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Sheila L. Williamson[a]; Charles L. McCormick[a]
[a] Department of Polymer Science, The University of Southern Mississippi, Hattiesburg

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CELLULOSE DERIVATIVES SYNTHESIZED VIA ISOCYANATE AND ACTIVATED ESTER PATHWAYS IN HOMOGENEOUS SOLUTIONS OF LITHIUM CHLORIDE/N,N-DIMETHYLACETAMIDE

Sheila L. Williamson and Charles L. McCormick
Department of Polymer Science
The University of Southern Mississippi
Hattiesburg, MS 39406-0076

ABSTRACT

Cellulose carbamate and ester derivatives were synthesized in homogeneous solutions of lithium chloride (LiCl)/N,N-dimethylacetamide (DMAc) by the reaction of cellulose with ethyl 4-isocyanatobenzoate and the activated esters of N,N-dimethylaminobenzoic acids. Comparative reactions were performed with phenyl isocyanate and the activated ester of benzoic acid. All reactions were followed spectroscopically by FTIR, ^{1}H NMR, and ^{13}C NMR. Degrees of substitution were calculated utilizing UV spectroscopy. The isocyanate reactions are facile allowing controllable degrees of substitution and high yields. By contrast, the activated ester pathway inherently results in lower degrees of substitution and lower yields due in part to undesirable side reactions.

INTRODUCTION

Cellulose (poly(1→4-β-D-glucose)) is the most abundant polysaccharide found in nature since it is the major component of nearly all forms of plant life. Thus, cellulose is economically attractive as a raw material since it is available from renewable resources and waste products. In addition, the environmental

advantages of cellulose are its biodegradable nature and soil nutritive properties. However, the full utility of chemically derivatized cellulose has not been attained commercially due to processing difficulties arising from intractability and lack of suitable solvents. For example, most commercial cellulose derivatives are prepared by heterogeneous processes which often lead to difficulty in maintaining quality control in the resulting materials. To date, the markets for cellulose have been limited to esters and ether derivatives. The principal ester derivatives include cellulose nitrate, acetate, propionate, and butyrate. A number of cellulose ethers including methyl cellulose and carboxymethyl cellulose are useful as gelling agents and rheological modifiers.

Several solvents have been reported for cellulose dissolution [1,2,3,4,5]. Among the non-degrading solvents is lithium chloride (LiCl)/N,N-dimethyacetamide (DMAc), first reported by our laboratories in 1979 [6, 7, 8]. This solvent had been previously utilized for dissolution of polyamides[9,10] and chitin [3, 11]. Subsequently we reported a number of synthetic transformations of cellulose to a variety of derivatives [12, 13, 14]. The most effective reactions studied thus far have been reactions of isocyanates or acid chlorides with cellulose to yield high degree of substitution (DS) values [10]. Glasser and Samaranayake [15] recently reported derivatization of cellulose in 9% LiCl/DMAc using N,N-dicyclohexylcarbodiimide (DCC), 4-pyrrolidinopyridine (PP) and various aliphatic carboxylic acids [16, 17].

In this contribution, we report new derivatives of cellulose prepared under homogeneous reaction conditions in 9% LiCl/DMAc via isocyanate and activated ester pathways. Methods of purification and solubility characteristics of the final derivatives are also reported. These derivatives have potential for facile transformation into water soluble cellulose derivatives.

EXPERIMENTAL

Materials

Reagent grade cellulose (J. T. Baker) was used without purification. All other reagents were obtained from Aldrich and used as received. Lithium chloride (LiCl) solutions (9% wt/wt) in N,N-dimethylacetamide (DMAc) were prepared at 100°C to eliminate traces of water and were allowed to cool to room temperature before use. To facilitate dissolution, the cellulose was pre-swollen utilizing a technique previously reported by McCormick and Dawsey [12]. This procedure has been modified in our current work by initially vacuum drying

cellulose and lithium chloride, drying N,N-dimethylacetamide (DMAc) over barium oxide and eliminating the deionized water step in the swelling procedure. These steps were performed to eliminate water from the system so as to increase the efficiency of the isocyanate and activated ester reactions.

