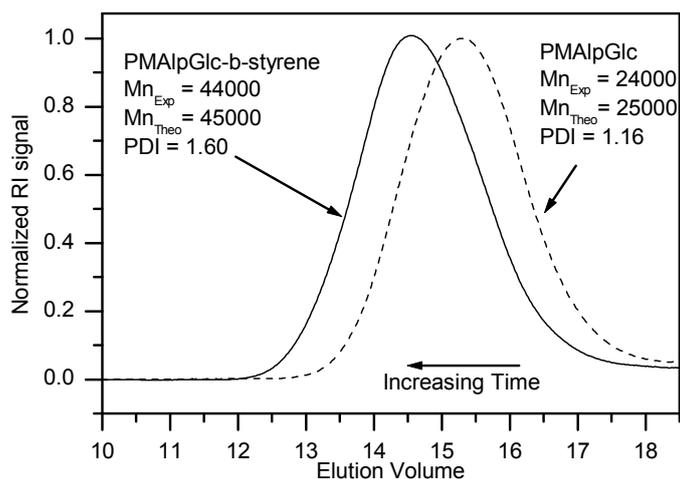


Figure 3.4 SEC traces for the RAFT mediated copolymerization of PMAIpGlc and styrene in toluene (25% w/v monomer) at 80 °C. (Starting compositions are tabulated in Table 3.1)

3.3.3 Deprotection of MAIpGlc units to form MAIGlc units

Polymer samples were treated with HCl. Figure 3.5 shows typical ^1H NMR spectra recorded before and after acidolysis. Acidolysis resulted in the complete disappearance of the isopropylidene protons (1.2 - 1.4 ppm in Figure 3.5a) and instead, a broad signal assignable to the anomeric hydroxyl groups of the sugar moiety (6.4 - 7.0 ppm in Figure 3.5b) appeared. The spectral data obtained was in agreement with existing literature^{16,21} and hence the quantitative deprotection of the isopropylidene groups, were verified.

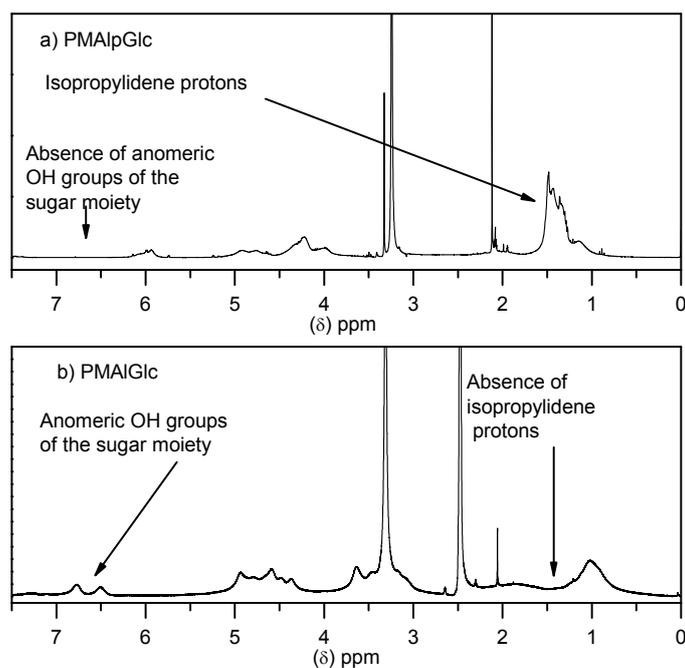


Figure 3.5 Typical ^1H NMR spectra recorded (a) before and (b) after the acidolysis of PMAIpGlc. The solvents were (a) CDCl_3 and (b) DMSO-d_6 .

3.3.4 Self-assembly/aggregation studies

The cmc of the diblock glycopolymers was determined by conductivity: conductivity was measured in microsiemens for various polymer concentrations in water.

Figures 3.6 and 3.7 show that self assembly/cmc occurs at $0.12 (\pm 0.01)$ and $0.13 (\pm 0.01)$ g/L for PMAIGlc-b-poly(styrene) and PMAIGlc-b-poly(methyl acrylate), respectively. These results are an average of three measurements carried out at 295 K. The hydrophobicity of poly(methyl acrylate) and poly(styrene) is similar, relative to that of the glycomoiety, and hence the cmc values recorded are similar.

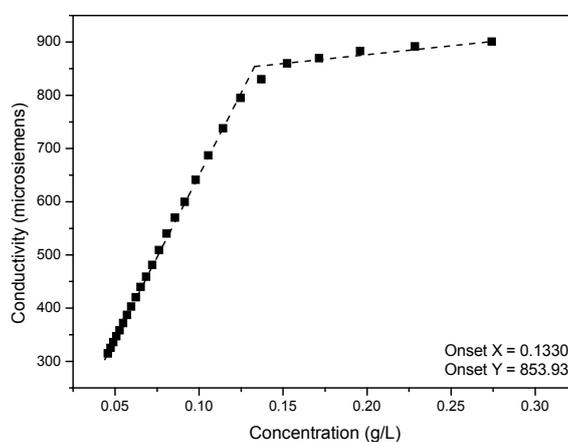


Figure 3.6 Change in conductivity with concentration of PMAIGlc-b-poly(styrene) in an aqueous solution at 295 K.

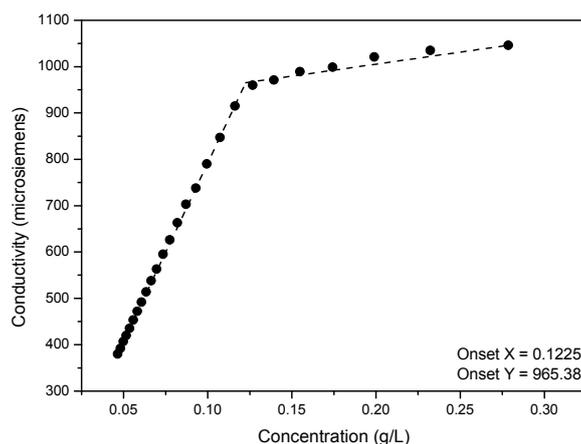


Figure 3.7 Change in conductivity with concentration of PMAIGlc-b-poly(methyl acrylate) in an aqueous solution at 295 K.

Micellar behaviour of sugar-containing polymers in aqueous solutions has been reported by Auodia and Zana.³⁶ A direct comparison between their results and results recorded in this study

can not be made due to the novel glycopolymers used in this study, in terms of monomer compositions, molecular weights and architectural design. For example, Goto et al.³⁷ documented the cmc value of poly(N-p-vinyl-benzyl-O- β -D-galactopyranosyl-[1~4]-D-gluconamide) to be about 4 g/L. In their study an amphiphilic homopolymer was used: the hydrophilic head group is part of the monomer itself and thus homogeneously distributed along the main polymer backbone. In this study, however, there is a diblock copolymer, which behaves as a giant classical surfactant. Isometrically pure sugar surfactants of β -D-alkylmaltoside and β -D-alkylglucosides, with molecular weights of 510 and 292 g/mol in the case of dodecyl- β -D-maltoside and 1-O-n-octyl- β -D-glucoopyranoside, respectively, have also been studied.³⁶ Once again, the cmc values recorded in that study, namely, 0.1 and 7.0 g/L are not comparable to those noted in this study due to the polymers' molecular weight, monomer compositions and architectural design.

3.3.5 Particle morphologies *above* their cmc value

Figure 3.8 demonstrates the self-assembling spherical core-shell nanoparticles for the amphiphilic diblocks, whereby styrene or methyl acrylate aggregates form the inner core and are encapsulated by a hydrophilic carbohydrate based outer shell. Inverted core-shell particles were also prepared (Figure 3.9) 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.

Detectable changes in water and toluene are noted. Figure 3.8b clearly shows that in the water medium the methyl acrylate polymer has undergone minor swelling, whilst the sugar component shows a 'halo' around the central particle of acrylate. In toluene medium (Figure 3.9b), the sugar shrinks to theta conditions and is buried in the methyl acrylate, which has now swelled to double its diameter in toluene.

The styrene-based sugars are more complicated. In water the styrene moiety shows a very small encapsulated phase surrounded by a swollen sugar, whereas in toluene the particles are similar in size, yet now the sugar is buried within the swollen styrene particles. The styrene moiety will actively try to dissolve in toluene but in doing so, it is restricted by the sugar moiety.

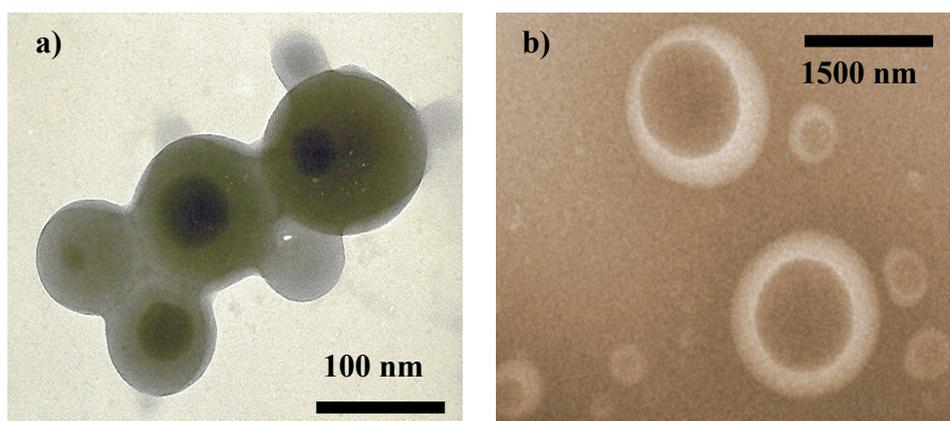


Figure 3.8 TEM image illustrating the core-shell self-assembling behaviour of (a) PMAIGlc-b-styrene in water (0.15 g/L) after 20 min, and (b) PMAIGlc-b-methyl acrylate in water (0.15 g/L) after 20 min.

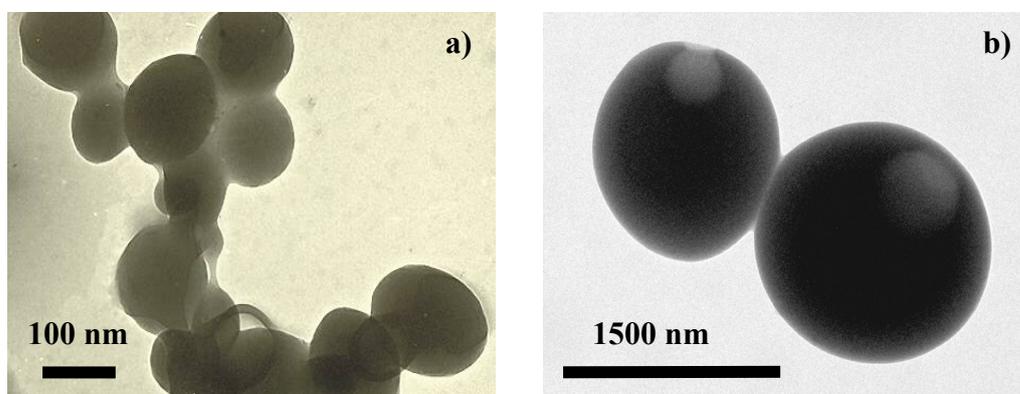


Figure 3.9 TEM image illustrating the inverted core-shell self-assembling behaviour of (a) PMAIGlc-b-styrene in toluene (0.12 g/L) after 20 min and (b) PMAIGlc-b-methyl acrylate in toluene (0.13 g/L) after 20 min.

3.4 Conclusions

The RAFT mediated synthesis of novel block glycopolymers with well-defined architectures was successfully carried out with cumyl phenyl dithioacetate. 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 molecular weight distributions. After acidolysis, their amphiphilic self-assembling character was determined after these diblock copolymers formed spherical core-shell nanoparticles, in which the hydrophobic and hydrophilic moieties were distinguishable. The formation of an encapsulated glycopolymERIC core, as described in this project, was achieved, and it was found to be exchangeable by the type of solvent used.

3.5 References

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Chapter 4

Crystallization of CaCO₃ in the presence of acrylic acid based glycopolymers

Abstract

The synthesis and characterization of 'sugar-coated' CaCO₃ nanoparticles, using a glycopolymer containing poly(AA), is described. A schematic study was carried out, which involved changing the pH, the temperature and the time of the reaction. TGA and SEM confirmed that the modified inorganic particles have an increased adherence to cellulose compared to unmodified inorganic particles. In addition, interesting new pH-dependent amphiphilic core-shell behaviour is reported.

In part, reproduced from:

Crystallization of calcium carbonate in presence of acrylic acid based glycopolymers

Vernon Ramiah, Howard Matahwa, Johannes C. Terblanche and Ron D. Sanderson, submitted to **Journal of Crystal Growth**, 2008

4.1 Introduction

For the past half century, retention aids have generally comprised cationic polyelectrolytes. The latter can complex with fines, fillers and pigments, and in doing so promote their attachment to the fiber surface - forming what is known as a polyelectrolyte complex.^{1,2} However, in the wet-end of a paper-making machine, anionic dissolved and colloidal substances (DCSs), which comprise dissolved lignin, hemicelluloses, soluble extractives, colloidal wood resins, etc. exist, and compete with fibers and pigments for retention aids. As a consequence, the efficiency of retention aids is substantially decreased.³⁻⁶ This has resulted in extensive research being focused on identifying and/or synthesizing the ideal retention aid for an optimum paper-making process.

Consequently, extensive research has been carried out into modifying the surface charge of the CaCO₃ filler with oppositely charged polymers prior to its use. For instance, Nystrom et al.⁷ pretreated cationic CaCO₃ with an anionic poly(sodium acrylate), which allowed the resulting anionic particles to subsequently adhere onto cationic starch. Cationic starch is commonly used as a strength additive in the wet-end of the paper-making process. In another case, a route was described by Suty and Luzakova in 1998.⁸ They investigated the effect of absorbing cationic polyethylenimine (PEI) onto negatively charged CaCO₃ particles prior to its addition to negatively charged fibers. They investigated the degree of deposition of the PEI-absorbed-CaCO₃ aggregates on the fibers, the deposition time and the capture efficiency of both the fibers and the aggregates. Results showed that the positively charged filler aggregates deposit faster than both dispersed particles as well as to PEI-absorbed fibers. In theory, these protocols are scientifically defined and, to the best of the author's knowledge, there has been no report on the industrial inappropriateness of using surface-charged modified fillers to improve filler retention. However, drawbacks of this technology is the cost incurred in accommodating the high addition ratio of polymer (raw material) to filler needed, followed by rebalancing the desired properties of the final product. In addition, with charged DCSs present and also competing in the paper-making system there will be a reduction in retention efficiency.

This study proposes an innovative approach to determining the crystallization of CaCO₃ in the presence of an acrylic acid-based diblock (AB) glycopolymer, PMAIGlc-b-poly(AA). The rationale is that the poly(AA) moiety will provide a nucleation site for CaCO₃ crystallization (a mechanism that has been documented extensively in literature⁹⁻¹³), whilst the glycomoiety will adhere to a cellulose

substrate via hydrogen bonding, and facilitate a *bridging mechanism** between the inorganic particle and the fiber. The advantage of this technology includes the low levels of polymer needed, as CaCO₃ only crystallizes on the polymer, resulting in an increase in retention efficiency. In addition, further fine-tuning of the properties (and subsequent costs) of the desired product could be achieved by varying the fillers growth rate, size, shape and polymorph. Finally, the effects that polymer concentration, reaction pH, temperature and time have on CaCO₃ crystallization and morphology were also investigated.

4.2 Methodology

A dual synthetic approach was undertaken to obtain a RAFT mediated diblock copolymer of poly(3-O-methacryloyl-1,2:5,6-di-O-isopropylidene-D-glucofuranose) (PMAIpGlc) and poly(AA) (Scheme 4.1). The two routes diverged once the macro-RAFT was prepared. **Route 1** involved the use of an organic soluble, protected acrylic acid (1-ethoxyethyl acrylate) [EEA], whilst in **Route 2** the macro-RAFT agent was made water soluble, by acidolysis, and thereafter reacted with water soluble acrylic acid. The RAFT agent CPDA was used in both cases as it has been successfully used for the controlled polymerization of (meth)acrylates.¹⁴

4.3 Experimental

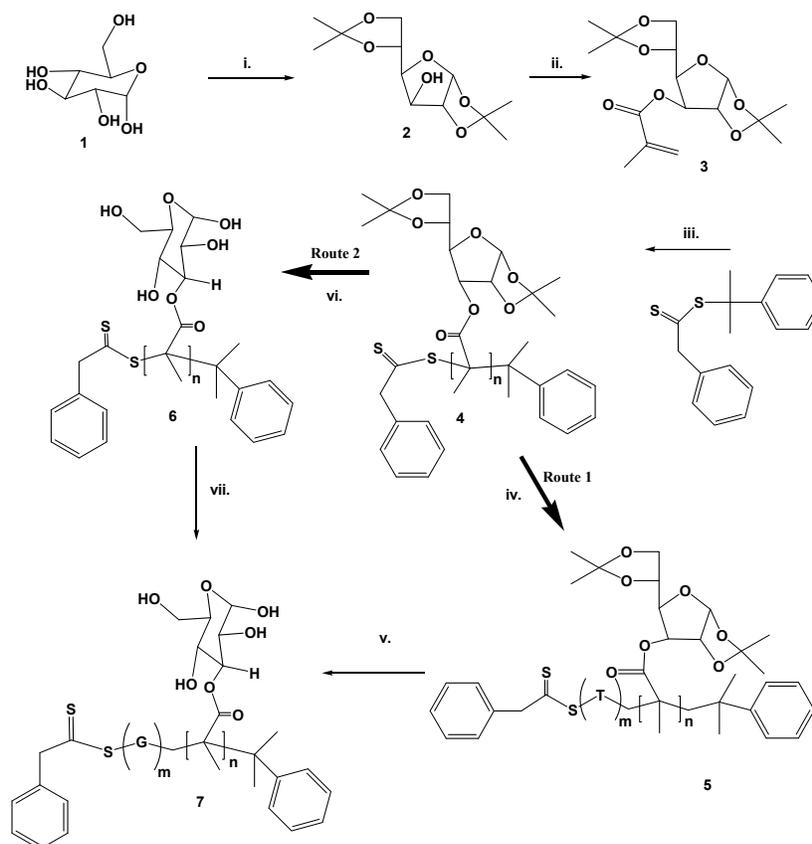
4.3.1 Materials

Unless otherwise specified, all chemicals were of analytical grade and reagents were prepared as described in Chapter 3. The chromatographic staining agent (aniline phthalate) was prepared by dissolving 0.93 g aniline (CP; Holpro Analytics) and 1.66 g *o*-phthalic acid (99%; Fluka) in 100 mL *tert*-butanol (99.5%; Acros Organics) and saturated in water, prior to its use. EEA was prepared as described in the literature.¹⁵⁻¹⁷

* *Bridging mechanism* involves the adsorption of different segments (terminal and/or intermediary) of a polymeric chain to a particle, resulting in the formation of an aggregate.

4.3.2 Characterization

SEM images were obtained using a Leo 1430VP SEM. TEM images were obtained using a LEO 912 Omega TEM. TGA was carried out using a Perkin Elmer Pyris 7 TGA.



Scheme 4.1 The dual synthetic approach used to prepare well-defined diblock acrylic acid-based glycopolymers. i. Acetone/ZnCl₂/H₃PO₄/NaOH; ii. Pyridine/pentane and methacrylic anhydride; iii. ethyl acetate, AIBN, 75 °C; iv. EEA, ethyl acetate, AIBN, 60 °C; v. and vi. HCl, NaOH and 100 °C; vii. DDI, KPS, acrylic acid, 75 °C. T = EEA and G = acrylic acid moiety.

