Macromol. Symp. ***174,*** *155–163 (2001)*

Recent Developments in Cellulose Grafting Chemistry Utilizing Barton Ester Intermediates and Nitroxide Mediation

William H. Daly, Timothy S. Evenson†, Scott T. Iacono, R. Walker Jones*

Macromolecular Studies Group, Department of Chemistry, Louisiana State University, Baton Rouge, Louisiana, 70803-1804, USA

SUMMARY: Esters or carbonates of N-hydroxypyridine-2-thione (Barton esters) were appended to either carboxymethyl or hydroxypropyl cellulose. Irradiation of the cellulose bound Barton esters in monomer initiated free radical graft copolymerization with minimal concomitant homopolymerization. Grafting of styrene to carboxymethyl cellulose was accompanied by backbone cleavage. The hydroxypropyl spacer group minimized backbone degradation; styrene, acylamide and N-isopropyl acrylamide could be grafted to hydroxypropyl cellulose in tetrahydrofuran solution. Treatment of Barton carbonate modified hydroxypropyl cellulose with styrene in the presence of TEMPO afforded corresponding TEMPO adducts, which can be used to promote the controlled radical graft polymerization of styrene. Grafts were analyzed independently after hydrolysis of the cellulose backbone.

Introduction

Since cellulose is a ubiquitous and renewable resource, efforts to improve its properties and utility by grafting to the anhydroglucose backbone continues to receive extensive attention. Chemical initiation by activated anhydroglucose units in the polymer backbone has been the dominate technique examined in cellulose grafting research[1] and it remains the main focus as illustrated by the following selection of recent papers.

Cellulose activation by ceric salt oxidation in the presence of ultrasound is an interesting innovation to this classic technique[2]. Grafting of methyl methacrylate to regenerated cellulose film was achieved with higher weight gain, higher efficiency, and smoother surface coverage when the films were agitated by ultrasound. Analogous improvements were observed in grafting acrylonitrile to cellulose fibers. The ultrasound enhanced the diffusion of Ce^{+4} into the cellulose substrate, which promoted the formation of anhydroglucose initiating radicals, as well as enhancing the dispersion and absorption of the organic monomers onto the hydrophilic cellulose surface.

†Deceased, March 28, 1999.

CCC 1022-1360/00/$ 17.50+.50/0

A percarboxymethyl cellulose initiator was prepared by treating carboxymethyl cellulose with hydrogen peroxide in sulfuric acid, and evaluated as a polymeric initiator for acrylic acid, acrylamide and N-isopropylacrylamide graft copolymerization[3)]. Photochemical decomposition of the peracid groups proved to be most effective; a high percentage of grafting could be achieved, but the efficiency of grafting was only 35%. Poly(acrylic acid) grafts enhanced the water absorbency of the cellulose as expected. By copolymerization of acrylic acid with N-isopropylacrylamide in the graft segments, water absorbency decreased when the temperature exceeded the LCST of poly (N-isopropylacrylamide).

If the conditions are chosen to minimize degradation, ozone can be used to activate the surface of cellulose fibers by introducing hydroperoxide substituents. Immersion of the treated fibers in 2-hydroxyethyl methacrylate/diethyleneglycol dimethacrylate mixtures yielded completely coated fibers containing up to 300% HEMA with interesting morphologies[4)]. The influence of the crosslinking agent on the extent of substitution and the effectiveness of coating is significant. If the no diethyleneglycol dimethacrylate is present, the grafts do not completely fill the pores and the coating failed to cover the surface of the substrate.

Grafting of polymers with controlled molecular weight to cellulose has been reported, but the experimental conditions required are rather demanding, i.e. inert atmosphere and anhydrous conditions. Elaboration of mesylated cellulose acetate with living anionically initiated polystyrene terminated by a carboxylate group produced thermoplastic graft copolymers[5)]. If cellulose with anhydroglucose units containing amino substiuents was employed as the substrate, coupling of a polymeric graft prepared using living cationic techniques was possible, but the number of polymer chains grafted decreased proportionally as the molecular weight of the graft increased[6)]. In this paper we report the application of Barton ester (BE) intermediates to promote free radical grafting to cellulose derivatives and show that controlled free radical grafting moderated by TEMPO can be achieved under typical conditions for free radical polymerization.