Cellulose Carbamates

Cellulose phenyl carbamate

9% LiCl/DMAc (50ml) and solvent swollen cellulose (1.6 g, 0.02 mol of hydroxyl groups) were added to a dry, 250 ml three-necked flask fitted with nitrogen inlet/outlet, addition funnel, and mechanical stirrer. Upon dissolution of the cellulose, a solution of pyridine (2.5 ml, 0.022 mol) in DMAc (25 ml) was added dropwise. A solution of phenyl isocyanate (6.0 ml, 0.055 mol) in DMAc (40 ml) was then delivered into the reaction vessel dropwise over a one hour period. The reaction mixture was stirred overnight (~12 hours) at room temperature. The product was then isolated by precipitation into a water/methanol mixture (50:50), filtered, washed with methanol, and vacuum dried at 50°C. The resulting polymer was purified by soxlet extraction with methanol for 24 hours followed by vacuum drying. The polymer was purified further by dialysis in acetone using regenerated cellulose Spectra-por dialysis tubing (MWCO = 12-14K). The overall yield (based on a degree of substitution of 3) of this reaction was 9.21 g (89%). Infrared spectrum: amide N-H, 3300; aromatic C-H, 3050; amide C=O, 1730; aromatic C=C, 1600 cm^{-1}. ^1H NMR spectrum (Acetone-d_6/TMS): δ 3.30-5.20 (cellulosic methine and methylene groups), 6.60-7.40 (m, aromatic hydrogens of phenyl moiety), 8.30-8.40 ppm (m, N***H*** of phenyl moiety). Residual solvent: 2.10 (m, residual acetone), 2.90 (m, absorbed $\boldsymbol{H}_2O$). ^{13}C NMR spectrum (Acetone-d_6) (Figure 1): δ 70.0-110.0 (m, methine and methylene carbons of cellulose), 130.0-150.0 (m, aromatic carbons of phenyl moiety), 162.4 (carbonyl carbon of phenyl moiety). (Calculated degree of substitution (DS) = 2.6).

Cellulose (p-ethylbenzoate) carbamate

A similar procedure to that for the phenyl isocyanate reaction was followed. The stoichiometry was altered to prepare a target derivative with a DS of 1, only a slight excess of reagent 1.40 g ethyl 4-isocyanatobenzoate (0.007 mol reagent: 0.02 mol OH) was utilized. The product was purified by dialysis in N,N-dimethylformamide (DMF). The overall yield (based on DS = 1) of this reaction was 6.48 g (92%). Infrared spectrum: hydroxyl O-H, 3450; amide N-H, 3300; aromatic C-H, 3000; amide C=O, 1740; ester C=O, 1650; aromatic C=C, 1575 cm^{-1}.

