

CRYSTAL OR ORDERED STRUCTURES OF CHITOSAN DERIVATIVES

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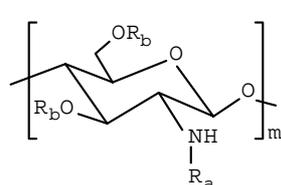
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Key words: crystal, ordered structure, chitosan derivatives

INTRODUCTION

Chitosan is a well known crystalline natural polymer. Most chitin has the α -crystal form but the β -chitin form appears mainly in the pen of squid. Despite the different structures, they are found to form the same crystal structure of chitosan after alkali-treatment. Chitosan, but not chitin, can be easily dissolved in acid solutions. Therefore, it is easy to prepare fibers, beads, or films from chitosan solutions. At that time, polymorphs of solvated chitosan crystals appear [1,2]. While lyotropic liquid crystals are obtained from concentrated chitosan solutions [3], some chitosan derivatives also form liquid crystals [4]. Meanwhile, partial N-acetylation affords amorphous chitosan with water-solubility [5].

From a chemical point of view, a variety of molecular designs has been made with chitosan to possess characteristic properties. Among them, the following are attractive; N-acyl chitosan gels with selective sorption of D, L-amino acid [6], benzoyl chitosan membrane with permselectivity [7] and N-acyl chitosan with long fatty acyl chains [8] available as a drug delivery system. In this way, chemical modification has led the application of chitosan but the relationship between chemical properties and certain ordered structure of chitosan derivatives has not yet been clarified. In this study, we



	R_a	R_b
Chitosan	H	H
C_n -CS	$-\text{CO}(\text{CH}_2)_{n-2}\text{CH}_3$	H
C_n -CinCS	$-\text{CO}(\text{CH}_2)_{n-2}\text{CH}_3$	$-\text{COCH}=\text{CH-Phenyl}$

discuss the structure of acyl chitosan derivatives (N- and N,O-acyl chitosans) as well as their solubility in common organic solvents.

EXPERIMENTAL AND RESULTS

Syntheses of structures of acyl chitosan derivatives

N-acyl chitosans (C_n -CS) having aliphatic ($C_nH_{2n-1}O$; $n = 2, 4, 8, 12$ and 18) side groups were prepared by treating chitosan powder ($M_v=1,090,000$, $DAC=97\%$) and acyl anhydrides in 10% acetic acid and methanol as previously reported [9]. *N,O*-acyl chitosans (C_n -CinCS) having both aliphatic and aromatic (cinnamoyl) side groups were prepared by a two-step method using an *O*-dicinnamoyl chitosan (prepared by an amino protection method through methanesulfonic acid) as a precursor [10].

The chemical structures of the acyl chitosans were identified by IR and NMR (500 MHz for 1H NMR) experiments. The degree of substitution (DS) per a glucosamine unit was evaluated by 1H NMR and IR measurements. The DS of cinnamoyl groups is 2.0, and that of aliphatic chains at N position is almost 1.0 (see Table 1).

Table 1. Characterization results of acyl chitosans

Code	Substituent (DS)	
	R_a	R_b
C_2 -CinCS	-COCH=CH-Phenyl (2.0)	-COCH ₃ (1.0)
C_4 -CinCS	-COCH=CH-Phenyl (2.0)	-CO(CH ₂) ₂ CH ₃ (1.0)
C_8 -CinCS	-COCH=CH-Phenyl (2.0)	-CO(CH ₂) ₆ CH ₃ (1.0)
C_{12} -CinCS	-COCH=CH-Phenyl (2.0)	-CO(CH ₂) ₁₀ CH ₃ (0.9)
C_{18} -CinCS	-COCH=CH-Phenyl (2.0)	-CO(CH ₂) ₁₆ CH ₃ (0.9)
C_2 -CS	—	-COCH ₃ (0.8)
C_4 -CS	—	-CO(CH ₂) ₂ CH ₃ (0.9)
C_8 -CS	—	-CO(CH ₂) ₆ CH ₃ (0.9)
C_{12} -CS	—	-CO(CH ₂) ₁₀ CH ₃ (1.0)
C_{18} -CS	—	-CO(CH ₂) ₁₆ CH ₃ (0.8)

Solid state structures

C_n -CinCS series

The WAXD profiles of C_n -CinCS are shown in Figure 1. All of the samples gave a broad halo at the wide-angle region (ca. $2\theta=20^\circ$), suggesting this type of acyl chitosans is substantially amorphous. However, a fairly sharp peak also appears at lower angles except C_2 -CinCS. The results imply that these polymers form layered structures associated by the interaction of the hydrophobic alkyl chains. From the plot of the spacing vs. the number of the carbon atoms (n) of the aliphatic chains (Figure 2), the increment of the layer spacing was estimated to be 0.08 nm, corresponding to the increase of “one carbon atom” in the aliphatic chain. Based on these results, such a layered mesophase structure is proposed for the C_n -CinCS (Figure 3), in which the rigid polymer backbones associate into a layered array, while those aliphatic side chains occupy the spaces between layers. Taking it into account that the increment of 0.08 nm is less than the corresponding length of 0.125 nm calculated for the case that the

aliphatic chains are extended and completely interdigitated, the flexible side chains between the layers may be highly interdigitated and tilted with respect to the layer sheet.

