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**Polysaccharide Materials:
Performance by Design**

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Chapter 13

Synthesis and properties of regioselectively substituted cellulose cinnamates

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Regioselectively substituted cellulose cinnamates were synthesized in order to obtain potentially versatile functional materials. The introduced cinnamoyl groups are expected to be photosensitive and electroconductive. At the same time, regioselective substitution may strongly impact derivative properties. Thus, this paper will report the synthesis procedure, and the thermal behaviors of these regioselectively substituted cinnamoyl derivatives.

Introduction

Hydrogen bonds in cellulose and cellulose derivatives are among the most influential factors on their physical- and chemical properties. To date we have attempted to probe this structure-property relationship using regioselectively functionalized methyl celluloses¹⁻¹² like 2,3-di-*O*-methyl cellulose (23MC)¹³, 6-mono-*O*-methyl cellulose (6MC)¹⁴, 3-mono-*O*-methyl cellulose (6MC)¹⁵ and 2,3,6-tri-*O*-methyl cellulose (236MC)¹⁶ as model compounds. In addition, the functionalization pattern of the methyl ether groups also had an influence on the enzymatic hydrolysis of methyl cellulose by cellulase.¹⁷ Through those investigations, the intramolecular hydrogen bonds between the OH groups of position 3 and the ring oxygen of the adjacent anhydroglucose unit (*O*-5), which is supposed to determine the molecular stiffness, have also been confirmed as a key factor for properties of cellulosic materials.¹⁸

Cinnamic acid is well known to be capable of photo-cycloaddition, and syntheses of polymers containing the cinnamoyl substituents have been reported in the last decade¹⁹⁻²¹. Such polymers are expected to exhibit photoconductivity through electron accepting groups within the molecule. The preparation and the behavior under photo-irradiation of cellulose cinnamates have been extensively studied²²⁻²⁸ in the 1990's, including interpenetrating polymer networks²⁶ and a photosensitive comb-like polymer²³. In addition, cellulose cinnamates at a critical concentration in some organic solvents exhibited chiral nematic mesophases²⁵. More recently, isopentylcellulose cinnamate as cross-linked Langmuir-Blodgett films sandwiched between a polymeric diffusion couple was investigated to provide a system for probing fundamental transport process across the ultrathin membranes²⁷.

Regioselectively functionalized polysaccharide cinnamates display some unique properties. The absolute helicities of acylated chitosan derivatives bearing cinnamate chromophores²⁰ vary depending on the degree of substitution (DS) of cinnamoyl groups, but are nearly independent of thermal stimulus. Molecular interactions including hydrogen bonding and hydrophobic interaction may be involved in this behavior. Therefore, regioselectively functionalized cellulose cinnamates would enable us to further elucidate the involvement of the inter- and intramolecular hydrogen bonds as well as photo-crosslinking behavior and other factors.

In this paper, regioselectively substituted cellulose cinnamates were synthesized in order to obtain potentially versatile functional materials. Thus, this paper will report the synthesis procedure and the thermal behaviors of these regioselectively substituted cinnamoyl derivatives in order to understand the principles of molecular design to exploit desired functional bio-based materials.

Syntheses of regioselectively substituted cellulose cinnamates

The cellulose cinnamates synthesized in this study were cellulose tricinnamate (a), cellulose-2,3-*di*-cinnamate (b), cellulose-6-*mono*-acetate-2,3-*di*-cinnamate (c), and cellulose-2,3-*di*-acetate-6-*mono*-cinnamate (d), respectively.

(i) Preparation of cellulose tricinnamate (1)

Figure 1 shows the synthesis scheme of cellulose tricinnamate. Basically, the process followed previous reports^{22,24}. The starting material was commercially available microcrystalline cellulose powder (Funacell, Funakoshi Co., Japan) with a nominal degree of polymerization (DP) of *ca.* 220. The sample was dried at 105 °C for 3 hours. Pyridine was dehydrated over 3Å molecular sieves. Reagent-grade solvents and cinnamoyl chloride (Aldrich Gold Label) were used without further purification. The procedure was as follows: After 1.5 g cellulose powder was dispersed in 60 mL pyridine at 100°C for 1 hour with constant stirring, 1.5 moles of cinnamoyl chloride per mole of hydroxyl groups were added to the solution. Then, the mixture was kept at 50 °C with stirring for 5 hours.