Thiohydroxamic esters, including esters of N-hydroxypyridine-2-thione, were first used as free-radical precursors by Derek Barton[7)], and have come to be known as Barton esters. N-hydroxypyridine-2-thione esters were synthesized by reacting the sodium salt of N-hydroxypyridine-2-thione and an acid chloride [7b)]. The decomposition of Barton esters by heat or visible light initially yielded acyloxy radicals and pyridine thiol radicals. Laser flash photolysis studies have shown that the pyridine thiol radical was consumed by attacking the pyridine thione ring of the starting Barton ester producing 2,2’-dipyridyl disulfide and a second acyloxy radical[8)]. Barton esters are effective chain transfer agents in free-radical polymerizations. The chain transfer constants (C_x) for the various Barton esters ($R=C_{15}H_{31}$, Bz, or Ph) were reported[9)]. The chain transfer mechanism involves induced decomposition of the BE by propagating radical attack on the thiocarbonyl of the BE.

The asymmetric decomposition of BE's promoted by either heat or light to acyloxy radicals and pyridine disulfide allows selective initiation by the acyloxy radical fragments[10)]. If these acyloxy fragments are attached to the grafting substrate, initiation and propagation of grafted chains is favored and concomitant homopolymerization is minimized. Barton esters can be used to modify polymer film surfaces by grafting[11)] Efficient grafting of vinyl monomers from BE-modified poly(arylene ether sulfone) is readily achieved[12)]. In this paper we report the application of BE intermediates to promote free radical grafting to cellulose derivatives. Additionally, utilization of bound Barton esters as free radical sources allows for the formation of bound TEMPO unimers

Experimental

Grafting from Carboxymethyl Cellulose Carboxymethyl cellulose, CMC, samples (M_w ca. 250,000, Aldrich) with D.S. = 0.7, 0.9, or 1.2 (1.07-1.56 g, 5 mmol carboxylic acid) were slurried in pyridine in 1% w/v concentration. The mixtures were cooled to -15°C. Isobutyl chloroformate, 0.69 g (5 mmol), was added and stirred for 20 minutes under nitrogen atmosphere. Sodium 2-mercaptopyridine-N-oxide, 0.75 g (5 mmol), was then added and the mixture was stirred in the dark for 1 hour under nitrogen at -15°C. The solvent was evaporated from the BE modified CMC using a nitrogen stream at room temperature. Quantitative conversion of Barton ester was confirmed by UV spectroscopy ($CHCl_3$, 0.2 mg/mL, 367 nm, $\varepsilon=4200$). The BE-CMC was slurried in 55 mL styrene and the sample was irradiated with visible light from a 150 W tungsten lamp placed 30 cm from the reaction flask at 25°C for 24 hours. The resulting copolymer was diluted with 10 mL THF, precipitated in 700 mL methanol, filtered, and dried. The graft copolymers were extracted with cyclohexane at 34°C, weighed, then analyzed by NMR, IR, and SEC. NMR ($CDCl_3$) δ(ppm): 1.30-1.60 (2H, PS CH_2), 1.70-2.0 (PS CH), 3.65-3.80 (2H, O-CH_2-COO), 5.26, 5.78 (2H, C(6)H_2). IR (NaCl): 3025, 2922 cm^{-1} (C-H), 1600, 1491, 1450 cm^{-1} (PS), 1119 cm^{-1} (Py-S-). SEC, M_w=200,000, 180,000, and 170,000 for DS=0.7, 0.9, and 1.2 respectively. The data from these experiments are reported in Table 1.

Grafting from Hydroxypropyl Cellulose To a solution of hydroxypropyl cellulose, HPC (0.6 g M_w, 60,000), in 60 mL THF shielded from light under a nitrogen atmosphere, 0.20 mL pyridine and 0.323 g (1.70 mmol) 1-oxa-2-oxo-3-thiaindolizinium chloride, **1**, were added. The mixture was stirred at 60°C for 16 hours. After cooling to room temperature, formation of a Barton carbonate was confirmed by UV spectroscopy (1% reaction mixture in THF, 327 nm, ε=4200); yield=92%. THF was removed from HPC-Barton carbonate, **2**, by rotary evaporation. NMR ($CDCl_3$) δ (ppm): 1.10 (3H, CH_3), 3.41 (2H, CH_2), 3.88 (1H, CH), d 7.76, t 7.95, t 8.43, d 8.88 (4H, CH=CH-CH=CH). Polymer **2** was dissolved in 42 g of a solution of 75 mole% styrene in DMF. The solution was purged with nitrogen and then exposed to visible light at 25°C for 24 hours. The resultant copolymer was precipitated with methanol, filtered and dried. The copolymer recovered, 2.76 g (360 % mass increase, 6 % styrene conversion), calculated graft length, 13, was analyzed by NMR, IR, and SEC. NMR ($CDCl_3$) δ(ppm): 0.90 (3H,CH_3), 1.25-1.65 (2H, PS CH_2), 1.70-2.05 (1H, PS CH), 3.55-3.70 (2H, CH_2), 4.11 (1H, CH), 5.27, 5.76 (2H, C(6)H_2), 6.60-7.20 (5H, PS Ar). IR (NaCl): 3025, 2922 cm^{-1} (C-H), 1743 cm^{-1} (C=O), 1600, 1491, 1450 cm^{-1} (PS), 1110 cm^{-1} (Py-S-), SEC (THF), M_w=143,000.