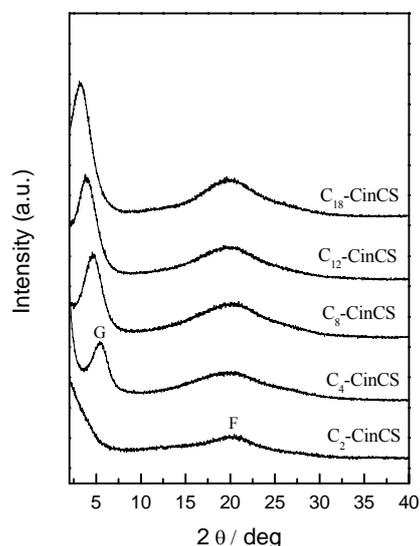


Fig. 1 WAXD profiles of C_n -CinCS.

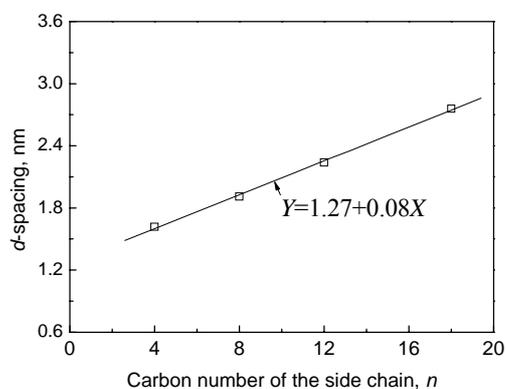


Fig. 2 d -spacing vs. carbon atom, n , of the aliphatic side chain. C_n -CinCS.

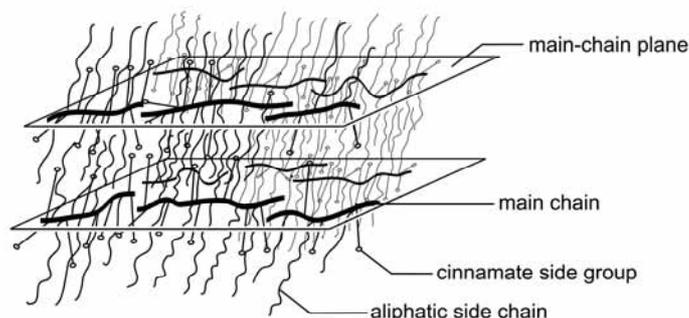


Fig. 3 A layer model of molecular arrangement in C_n -CinCS.

C_n -CS series

WAXD profiles of C_n -CS, together with that of α -chitin, are displayed in Figure 4. Each of C_n -CS gave rise to the crystalline reflections similar to those of α -chitin. The fact suggests that these polymers are semi-crystalline. As a matter of fact, from the IR measurements, the absorption bands due to NH and OH stretching of C_n -CS remain at the same positions (3270 cm^{-1} and $3450, 3110\text{ cm}^{-1}$, respectively) as in α -chitin. Therefore, it can be considered that every C_n -CS forms the same H-bond networks as α -chitin, so that each one has the similar orthorhombic unit cell of crystal. Moreover, the reflection peaks (corresponding to the (020) plane of α -chitin) shifts to lower angles

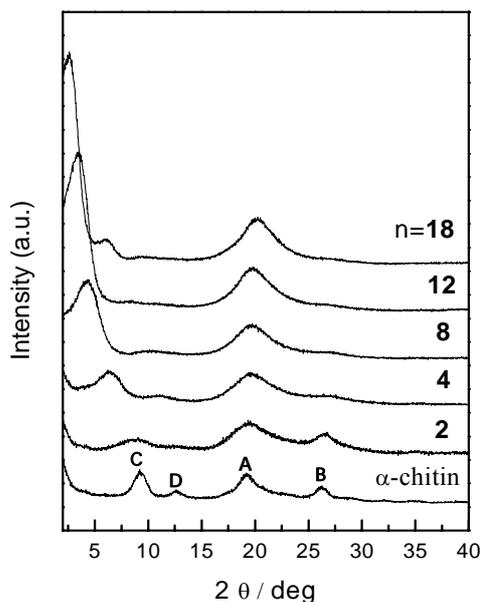


Fig. 4 WAXD profiles of C_n -CS.

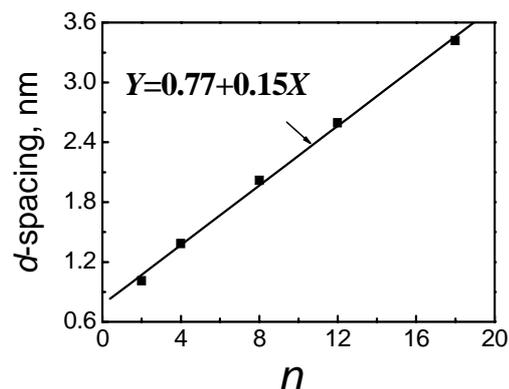


Fig. 5 d -spacing vs. carbon atom, n , of the aliphatic side chain. C_n -CS.