4.3.3 Macro-RAFT agent synthesis: Poly(3-*O*-methacryloyl-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose), (PMAIpGlc)

The macro-RAFT agent was prepared according to the method described in section (3.2.5), whereby polymerizations were carried out with MAIpGlc (10.05 g; 30.61 mmol) and CPDA (0.072 g; 0.2514 mmol), using AIBN (0.0041 g; 0.025 mmol) as the free radical initiator and ethyl acetate (25% w/v monomer) as the solvent, at 75 (± 1) °C. Termination of the reaction was achieved by cooling the

system in an ice-bath. The macro-RAFT agent was precipitated in an excess of methanol and filtered off. \overline{M}_n (SEC) = 12000, \overline{M}_n (MALLS) = 39000, \overline{M}_n (theor) = 40000 and PDI (MALLS) = 1.19.

4.3.4 Diblock synthesis routes

4.3.4.1 Route 1: Synthesis of PMAIpGlc-b-poly(1-ethoxyethyl acrylate)

This reaction entailed adding macro-RAFT agent (5.0 g; 0.1282 mmol) and ethyl acetate (25% w/v monomer) into a temperature regulated reaction vessel at 60 (\pm 1) °C under nitrogen purge. Quantities of AIBN (0.0021 g; 0.01282 mmol) and EEA (1.0256 g; 14.22 mmol) were added as the free radical initiator and comonomer, respectively, after 30 min. EEA comonomer conversion was determined gravimetrically. The resulting copolymer was precipitated and washed in excess methanol as the poly(EEA) homopolymer (that might have formed during the course of the reaction) remained in solution. \overline{M}_n (SEC) = 15000, \overline{M}_n (MALLS) = 46000, \overline{M}_n (theor) = 48000 and PDI (MALLS) = 1.33.

4.3.4.2 Deprotection by acidolysis

¹³C NMR spectroscopy indicated that the 1-ethoxyethyl protecting group was not removed during the EEA chain extension reaction as peaks for [-OCH₂CH₃] and [-COOCH(CH₃)] still appeared at 15.1 and 21.0 ppm, respectively. Therefore, acidolysis was carried out analogous to procedures documented previously in Section 3.3.3. Acidolysis allows for the removal of the 1-ethoxyethyl and acetal protecting groups on the acrylic acid and glycopolymers, respectively. ¹H and ¹³C NMR data verified the resulting deprotected polymer PMAIpGlc-b-poly(AA). The latter was obtained as a white powder, in a quantitative yield.

4.3.4.3 Route 2: Synthesis of PMAIpGlc-b-poly(acrylic acid)

This approach involved carrying out an acidolytic reaction on the macro-RAFT agent (PMAIpGlc) to yield PMAIpGlc, which is highly water soluble. Thereafter, chain extending the PMAIpGlc polymer with repeat units of water soluble AA was undertaken. The formulation and reaction procedure included premixing PMAIpGlc (0.501 g, 0.013 mmol) and acrylic acid (0.125 g, 1.74 mmol) in nitrogen-purged DDI water (purging was carried out for 24 h) at 60 °C. A water soluble initiator, potassium persulphate (KPS) (0.0012 g, 0.0063 mmol) was then added and the reaction was allowed to run for 24 h.

4.3.5 CaCO₃ crystallization studies

A typical CaCO₃ crystallization reaction was carried out by separately dripping equimolar amounts (0.025 M) of aqueous solutions of calcium chloride and sodium carbonate in a sealed 50 mL two-neck round bottom flask fitted with a condenser and a dripping funnel. The reaction temperature was regulated at 25 (±1) °C throughout the 24 h period of the reaction. 0.5 g of glycopolymer additives, when used, were added to an aqueous solution of calcium chloride (0.025 M) prior to the dripwise addition of an aqueous solution of sodium carbonate (0.025 M) into the reaction vessel. Crystallization was terminated by filtering the resulting solution through a 0.22 μm filter. The residue was collected and washed several times with DDI, prior to analysis.

4.4 Results and discussion

4.4.1 Diblock synthesis: Routes 1 and 2

Route 1: In an effort to synthesize diblock glycopolymers, the PMAIpGlc homopolymer was used as a macro-RAFT agent for the block copolymerization of EEA.

Figure 4.1 illustrates the evolution of molecular weight over time for the successful chain extension of PMAIpGlc with EEA. The percentage conversion was used to calculate \overline{M}_n (theor) value. The observed blocking efficiency confirmed the retention of the ‘living’ character of the resulting polymer, with RAFT chain-end functionality. The dn/dc values for the MALLS measurement of the final precipitated polymers were calculated (in duplicate) to be 0.0791 (± 0.0001) mL/g with a correlation coefficient of 0.999 (± 0.002), and 0.0994 (± 0.0001) mL/g with a correlation coefficient of 0.999 (± 0.001), for PMAIpGlc and PMAIpGlc-b-poly(EEA), respectively. The resulting diblock glycopolymer was subjected to acidolysis to yield the deprotected form: PMAIGlc-b-poly(AA).

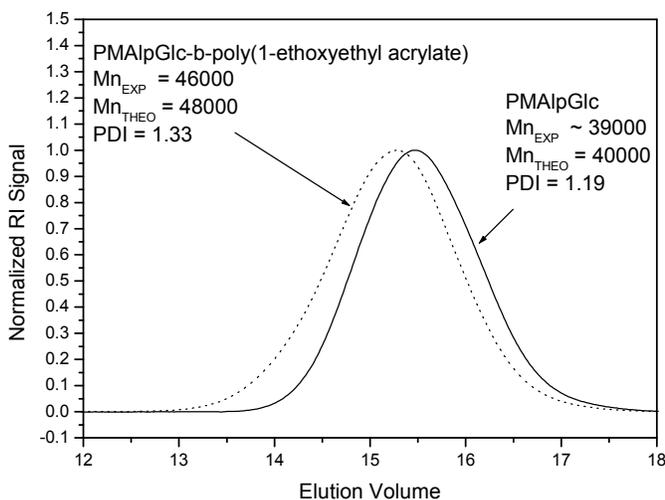


Figure 4.1 SEC chromatograms for the products of the RAFT mediated copolymerization of PMAIpGlc and EEA in ethyl acetate (25% v/v monomer) at 60 °C. Starting compositions: PMAIpGlc (0.1282 mmol), EEA (14.22 mmol) and AIBN (0.01282 mmol).

Route 2: The acidolysis reaction exposes the macro-RAFT agent to extremely harsh conditions (1 N HCl, 4 N NaOH, 100 °C and 2 h). Hence, prior to attempting an acrylic acid chain extension reaction of PMAIGlc the presence of the RAFT agent at the terminal ends of the macro-RAFT agent need to be verified. UV analysis was used for this purpose. Results indicated that after several washing steps some of the RAFT agent remained after acidolysis, as seen in Figure 4.2. In the light of this, the acrylic acid chain extension experiment was carried out and the resulting product was characterized using aqueous SEC. Results illustrated in Figure 4.3, show that no poly(AA) chain extension of PMAIGlc occurred, and only uncontrolled poly(AA) formed during the experiment.

The question that arose at this stage was: Why did no apparent poly(AA) chain extension occur even though UV studies showed evidence of the presence of RAFT agent? The only plausible reason, and one that has been documented in literature,¹⁸⁻²¹ is that partial hydrolysis of the terminal RAFT agent occurs during acidolysis and neutralization of the macro-RAFT agent. Using ^1H NMR spectroscopy, Baussard et al.²² showed that hydrolysis of dithio-RAFT agents results in degradation products, such as dithiobenzoic acid, with absorbance wavelengths that are similar to the parent RAFT agent. Therefore, residual absorbance is still observed even if the compound is partially hydrolyzed, according to ^1H NMR results. Having achieved success with using Route 1 to prepare well-defined block glycopolymers, Route 2 was subsequently abandoned.

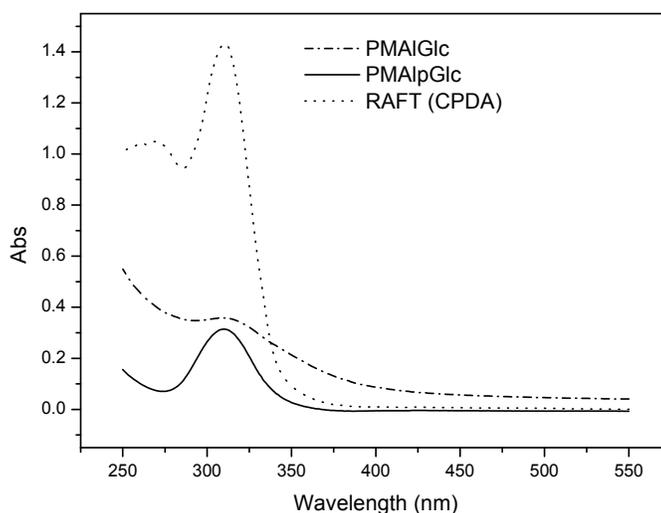


Figure 4.2 UV analysis of (i) RAFT agent CPDA, (ii) PMAIpGlc and (iii) PMAIGlc.

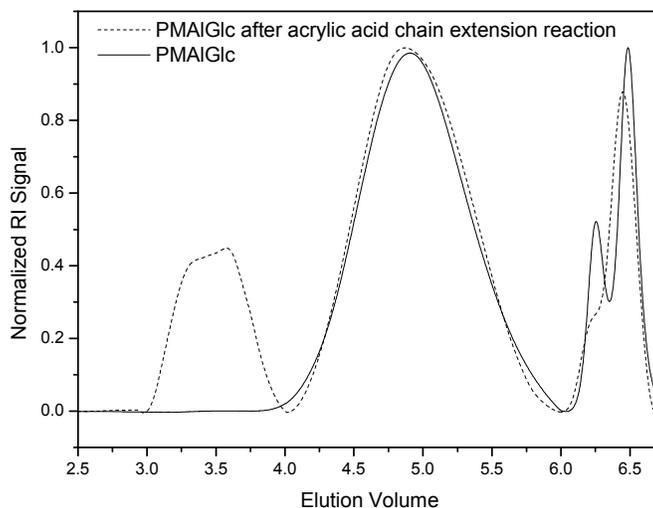


Figure 4.3 Aqueous SEC analysis of PMAIGlc before and after the acrylic acid chain extension reaction.

4.4.2 Self-assembly/aggregation studies

The cmc of the diblock glycopolymer was investigated by determining its conductivity. Conductivity (measured in μs) was measured for various polymer concentrations in water at pH 4, 7 and 9 and 295 K. Figure 4.4 shows that the cmc occurs at $0.15 (\pm 0.01)$, $0.17 (\pm 0.01)$ and $0.18 (\pm 0.02)$ g/L for PMAIGlc-b-poly(AA) at pH 4, 7 and 9, respectively. Each of these results is an average of three measurements. As the same polymer composition was used in all three cases, the cmc values obtained in this study were similar.

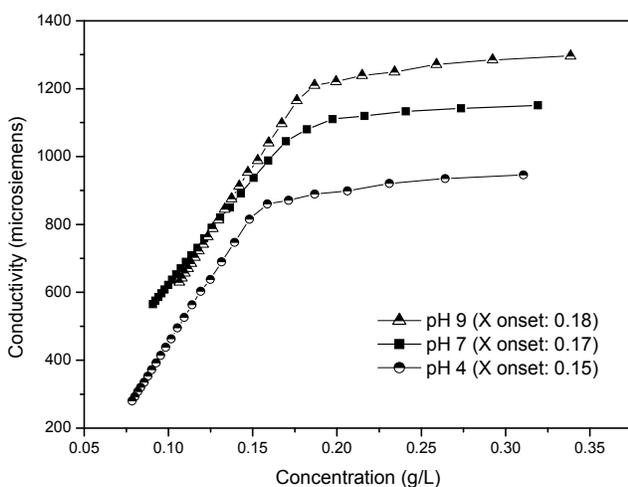


Figure 4.4 Changes in conductivity with concentration of PMAIGlc-b-poly(AA) in an aqueous solution at pHs 4, 7 and 9.

Although the self assembly capabilities of sugar-containing²³ and acrylic acid-containing^{24,25,26} polymers in aqueous solutions have been reported by other researchers, a direct comparison between

their results and those obtained in this study cannot be drawn, due primarily to the novel poly(AA) based glycopolymers (in terms of monomer compositions and molecular weights and architectural design) produced in this study. For instance, cmc values of 0.1 and 7.0 g/L obtained when dodecyl- β -D-maltoside and 1-O-n-octyl- β -D-glucopyranoside were studied,²³ and a cmc value of 0.1 g/L was obtained when oligo(methyl methacrylate) was AB copolymerized with poly(AA)²⁷, is an excellent example of how the above-mentioned factors make it academically unsound to compare cmc values.

4.4.3 Particle morphologies above their cmc value

Sample preparation for self-assembly studies involved preparing 0.2 g/L solutions of the diblock copolymers in water at pHs 4, 7 and 9, respectively, and then staining the respective solutions with uranyl acetate (a stain used in TEM studies to identify carboxylic acids^{28,29}) for 30 min. 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.³⁰ TEM images (Figure 4.5) show that the diblock glycopolymer does exhibit core-shell amphiphilic behaviour and that its core-shell configuration assembly is pH dependent. At pH 4 the acrylic acid moiety forms the inner core, encapsulated by the glycomoiety, which forms the periphery of the particle.

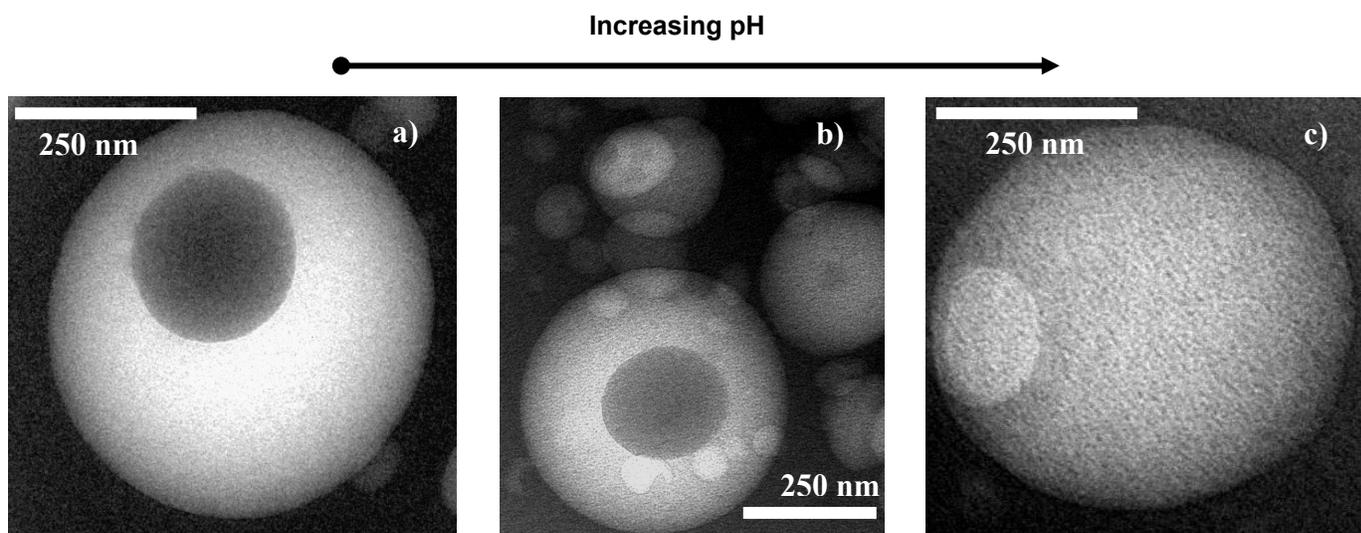


Figure 4.5 TEM images illustrating the core-shell amphiphilic behaviour of PMAIGlc-b-poly(AA) [\overline{M}_n (MALLS) = 46000] after 20 min in an aqueous solution. (a) At pH 4, the glycomoiety forms the periphery of the nanoparticle encapsulating the acrylic acid moiety in the core. (b) At pH 7, a mixture of core-shell configurations was found. (c) At pH 9, deprotonation of the acrylic acid moiety occurs, resulting in the glycomoiety being encapsulated by an acrylic acid based outer shell. (Uranyl acetate was used to stain the acid moiety)

However, at pH 9 there is an increase in the degree of ionization of the poly(AA) moiety,^{26,31-34} which results in it having a higher water solubility than that of the glycomoiety. Subsequently at this high pH the acrylic acid moiety self assembles to form the periphery of the particle encapsulating a glyco-based inner core. At neutrality interestingly, TEM indicates that there is a combination of both core-shell configurations, as shown in Figure 4.5b. It is also interesting that at extreme pH conditions (pH 4 and 9) the sugar moiety shrinks, whereas the acrylic acid moiety expands in such a way that the particle dimensions remain the same. At the interim pH 7, the particle shrinks to roughly half the diameter.