The reaction mixture was cooled to room temperature and poured into methanol. The precipitate was dissolved in chloroform, the chloroform layer was extracted with water three times, and then evaporated under reduced pressure at 60°C to a syrup. The product was precipitated from the syrup by the addition of methanol, filtered off, and dried under vacuum at 60°C for 5 hours. The yield of product **1** was 80 %.

Cellulose 2,3-dicinnamate (**4**), cellulose 6-monoacetate-2,3-dicinnamate (**5**), and cellulose 2,3-diacetate-6-monocinnamate (**8**) were prepared starting from 6-*O*-triphenylmethyl ("trityl") cellulose in which the C-6 hydroxyl is regioselectively substituted. Tritylcellulose (**2**) was used as a starting material, since the trityl group can be easily removed by exposing the cellulose derivatives to acidic conditions²⁸. This allows the preparation of cellulose derivatives that are regioselectively substituted at C-2 and C-3. Tritylcellulose was prepared according to our previous papers^{13,14}. Regenerated cellulose (32.5 g) was added to 300 mL of dry pyridine, which was then heated for 3 hours at 80°C and filtered off, in order to remove water. This procedure was repeated three times.

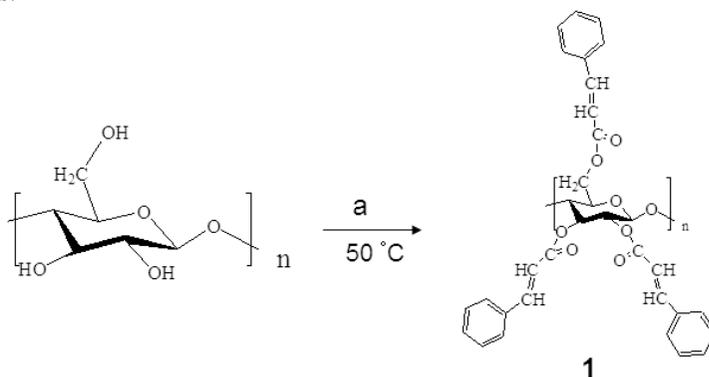


Figure 1. Synthesis of tricinnamate **1**.
a – 1.5 equiv/OH cinnamoyl chloride

Then the cellulose was added to 500 mL of anhydrous pyridine and triphenylmethyl chloride (142.0 g, 2.5 moles per mol of hydroxyl group) in a 1000 mL three-necked round-bottom flask equipped with a condenser, stirrer and drying tube. The mixture was heated for 26 hours at 95°C, then cooled to room temperature and poured into methanol. The precipitate was isolated and washed in methanol for 12 hours. After a second washing, the precipitate was filtered off and dried at 100°C under vacuum. The yield of the product was 95% and the degree of substitution of trityl groups was 1.07 by ¹H-NMR measurements.

(ii) Preparation of cellulose-2,3-dicinnamate (**4**) and cellulose-6-mono-acetate-2,3-dicinnamate (**5**)

The method for the preparation of cellulose tricinnamate was applied to the preparation of cellulose 2,3-dicinnamate (**4**) as shown in Figure 2. Thus,

tritylcellulose (**2**: 1.0 g) was dissolved in pyridine (60 mL). After 1 h stirring under nitrogen, cinnamoyl chloride (5.2 g, 6.0 moles per mole of hydroxyl groups) was added to the solution. Then, still under a nitrogen atmosphere, the temperature was raised to 90°C and kept there for 5 hours. The mixture was cooled to room temperature and the product was isolated and purified as described for the preparation of cellulose tricinnamate. Following cinnamylation the product (**3**) was detritylated and the sample was isolated as follows: the sample was detritylated by treating 1.0 g of the polymer (**3**) in 30 mL of dichloromethane with hydrogen chloride gas at 0°C for 4 minutes^{13,14}. After the reaction, the detritylated mixture was poured into 50 mL of methanol. The product was isolated by centrifugation, washed with methanol, filtered and dried under vacuum at 60°C. The yield of the detritylated product **4** was approximately 65%.