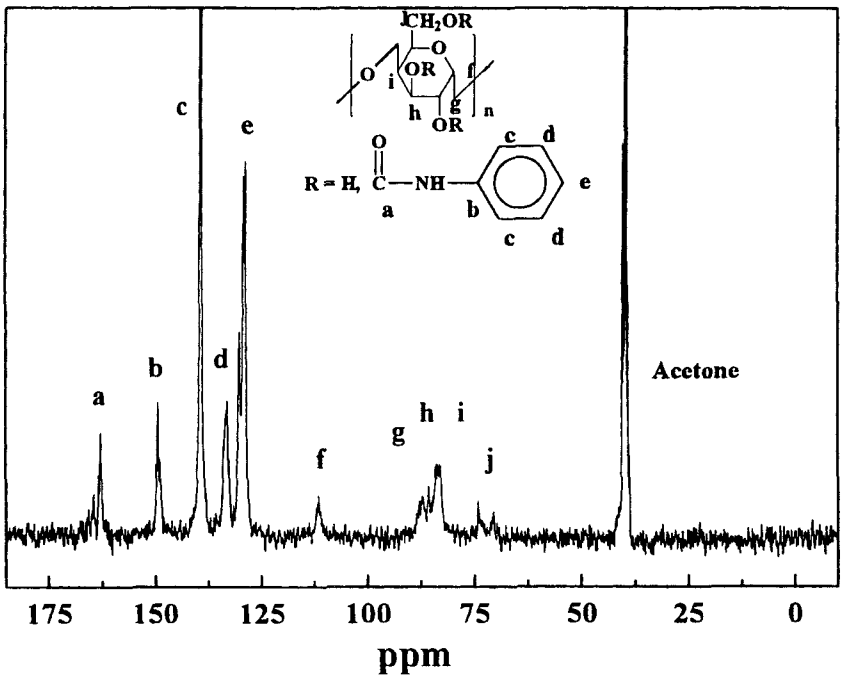


Figure 1. ^{13}C NMR spectrum of cellulose phenyl carbamate (Acetone-d_6).

^1H NMR spectrum (DMSO-d_6/TMS): δ 1.20-1.40 (m, C***H***$_3$ of ethyl 4-isocyanatobenzoate (EIB) moiety), 2.50 (s, C***H***$_2$ of cellulose), 3.20-3.90 (C***H*** of cellulose), 4.10-4.40 (s, C***H***$_2$ of EIB moiety), 7.40-7.70 (s, N***H*** of EIB moiety), 7.80-8.00 ppm (m, aromatic hydrogens), 2.00 (s C***H***$_3$CON(CH$_3$)$_2$). Residual solvent: 2.70-2.90 (m, (C***H***$_3$)$_2$NCOCH$_3$). ^{13}C NMR spectrum (DMSO-d_6) (Figure 2): δ 14.5 (s, ***C***H$_3$ of EIB moiety), 59.0 (s, ***C***H$_2$ of EIB moiety), 60.0-105.0 (m, methine and methylene of cellulose), 116.0-145.0 (aromatic carbons multiple substitution), 152.0 and 165.0 (carbonyl carbons), 168.0 (carbonyl carbon of ethyl ester of EIB). Calculated DS = 1.0.

Cellulose Esters

Cellulose benzoate

9% LiCl/DMAc (50 ml) and solvent swollen cellulose (1.6 g, 0.02 mol of hydroxyl groups) were added to a dry, 250 ml three-necked flask fitted with nitrogen inlet/outlet, addition funnel, and mechanical stirrer. After the dissolution of cellulose, dicyclohexylcarbodiimide (DCC) (8.25 g, 0.0 mol) was