4.4.4 CaCO_3 crystallization studies

TEM was used to image the crystal morphology. Crystallization reactions were carried out in the absence of a polymer (control sample), and in the presence of either PMAIpGlc-b-poly(EEA) or PMAIGlc homopolymer or PMAIGlc-poly(AA). Results (shown in Figures 4.6 and 4.7) indicate that for the former three reactions, single and randomly aggregated cubic-like structures formed, whilst for the latter sample (i.e. PMAIGlc-b-poly(AA)) an array of randomly structured round-edged arrangements formed. These results agree well with what is reported in literature,³⁵⁻⁴⁰ round-edged calcite crystal morphologies were observed when CaCO_3 was formed in the presence of a polycarboxylic acid such as poly(AA).⁴¹⁻⁴⁴

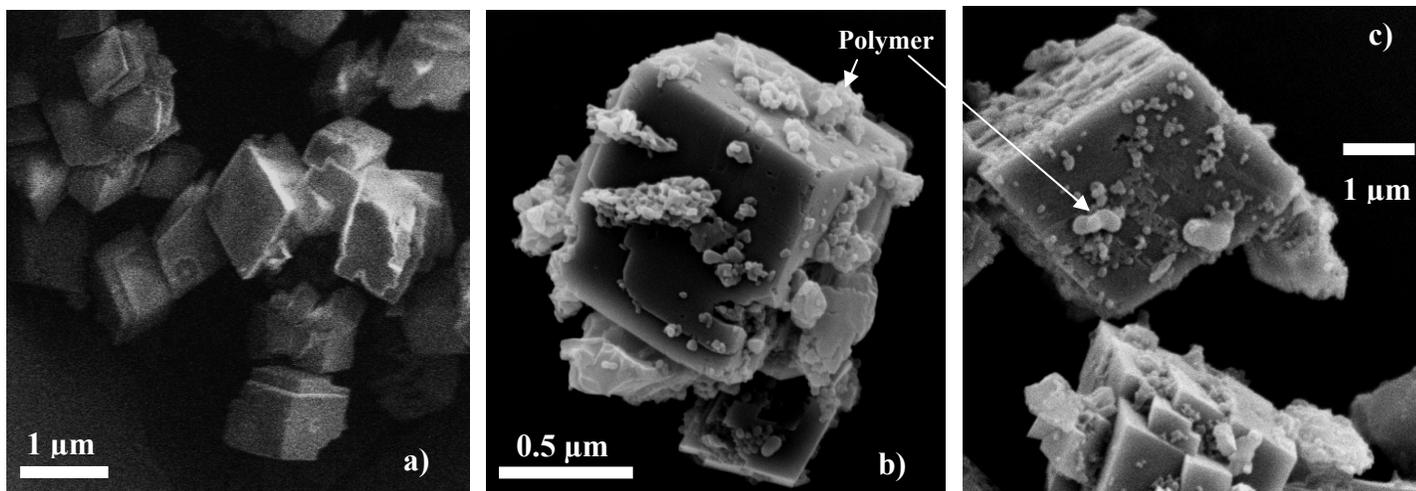


Figure 4.6 SEM images of CaCO_3 crystals grown (a) as the control sample; (b) in the presence of PMAIpGlc-b-poly(EEA) and (c) in the presence of the PMAIGlc homopolymer. (See Section 4.3.5 for reaction conditions)

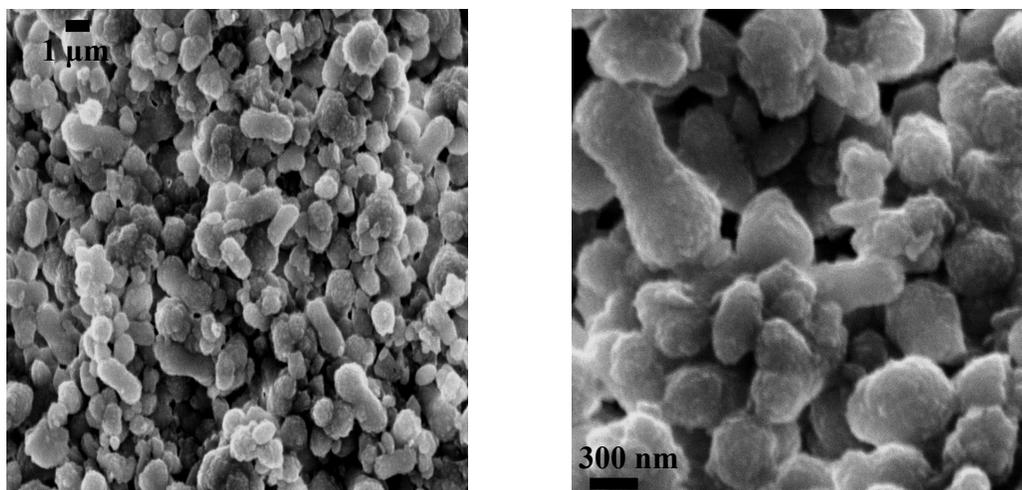


Figure 4.7 SEM images illustrating the surface modifying effect that the poly(AA) moiety on the diblock copolymer PMAIGlc-b-poly(AA) has on the final crystal size and morphology of the crystallized CaCO_3 . (See Section 4.3.5 for reaction conditions)

The effect of PMAIGlc-b-poly(AA) on the crystallization of CaCO_3 , achieved by changing the pH, the reaction temperature and time, and the polymer concentration, was also studied. The experimental conditions and the results are tabulated in Table 4.1. It can be seen that reaction time has an influence on CaCO_3 crystallization (samples 5 to 10). Results show that as the reaction time was increased from 12 to 48 h the average particle size subsequently increased from ± 0.3 to $1.3 \mu\text{m}$. However, there was no change in the polymorphism (calcite) or the overall particle shape of these samples, as shown by XRD and SEM (Figure 4.8), respectively. There was however a significant difference in particle shape between the control samples (samples 5, 7 and 9) and the samples which were carried out in the presence of the polymer substrate (samples 6, 8 and 10). SEM showed that strictly rhombedral particles (Figure 4.8a) and spherical particles (Figure 4.8b) formed, respectively. Therefore, in these experiments the evolution of crystal polymorphism was unaffected by the presence of the polymer or by the reaction time. However, the crystal morphology was significantly affected. These results are consistent with the crystallization of CaCO_3 in the presence of poly(AA).⁹

In order to evaluate the effect of pH on the morphosynthesis of CaCO_3 the pH of the systems were adjusted using 0.02 M HCl or 0.02 M NaOH, whilst other conditions such as reaction time, temperature and polymer concentration were kept constant. In all cases the pH was adjusted after Na_2CO_3 addition. Results showed that there were only small changes in particle polymorphism, shape and size for reactions carried out at pH 7 (sample 5), compared to reactions carried out at pH 3 (sample 12).

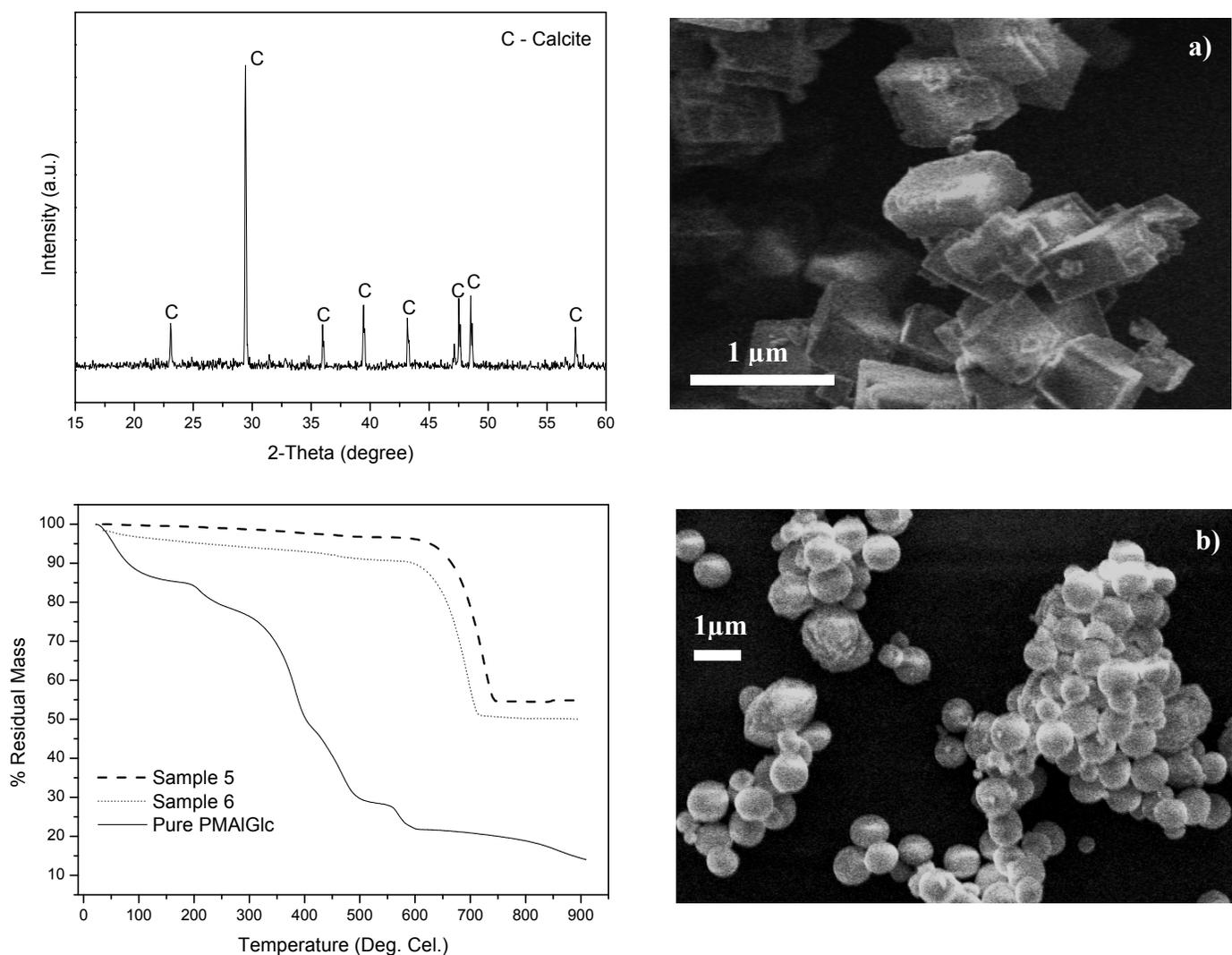


Figure 4.8 A typical XRD pattern (top left) and TGA (bottom left) of CaCO_3 , obtained at 25 °C for 24 h, pH 7 in (a) the absence of PMAIGlc-b-poly(AA) [sample 5] and (b) the presence of PMAIGlc-b-poly(AA) [sample 6]. SEM images are shown on the right.

However, when the pH was adjusted to 10 a difference in particle polymorphism, shape and size was detected. The evident increase in particle size is to be expected, according to literature.⁹ The predominant polymorph was calcite, with traces of vaterite and aragonite (levels in order given) also present. The resulting particle shape was oval, with traces of irregular structures, and subsequently particle size was affected (Figure 4.9). Interestingly, similar particle morphologies and sizes were obtained for reactions carried out at higher temperature (80 °C). These results imply that as one increases the reaction temperature or pH a mixture of the three polymorphs (calcite, vaterite and aragonite) is found. As temperature is increased the aragonite polymorphism is favoured as it is more stable at higher temperatures. At a basic pH, since deprotonation of poly(AA) occurs, its interactions

with growing CaCO_3 nuclei are increased, thereby stabilizing the less thermodynamically stable polymorph (vaterite and aragonite).

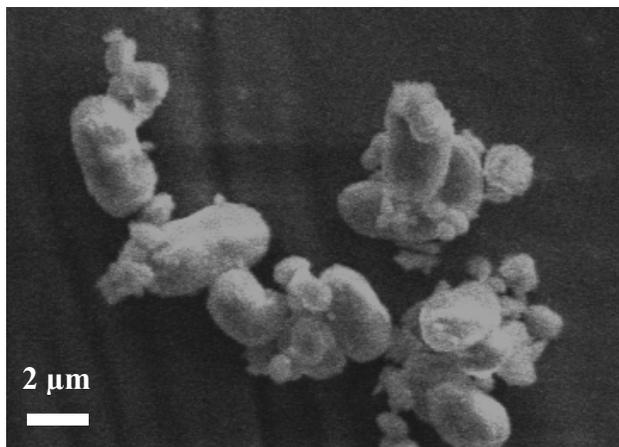
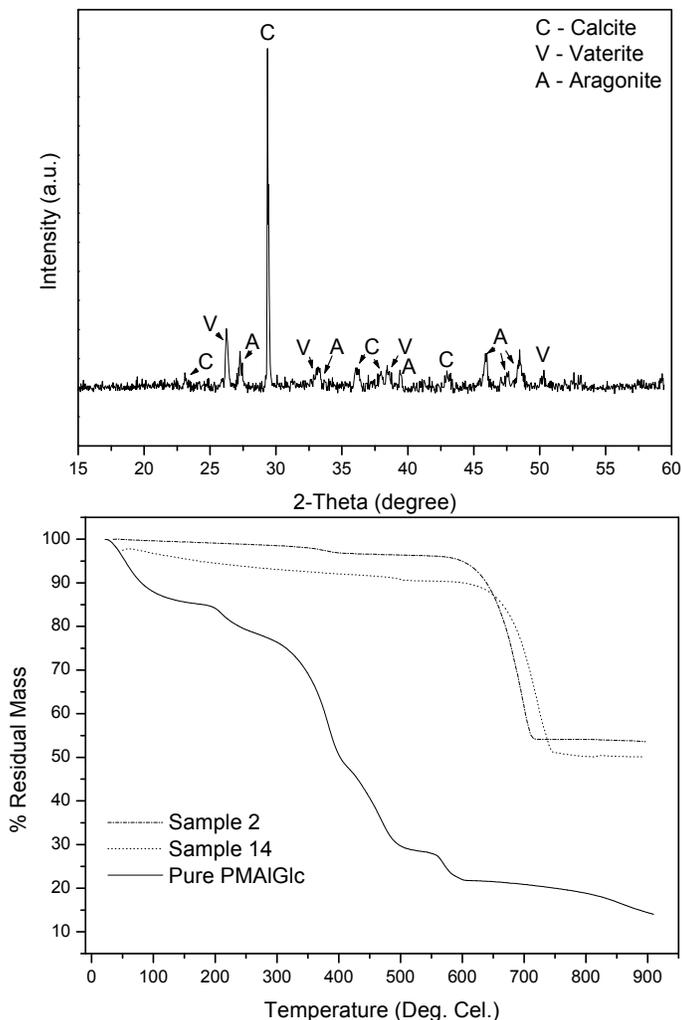


Figure 4.9 A typical XRD pattern (top left) and TGA (bottom left) of CaCO_3 , obtained at 25 °C for 24 h, pH 10 and at 80 °C for 24 h, pH 7, in the presence of PMAIGlc-b-poly(AA). SEM illustrating the oval irregular particles that were formed under these conditions (samples 1, 2 and 13, 14).

Results in Table 4.1 also indicate that polymer concentration, ranging from 0.501 to 1.011 g/L, has a greater effect on particle size, percentage yield and percentage of polymer attached to the surface of crystallized CaCO_3 than its effect on polymorphism during CaCO_3 crystallization. As the polymer concentration was increased there was a subsequent decrease in particle size. This is probably due to the statistical increase in CaCO_3 nucleation sites across this series of reactions. The inhibitory effect that acrylic acid has on the rate of CaCO_3 crystallization may also result in reduced particle sizes.^{10,35}

Table 4.1 Formation of crystalline CaCO₃ in the presence of PMAIGlc-b-poly(AA) at different reaction temperatures, reaction times, pH conditions and polymer concentrations (PMAIGlc-b-poly(AA) $\overline{M}_n = 48000$)

Sample No.	PMAIGI-b-P(AA) (g/L)	Temp (°C)	Time (h)	pH	Polymorph ^a	Shape of particles ^b	CaCO ₃ particle size ^c (µm)	Yield ^d (%)	Percentage of polymer absorbed on particles ^e (%)
1	-	80	24	7	C, V and A	Oval, irregular	1.8 ± 0.7 ^f	86.4	-
2	0.502	80	24	7	C, V and A	Oval, irregular	1.5 ± 0.6 ^f	72.1	53
3	-	50	24	7	C and V	Rhombhedral	1.1 ± 0.2	91.3	-
4	0.501	50	24	7	C and V	Spherical	1.0 ± 0.3	75.5	54
5	-	25	24	7	C	Rhombhedral	0.9 ± 0.3	89.7	-
6	0.501	25	24	7	C	Spherical	0.7 ± 0.3	69.6	57
7	-	25	48	7	C	Rhombhedral	1.5 ± 0.3	78.1	-
8	0.502	25	48	7	C	Spherical	1.3 ± 0.3	69.8	58
9	-	25	12	7	C	Rhombhedral	0.5 ± 0.3	96.4	-
10	0.503	25	12	7	C	Spherical	0.3 ± 0.1	77.6	58.5
11	-	25	24	3	C	Rhombhedral	1.3 ± 0.4	88.1	-
12	0.501	25	24	3	C	Spherical	1.1 ± 0.1	72.1	58
13	-	25	24	10	C, V and A	Oval, irregular	1.9 ± 0.6 ^f	77.8	-
14	0.501	25	24	10	C, V and A	Oval, irregular	1.9 ± 0.8 ^f	73.9	57
15	0.751	25	24	7	C	Spherical	0.5 ± 0.2	67.2	63
16	1.011	25	24	7	C	Spherical	0.3 ± 0.1	55.1	68
17	<i>g (Blank)</i>	25	24	7	C	Rhombhedral	0.6 ± 0.1	89.2	0
18	<i>h (Blank)</i>	25	24	7	C	Spherical	1.8 ± 0.3	68.4	100

^a Polymorphism was characterized by XRD (V: Vaterite, C: Calcite and A: Aragonite). ^b The shape of the particles was observed by SEM. ^c The size of the particles was measured by SEM. ^d The yield was calculated using the final crystal weights compared with the theoretical weights of CaCO₃ from the injected calcium reagents. ^e The absorbed amount of polymer was measured by TGA (heating rate: 10 °C/min under air atmosphere) [See Appendix A-1]. ^f Size measured along the length of the oval shaped crystals. ^g Glyco-homopolymer added (0.501 g). ^h Poly(AA) homopolymer added (0.500 g).

TEM analysis of these particles indicated that glycopolymers had absorbed onto the surface of the CaCO₃ particles (Figure 4.10). This is possibly due to the excess amounts of glycopolymers used in these reactions, compared to quantities used in literature.⁴⁵ Thus, apart from affecting crystal morphology and size, these glycopolymers formed a ‘coated’ layer on the surface of the crystals. This absorption phenomenon is facilitated by the poly(AA) moiety of the glycopolymer, which is known to

be an effective disperser of CaCO_3 .⁴⁶⁻⁴⁹

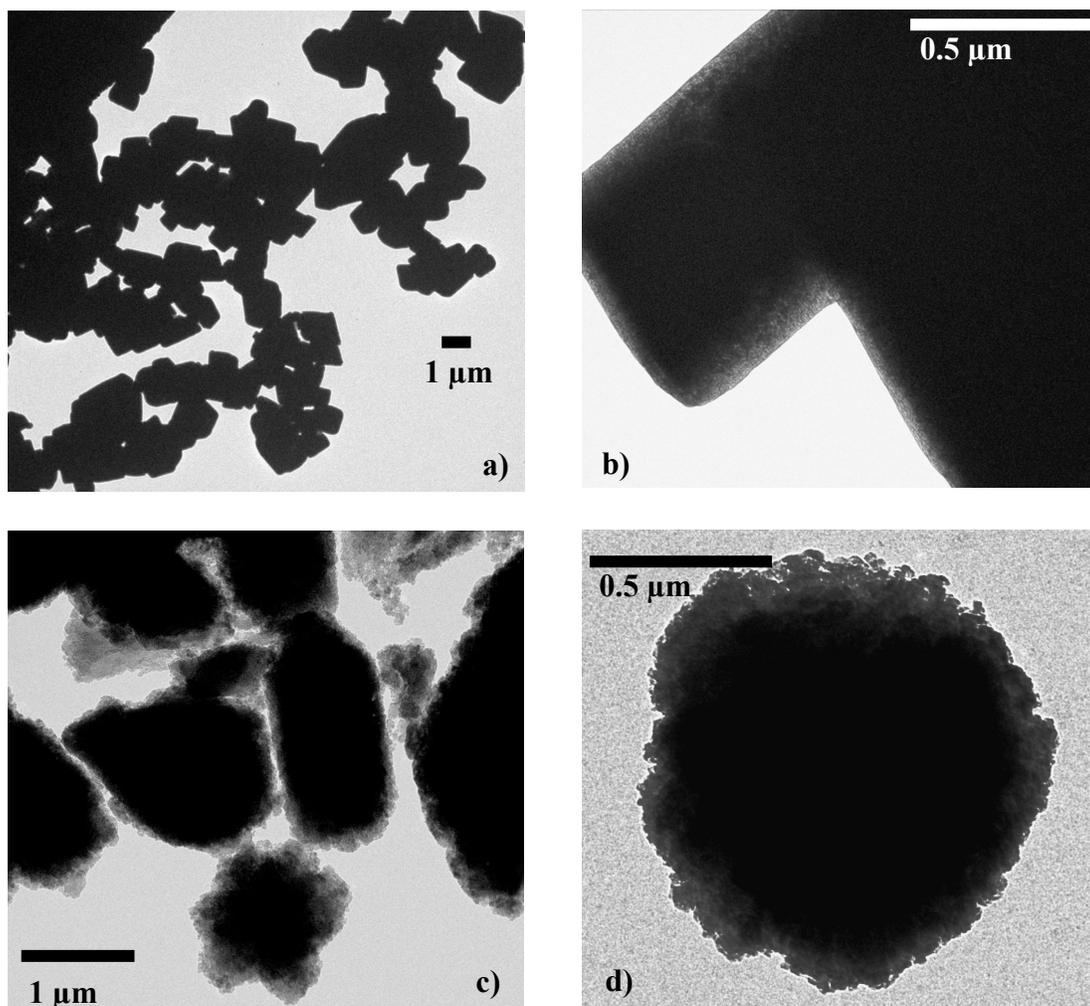


Figure 4.10 TEM images of the CaCO_3 crystallization reactions conducted in (a) and (b) the absence of the PMAIGlc-b-poly(AA) diblock glycopolymer [Control], (c) and (d) conducted in the presence of the diblock glycopolymer. In images (c) and (d), a ‘fluffy’ carbohydrate based polymer is shown to surface modify the CaCO_3 crystal.