For acetylating compound **4**, acetic anhydride (5.8 mL, 25 moles per moles of hydroxyl group) was added to the pyridine solution containing 1.0 g of compound **4**. Then, the mixture was kept at 90 °C with constant stirring for 48 hours. After the reaction, the mixture was poured into 50 mL of methanol to obtain a precipitate.

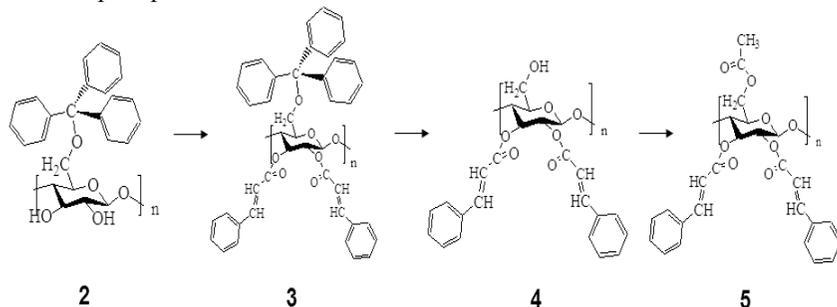


Figure 2. Synthesis of cellulose-2,3-dicinnamate **4** and cellulose-6-acetate-2,3-dicinnamate **5**.

The precipitate was dissolved in dichloromethane, the CH_2Cl_2 layer was extracted with water twice, and then the combined extracts were evaporated under reduced pressure at 60°C to a syrup. The product (**5**, Fig. 2) was precipitated from the syrup by the addition of methanol, filtered off, and dried under vacuum for 5 hours at 60°C. The yield of product **5** was 74%.

(iii) Preparation of cellulose 2,3-diacetate-6-mono-cinnamate (**8**)

Figure 3 shows the synthesis of cellulose-2,3-diacetate-6-monocinnamate (**8**). 6-Tritylcellulose (**2**: 1.0 g) was dissolved in 40 mL of pyridine with constant stirring at 60°C for 1 h. Then, acetic anhydride (12.0 mL, 25 moles per moles of hydroxyl group) was added to the pyridine solution. The mixture was kept at 90°C with constant stirring for 48 h. Following the reaction, the mixture was poured into 150 mL of methanol to yield a precipitate. The precipitate was dissolved in dichloromethane/methanol (3/1 v/v) mixture, and filtered off. The

product was reprecipitated by addition of methanol. The reprecipitation procedure was repeated twice, and then the product (**6**) was dried under vacuum at 60°C for 5 h. The products (**6**) were detritylated in 30 mL of dichloromethane according to the same procedure described above to provide cellulose 2,3-diacetate (**7**).

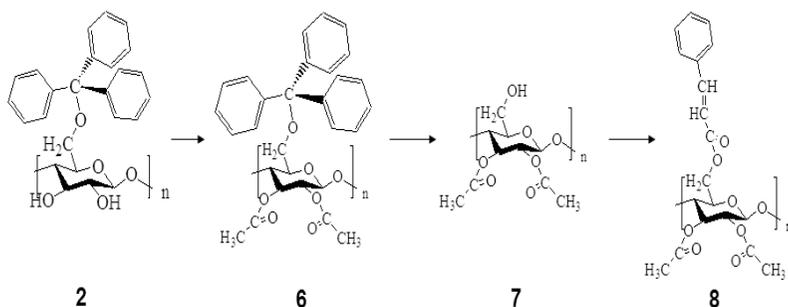


Figure 3. Synthesis of cellulose-2,3-diacetate-6-monocinnamate **8**.