Acrylamide Grafts Acrylamide, (13.60 g, 0.1914 mol) was added to a THF solution of BE modified HPC carbonate, **2**, DS = 0.73, which was then purged with nitrogen. The solution was exposed to visible light for 18 hr. The copolymer precipitated throughout the polymerization. Finally, the copolymer was filtered and washed with 60 mL THF, then vacuum dried at room temperature for 48 hours; yield = 4.77 g, NMR (D_2O) δ (ppm): 1.15 (3H, CH_3), 1.55-1.85 (2H, CH_2), 1.91-2.22 (1H, CH), 3.08 (2H, CH_2), 3.74 (1H, CH), 5.90, 6.23 (2H, C(6)H_2).

Controlled Radical Grafting from Hydroxypropyl Cellulose 2.2,6,6-Tetramethylpyridinyloxyl, TEMPO, (0.5340 g, 3.41 mmol), was added to a solution of 0.6 g BE (D.S. = 0.84) modified HPC dissolved in 11.6 g of the styrene and 3.85 g DMF. The solution was purged with argon before exposure to visible light from a tungsten lamp at 25°C for 40 h. The volume of solution was reduced by rotary evaporation, and then the polymer was precipitated with a 90 % v/v hexane/acetone solution, filtered, and dried. NMR ($CDCl_3$), δ (ppm): 1.11 (3H, CH_3), 0.88, 1.26, 1.38, 1.54-1.58, 1.71 (18H, TEMPO), 2.88, 2.96, 4.31 (3H, styryl CH_2-CH), 3.35-4.00 (3H, HPC CH_2-CH), 7.07-8.02 (5H, Ar), yield=0.73 g. Based upon the NMR, a TEMPO adduct with a DS= 0.41 (49% yield) was isolated.

The TEMPO-modified polymer, **4**, was dissolved in 59.20 g styrene, 10.66 g DMF; 0.0178 g (0.11 mmol) TEMPO was added, and the solution purged with argon. A 20.42 g sample of the solution was heated to 130°C for 48 hours. Aliquots (1 mL) were taken every 12 hours for analysis. Samples of graft copolymer, **5,** were precipitated in methanol, filtered and dried. The copolymers (0.1 g) were dissolved in 12 mL THF and 3.0 mL 6 M HCl and refluxed for 48 hours. The liberated polystyrene grafts were precipitated in mixtures of 60 mL methanol and 6.0 mL of 3 M NaOH., filtered and washed with 20 mL distilled water and 20 mL methanol, then vacuum dried. The polystyrenes in THF were analyzed by SEC, and the results compiled in Table 2.

Results and Discussion

The carboxymethyl substituents of CMC can be converted to Barton esters using a mixed anhydride intermediate[13)]. First the carboxylate groups were reacted with isobutyl chloroformate to form a mixed anhydride, then sodium 2-mercaptopyridine-N-oxide was added to form the Barton ester modified CMC. The modified cellulose samples (BE-CMC) were isolated and characterized; conversion of the carboxymethyl group to Barton ester groups was effectively quantitative. The BE-CMC was slurried in styrene and subjected to visible light to form graft copolymers (Table 1). Copolymer samples were subjected to extraction by cyclohexane to determine the homopolystyrene content; less than 7 wt % polystyrene was detected. The graft copolymers were predominately soluble in chloroform, THF and toluene, but an insoluble component (5-10 wt%) was observed in these solvents. The polystyrene graft lengths were calculated with NMR by comparing the aromatic polystyrene peaks (8H, 1.2-2.2, 6.3-7.2) with carboxymethyl and cellulose C6 protons (4H, 3.5-3.9, 5.1-5.4, 5.6-5.9). and correcting for degree of substitution. The graft lengths calculated from NMR and mass increase were in agreement.