Apart from electron microscopy analyses, an additional analytical technique was also used to confirm the presence of the glycomoiety on the periphery of the CaCO_3 crystal. This involved the use of a chromatographic staining agent, aniline phthalate, which is used to strictly identify reducing sugars. Reducing sugars stain brown after being heated to 150 $^{\circ}\text{C}$ in a drying oven. CaCO_3 crystallized in the presence of PMAIGlc-b-poly(AA) stained brown, as seen with a light microscope, whilst the colour of the CaCO_3 crystallized in the absence of PMAIGlc-b-poly(AA) remained unchanged (Figure 4.11). This further confirmed the presence of the glycomoiety on the periphery of the CaCO_3 crystal.



Figure 4.11 Photographic images taken after staining and heating of a pure CaCO_3 sample (left) and a CaCO_3 sample prepared in the presence of a glycomoiety (right). The brown colour confirms the presence of a glycomoiety on the periphery of a CaCO_3 crystal.

Furthermore, the ability of these ‘sugar-coated’ particles (SCPs) to adhere to cellulose was quantified and qualified by TGA and SEM, respectively. Experiments were carried out by stirring 0.25, 0.5 and 0.75 g of SCP together with 0.5 g of cellulose in an aqueous solution (pH 7) at ambient temperature for 24 h. The resulting mixture was filtered through a 4.5 μm filter paper and then washed several times (5 - 7) with DDI water prior to analysis.

Results of TGA analyses (shown in Figure 4.12) confirmed that 27, 52 and 64% adherence was obtained when 0.25, 0.50 and 0.75 g SCP was used (calculation shown in Appendix A-2), whilst only 15% cellulose adhered to the uncoated CaCO_3 particles (control sample). Visually, SEM verified these TGA results by showing that the SCP particles synthesized in this study have a greater affinity for cellulose than the uncoated CaCO_3 particles (Figure 4.13). This increased adherence is due to hydrogen bonding between the hydroxyl groups of the glycomoiety and the cellulose.

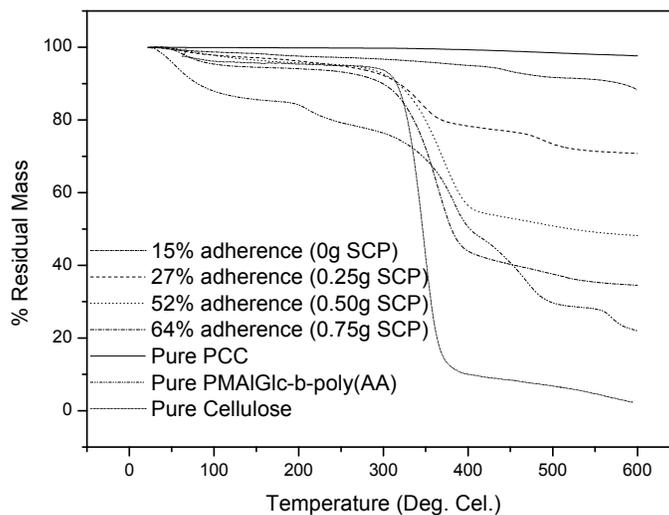


Figure 4.12 TGA used to determine the percent cellulose that adhered onto various percentages of SCP.

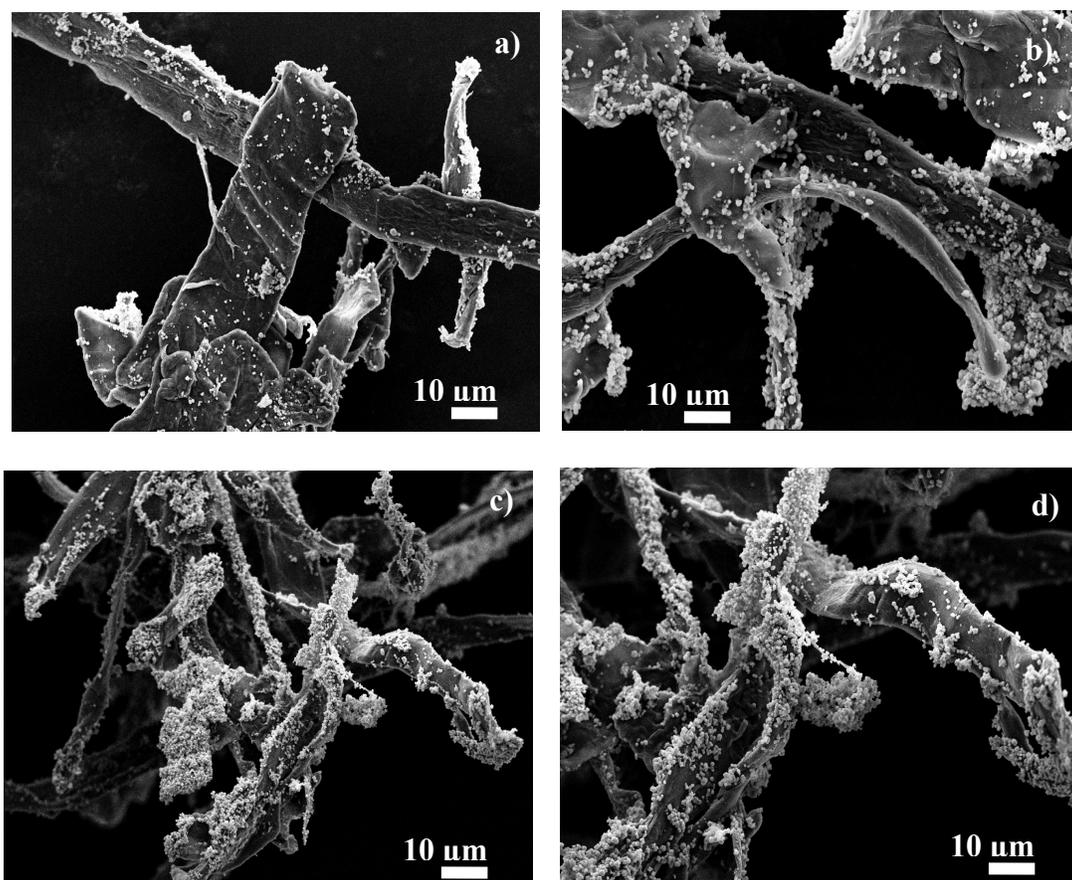


Figure 4.13 SEM images of cellulose after interaction at pH 7 with (a) uncoated CaCO_3 particles [control sample] and (b) 0.25 g ‘sugar-coated’ CaCO_3 particles, (c) 0.5 g ‘sugar-coated’ CaCO_3 particles and (d) 0.75 g ‘sugar-coated’ CaCO_3 particles.

4.5 Conclusions

A novel amphiphilic diblock glycopolymer poly(3-O-methacryloyl-1,2:5,6-di-O-isopropylidene-D-glucofuranose)-b-[poly(AA)] was synthesized via the RAFT polymerization process. TEM illustrated the formation of nano-sized core-shell particles in aqueous solution. The acrylic moiety aggregated to form the inner-core and was encapsulated by the glycomoiety at pH 4, whilst at pH 9 particle inversion occurred. The crystallization of CaCO_3 was carried out in the presence of the diblock glycopolymer. SEM analysis indicated that the acrylic acid moiety surface-modified crystal growth, resulting in an array of randomly structured round-edged arrangements. This result correlates well with existing literature. TEM and the use of a chromatographic staining agent (aniline phthalate) confirmed the synthesis of nano-sized ‘sugar-coated’ CaCO_3 . SEM showed the increased adherence capabilities of these ‘sugar-coated’ particles to cellulose.

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Chapter 5

Identifying the ideal acrylic acid based glycopolymer configuration

Abstract

A series of polymer configurations were synthesized with various ratios of glycomoiety to poly(AA). MALLS was used to characterize the polymers in terms of molecular weight and its molecular weight distributions. CaCO₃ crystallizations were carried out utilizing the polymers as substrates. SEM confirmed that there was no apparent change in particle shape or size across the series. XRD confirmed the dominating calcite polymorphism. TEM illustrated that polymers could attach to precipitated CaCO₃ and TGA was once again admired for its quantitative ability.

In parts, reproduced from:

Crystallization of calcium carbonate in presence of acrylic acid based glycopolymers: PART 2

Vernon Ramiah, Howard Matahwa, Johannes C. Terblanche and Ron D. Sanderson, submitted to **Journal of Crystal Growth, 2008**

Novel retention aids

Vernon Ramiah, Howard Matahwa, Johannes C. Terblanche and Ron D. Sanderson, to be submitted to **TAPPI, 2008** (In preparation)

5.1 Introduction

This extremely important chapter is aimed at identifying the influence of the diblock configuration on the absorption of CaCO_3 to cellulose.

In light of this, the objectives of this chapter are four-fold:

- Devise a protocol for the synthesis and characterization of various polymer configurations as presented in Figure 5.1.
- Determine the effect of the various polymer configurations on CaCO_3 crystallization
- Determine the effect of the resulting CaCO_3 crystallization study products and these products absorption capabilities to cellulose
- Determine if there are any physical interactions between these synthesized polymers and precipitated CaCO_3 and/or cellulose.

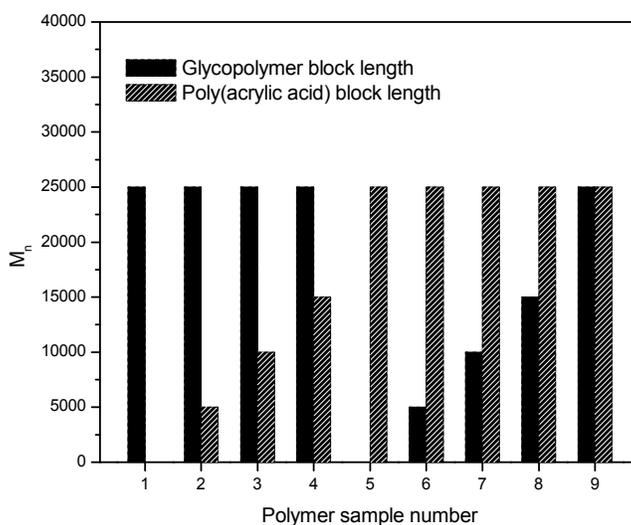


Figure 5.1 A proposal of the different block compositions used to determine the ideal ratio of poly(AA) to glycopolymer for maximum absorption of PMAI₂Glc-b-poly(AA) onto cellulose and CaCO_3 .

5.2 Experimental

5.2.1 Synthesis of polymer samples 1 to 5

The synthesis of polymer samples 1 to 4 involved the initial bulk synthesis of the macro-RAFT agent, PMAI₂Glc, which was prepared according to the method described in the Section 3.2. This resulting polymer was divided into equi-molar quantities and chain extended with EEA. The starting compositions are tabulated in Table 5.1 (Section 5.2.2). Termination of the reaction was carried out by

cooling the system in an ice bath. The resulting product was precipitated in an excess of methanol and filtered.

Removal of the 1-ethoxyethyl and acetal protecting groups was carried out by acidolysis, analogous to procedures described previously (Section 3.4.7). The resulting products were characterized by ^{13}C and ^1H NMR. The products were white powders, obtained in a quantitative yield.

5.2.2 Synthesis of polymer samples 6 to 9

When two different leaving groups are subjected to RAFT polymerization an intermediate radical is formed. The latter will have preference to fragment in a direction based on the leaving group potential of the two radicals. This proven concept provides a preferred monomer addition sequence for the production of block copolymers in methacrylates > styrenic > acrylate monomers.¹ In the light of this, a unique synthetic route was used for the synthesis of polymer samples 6 to 9. Various glycopolymeric chain lengths were initially produced, followed by chain extension with similar chain lengths of EEA. Starting compositions are tabulated in Table 5.1. Acidolysis was carried out as for samples 1 to 5.

Table 5.1 Starting compositions used for the synthesis of polymer samples 1 to 9. All reactions were carried out in ethyl acetate (25% w/v monomer) and at 60 °C. Details of the starting compositions for the synthesis of PMAIpGlc are given in the footnote.

Polymer	PMAIpGlc (Macro-RAFT agent) [mmol, g]	AIBN [mmol, g]	EEA [mmol, g]
1 ^a	-	0.0607, 0.0100	-
2	0.0874, 2.01	0.0084, 0.0013	3.031, 0.437
3	0.0870, 2.00	0.0084, 0.0015	6.031, 0.870
4	0.0874, 2.01	0.0084, 0.0012	9.093, 1.311
5 ^b	-	0.0289, 0.0047	34.68, 5.001
6 ^c	0.4020, 2.01	0.0574, 0.0094	69.71, 10.05
7 ^d	0.2000, 2.00	0.0402, 0.0065	34.68, 5.001
8 ^e	0.1341, 2.01	0.0268, 0.0044	23.23, 3.352
9 ^f	0.0838, 2.01	0.0201, 0.0033	13.94, 2.010

^a MAIpGlc = 45.71 mmol, 15.01 g; CPDA = 0.6074 mmol, 0.1740 g

^b CPDA = 0.2023 mmol, 0.0580 g

^c PMAIpGlc: (MAIpGlc = 9.17 mmol, 3.01 g; CPDA = 0.6389 mmol, 0.1830 g; AIBN = 0.0913 mmol, 0.0150 g)

^d PMAIpGlc: (MAIpGlc = 9.14 mmol, 3.00 g; CPDA = 0.3090 mmol, 0.0885 g; AIBN = 0.0441 mmol, 0.0072 g)

^e PMAIpGlc: (MAIpGlc = 9.17 mmol, 3.01 g; CPDA = 0.2045 mmol, 0.0586 g; AIBN = 0.0292 mmol, 0.0048 g)

^f PMAIpGlc: (MAIpGlc = 9.20 mmol, 3.02 g; CPDA = 0.1222 mmol, 0.0350 g; AIBN = 0.0031 mmol, 0.0050 g)

5.2.3 Self assembly/aggregation studies

The cmc of the diblock glycopolymers was investigated by means of conductivity, at various polymer concentrations in water at pH 4, 7 and 9. These results are expressed as an average of triplicate measurements, carried out at 295 K.

5.2.4 Substrate - substrate interactions

5.2.4.1 Polymer - CaCO₃ (PCC) interactions

The absorption of polymer samples onto precipitated CaCO₃ (PCC) was evaluated by stirring various ratios of the glycopolymers to PCC, at 25, 50 and 80 °C, for 12, 24 and 48 h, at pH 4, 7 and 9. Typical ratios were from 1:1, 0.8:0.2, 0.6:0.4, 0.4:0.6 and 0.2:0.8. The resulting solutions were filtered and then washed several times with DDI water. The collected precipitates were characterized by TEM and the percentages of the diblock glycopolymer attached to PCC were quantified using TGA.

5.2.4.2 Polymer - cellulose interactions

Thin-layer chromatography (TLC) was used to qualify the absorption of these polymer samples (1 to 9) onto cellulose. This was done by spotting aqueous solutions of the resulting polymers (50% w/v) on pure Baycell pulp hand-sheets (80 g/m² grammage). Polymer samples that contained a glycomoiety were identified by application of a chromatographic staining agent (aniline phthalate), whilst the poly(AA) homopolymer was visible under UV at 254nm. Analysis was done in triplicate and the average R_f values* were reported for an acidic (HCl modified), basic (NaOH modified) and neutral eluent system at 25 (± 1) °C.

The absorption of these polymer samples onto cellulose was quantified by stirring various ratios of the glycopolymers to cellulose at 25, 50 and 80 °C for 12, 24 and 48 h at pHs 4, 7 and 9. The added ratios varied from 1:1, 0.8:0.2, 0.6:0.4, 0.4:0.6 and 0.2:0.8. The resulting solutions were filtered off, washed several times (5 to 7) with DDI water and the collected precipitates were subjected to TGA to evaluate the percentages of the diblock glycopolymer attached to cellulose.

* R_f value: migration of a sample/ migration of a eluent.

5.2.4.3 Cellulose - polymer - CaCO₃ interactions

Study utilizing crystallized CaCO₃

A quantity of prepared ‘sugar-coated’ CaCO₃ particles (0.100 g) was stirred in an aqueous solution of cellulose (0.100 g). The resulting product was filtered (Whatmann No.1), washed several times (5 to 7) with DDI water, air dried, and collected for further characterization. The effect of reaction pH, time and temperature on the attachment of cellulose to ‘sugar-coated’ CaCO₃ particles was investigated using TGA.

Study utilizing precipitated CaCO₃ (PCC)

Four different methods were investigated using TGA and SEM:

Method A: Each diblock copolymer (0.800 g of polymer samples 1 to 9) was premixed with PCC (0.100 g) and then added to an aqueous solution of cellulose (0.100 g). After adjusting the pH of the solution to 9 with 0.01 M NaOH the solution was allowed to stir for 48 h at 80 °C. The resulting solution was filtered, washed with an excess of DDI water, and then characterized. *Method B:* The procedure was very similar to that used in Method A, however, in this case: 0.800 g of each diblock copolymer (polymer samples 1 to 9) was first premixed with 0.200 g of cellulose and then added to an aqueous solution to 0.100 g of PCC. *Method C:* Here, 0.500 g of PCC was first premixed with 0.500 g cellulose and then added to aqueous solutions of each of the diblock copolymers (polymer samples 1 to 9). Reaction conditions were once again at pH 9, 80 °C and 48 h. *Method D:* This entailed mixing 0.500 g of each reactant together in an aqueous solution (pH 9, 80 °C, 48 h), followed by TGA and SEM characterization.

Controls reactions were carried out in the absence of each diblock copolymer (polymer samples 1 to 9).
[Reaction conditions: pH 9, 80 °C and 48 h]

5.3 Results and discussion

5.3.1 Polymer characterization

In this study a well-defined living homopolymer PMAIpGlc was prepared via the RAFT process using CPDA as the CTA agent. This homopolymer was then further used as a macro-RAFT agent for the block copolymerization of EEA.

Summarized in Table 5.2 are MALLS results obtained for polymer samples 1 to 9. The similarity of the \overline{M}_n (exp) values to the \overline{M}_n (theor) values confirms the successful chain extension of PMAIpGlc with EEA. The resulting diblock glycopolymer was subjected to acidolysis, yielding the deprotected form, namely PMAIGlc-b-poly(AA).

Table 5.2 Summary of the MALLS analyses of polymer samples 1 to 9.