Cinnamoyl chloride (17.1g, 12 moles per moles of hydroxyl group) was added to a solution of cellulose 2,3-diacetate (**7**, 1.0 g) in pyridine. Then, the temperature was raised to 95°C and kept there for 5 h. The mixture was cooled to room temperature and poured into 95% (v/v) aq. methanol to precipitate the product. The isolation and purification was followed as described above for the case of 6-*O*-trityl-cellulose 2,3-diacetate. The yield of product (**8**) was 88 %.

Characterization of regioselectively substituted cellulose cinnamates

The obtained products, cellulose tricinnamate (**1**), cellulose 2,3-dicinnamate (**4**), cellulose-6-monoacetate-2,3-dicinnamate (**5**), and cellulose-2,3-diacetate-6-monocinnamate (**8**) were characterized using FTIR and ¹³C-NMR spectroscopy. In particular, since compounds **1**, **5**, and **8** lacked hydroxyl groups, IR spectra showing no absorption bands due to stretching vibration of OH groups indicated complete substitution (data not shown).

Figure 4 shows ¹³C NMR spectra of compounds **1**, **4**, **5** and **8**. As shown in each spectrum, signals were all clearly assigned to the individual chemical shifts of the component carbons. Thus, ¹³C NMR confirmed the expected structures. Further, using ¹H NMR spectroscopy, the degrees of substitution (DS) of cinnamoyl group in the 4 products were found to be 3.0 for **1**, 2.1 for both **4** and **5**, and 0.86 for **8**, respectively.

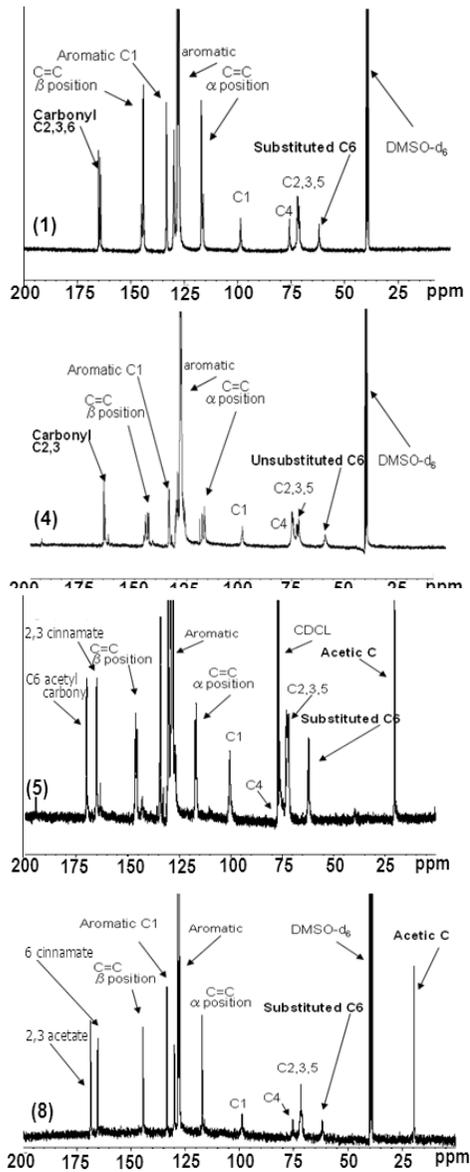


Figure 4. ^{13}C -NMR spectra of cellulose-tricinamate (1), cellulose-2,3-dicinamate (4), cellulose-6-monoacetate-2,3-dicinamate (5) and cellulose-2,3-diacetate-6-mono-cinnamate (8).