Molecular weights (M_w) of the copolymers were measured in THF by SEC applying the dn/dc for polystyrene. The reduction in Mw as the DS increases suggests that backbone chain breaking reactions are occurring. No peaks characteristic of carbonyl groups could be identified by FTIR, indicating that decarboxylation occurs before any reactions with styrene. Backbone cleavage of cellulose has been previously noted as a side reaction to free radical grafting[14)], probably through eliminations beginning with the formation of formaldehyde as noted by Bough[14b)] and Phillips[14c)].

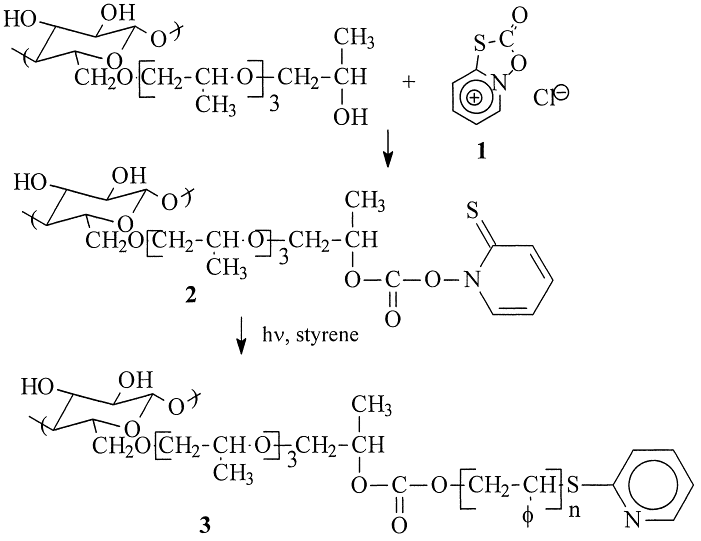
Table 1. Carboxymethyl cellulose-*graft*-polystyrene copolymers

DS	Substrate mass[a] (g)	% Mass increase	Graft DP (by mass)	Graft DP (by NMR)	Toluene sol, wt %	Mw (SEC) x 10^{-3}
0.7	1.56	319	13	12	90	200
0.9	1.3	422	11	13	93	180
1.2	1.07	635	11	13	95	170

[a)] [BE](mM) = 91, in styrene

Grafting to Hydroxypropyl Cellulose Barton Carbonates

Hydroxypropyl celluloses (HPC) with molecular weights of 100,000 or less are soluble in THF allowing for convenient conversion to Barton ester derivatives under anhydrous conditions. Reaction of the hydroxyl groups of HPC with 1-oxa-2-oxo-3-thiaindolizinium chloride, **1**, in THF yields the Barton carbonate derivative **2 (Scheme 1)**. Dissolution of **2** in a stock solution of styrene (75 mole % in DMF) and subsequent photolysis of the Barton carbonate provided the HPC-*graft*-polystyrene **3**. The molecular weight of the copolymer (M_w=143,000) was more than double that of the starting HPC (M_w=60,000). The increase in molecular weight indicates that chain cleavage is minimized. Our hypothesis that reactions occur at the pendant hydroxypropyl spacer groups, which ameliorates chain scission, is based on the intramolecular hydrogen bonding that makes the anhydroglucose hydroxyl groups in the main chain less accessible. FTIR analysis reveals a carbonyl peak at 1743 cm^{-1} indicating that decarboxylation does not occur before styrene monomer addition. The greater stability of the carbonate radical (25) relative to the carboxylate radical minimizes the decomposition of the anhydroglucose substrate. Chain transfer to pendant Barton carbonate substituents leads to relatively short polystyrene grafts (DP= 13) terminated with thiopyridine groups.