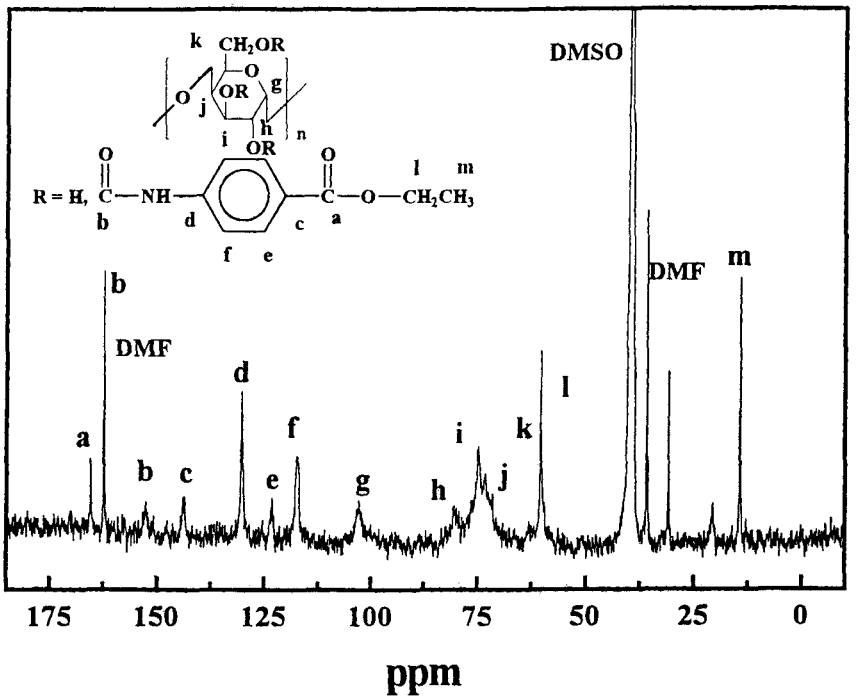


Figure 2. ^{13}C NMR spectrum cellulose (*p*-ethylbenzoate) carbamate (DMSO-d_6).

added. To this solution, benzoic acid (BA) (4.88 0.0 mol) was added. After addition of the carboxylic acid, N,N-dimethylaminopyridine (DMAP) (0.5 g, 0.004 mol) was added to catalyze the reaction. The product was isolated by filtration of the dicyclohexyl urea (DCU) from the reaction mixture and precipitation of the supernatant into a 50:50 mixture of methanol and deionized water. The precipitate was then washed with several aliquots of methanol. The method of purification involved the direct dilution of the filtered reaction mixture with DMF and organic dialysis against DMF. The resulting product was isolated by rotary evaporation of the DMF and vacuum drying at room temperature with a yield of 6.09 g (64%) (based on DS = 3). Infrared spectrum: hydroxyl OH, 3500-3100; aromatic C-H, 3000-2900; ester C=O, 1675 and 1600; aromatic C=C, 1550 cm^{-1}. ^1H NMR spectrum (9% LiCl/DMAc (DMSO-d_6/TMS)) (Figure 3): δ 3.3-5.5 (CH_2 and C*H* of cellulose), 6.90-8.00 ppm (s, aromatic hydrogens). Residual reagents and solvent: 1.00-1.80 (m, DCC), 2.40 (m, *H*CON$(CH_3)_2$), 2.60-3.30 (m, $(CH_3)_2$NCOH), 3.40 (s, DCC). Calculated DS = 0.33.

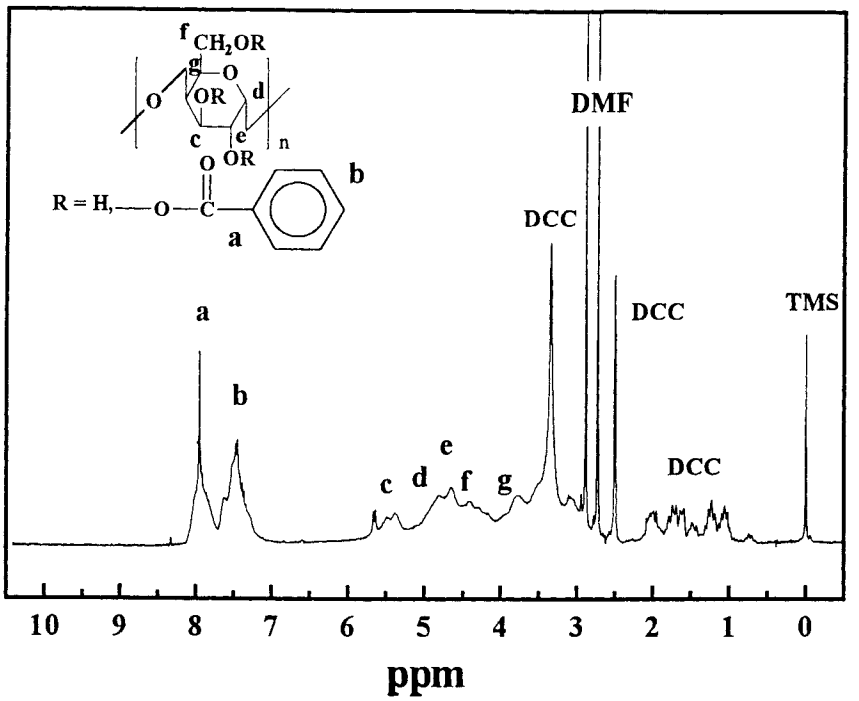


Figure 3. ^{1}H NMR spectrum of cellulose benzoate (DMSO-d_6).