The thermal behavior of those products exhibiting melting transition by DSC, compounds **1**, **5**, and **8**, were investigated by obtaining equilibrium melting points ($T_{m_{eq}}$) from Hoffman-Weeks plots²⁹. The $T_{m_{eq}}$ was determined from DSC measurements as follows: differential scanning calorimetry (DSC) was performed under a nitrogen atmosphere using a Perkin-Elmer DSC-7. The instrument was calibrated with an indium standard. Film specimens weighing from 5 to 17 mg each were placed in aluminum sample pans which were then heated to 200°C and maintained at this temperature for 7 min to eliminate any residual crystallinity. The samples were then quenched to the selected isothermal crystallization temperature, T_{ic} , and held at this temperature for 5 h. The samples were then cooled to 25 °C and the melting point T_m was then measured using a heating rate of 10 °C/min. Subsequently by using Hoffman-Weeks plots³⁰ of the T_m points thus obtained, an equilibrium melting point ($T_{m_{eq}}$) was determined for each film as shown in Figure 5.

The measured values of $T_{m_{eq}}$ for cellulose tricinnamate (**1**), cellulose 6-monoacetate-2,3-dicinnamate (**5**), and cellulose 2,3-diacetate-6-monocinnamate (**8**) were 146 °C, 156 °C and 160 °C, respectively. This data indicates that as the DS (cinnamate) increased, $T_{m_{eq}}$ decreased.

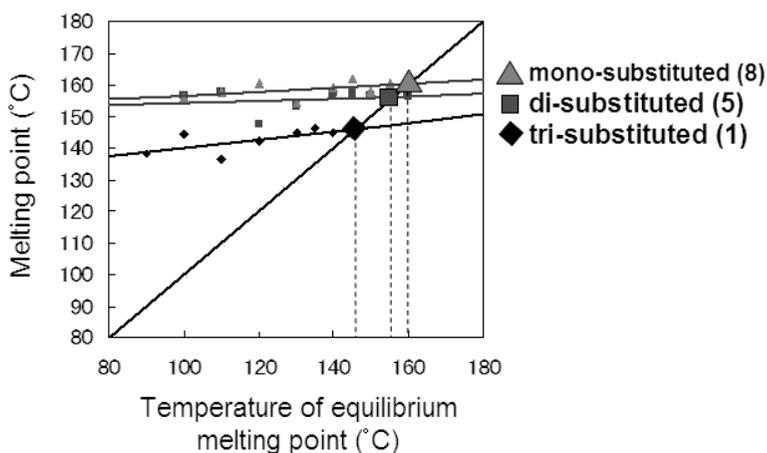


Figure 5. Equilibrium melting points of cellulose derivatives by Hoffman Weeks Plots^[29]. Samples 1, 5 and 8 correspond to the compounds shown in Figs 1-3.

In order to examine the changes in morphology of products **1**, **5** and **8** with increasing temperature, we observed these samples using polarized microscopy together with DSC. Observations were carried out for cast films of **1**, **5**, and **8** after isothermal crystallization at various temperatures, at the heating rate of 1 °C/min, with an Olympus polarized microscope BHA equipped with a hot stage (FP90, Mettler Toledo Inc.).

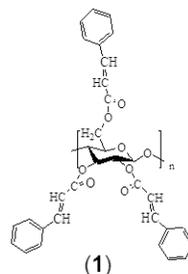
The T_m 's determined for compounds **1**, **5** and **8** by DSC following isothermal crystallization are listed in Table 1.

Table 1. Temperature of endothermal peaks of 3 cellulose derivatives (1,5,8) in the DSC scans

cellulose tricinnamate (**1**)

equilibrium melting point: 146 °C

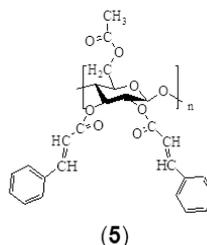
Isothermal crystallization	1 ST peak(ΔH)	2 ND peak(ΔH)
80 ° C 5h		
90 ° C 5h	123 ° C (0.46J/g)	138 ° C (0.72J/g)
100 ° C 5h	130 ° C (0.23J/g)	141 ° C (0.11J/g)
110 ° C 5h	137 ° C (0.82J/g)	
120 ° C 5h	143 ° C (0.97J/g)	
130 ° C 5h	146 ° C (1.15J/g)	
135 ° C 5h	147 ° C (1.26J/g)	
140 ° C 5h	145 ° C (0.58J/g)	