Polymer	dn/dc Values and correlation coefficients (mL/g)	PMAIGlc moiety		Poly(AA) moiety		\overline{M}_n (Total)	PDI
		\overline{M}_n	\overline{M}_n	\overline{M}_n	\overline{M}_n		
		(exp)	(theor)	(exp)	(theor)		
1	0.0856 (\pm 0.0003), 0.999 (\pm 0.001)	24000	23000	-	-	23000	1.18
2	0.0794 (\pm 0.0001), 0.999 (\pm 0.003)	24000	23000	4000	3000	26000	1.19
3	0.0998 (\pm 0.0001), 0.999 (\pm 0.002)	24000	23000	10000	11000	34000	1.21
4	0.0877 (\pm 0.0002), 0.999 (\pm 0.002)	24000	23000	15000	14000	37000	1.33
5	0.0774 (\pm 0.0001), 0.999 (\pm 0.001)	-	-	23000	24000	24000	1.48
6	0.0861 (\pm 0.0001), 0.998 (\pm 0.004)	5000	6000	24000	23000	29000	1.26
7	0.0976 (\pm 0.0003), 0.999 (\pm 0.001)	10000	9000	23000	22000	31000	1.38
8	0.1101 (\pm 0.0002), 0.999 (\pm 0.001)	14000	15000	25000	24000	39000	1.43
9	0.1002 (\pm 0.0001), 0.999 (\pm 0.003)	24000	23000	25000	26000	49000	1.56

5.3.2 Self assembly/aggregation studies

In principle, as one increases the degree of hydrophobicity as well as the molecular weight of a surface active agent the cmc will decrease.² At pH 4, the acrylic acid moiety is the hydrophobic component, whilst at pH 9 the glycomoiety is the hydrophobic component. This is because at high pH there is an increase in the degree of ionization of the poly(AA) moiety,³⁻⁷ which results in it having a higher water solubility than that of the glycomoiety.

Hence, the results obtained in this study are expected. At pH 4, for polymer samples 2 to 4 where one increases the acrylic acid moiety (hydrophobic component), there is decrease in the cmc value. For polymer samples 6 to 8, it was observed that as the hydrophilic component is increased, a resulting increase in the cmc occurred. At pH 7, hydrophilic and hydrophobic components compete with each other, resulting in no observable trend when one increases either component. At pH 9, for polymer samples 2 to 4 (the acrylic acid moiety (hydrophilic component) is increased, there is an increase in the cmc value. However, for polymer samples 6 to 8, it was observed that as the hydrophobic component (glycomoiety) is increased, a resulting decrease in the cmc occurred. From the data (Table 5.3), especially for polymer sample 9, it becomes clearly evident that the lowest cmc value was obtained when there was a 1:1 molecular weight ratio of poly(AA): PMAIGlc.

Table 5.3 Cmc values of polymer samples 1 to 9, determined by conductivity.

Polymer	PMAIGlc-b-poly(AA)		Cmc at 295 K (g/L)		
	Mw: PMAIGlc moiety	Mw: Poly(AA) moiety	pH 4	pH 7	pH 9
1	23000	-	-	-	-
2	23000	3000	0.13	0.15	0.14
3	23000	11000	0.12	0.11	0.15
4	23000	14000	0.10	0.07	0.19
5	-	24000	-	-	-
6	6000	23000	0.11	0.13	0.24
7	9000	22000	0.15	0.18	0.20
8	15000	24000	0.18	0.23	0.16
9	23000	26000	0.02	0.02	0.05

A TEM image of these particles was shown in Figure 4.5 (Section 4.3.4).

5.3.3 CaCO₃ crystallization studies (synthesis of ‘sugar-coated’ CaCO₃ particles)

The effect of various configurations of PMAIGlc-b-poly(AA) on the crystallization of CaCO₃ was studied. Results are tabulated in Table 5.4. In the case of polymer samples 1 to 4, as the molecular weight of the poly(AA) was increased there was a subsequent increase in the particle size, as well as a decrease in the percentage yield of the reaction. This phenomenon is highly expected as, in the former case, the surface area of the template for CaCO₃ crystallization increased, facilitating a statistical

increase in CaCO₃ particle size. Poly(AA) has been documented to have a somewhat inhibitory effect on the rate of CaCO₃ crystallization.^{8,9} In the light of this, interestingly enough, results showed that for polymer samples 5 to 9 there were very small changes in particle size and percentage yield as the molecular weight of the poly(AA) moiety remained constant.

Table 5.4 Formation of crystalline CaCO₃ in the presence of different configurations of PMAIGlc-b-poly(AA).

Polymer	PMAIGl-b-P(AA) (g/L)	Polymorph ^a	Shape of particles ^b	CaCO ₃ particle size, ^c (μ m)	Yield ^d (%)	Percent of polymer absorbed on particles ^e (%)
1	<i>G</i>	Calcite	Rhombhedral	0.6 \pm 0.1	89.2	0
2	0.502	Calcite	Spherical	0.8 \pm 0.3	85.4	51
3	0.500	Calcite	Spherical	1.1 \pm 0.2	83.6	54
4	0.501	Calcite	Spherical	1.3 \pm 0.3	79.1	75
5	<i>H</i>	Calcite	Spherical	1.8 \pm 0.3	68.4	100
6	0.501	Calcite	Spherical	1.6 \pm 0.3	69.6	91
7	0.502	Calcite	Spherical	1.5 \pm 0.4	70.1	88
8	0.502	Calcite	Spherical	1.6 \pm 0.2	71.3	82
9	0.503	Calcite	Spherical	1.6 \pm 0.3	69.2	93
10 ^f	-	Calcite	Rhombhedral	0.8 \pm 0.1	91.3	-

^a Polymorphism was characterized by XRD. ^b The shape of the particles was observed by SEM. ^c The size of the particles was measured by SEM. ^d The yield was calculated by the final crystal weights compared with the theoretical weights of CaCO₃ from the injected calcium reagents. ^e The absorbed amount of polymer was measured by TGA (heating rate: 10 °C/min in an air atmosphere. ^f Control sample. ^g Glycopolymers added (0.501 g). ^h Poly(AA) homopolymer added (0.500 g). Reactions carried out at 24 °C, pH 7 for 24 h.

SEM analysis of the resulting products of crystallization confirmed that spherical particles were obtained in most cases. Reactions carried out in the presence of the glycopolymer (polymer sample 1) and in the absence thereof (polymer sample 10) resulted in the formation of rhombhedral particles. These results correlate well to data presented in Section 4.3.2. Upon comparing the SEM images of polymer samples 1, 5 and 10 (see Figure 5.2) it was concluded that only the poly(AA) moiety on the glyco diblock copolymer has an influence on the particle shape and size, and percentage yield.

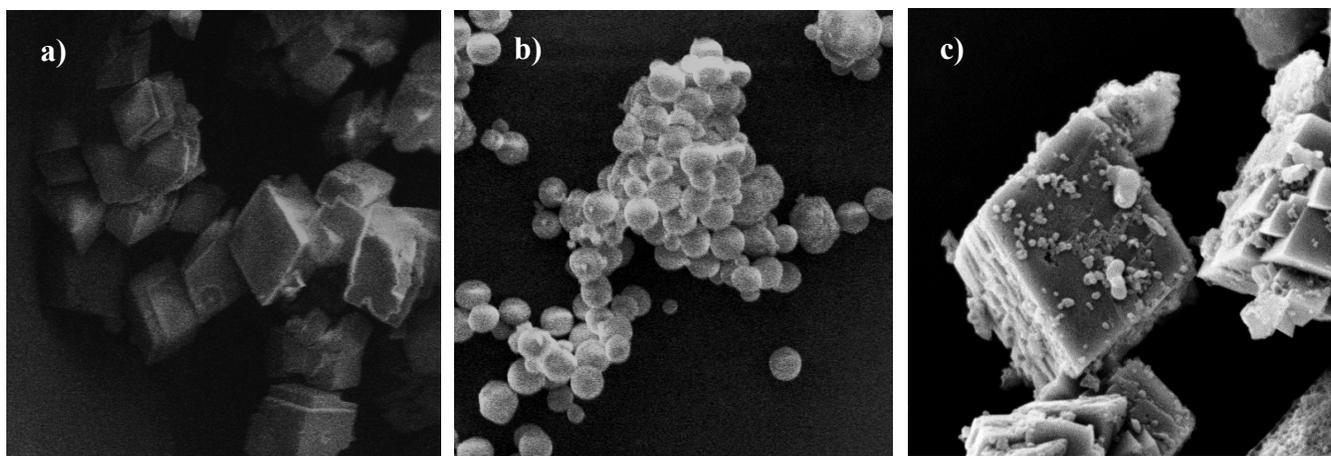


Figure 5.2 SEM images of (a) polymer sample 10 (control sample), (b) polymer sample 5 (where poly(AA) showed a dramatic effect on crystal growth and (c) polymer sample 1 (where the glycopolymer homopolymer showed no effect of crystal growth).

TGA results, tabulated in Table 5.4 and illustrated in Figure 5.3, indicate that as one increases the acrylic acid moiety of the diblock copolymer an increased attachment of the polymer onto crystallized CaCO_3 occurs. This ‘increased attachment phenomenon’ is expected primarily due to the statistical increase in nucleation sites for CaCO_3 crystallization in a reaction system. XRD analysis (Figure 5.3) confirmed the calcite polymorph of CaCO_3 , found in all cases. In the light of these results, polymer sample 9 was used for further studies in the sections that follow.

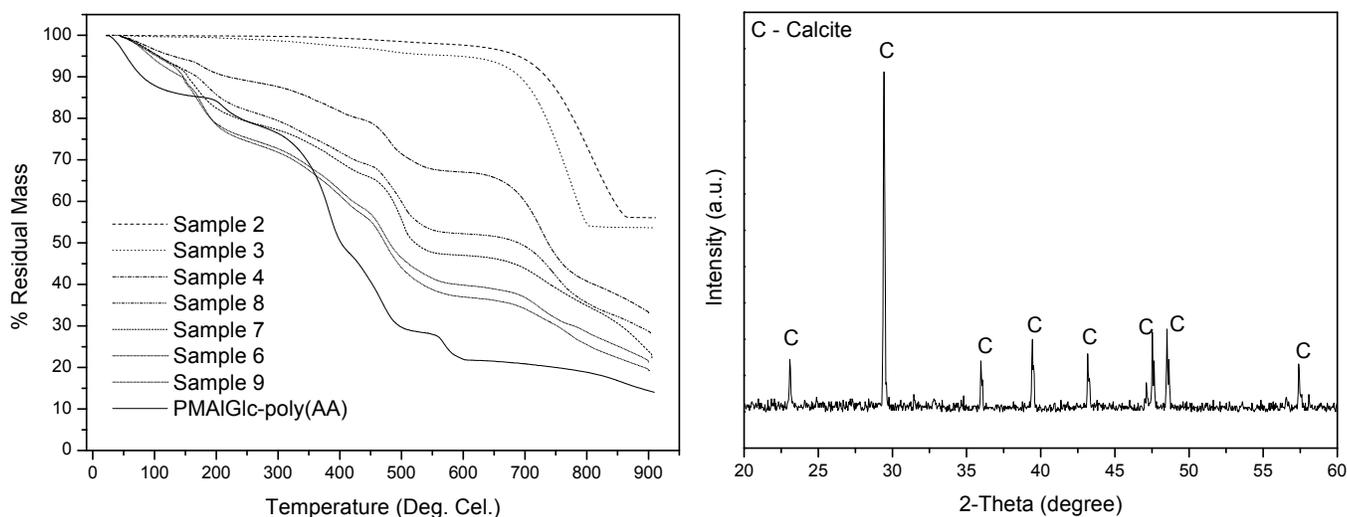


Figure 5.3 TGA of polymer samples 2 to 9, illustrating the percent of PMAIGlc-poly(AA) attached to crystallized CaCO_3 (left), and a typical XRD pattern showing that the calcite polymorph was synthesized in all cases (right).

5.3.4 Substrate - substrate interactions

5.3.4.1 Polymer - CaCO₃ (PCC) interactions

It is well known that poly(AA) acts as a dispersant of CaCO₃.¹⁰ It is for this reason that one would expect the PMAIGlc-b-poly(AA) polymers to adsorb onto the surface of PCC. By comparing the TEM images of the control sample (PCC in the absence of polymer) and the products of experiments carried out with PCC in the presence of either PMAIGlc-b-Poly(AA) or PMAIGlc (Figure 5.4), it is evident that the diblock glycopolymer strongly adsorbs onto the surface of the PCC particle (Figure 5.4c and d), whilst the glycohomopolymer (PMAIGlc) only partially attaches, and appears much less on the surface but rather more agglomerated with itself (Figure 5.4b).

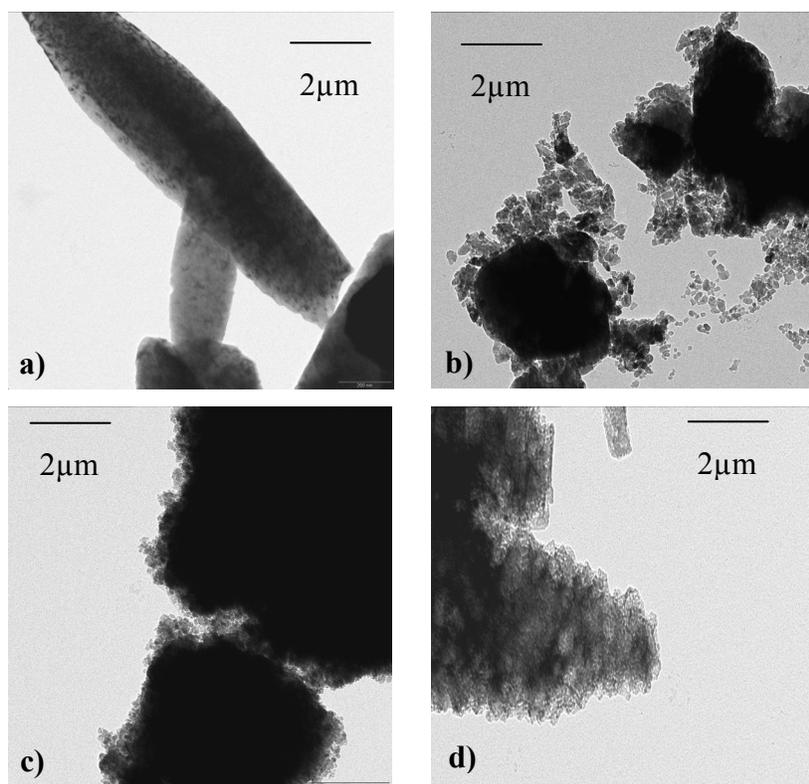


Figure 5.4 TEM images illustrating (a) PCC (control sample), (b) PCC in the presence of PMAIGlc homopolymer, (c) and (d) PCC in the presence of PMAIGlc-b-poly(AA).

Results tabulated in Table 5.5 and depicted in Figure 5.5 illustrate that as the polymer concentration is increased there is a subsequent increase in its adsorption onto PCC. The effect of reaction pH, temperature and time was also evaluated (Table 5.6) and it was found that maximum absorption of the polymer onto PCC is dependent on a high reaction pH and temperature, over a long period of time.

Table 5.5 Percentage of a single polymer of PMAIGlc-poly(AA)-3 absorbed onto the surface of PCC at various starting compositions.

Sample	Starting Compositions		% PMAIGlc absorbed on PCC surface
	PCC (%)	PMAIGlc (%)	
PCC-PMAIGlc-poly(AA)-a	80	20	12
PCC-PMAIGlc-poly(AA)-b	60	40	25
PCC-PMAIGlc-poly(AA)-c	40	60	44
PCC-PMAIGlc-poly(AA)-d	20	80	71
PCC-PMAIGlc-poly(AA)-e	50	50	51
PCC	100	-	-
PMAIGlc-poly(AA)-3	-	100	-

Table 5.6 The effect of reaction pH, temperature and time on the absorption of PMAIGlc-poly(AA)-3 onto the surface of PCC.

Reaction conditions	pH			Temp. (°C)			Time (h)		
	4	7	9	25	50	80	12	24	48
% PMAIGlc-poly(AA)-3 absorbed on PCC surface	41	51	68	51	60	76	47	51	79

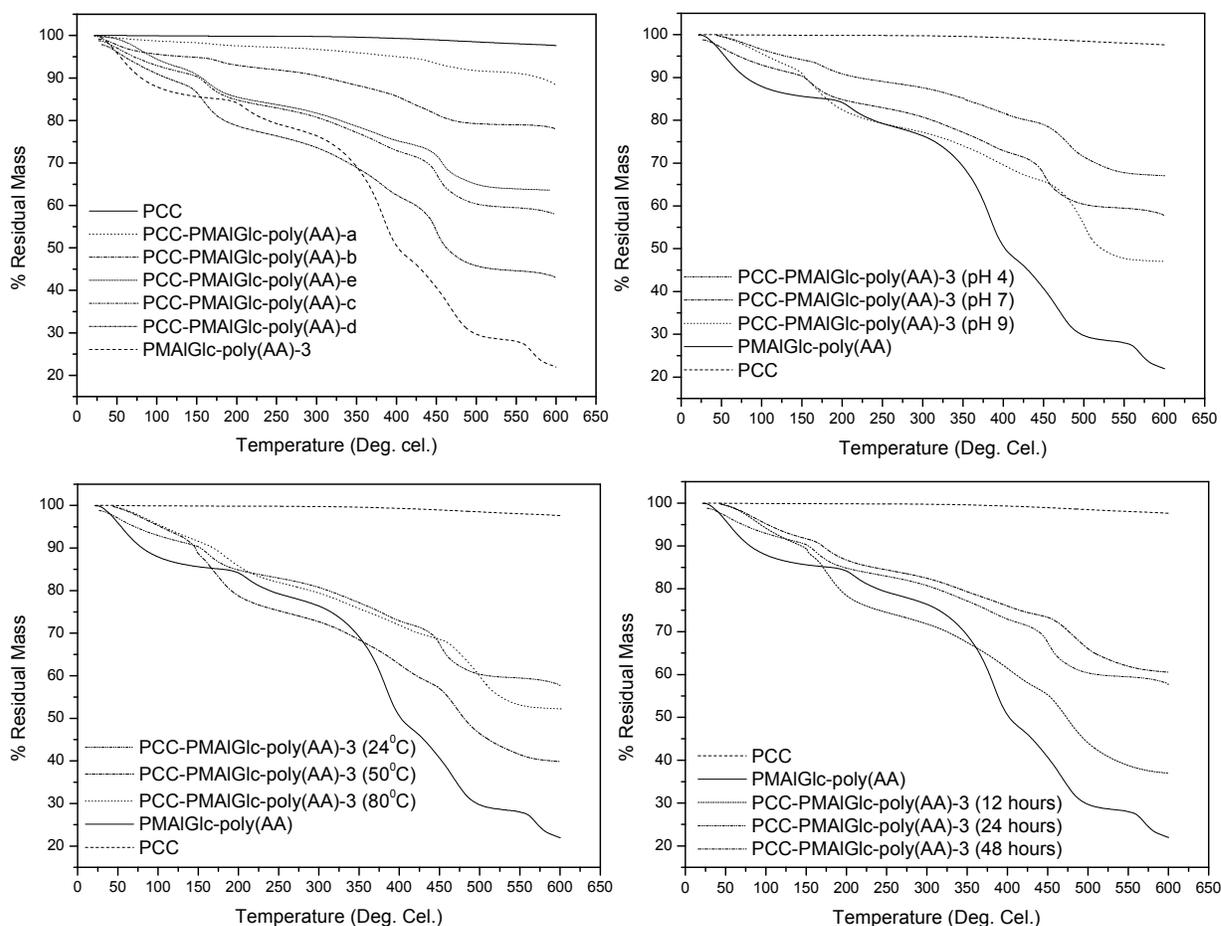


Figure 5.5 TGA used to evaluate the percentage of PMAIGlc-poly(AA)-3 absorbed on the surface of PCC at various addition ratios of PMAIGlc-poly(AA)-3 and PCC, as well as at different reaction pHs, temperatures and times.

5.3.4.2 Polymer - cellulose interactions

This investigation showed that an interaction occurs between the glycomoiety and cellulose, but this interaction can be over-ridden by the presence of acrylic acid. Figure 5.6 illustrates that if one increases the ratio of poly(AA) to the glycomoiety then a decrease in cellulose - polymer interaction is observed in an acidic medium. In a neutral and basic medium, there will be an increasingly significant interaction between the polymer and cellulose. Poly(AA) is known to not interact with cellulose. However, if one considers the glyco-poly(AA) core-shell particles that can be obtained, whereby poly(AA) forms the inner core encapsulated by the glycomoiety shell in an acidic medium, and vice versa in a basic medium, then these results are expected.