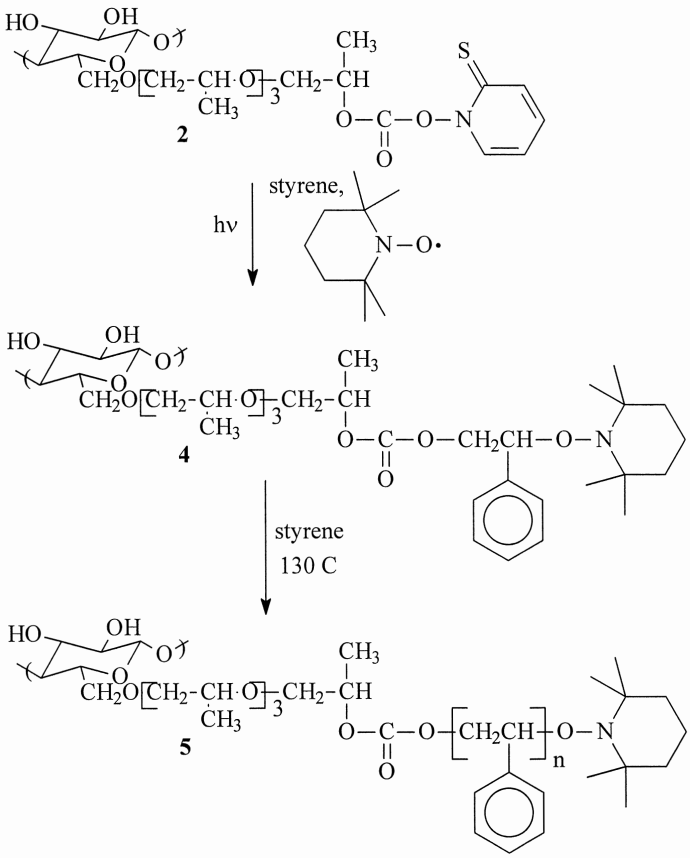
Scheme 1. Grafting of styrene to hydroxypropyl cellulose

The chain transfer constant of O-phenyl- N-hydroxypyridine-2-thione carbonate with acrylamide was found to be 0.02, which is two orders of magnitude lower than that for styrene. Thus, it should be feasible to prepare graft copolymers with longer side chains using acrylamide. Indeed, grafting of acrylamide from Barton carbonate **2** could be achieved readily; mass increases up to 695% were observed; and the NMR (D_2O) analysis was consistent with a polyacrylamide graft length of 20-25. The copolymers are completely soluble in water and insoluble in organic solvents so the short chain grafts effectively shield the hydroxypropyl backbone. The potential application of these water soluble cellulose brushes as chiral packing materials is currently being investigated.

Controlled Grafting from Hydroxypropyl Cellulose

The use of nitroxide mediated polymerization to control molecular weight is well documented16). Since the chain transfer properties of the Barton derivatives limit the molecular weights of the grafts formed, switching to a nitroxide mediated controlled radical process affords an opportunity to produce both long chain grafts and grafts with controlled chain length. Conversion of Barton esters and carbonates to the corresponding styrene TEMPO unimer17) proceeded cleanly when the Barton carbonate was decomposed under photolytic conditions in the presence of excess TEMPO and styrene.

Controlled radical grafting from HPC was accomplished utilizing TEMPO monoadducts formed from the HPC-Barton carbonate derivative **2** (Scheme 2). Photolysis of **2** in styrene and TEMPO provided adduct **4**. The conversion to the TEMPO adduct was 49%; a yield consistent with that observed using benzoyl peroxide as the radical source17). Heating the macroinitiator in styrene and removing aliquots at selected polymerization times afforded a series of graft copolymers **5** with increasing molecular weights (Table 2). After heating for 48 hours, the total styrene conversion to graft was 36 %. Direct graft copolymer analysis by SEC was did not indicate a significant increase in the molecular weight. The change in hydrodynamic volume that accompanies grafting lead to underestimation of the molecular weight. The branched copolymers also exhibited high polydispersities (1.86, 1.87, 2.03, and 2.03 respectively as the polymerization time increased). Acid hydrolysis of the cellulose backbone liberates the polystyrene grafts for independent analysis. The analysis of the purified polystyrene grafts by SEC yielded the molecular weights and polydispersities of the polystyrene grafts contained in Table 2. The increase in graft length with increasing polymerization time is apparent. Further, the polydispersity of the grafts ranged from 1.3 - 1.5, so some control of the grafting process was achieved.



Scheme 2. Controlled radical grafting from hydroxypropyl cellulose

The styrene grafting experiments show that TEMPO adducts can be formed utilizing Barton ester intermediates and demonstrate an effective procedure for controlled radical grafting from cellulose. The use of TEMPO to control radical grafting allows for higher molecular weight grafts to be formed, and the living nature of the polymerization gives potential for the formation of block copolymers as grafts.

Table 2. Molecular Weight and Polydispersities of Grafts from HPC-TEMPO Adducts.

Rxn time (hrs)[a]	Sample mass (g)	Copolymer Mn	Graft Mn	Graft PD
12	0.07	56,000	28,000	1.34
24	0.43	78,000	54,000	1.28
36	0.74	80,000	61,000	1.40
48	5.49	82,000	62,000	1.52

a) Time to removal of 1 mL aliquot

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