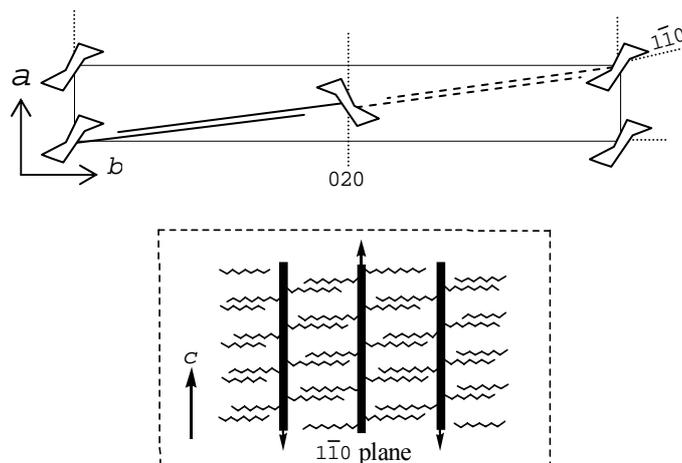


Fig. 6 A potential model for molecular arrangement in C_n -CS.

as the number of n increases. The corresponding spacings of (020) plane are plotted against n (see Figure 5), from which the increment of the spacing is estimated to be 0.15 nm per a carbon atom. This value is a little larger than the length of 0.125 nm in the extended chain. As a result, C_n -CinCS is considered to keep the crystal system of orthorhombic, in which the aliphatic side chains are partially interdigitated between the corner and the center backbone chains along the $(1\bar{1}0)$ plane or (110) plane (Figure 6).

Solubility

As C_n -CinCS are hydrophobic and substantially amorphous, they exhibited pretty good solubility in common organic solvents, including chloroform, dichloromethane, THF, dioxane, DMF, DMAc, DMSO, and so on. However, the reduction tendency was also observed in the solubility with an increase of the side chain length. In comparison, C_n -CS were non-soluble in the above organic solvents due to the compact crystal form as well as the strong H-bonds and the interactions of hydrophobic groups.

Thermal property

Figure 7 shows the thermoregulated WAXD profiles of C_{12} -CinCS recorded at 10 °C interval from 20 °C to 210 °C. While heating the sample, the broad halo remains almost unchanged, but the peak intensity at the lower angle gradually increases up to about 170 °C and then decrease up to 210 °C. The variation of the intensity of lower-angle peak may be due to the glass transition (T_g) of the amorphous polymer.

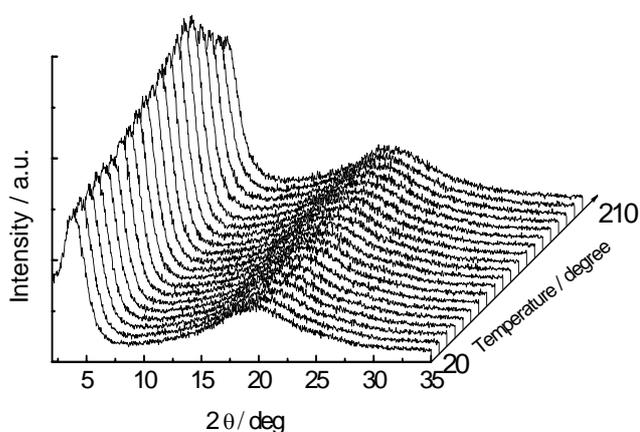


Fig. 7 Thermoregulated WAXD profiles of C_{12} -CinCS measured at 10 °C interval.

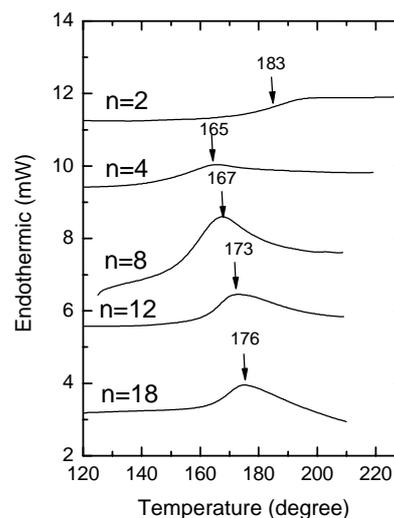


Fig. 8 DSC thermograms of C_n -CinCS (second heating scans).

Figure 8 shows the DSC thermograms of C_n -CinCS recorded for the second heating process. The observed endothermic peaks can be considered to be the glass transition temperatures. In the case of C_{12} -CinCS, the peak was observed at 173 °C, which is in good agreement with the thermoregulated WAXD measurement. Of particular interest for the C_n -CinCS system is the finding that they displayed flowability at higher temperature over T_g .

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