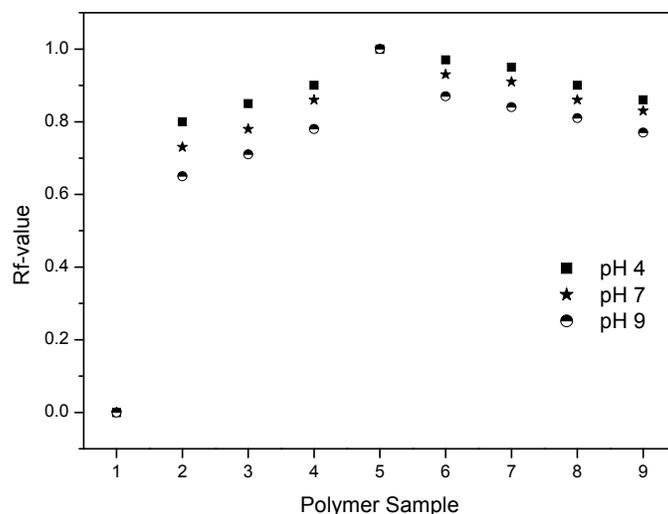


Figure 5.6 TLC analysis of polymer samples 1 to 9 at pHs 4, 7 and 9 (25 ± 1 °C). Sample 5: pure poly(AA)

Results tabulated in Table 5.7 indicate that as the polymer concentration is increased there is a subsequent increase in adsorption of these polymers onto cellulose. When considering the pH effect, TGA results are in accordance with results obtained from TLC analysis (Figure 5.6). Furthermore, the results indicate that irrespective of both adsorbing substrates (i.e. cellulose or PCC), maximum adsorption of the polymer occurs at conditions of high reaction pH and temperature, and long reaction times (Table 5.8).

Table 5.7 Percentage of a single polymer PMAIGlc-poly(AA)-3 absorbed on the surface of cellulose for various addition ratios.

Sample	Starting Compositions		PMAIGlc absorbed on cellulose surface (%)
	Cellulose (%)	PMAIGlc (%)	
Cellulose - PMAIGlc-poly(AA)-a	80	20	15
Cellulose - PMAIGlc-poly(AA)-b	60	40	31
Cellulose - PMAIGlc-poly(AA)-c	40	60	48
Cellulose - PMAIGlc-poly(AA)-d	20	80	70
Cellulose - PMAIGlc-poly(AA)-e	50	50	61
Cellulose	100	-	-
PMAIGlc-poly(AA)-3	-	100	-

Table 5.8 The effect of reaction pH, temperature and time on the absorption of PMAIGlc-poly(AA)-3 onto the surface of cellulose.

Reaction conditions	pH			Temp. (°C)			Time (h)		
	4	7	9	25	50	80	12	24	48
% PMAIGlc-poly(AA)-3 absorbed on cellulose surface	52	61	75	45	58	71	45	56	73

5.3.4.3 Cellulose - polymer - CaCO₃ interactions

Study utilizing crystallized CaCO₃

Results tabulated in Table 5.9 elucidate some key issues. Firstly, only the diblock copolymers can be used to increase adsorption of cellulose onto CaCO₃. This conclusion was drawn based on the fact that similar (but lower) percentage values were obtained for the control sample (sample 10) and for reactions carried out in the presence of the PMAIGlc and poly(AA) homopolymers (samples 1 and 5), compared to reactions carried out in the presence of diblock copolymers (sample 2 to 4, and 6 to 9).

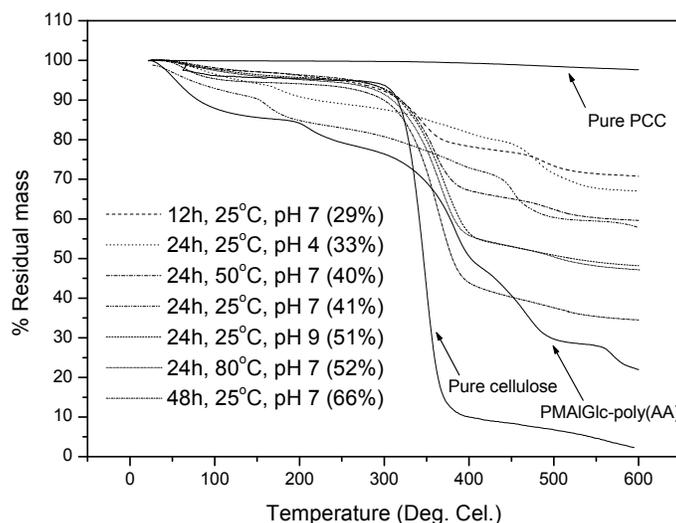
Secondly, the diblock configuration ratio plays a significant role in adsorption: when the poly(AA) ratio is higher than or equal to the PMAIGlc ratio in the diblock copolymer the higher adsorption results. This result is expected, as at higher poly(AA) to PMAIGlc ratios larger CaCO₃-PMAIGlc complexed particles with higher percentages of polymer adsorbed onto the CaCO₃ particles are observed (See Table 5.4). These larger particles with higher amounts of attached PMAIGlc will have a greater tendency to adhere to the surface of cellulose, resulting in higher values of adsorption than in the case of smaller particles with lower levels of PMAIGlc attached. The method used to wash and filter could also contribute to low levels of adsorption achieved with smaller 'low adhering ability' particles (i.e. low levels of PMAIGlc adsorbed).

Thirdly, the ideal experimental conditions used to achieve maximum adsorption of the two substrates are pH 9, 80 °C and 48 h. Interesting to note that these reaction conditions correlate well with the ideal reaction conditions used to obtain maximum adsorption of the polymer to PCC and the polymer to cellulose (See Section 5.3.4.1/2).

Table 5.9 Effects that various polymer configurations have on the percentage ‘sugar-coated’ CaCO₃ particles adsorbed onto cellulose, under various reaction conditions.

Polymer	Percent of polymer adsorbed on CaCO ₃ particles ^a (%)	Percentage of cellulose adsorbed onto polymer-coated CaCO ₃ particles (%)								
		24 h, 25 °C			pH 7, 25 °C			pH 7, 24 h		
		pH 4	pH 7	pH 9	12 h	24 h	48 h	25 °C	50 °C	80 °C
1 ^b	0	10	12	15	9	12	16	12	14	17
2	51	15	18	21	13	18	24	18	22	23
3	54	15	17	23	13	17	24	17	21	22
4	75	17	25	28	17	25	32	25	32	32
5 ^c	100	11	11	17	10	11	15	11	15	18
6	91	29	37	53	25	37	67	37	41	48
7	88	27	32	44	22	32	51	32	41	41
8	82	27	27	44	19	27	53	27	40	37
9 ^d	93	33	41	51	29	41	66	41	40	52
10 ^e	Control	10	11	16	10	11	16	11	16	18

^a Results tabulated in Table 5.4. ^b PMAIGlc homopolymer (0% attachment to CaCO₃). ^c Poly(AA) homopolymer. ^d The corresponding TGA series is shown in Figure 5.7. ^e Control sample (no polymer added). Shaded grey areas indicate identical experimental conditions. Calculations carried out as stipulated in the Appendix A.

**Figure 5.7** TGA series carried out for polymer sample 9 (in Table 5.9). The percentage cellulose attached to a polymer-coated CaCO₃ particle is shown in parenthesis.

Study utilizing precipitated CaCO₃ (PCC)

Results shown in Table 5.10 confirm once again that (a) CaCO₃ adsorption onto cellulose is increased in the presence of a PMAlGlc-b-poly(AA) copolymer and (b) the ratio of diblock copolymers PMAIGlc and poly(AA) moieties plays a major role in the extent of absorption.

Table 5.10 Effects that various polymer configurations have on the percentage of PCC absorbed onto cellulose under various mixing methods

Polymer	Percentage of cellulose absorbed onto PCC via:			
	Method A	Method B	Method C	Method D
1 ^a	17	19	17	16
2	41	38	42	37
3	56	49	55	51
4	63	59	61	57
5 ^b	18	17	17	17
6	41	41	39	43
7	56	51	53	55
8	62	51	53	49
9 ^c	76	69	68	67
Control ^d	17	18	17	16

^aPMAIGlc homopolymer. ^bPoly(AA) homopolymer. ^cThe corresponding TGA series is shown in Figure 5.7.

^dControl sample (no polymer added). Calculations carried out as stipulated in the Appendix.

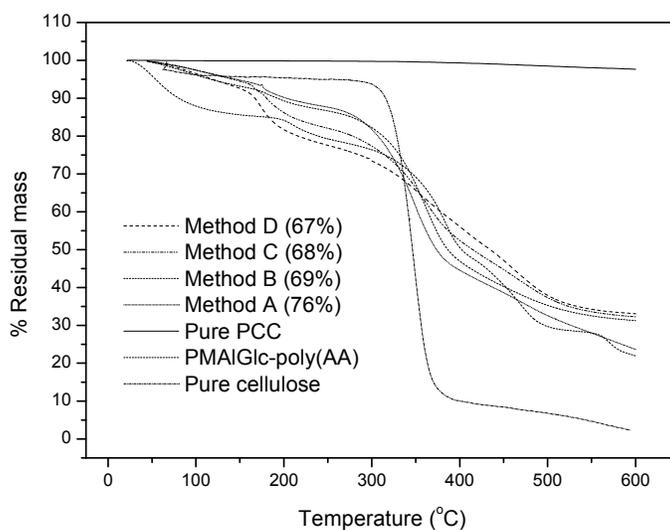


Figure 5.8 TGA series carried out for polymer sample 9 (refer to Table 5.10).

Here it is interesting to note the role that the method of addition of the three substrates (cellulose, CaCO₃ and polymer) played in adsorption. Figure 5.9 and Table 5.8 indicate that Method A was the best method. This is probably due to the fact that when the polymers are premixed within a highly complex cellulose fibrous network prior to PCC addition (Method B) they tend to coil-up into void fibril spaces, which become too small for 2 μm sized PCC particles to reach. This phenomenon would also support the low percentage values obtained for Methods D and C.

Upon considering the SEM images in Figure 5.9 and TGA data in Table 5.8, two crucial points are evident: (a) an increase in absorption of PCC onto cellulose is achieved when the diblock/difunctional glycopolymers are used and (b) the process selection is a determining factor in increasing the percentage absorption of PCC onto cellulose.

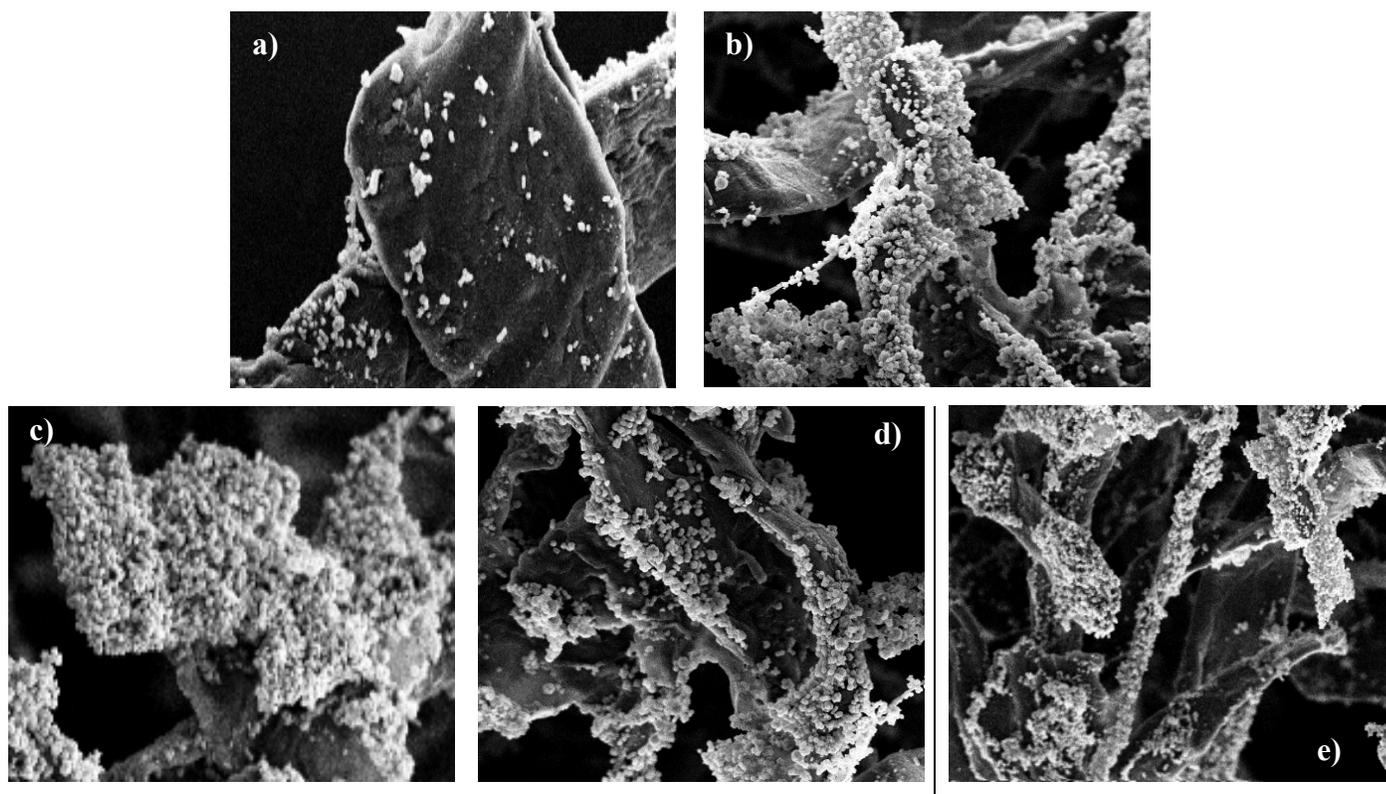


Figure 5.9 SEM images of the control sample (a) and polymer sample 9. SEM images (b) to (e) depict increased absorptions obtained for Methods A to D, respectively.

5.4 Conclusions

Nine different block copolymers having varying ratios of PMAIGlc and poly(AA) were synthesized and characterized. Results showed that when the poly(AA) moiety is used at a higher ratio than that of the PMAIGlc moiety, then:

- higher cmc values are observed
- larger-sized CaCO₃ particles are formed during CaCO₃ crystallization, with lower reaction percentage yields
- a higher percent of the copolymer is absorbed onto the crystallized CaCO₃ particle
- a decrease in cellulose - polymer interactions is observed in an acidic medium, whilst there is an increased interaction in a neutral or basic medium
- a higher adsorption to cellulose occurs irrespective of whether (i) the polymer was premixed with PCC, (ii) the polymer was premixed with cellulose before adding PCC, (iii) cellulose was premixed with PCC before adding the polymers, or (iv) all three substrates were mixed simultaneously.

It was found that the optimum reactions conditions needed to achieve maximum adsorption of all three substrates are the following: pH 9, 80 °C and 48 h, using Method A. In this method polymers are premixed with PCC before cellulose addition. Crystallized and/or precipitated CaCO₃ can be used.

5.5 References

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Chapter 6

Conclusions and Recommendations

6.1 Conclusions

The need for a new approach to achieving improved interaction between cellulose fibers and inorganic particles in order to get as much CaCO_3 attached to cellulose as possible, led to the conceptualization of this research project. For this purpose the use of a diblock copolymer containing both a carbohydrate-based moiety, which has the ability of adsorbing onto cellulose via hydrogen bonding, and a poly(acrylic acid) moiety, which can disperse inorganic particles, was proposed. The focus of this work was therefore to prepare well-defined diblock glycopolymers and to test their ability to increase the interaction between cellulose fibers and inorganic particles. Well-defined polymer architectures allow structure/property relationships to be investigated.

Well-defined glycopolymers were prepared via the RAFT polymerization process. This study is the first to describe the use of a novel RAFT agent, cumyl phenyl dithioacetate, in obtaining well-defined novel glycopolymers. These glycopolymers were used as macro-RAFT agents for the AB diblock synthesis of poly(styrene), poly(methyl acrylate) and poly(acrylic acid) based glycopolymers. Detailed polymerization kinetics confirmed the successful synthesis of well-defined controlled polymers.

The ability of the poly(acrylic acid) based AB diblock glycopolymers to increase interactions between cellulose fibers and inorganic particles was confirmed, in further analyses, dividing the study in two parts.

Part 1 involved crystallizing CaCO_3 in the presence of poly(acrylic acid) based glycopolymers prior to its addition to cellulose. This is the first report of such a reaction. The effects that various factors, including polymer concentrations and block to block configurations, reaction pH, temperature and time had on the final CaCO_3 crystal morphology, morphism, rate of growth and percentage yield, were determined. Optical microscopy confirmed the presence of a glyco-encapsulated CaCO_3 particle “sugar-coated particle”. TGA quantified and SEM illustrated that these surface modified inorganic particles have a heightened adherence to cellulose when compared to the unmodified inorganic particles.

Part 2 involved preparing various molecular weight configurations of the poly(acrylic acid) block to the glyco-block in the AB diblock copolymer and then determining the resulting polymers' ability to adhere to CaCO_3 or cellulose under various reaction conditions (temperature, time, pH and polymer concentration). This was qualitatively determined by TEM and TLC, and quantitatively by TGA. Furthermore, it was possible to quantify the percentage adherence of inorganic particles to cellulose fibers in the presence of the poly(acrylic acid) based glycopolymer. Significant success was achieved in terms of the structure/property relationship study.

Four different methods of addition of cellulose, CaCO_3 and glycopolymers were outlined (using constant reaction conditions: pH 9, 80 °C and 48 h). It was found that maximum adherence was obtained when cellulose was added to a premixed solution of diblock copolymer and CaCO_3 .

Overall, it can be concluded that the original hypothesis of the study could be confirmed: Tailored glycopolymers, more especially poly(acrylic acid) based glycopolymers show significant interaction between cellulose fibers and inorganic particles. The quantitative variation in adhesion as a function of structure was also achieved.

Besides being able to draw successful conclusions to the main objectives of this study, a final interesting conclusion is made. The self-assembling nature of these glyco-based polymers was

also determined. This study is the first to report tailored-made glycopolymeric core-shell particles that can either be solvent or pH invertible, depending on the final desired application.

6.2 Recommendations

- 6.2.1 Compare the technology outlined in this study to current commercially available retention aids.
- 6.2.2 Carry out industrial testing of these glycopolymers
- 6.2.3 Experiment with new/existing RAFT agents and monomer systems in specific applications within several other fields of science (i.e. in vivo drug release technology).

Appendix A

Calculations

A-1. Calculation of the percentage of PMAIGlc attached to crystallized CaCO₃, via TGA

The following mathematical equation was used to theoretically calculate the percentage of PMAIGlc in a CaCO₃-PMAIGlc composite:

$$\% \text{ PMAIGlc in a CaCO}_3\text{-PMAIGlc composite} = \left(\frac{y}{x + y} \right) \quad (\text{A.1})$$

where: % CaCO₃ = x and % PMAIGlc = y .

However, the % residual mass (RM) obtained experimentally, via TGA, can be related to x , y and z as follows:

$$\%RM_{Exp} = \left(\frac{RM}{IM} \right) = \left(\frac{x + 0.13y}{x + y} \right) \quad (\text{A.2})$$

where IM is the initial mass.