Cellulose (p-N,N-dimethylamino)benzoate

This reaction followed the same procedure as the previous cellulose reaction with BA. N,N-dimethylaminobenzoic acid (DMABA) (6.61 g, 0.04 mol) was added instead of the BA. The purification of the product with organic dialysis was employed as described for the BA derivative with a yield of 4.76 g (39%) (based on DS = 3). Infrared spectrum: hydroxyl OH, 3450; aromatic C-H, 3000; methylene of DCC, 2850; ester C=O, 1650; aromatic C=C, 1550 cm^{-1}. ^{1}H NMR spectrum (9% LiCl/DMAc (D_2O-d_6/TMS)) (Figure 4): δ 2.50-3.40 ((CH_3)$_2$ of DMABA moiety), 3.50-4.50 (methylene and methine ***H*** of cellulose backbone), 6.50-9.00 (aromatic hydrogens of DMABA moiety). Residual reagent and solvent: 0.90-1.80 (DCC). 2.00 (m, ***H***CON(CH_3)$_2$), 2.50-3.40 (m, (CH_3)$_2$NCOH). Calculated DS = 0.2.

Spectroscopy

Fourier transform infrared (FTIR) spectra were obtained with a Mattson Instruments Galaxy Series FT-IR 2020. ^{1}H and ^{13}C NMR spectra were obtained

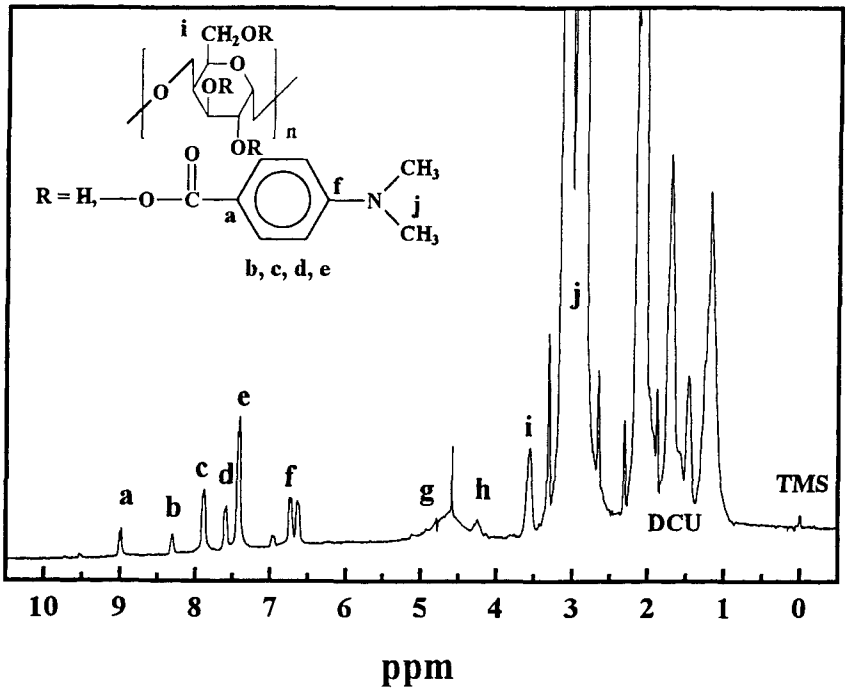


Figure 4. ^{1}H NMR spectrum of cellulose (*p-N,N*-dimethylamino)benzoate (DMSO-d_6).