cellulose-6-monoacetate-2,3-dicinnamate (**5**)

equilibrium melting point: 156 °C

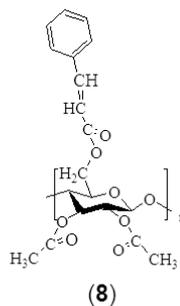
Isothermal crystallization	1 ST peak(ΔH)	2 ND peak(ΔH)
100°C 5h	136°C (0.11J/g)	157°C (1.85J/g)
110°C 5h	141°C (0.40J/g)	159°C (0.96J/g)
120°C 5h	147°C (0.48J/g)	
130°C 5h	154°C (2.49J/g)	
140°C 5h	158°C (2.16J/g)	
145°C 5h	158°C (1.95J/g)	
150°C 5h	156°C (0.53J/g)	
155°C 5h	156°C (1.18J/g)	
160°C 5h	156°C (1.58J/g)	



cellulose 2,3-diacetate-6-monocinnamate (**8**)

equilibrium melting point: 160 °C

Isothermal crystallization	1 ST peak(ΔH)	2 ND peak(ΔH)
100°C 5h	158°C (0.94J/g)	
110°C 5h	142°C (0.38J/g)	155°C (0.44J/g)
120°C 5h	147°C (0.76J/g)	162°C (0.10J/g)
130°C 5h	154°C (1.43J/g)	
140°C 5h	160°C (1.48J/g)	
145°C 5h	162°C (1.87J/g)	
150°C 5h	158°C (1.10J/g)	
155°C 5h	160°C (0.37J/g)	
160°C 5h	164°C (1.03J/g)	



Each product displayed one main endothermal peak, and depending upon the annealing temperature, a second peak at a lower temperature. The images from polarized microscopy indicated that the lower endotherm was not melting of the bulk sample. On the other hand, after traversing the higher endotherm, the images disappeared in the polarized microscopic observation. This indicates that the higher endotherm is melting of the polymer.

In cellulose tricinnamate (**1**), there appeared two endothermal peaks, one at 130°C or less and a 2nd in the range of 140-150°C. Cellulose-6-monoacetate-2,3-dicinnamate (**5**) and cellulose 2,3-diacetate-6-monocinnamate (**8**) exhibited two endothermal peaks at 140 °C and at 160 °C. Taking the results from the polarized microscopy into account, the peak at the lower temperature could be due to two possibilities; crystallization of side chain substituents independent of the bulk polymer, which is not a common event, and melting of poorly formed cellulose ester crystals as polymorphs, which is also a function of the annealing (isothermal crystallization) temperature. This commonly occurs when the annealing temperature is close to the T_g . Since there is not sufficient data at present, it would be reported in the future paper. On the other hand, the higher temperature peak could be due to melting of the crystals of cellulose main chains. Occurrence of the two kinds of crystallization growth may depend on the T_{ic} (Isothermal crystallization temperature).

In addition, cellulose tricinnamate (**1**) displayed thermotropic liquid crystalline behavior. The film subjected to isothermal crystallization at 100°C for 36 hours exhibited polarized images again at higher temperature (190°C) after melting. Compounds **5** and **8** did not display such behavior with increasing temperature.

Summary

Regioselectively substituted cellulose cinnamates were synthesized in hopes of obtaining versatile, functional cellulose derivatives. The thermal behavior of the regioselectively substituted cellulose esters depended on the DS of cinnamate. Interestingly, two melting peaks appeared depending on the thermal history at the isothermal crystallization temperature. The lower temperature peaks could be due either to crystals of poorly formed cellulose ester polymorphs or side chain crystals of cinnamoyl groups, whereas the higher temperature peaks were due to melting of the crystals of cellulose main chains. Accordingly, the basic properties of cellulose cinnamate derivatives are strongly affected by the distribution of the substituents. The information concerning the thermal behaviors in this study could provide fundamental understanding to those wishing to modify physicochemical processes, leading to desired functional bio-based materials such as photo-sensitive materials and interpenetrating polymeric materials.

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