Therefore, by combining equations A.1 and A.2:

$$\% \text{ PMAIGlc in a sample} = 100 \times \left(\frac{1 - \%RM_{Exp}}{1 - 0.13} \right) \quad (\text{A.3})$$

A-2. Calculation of the percentage of cellulose attached to polymer coated CaCO₃ particles, via TGA

The following mathematical equation was used to theoretically calculate the percentage cellulose in a CaCO₃-PMAIGlc-cellulose composite:

$$\% \text{ Cellulose in a CaCO}_3\text{-PMAIGlc-cellulose composite} = \left(\frac{y}{x + y + z} \right) \quad (\text{A.4})$$

where: % cellulose = y , % CaCO₃ = x and % PMAIGlc = z .

However, the % residual mass (RM) obtained experimentally, via TGA, can be related to x , y and z as follows:

$$\%RM_{Exp} = \left(\frac{RM}{IM} \right) = \left(\frac{y + 0.96x + 0.21z}{x + y + z} \right) \quad (\text{A.5})$$

where IM is the initial mass.

Therefore, by combining equations A.4 and A.5:

$$\% \text{ cellulose in a sample} = 100 \times \left(\frac{1 - \%RM_{Exp}}{1 - 0} \right) \quad (\text{A.6})$$

Appendix B

Peer-reviewed publications

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

V. Ramiah, H. Matahwa,* W. Weber, J. B. McLeary, R. D. Sanderson

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) (PMAlpGlc), 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 (PMAlpGlc-b-styrene and PMAlpGlc-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 ¹H, ¹³C 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 Controller 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- α -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. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ (ppm): 1.25–1.50 (m, 12H, 4 CH_3); 1.95 (s, 3H, $\text{CH}_3\text{-C}=\text{CH}_2$); 5.70 (m, 1H, $\text{CH}_2=\text{C-}$, E form H); 6.00 (m, 1H, anomeric proton of sugar moiety); 6.15 (m, 1H, $\text{CH}_2=\text{C}$, 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

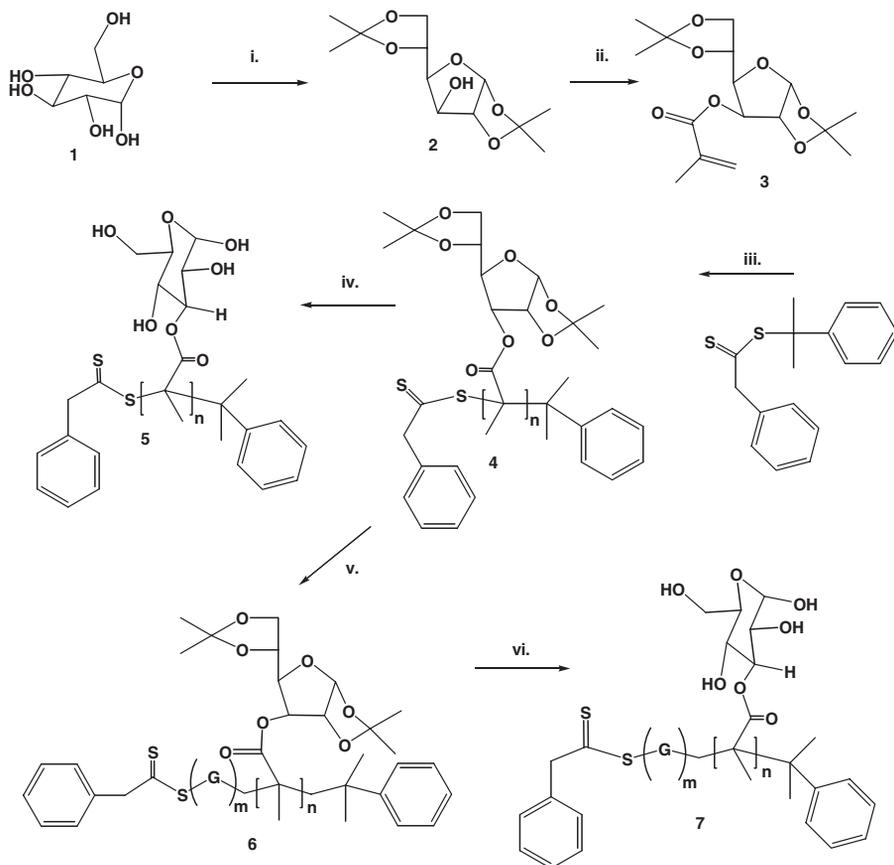
prepared from benzyl chloride (50.60 g, 0.40 mol), magnesium turnings (10.90 g, 0.45 mol) and catalytic amounts of iodine in 300 ml dry ether. After the dropwise addition of benzyl chloride the solution was refluxed for an hour and cooled to ambient temperature. CS_2 (30.40 g, 0.40 mol) was added within 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) $^1\text{H NMR}$, (600 MHz, CDCl_3) δ (ppm): 2.00 (s, 6H, 2 CH_3); 4.2 (s, 2H, CH_2); 7.2–7.6 (m, 10H, H_{ar}). $^{13}\text{C NMR}$, (300 MHz, CDCl_3) δ (ppm): 27.6 (2 CH_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/ $\text{ZnCl}_2/\text{H}_3\text{PO}_4/\text{NaOH}$; 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 con-

centration, 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)} MAIpGlc: 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. $^1\text{H-NMR}$ (600 MHz, acetone-*d*8) 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 $^1\text{H-NMR}$ 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 glycomonomer. 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. $\overline{M}_n(\text{SEC})$: 12000, $\overline{M}_n(\text{MALLS})$: 24500, $\overline{M}_n(^1\text{H-NMR})$: 24000 and PDI (MALLS): 1.16. $^1\text{H-NMR}$ (acetone-*d*8, 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, ^1H , anomeric proton of sugar moiety) and between 7.2–7.8 (aromatic protons of CPDA).

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

The reaction procedure was very similar to the synthesis of the homopolymer PMAIpGlc except that the (i) monomer (styrene and methyl acrylate) conversion was determined gravimetrically, (ii) PMAIpGlc 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 PMAIpGlc-b- (methyl acrylate): at 82% conversion, $\overline{M}_n(\text{SEC})$: 22000, $\overline{M}_n(\text{MALLS})$: 49000, $\overline{M}_n(^1\text{H-NMR})$: 52000, $\overline{M}_n(\text{Theo})$: 50000 and the PDI (MALLS): 1.56. $^1\text{H-NMR}$ (acetone-*d*8, 600 MHz) (Scheme 1, compound 5): δ (ppm) 0.9–1.8 (m, 12H, CH_3), 4.0–5.2 (4H,

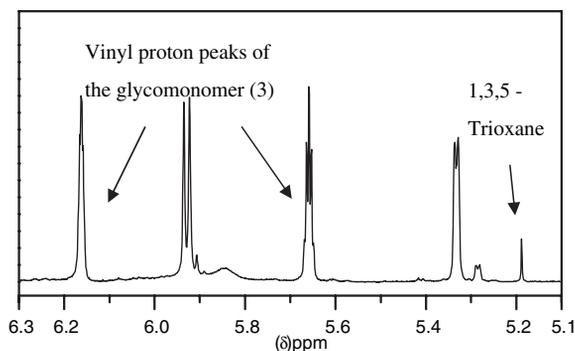


Figure 1.

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

sugar moiety), 5.7–6.0 (m, ^1H , 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 PMAIpGlc-b-(styrene): at 40% conversion, $\overline{M}_n(\text{SEC})$: 36000, $\overline{M}_n(\text{MALLS})$: 44000, $\overline{M}_n(\text{Theo})$: 45000 and PDI(MALLS): 1.60. $^1\text{H-NMR}$ 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 $^1\text{H NMR}$) 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-glucufuranose), (PMAIpGlc) (4)

The homopolymerization of MAIpGlc proceeded with 90% conversion being achieved within five and a half hours ($\overline{M}_n(\text{SEC})$: 12000, $\overline{M}_n(\text{MALLS})$: 24500, $\overline{M}_n(^1\text{H-NMR})$: 24000, $\overline{M}_n(\text{Theo})$: 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 $^1\text{H-NMR}$ and MALLS.

In the case of $^1\text{H-NMR}$, 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) $\overline{M}_n(\text{Exp})$ and $\overline{M}_n(\text{Theo})$ versus time, (ii) % conversion versus time, and (iii) the UV (310 nm) and RI normalized responses for the homopolymerization of MAIpGlc. 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

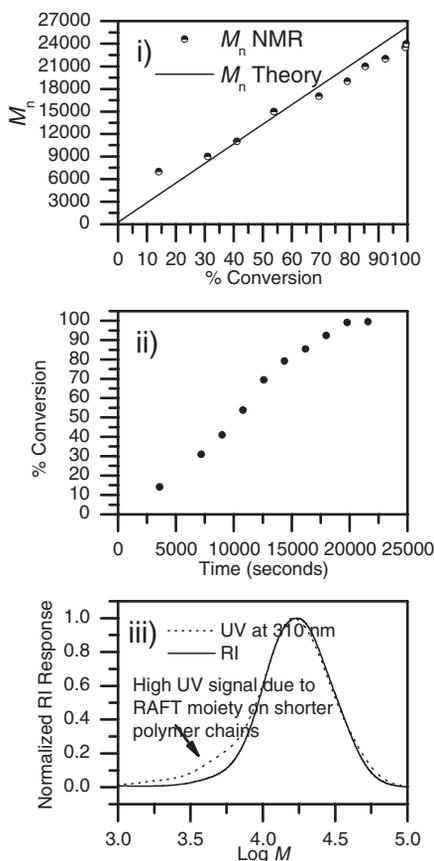


Figure 2.

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 MAIpGlc in ethyl acetate (25% w/v monomer) at 75 °C.

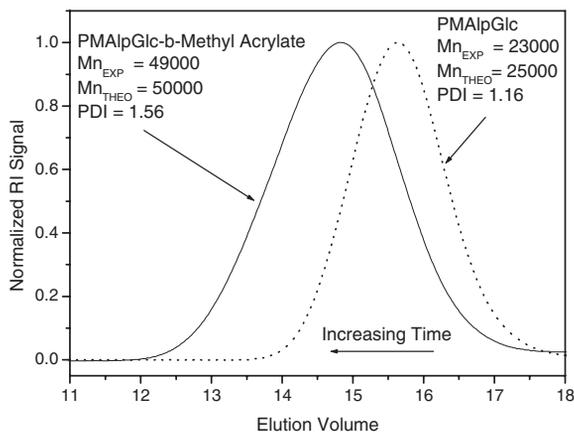


Figure 3.

SEC traces for the RAFT mediated copolymerization of PMAIpGlc 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 PMAIpGlc 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 PMAIpGlc 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 (PMAIpGlc) present in the system. Although the $\overline{M}_n(\text{Exp})$ corresponded well with the $\overline{M}_n(\text{Theo})$, the final polydispersities were relatively large 1.56 and 1.60 for PMAIpGlc-b-(methyl acrylate)

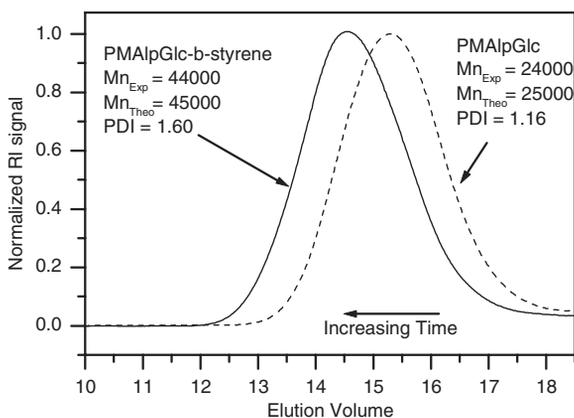


Figure 4.

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

and PMAIpGlc-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 PMAIpGlc-b-(methyl acrylate) and PMAIpGlc-b-(styrene), respectively. In $^1\text{H-NMR}$ 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 $\overline{M}_n(\text{Exp})$ value. However, this approach could not be used for PMAIpGlc-b-(styrene) as there was an overlap of the aromatic protons of CPDA and styrene.

Deprotection of MALpGlc Units into MAIGlc Units

All polymer samples were treated with hydrochloric acid. Figure 5 shows typical $^1\text{H NMR}$ 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 PMAIGlc-b-poly(styrene) and PMAIGlc-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

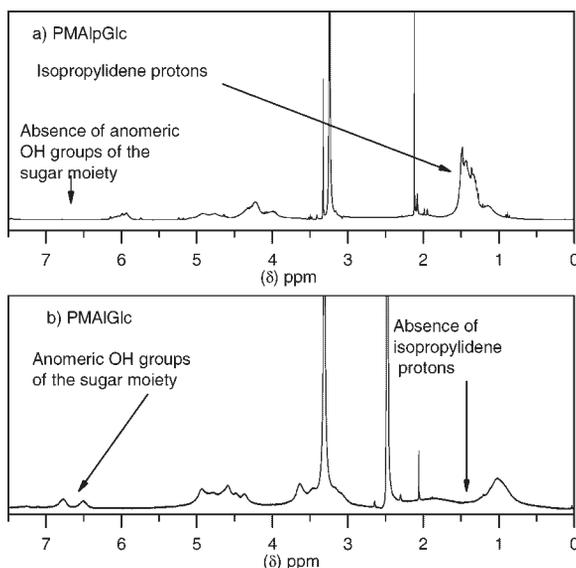


Figure 5.

Typical $^1\text{H NMR}$ spectra taken a) before and b) after the acidolysis of PMAIpGlc. The solvents were a) CDCl_3 and b) $\text{DMSO-}d_6$.

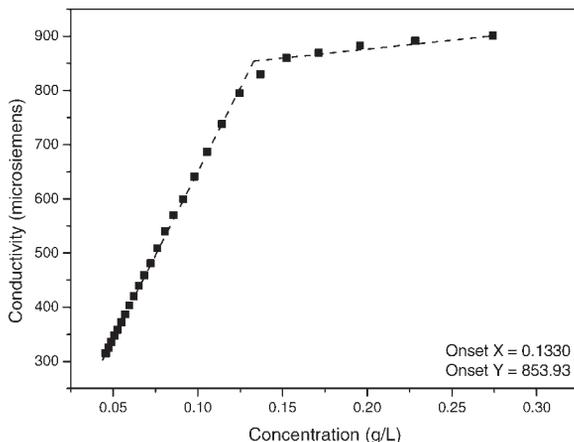


Figure 6.

Variation of conductivity with concentration of PMAIGlc-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-(1~4)-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

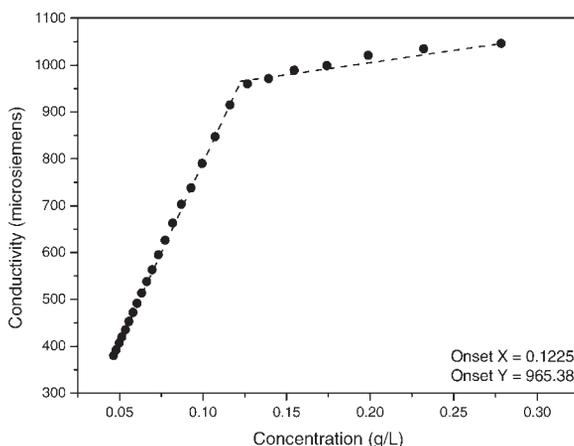


Figure 7.

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

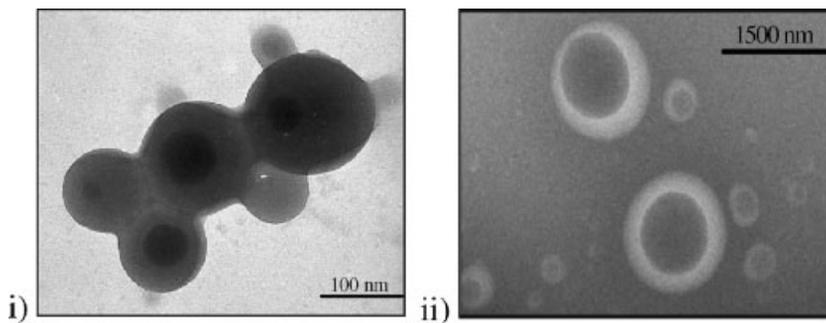


Figure 8.

TEM image illustrating the core-shell self-assembling behaviour of i) PMAIGlc-b-styrene in water (0.12 g/L) after 20 minutes, and ii) PMAIGlc-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,

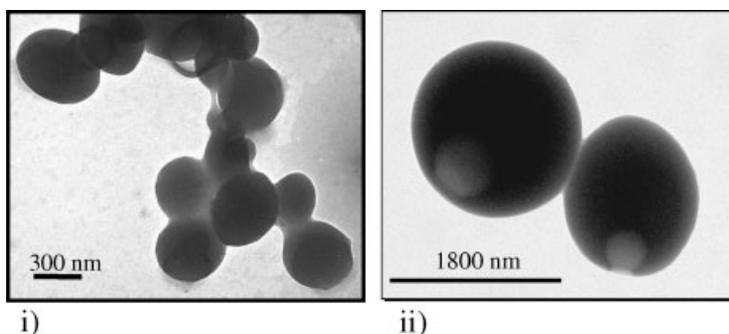


Figure 9.

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

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Microwave Assisted Graft Copolymerization of N-Isopropyl Acrylamide and Methyl Acrylate on Cellulose: Solid State NMR Analysis and CaCO₃ Crystallization

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Summary: Graft copolymerization of N-isopropyl acrylamide and methyl acrylate on α -cellulose was carried out under microwave irradiation at specific cut off temperatures with cerium (IV) ammonium nitrate and potassium persulfate (KPS) as the initiating system. The role of KPS was to oxidize Ce (III) to Ce (IV) which is the active species in radical formation. The reactions at a temperature cut off of 60 °C were confirmed by ¹³C nuclear magnetic resonance cross-polarization with magic-angle spinning (¹³C NMR CP/MAS) and Fourier-transform infrared spectroscopy (FTIR). The extent of grafting was calculated from weight gain and ¹³C resonances. The grafted cellulose was thermally more stable than the parent cellulose. An attempt to do grafting at a higher cut off temperature of 80 °C was made, however, no grafting was observed from ¹³C NMR CP/MAS but TGA results showed that a cellulose having more thermal stability resulted which was attributed to cross linking. Crystallization of CaCO₃ was carried out using the grafted materials as templates showed better nucleation and different crystal structure was observed.

Keywords: ¹³C NMR P/MAS; crystallization; FT-IR; graft copolymers; nucleation

Introduction

Cellulose is one of the most abundant naturally occurring polysaccharides consisting of glucose units joined together by β 1-4 linkages. The extensive hydrogen bonding that exists between the chains renders it highly crystalline and resistant to dissolution by normal organic solvents. Thus, most grafting reactions are done in a heterogeneous system where the cellulose fibers are swollen by solvent. A wide range of vinyl monomers can be grafted on cellulose to produce a wide range of biodegradable materials with different chemical and

physical properties. Cellulose and cellulosic materials have applications in the paper, food, paint & pharmaceutical industries.