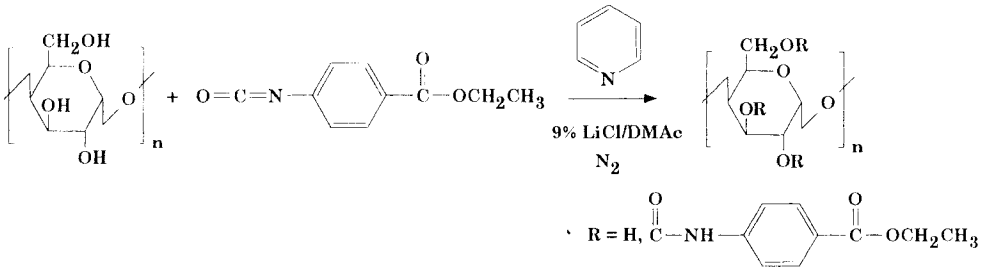
with a Bruker 300 MHz nuclear magnetic resonance spectrometer. UV spectroscopy was performed on model compounds and derivatives with a Hewlett-Packard 8452A diode array spectrophotometer to determine the degree of substitution.

Molecular Weight

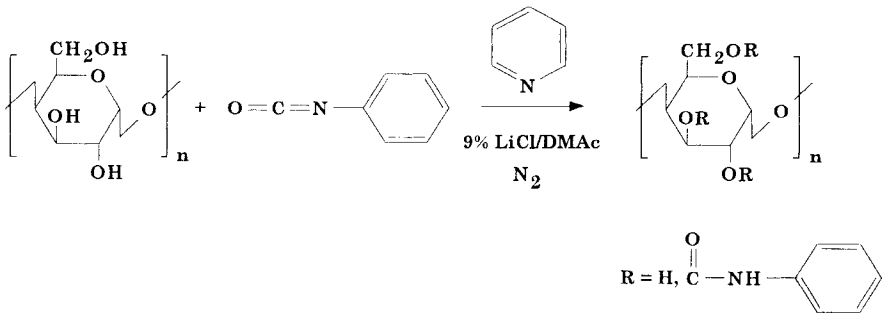
The cellulose (J. T. Baker) was reported to have a weight average molecular weight of 320,000 as determined by McCormick, Callais, and Hutchinson [18].

RESULTS AND DISCUSSION

Previously, our laboratory described the reactions of phenyl isocyanate and acetyl chloride with cellulose in 9% LiCl/ DMAc [12]. The highest degrees of substitution attainable were between 2.6-2.8, even with three-fold excess of reagent. It was suggested that the high viscosity of the LiCl/DMAc reaction



Scheme 1. Reaction of cellulose with ethyl 4-isocyanatobenzoate.



Scheme 2. Reaction of cellulose with phenyl isocyanate.

medium or inaccessibility of highly ordered regions could lead to diffusion controlled kinetics which would limit complete substitution.

Cellulose Carbamates

In the first part of the work presented here, isocyanate chemistry was utilized to prepare a new cellulose derivative with ethyl 4-isocyanatobenzoate (EIB) (Scheme 1). The reaction was compared to the model reaction of cellulose with phenyl isocyanate (PI) (Scheme 2). Both of these reactions were facile with high yields (89% for phenyl isocyanate and 92% for ethyl 4-isocyanatobenzoate). There are no side products produced during these carbamate forming reactions and, therefore, only minor purification was required. The respective syntheses of cellulose carbamates were accomplished by allowing reaction of the backbone hydroxyl groups with isocyanates in the presence of a tertiary amine catalyst. These reactions were monitored by the disappearance of the isocyanate absorbance (2280-2260 cm^{-1}) and the appearance of the carbamate carbonyl absorbance (1730-1660 cm^{-1}).