Grafting of cellulose and other polysaccharides can be initiated by various transition metal ions such as Fe⁺³, Cu⁺², Ce⁺⁴ e.t.c. via free radical initiation.^[1] Grafting of cellulose and its derivatives initiated by ceric (IV) ion has been widely studied.^[2–11] The mechanism of initiation is through the formation of free radicals directly on the cellulose backbone by cleaving the C2-C3 bond^[12,13] and oxidation of cellulosic chain ends containing hemiacetal linkages.^[14] Furthermore it has been suggested that the Ce⁺⁴ ions can also abstract protons from the hydroxyl groups of these polysaccharides thereby facilitating grafting resulting in the formation of ether linkages.^[13,15] The Ce⁺⁴ can also form radicals on the monomer and this results in homopolymer formation. Recently it has been

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shown that the addition of certain alcohols to Ce^{+4} initiated grafting of cellulose resulted in a higher percentage grafting as well as improved grafting efficiency.^[3] A double initiating system termed Ce^{+4} -KPS has been successfully used in grafting copolymerization of diallyldimethyl ammonium chloride (DADMAC) and acrylamide on starch.^[16] The inclusion of KPS in Ce^{+4} initiated reactions was shown to improve the percentage grafting, by oxidation of Ce^{+3} to Ce^{4+} , which is the active specie in grafting reactions. Grafting of itaconic acid on cellulose was also done using KPS as initiator and the mechanism of radical formation on cellulose backbone was explained to be via proton abstraction by initiator radicals.^[17]

Microwave assisted grafting of chitosan^[18] and guar gum^[19] has been carried out with and without the redox system $AgNO_3$ /KPS/ascorbic acid. Microwave activation was also used in homogeneous esterification of cellulose.^[20,21] The use of microwave in grafting reactions provided shorter reaction times compared to conventional methods.

In this study, we tested a combination of double initiating system (Ce^{4+} -KPS) under microwave irradiation on graft copolymerization of NIPAM and MA. Thus a series of reactions were done varying the microwave power as well as the reaction temperature to determine their effect on grafting of α -cellulose. We also studied the crystallization of calcium carbonate using the grafted α -cellulose as template.

Experimental Part

Materials

Methyl acrylate (MA) (Aldrich) was purified by first extracting stabilizers with aqueous sodium hydroxide 0.3 M and dried over magnesium sulfate, vacuum distilled and stored below 5 °C. N-isopropyl acrylamide (NIPAM) (Sigma) was recrystallized from methanol and stored below 5 °C, Cerium (IV) ammonium nitrate (CAN) (Fluka) and Potassium persulfate (KPS)

(Aldrich) were used as received. α -Cellulose (α -CE) was washed with water then ethanol and vacuum dried to a constant weight at 60 °C. Nitric acid 55 % (R & S Enterprises) was used as received.

Grafting Procedure

In a typical reaction, α -cellulose (0.5 g, 3.08×10^{-3} moles of anhydroglucose unit) was dispersed in 100 ml of 2.5×10^{-3} M HNO_3 and CAN (0.025 g, 9.5×10^{-5} moles) was added then stirred for 30 minutes. The two monomers (total moles 5.0×10^{-3} and mole ratio MA: NIPAM=1) were then added whilst vigorously stirring. The microwave oven was set at appropriate microwave power (MWP), temperature and run time of 10 minutes. At the end of the reaction, the products were precipitated from a mixture of water and methanol. The homopolymers were extracted with water/THF mixture. The resulting graft copolymer was then dried to constant weight and the percentage grafting (% G) was calculated. The graft copolymers (α -CE-g-NIPAM-co-MA) are referred as G1, G2, and G3 in order of increasing % grafting.

Crystallization of $CaCO_3$

The grafted materials were then used as templates for $CaCO_3$ crystallization. In a typical reaction, 0.025 g of α -cellulose or grafted α -cellulose was dispersed in 15 ml of 0.025 M $CaCl_2$ solution for 2 hrs after which 15 ml of 0.025 M Na_2CO_3 solution was added slowly whilst stirring. The pH was adjusted to neutral. After 24 hrs, the reaction was stopped and the product filtered through a 0.22 micron membrane filter paper. The harvested $CaCO_3$ and α -cellulose fiber were then dried and analyzed by scanning electron microscopy (SEM) and FT-IR.

Analysis

Gravimetric Analysis

The weight of the grafted cellulose after homopolymer extraction was used to

calculate the % G using the following equation:

$$(\%G) = \frac{W_1 - W_0}{W_0} \times 100 \quad (1)$$

Where W_1 and W_0 denote the weight of the grafted α -cellulose and the weight of the original α -cellulose respectively.

CP/MAS ^{13}C NMR

The anomeric and carbonyl ^{13}C NMR peak intensities were used to estimate the % G. The ^{13}C intensities from CP/MAS are not quantitative because the peak intensities depends on the rate of cross polarization which is usually different for different carbon atoms.^[22] Thus direct integration of ^{13}C peaks of different carbon nuclei type may give misleading peak ratios. In order to quantify using ^{13}C peak intensities, the following equation was used.^[23]

$$\frac{S(\tau)}{S_0} = \frac{1}{\lambda} \left[1 - \exp\left(\frac{-\lambda\tau}{T_{IS}}\right) \right] \exp\left(\frac{-\tau}{T_{1\rho}(^1H)}\right), \quad (2)$$

$$\lambda = 1 + \frac{T_{IS}}{T_{1\rho}(^{13}C)} - \frac{T_{IS}}{T_{1\rho}(^1H)} \quad (3)$$

Where S_0 is the “true” area of resonance; $T_{1\rho}(^1H)$ and $T_{1\rho}(^{13}C)$ are the proton and carbon spin lattice relaxation times in the rotating frame and T_{IS} is the cross relaxation time between protons and carbon. By fitting the experimental data obtained from a plot of area of resonance of both the anomeric carbon and carbonyl carbon versus contact time (Figure 1) to Equation (2), S_0 and $T_{1\rho}(^1H)$ for the three graft copolymers were calculated.

From the ^{13}C CP/MAS spectra, there are two side bands [SB1 (A) and SB2 (C)] which are due to the anomeric carbon. The two side bands were also used in the calculation with an assumption that the carbonyl carbon relaxation data is the same for the side bands as in the main carbonyl peak.

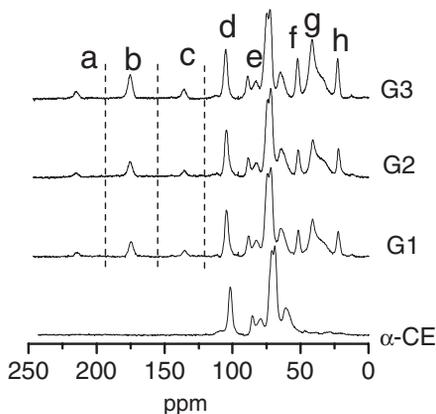


Figure 1.

^{13}C CP-MAS NMR spectra of α -CE and the graft copolymers G1, G2 and G3. a) and c) carbonyl side bands, b) carbonyl peak, d) Anomeric carbon, e) C2-C6 of cellulose, f) CH_3 carbon peak of MA, g) the carbon peaks of the grafted copolymer (NIPAM-co-MA), h) $2 \times \text{CH}_3$ carbons of NIPAM.

The % G was then calculated using the following equation

Corrected NMR % grafting

$$= \frac{S_0(T)}{S_0(T) + S_0(D)} \times 100 \quad (4)$$

and

$$S_0(T) = S_0(A) + S_0(B) + S_0(C) \quad (5)$$

Where $S_0(T)$ is the sum of the true area of resonance $S_0(A \rightarrow C)$ with B denoting the main peak of the carbonyl carbon whilst A and C denoting the side bands SB1 and SB2 respectively and $S_0(D)$ is the true area of resonance for the anomeric carbon.

However, besides using the corrected areas of resonance of the carbon peaks, direct integration of the ^{13}C peaks was made and the ratio of the carbonyl peaks (main peak and the side bands) to the anomeric carbon of α -cellulose was used to calculate % G and the results were compared to that of weight loss as well.

FT-IR Spectroscopy

A Perkin Elmer FT-IR transmission spectrophotometer ranging from 400–4500 cm^{-1} was used. KBr was used to prepare the sample disc for analysis.

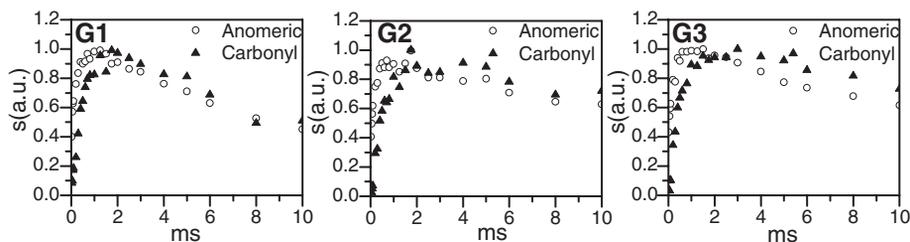


Figure 2.

Correlation between area of resonance C1 (Anomeric carbon) of α -cellulose and the area of resonance C⁺ (NIPAM/MA) of the two monomers used and the contact time for the three graft copolymers G1, G2 and G3.

Thermogravimetric Analysis (TGA)

The thermogravimetric curves for all the samples were obtained from a Shimadzu analyzer with a heating rate of 10 °C per minute.

Results and Discussion

The use of microwave irradiation on Ce⁺⁴-KPS initiated grafting of cellulose was carried out successfully with the reaction times reduced to 10 minutes. The peaks due to different carbon nuclei are shown in Figure 1. The carbonyl peaks (a, b and c) and the anomeric peak (d) were used to calculate % G whilst the MA peak (f) and the NIPAM peak (h) were used to estimate the % incorporation of each monomer in the graft copolymer.

In order to correlate the intensities of the anomeric carbon and carbonyl carbon peaks, the proton and carbon spin-lattice relaxation times were determined. A series of spectra were carried out with the contact time ranging from 0 to 12 ms and are shown in (Figure 2). The proton relaxation times measured on the anomeric carbon and carbonyl carbon were rather similar

(Figure 2) meaning that the system can be treated as homogeneous.^[8]

The % G calculated by i) direct integration of ¹³C NMR peaks and ii) correction of the area of resonance of the ¹³C CP/MAS peaks gave results that were similar to those calculated from gravimetric method. This showed that solid state NMR can be used to estimate % G of α -cellulose. The % incorporation of each monomer was also estimated from CP/MAS spectra and that MA incorporation was much higher than that of NIPAM (Table 1). This is expected as MA has higher reactivity than NIPAM. The microwave power had no effect on percentage incorporation of the monomers and small effect on % G. The FT-IR spectra (Figure 3) show the MA and NIPAM carbonyl absorption peaks of the grafted copolymers polymers at 1736 and 1650.cm⁻¹ respectively.

The TGA curves, Figure 4, show an increase in thermal stability with an increase in percentage grafting.

Analogous reactions at temperature cut-off at 80 °C of grafting α -cellulose with NIPAM and MA showed that there was no grafting from solid state NMR (Figure 5).

Table 1.

A comparison of the %G as calculated from three different methods as well as the % incorporation of each monomer.

Sample	MWP (W)	Carbonyl	SB1	SB2	Anomeric	%G	%G	%G	%MA	%NIPAM
						CP/MAS	Calc.	(WG)	(mol)	(mol)
G3	800	28.33	9.68	11.13	50.86	49.14	48.88	55.01	66	34
G2	600	20.65	7.82	8.81	62.71	37.29	38.42	42.12	64	36
G1	400	20.65	7.25	8.2	63.9	36.86	36.56	38.31	67	33

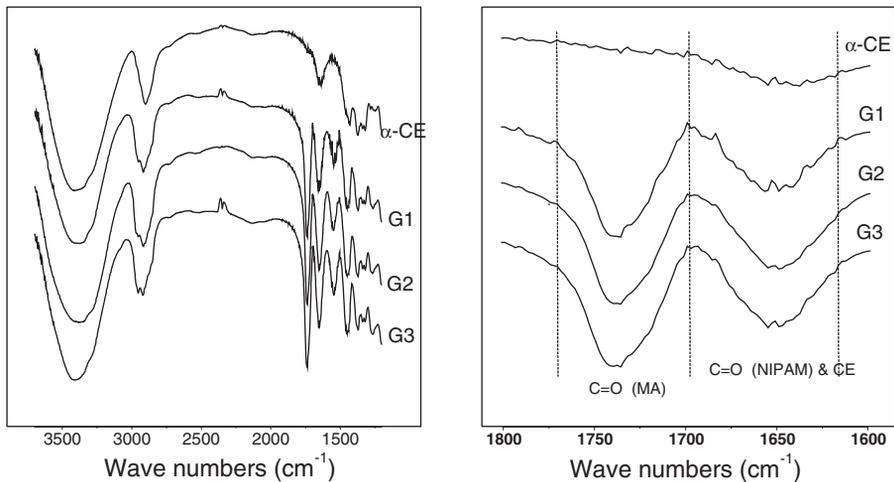


Figure 3.

A comparison of the FT-IR spectra of α -CE and the graft copolymers G1, G2 and G3 showing the carbonyl peaks due to the grafted polymers.

The NMR results showed that there was no polymer grafted on α -cellulose as the ^{13}C peaks of the polymer were absent. The carbonyl peak of the polymers was not observed in FT-IR spectra as well. However, the results from TGA showed an increase in thermal stability of the grafted materials which is typical for grafted materials as illustrated in (Figure 5). The reason for having an increase in the thermal stability of cellulose materials is suggested

to be due to the cross linking of cellulose. In previous studies of conventional cerium initiation, a decrease in %G and an increase in homopolymer formation as temperature was increased to 60°C was observed.^[2,6] We concluded that the Ce^{+4} -KPS initiation system is not suitable for microwave reactions above 60°C temperature cut off as only homopolymer is formed and cross linking is highly enhanced. The presence of a water soluble initiator KPS can also

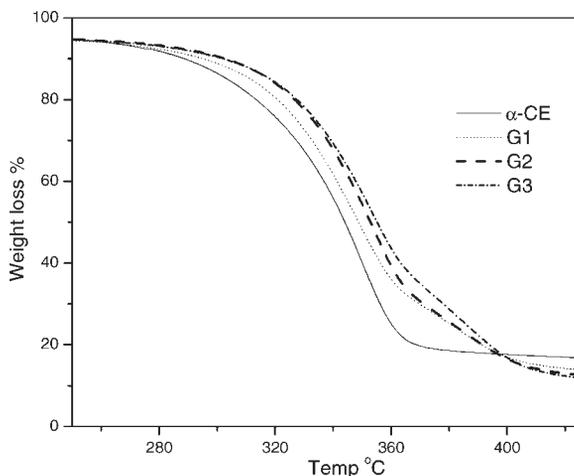


Figure 4.

TGA curves of α -CE and the graft copolymers G1, G2 and G3 showing an increase in thermal stability with % grafting.

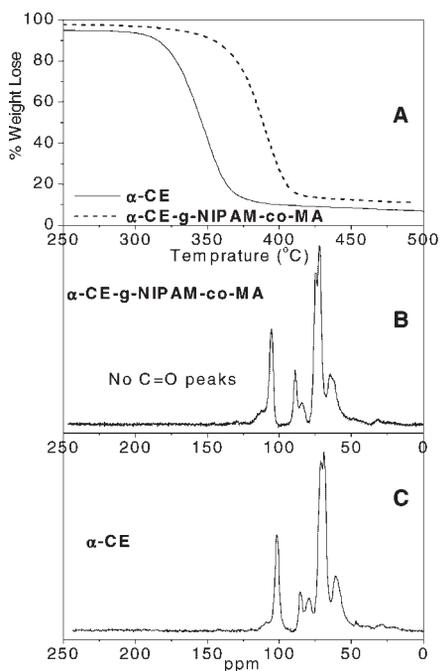


Figure 5.

A) TGA curves of α -CE and α -CE grafted with NIPAM showing the thermally more stable ungrafted material. C and B) ^{13}C NMR of α -CE and α -CE grafted with NIPAM and MA (α -CE-g-NIPAM-co-MA) respectively.

contribute to homopolymer formation rather than grafting at these high temperatures.

The crystallization of calcium carbonate results showed that the grafted cellulose can nucleate CaCO_3 crystal formation much better than ungrafted cellulose. Crystals formed in the presence of cellulose were rhombohedral single crystals whereas platelet like crystals that stacked together and cubical single crystals were formed in the presence of grafted materials.

Grafting can also aid the adsorption of these crystals on the surface of the fiber as many particles were adsorbed on the surface of the grafted fibers. However, there was no effect of % G on size and morphology of crystals of CaCO_3 . Calcium carbonate exists in three polymorphs: vaterite, aragonite and calcite in order of their thermodynamic stability and phase transformation possible.

From infrared spectroscopy, Figure 7, the peaks at 876 cm^{-1} and 711 cm^{-1} are due the calcite.^[24] The absence of aragonite and vaterite polymorphs' characteristic peaks at 1057 cm^{-1} ^[25] and 745 cm^{-1} ^[24] respectively means that the synthesized

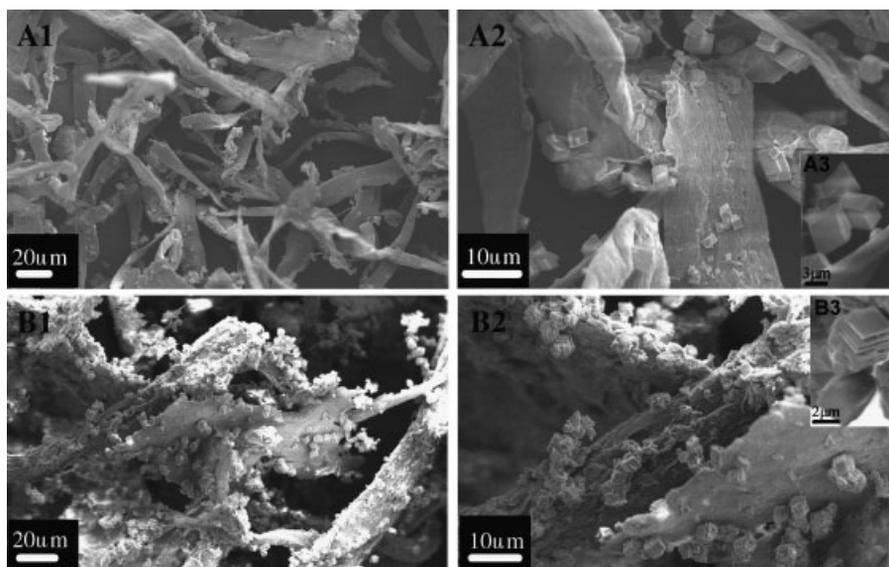


Figure 6.

SEM images of CaCO_3 crystals synthesized in the presence of A) alpha cellulose and B) CE grafted copolymerized with NIPAM with MA (G2). A2, A3, B2 and B3 are enlargements.

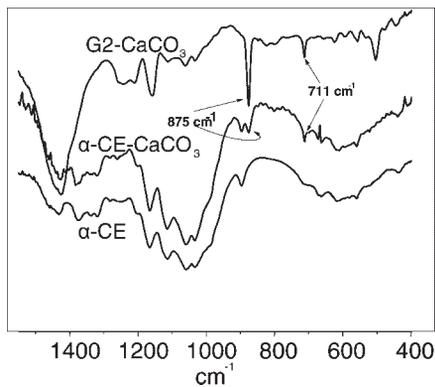


Figure 7.

A comparison of the FT-IR spectra of α -CE, α -CE- CaCO_3 and the graft copolymer G2- CaCO_3 showing the peaks due to the calcite and vaterite.

CaCO_3 consisted of mainly the calcite polymorph.

Conclusion

Grafting of cellulose was confirmed by solid state NMR, FT-IR as well as thermogravimetric analysis. The % G calculated from ^{13}C NMR correlated well with % grafting calculated from weight gain. It was found that microwave irradiation of cerium initiated grafting of cellulose is limited to temperatures lower than 60°C with higher temperatures resulting in cross linking of the celluloses as concluded from TGA curves and ^{13}C NMR spectra. The reaction times in microwave assisted grafting were reduced significantly and the effect of microwave irradiation power on % grafting was less significant. The grafted cellulose materials had better nucleating properties than cellulose as more crystals were formed on the surface of the fiber. The crystal morphology was different although the crystal sizes were relatively similar.

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