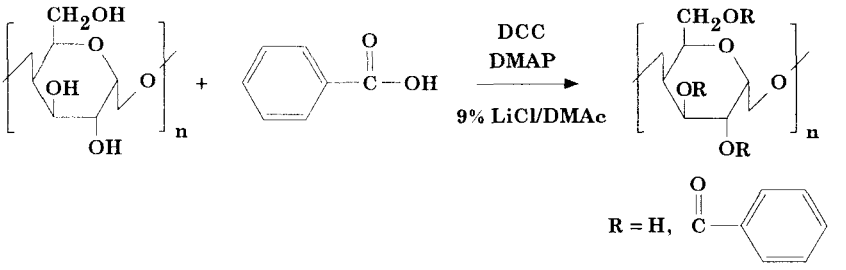
The ^{13}C NMR spectrum of the unmodified cellulose in LiCl/DMAc (DMSO-d_6) has previously been reported to exhibit five distinct peaks: the anomeric carbon C_1 at 103.5 ppm, the primary carbon C_6 at 60.7 ppm, C_2 at 74.5 ppm, C_3, C_5 at 76.3 ppm and C_4 at 79.5 ppm [19]. The ^{13}C NMR spectrum of cellulose phenyl carbamate (Acetone-d_6) (Figure 1) exhibits the expected peak pattern for the cellulose carbons (with a downfield shift due to the solvent change). Also observed in Figure 1, are resonances for carbamate carbonyl carbons at 162 and 164 ppm and aromatic carbons at 130-150 ppm. The phenyl isocyanate cellulose derivative is readily soluble in acetone. A degree of substitution of 2.6 was determined by UV spectroscopy.

The ^{13}C NMR spectrum of the cellulose (p-ethylbenzoate) carbamate derivative is shown in Figure 2. The carbamate carbonyl carbons appear at 152 and 165 ppm and the aromatic carbons at 116-145 ppm. The cellulose 4-ethyl benzoate carbamate derivative is soluble in DMAc, DMF, and N,N-dimethyl sulfoxide (DMSO). The target degree of substitution of 1 was achieved.

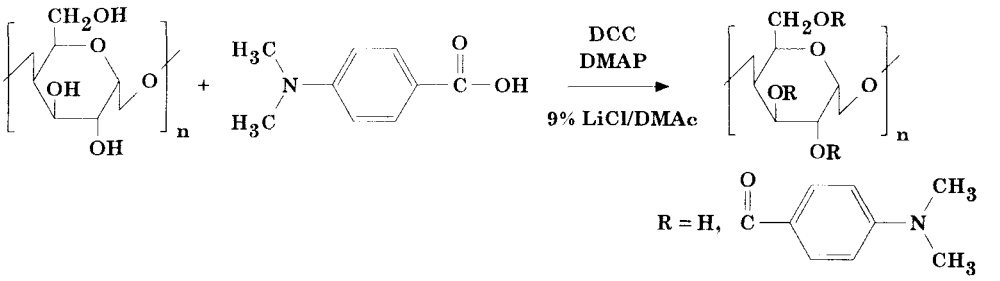
Cellulose Esters

Cellulose esters can be prepared by reaction with acyl halides, acid anhydrides, and carboxylic acids. The acyl halide pathway is effective for synthesis of some cellulose esters, but homogeneous reactions are often not possible due to insolubility of many acyl chlorides in the presence of an acid scavenger such as triethylamine. Acid anhydrides and carboxylic acids usually require activation for acylation. For example, N,N-dicyclohexylcarbodiimide (DCC)/4-pyrrolidinopyridine (PP) has been employed to activate acid anhydrides and carboxylic acids for acylation reactions with short chain alcohols [16] and with amines and carboxylic acids in peptide chemistry [17]. Glasser and Samaranayake [15] reported derivatization of cellulose in 9% LiCl/DMAc using DCC/PP with various aliphatic carboxylic acids.

In this contribution, we utilize an *in situ* DCC/PP activated ester pathway to prepare cellulose derivatives from benzoic acid (BA) and N,N-dimethyl-aminobenzoic acid (DMABA). Benzoic acid (Scheme 3) was selected as the simplest aromatic carboxylic acid that had literature precedence in activated ester reactions with appreciable yields [20, 21]. The tertiary amine group of the resulting cellulose (p-N,N-dimethylamino)benzoate (Scheme 4) from the DMABA reaction provides a site for eventual conversion to a quaternary ammonium derivative which imparts water solubility. The esterification reactions were monitored by the disappearance of DCC (2200 cm^{-1}) and the appearance of the ester absorbances (1600 and 1675 cm^{-1}).



Scheme 3. Reaction of cellulose with benzoic acid via an activated ester pathway.



Scheme 4. Reaction of cellulose with N,N-dimethylaminobenzoic acid via an activated ester pathway.

These activated ester reactions were not efficient in producing cellulose esters under homogeneous conditions in the LiCl/DMAc solvent. Quantitative control of the degree of substitution was not attainable, also lower degrees of substitution and yields were observed with the activated esters when compared to the isocyanates. Byproducts of the reactions were readily apparent upon attempted analysis of the NMR and IR spectra and purification proved problematic. The most successful purification method involved filtration of the DCU precipitant from the reaction mixture, followed by direct dilution with DMF, and subsequent dialysis against DMF. The resulting products exhibited limited solubility in DMAc, DMF, and DMSO.

The concentrations of the activated ester cellulose derivatives soluble in deuterated DMSO were lower than that required for ^{13}C NMR analysis; however, ^{1}H NMR was possible. Unmodified cellulose has also been characterized in LiCl/DMAc at 70°C utilizing ^{1}H NMR spectroscopic techniques [22]. The

hydroxyl moieties of unmodified cellulose have proton signals at 5.2, 5.3, and 5.65 representing C_3-OH, C_6-OH, and C_2-OH, respectively. Figure 3 shows the ^1H NMR spectrum of the cellulose benzoate derivative. The aromatic protons of the benzyl moiety are present at 6.90-8.00 ppm. The cellulosic proton region is broad and poorly resolved. The cellulose protons of the cellulose benzoate ester appear in the same region as the unmodified cellulose, but the peaks are much broader which is indicative of substitution. Some residual DCC/DCU (0.9-1.8 ppm) remains in the benzoic acid derivative, even after dialysis.

Possible explanations for the residual DCC/DCU are: (1) the impurity has a strong affinity for the cellulosic backbone or (2) the condensation of the carboxylic acid to the anhydride is not 100% efficient and some DCC is chemically bound to the backbone through a side reaction. The DCC/DCU impurity is also seen in the ^1H NMR spectrum of the cellulose (p-N,N-dimethylamino)benzoate derivative where the residual peak pattern of DCC/DCU appears at 0.90-1.80 ppm (Figure 4). The aromatic protons (7.30, 7.50 ppm) and the methyl groups of the tertiary amine (2.50, 3.40 ppm) are also present. This derivative has interesting phase behavior in that during organic dialysis, the polymer condenses into a solid gel in the dialysis tube. The gel product is soluble in DMAc, DMF, and DMSO. This may suggest that complexation is occurring, possibly hydrogen bonding, between the lone pairs of the tertiary amine nitrogens and the unreacted hydroxyl group protons.

CONCLUSION

Previously unreported cellulose derivatives were prepared in homogeneous solutions of LiCl/DMAc by reaction of isocyanate or activated ester reagents. The isocyanate reactions could be controlled (degree of substitution) by adjusting the stoichiometry of reagents. The highest degree of substitution obtainable was 2.6 for the formation of cellulose phenyl carbamate. These reactions were very facile with no indication of competing substitutions along the cellulose backbone.

The activated ester chemistry was found to be less efficient resulting in low degrees of substitution due to undetermined side reactions. Spectra of both the benzoate and N,N-dimethylaminobenzoate cellulose esters indicated byproducts strongly bound to the parent backbone. Purification of these systems in DMF proved to be helpful, but residual DCU derivatives, likely covalently attached, appear in the final products in small concentrations.

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