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PREPARATION OF CHITIN-*P*-TOLUENESULFONATE AND DEOXY(THIOCYANATO) CHITIN

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Abstract—Chitin-*p*-toluenesulfonate(tosyl-chitin) was prepared homogeneously in lithium chloride-N,N-dimethylacetamide (LiCl/DMAc). In this solvent system, the side reaction of O-acetylation often occurred by solvolysis of *p*-toluenesulfonyl(tosyl) chloride. The utilization of strong base either triethylamine or 4-dimethylaminopyridine, leads to highly tosylated chitin, with minimal incorporation of an O-acetyl group. Similar results were found in the substitution of N-methylpyrroridone (NMP) for DMAc. Chitin-4(methylamino)butylate was obtained with a pyridine catalyst. The degree of tosylation increased with increasing amount of tosyl chloride and became constant above 1. Tosyl-chitin obtained at high reaction temperature was highly chlorinated. The tosyl-chitin with high degree of substitution was readily soluble in various polar organic solvents such as dimethylsulfoxide (DMSO) and N,N-dimethylformamide (DMF). By X-ray analysis, it was observed that the crystallinity of tosyl-chitin became low as the reaction proceeded. Treating tosyl-chitin with potassium thiocyanate in DMSO produced deoxy(thiocyanato)chitin.

1. INTRODUCTION

Chitin has considerable interest because of its abundance and wide range of properties. The progress of chemical modifications and utilizations is quite slow because of lack of solubility in organic solvents. Chitin derivatives have mainly been prepared in strong acid or alkali solution, but these solvents cause extensive depolymerization and deacetylation. LiCl/DMAc is known as a non-degrading solvent of cellulose [1] and chitin [2], but only a few papers are reported about this solvent [3, 4].

As the *p*-toluenesulfonyl(tosyl) group is a good leaving group, many reports about tosyl-cellulose and their properties have been reported [5–8]. There are few reports with chitin [4, 9, 10]. Terjebovich *et al.* [4] attempted to synthesize tosyl-chitin in this solvent, but the degree of tosylation (DS) was very low [4]. For controlled modification of chitin, we need tosyl-chitin with high DS.

From these points of view, we studied the tosylation in the LiCl-DMAc homogeneous system. We have also examined the influences of various factors to obtain highly tosylated chitin, and some characteristics such as solubility and crystallinity were investigated. Utilizing the high reaction potential of tosyl-chitin, we prepared deoxy(thiocyanato)-chitin as a novel chitin derivative.

2. EXPERIMENTAL

2.1. Chitin sample and reagent

The chitin sample provided by Kyowa-Yushi Co. Ltd was pulverized to 40 mesh. Then, the powder was extracted with methanol at 60°C for 24 hr in a Soxlet extractor. The degree of deacetylation was 0.04 as determined by elemental analysis. Pyridine was dried with BaO and distilled. Reagent grade N,N-dimethylacetamide (DMAc) and N-methylpyrroridone (NMP) were dried with molecular sieves (3A). Other chemicals were of reagent grade and used without further purification.

2.2. Chitin solution

Chitin (3.0 g, 1.48×10^{-2} mol) was placed in a 500 ml three-necked flask equipped with nitrogen inlet/outlet and a magnetic stirrer. To this was added 100 ml of 5% (w/w) LiCl/DMAc solvent and stirred at 10°C for 20 min with nitrogen sparging. All subsequent reactions were performed under nitrogen atmosphere.

2.3. Tosylation of chitin

2.3.1. Chitin-p-toluenesulfonate(tosyl-chitin). To 10 ml of chitin solution (0.3 g of actual chitin weight) was added triethylamine (7.2 ml, 5.19×10^{-2} mol). Then a solution of tosyl chloride (9.86 g, 5.14×10^{-2} mol) in DMAc (10 ml) was added dropwise to this reaction mixture.

The reaction was carried out at 10°C for 24 hr. The reaction mixture was precipitated into cold water, filtered and dried *in vacuo* (yield 0.54 g, DS 1.07; anal. calc. for C, 48.69; H, 5.48; N, 3.93; S, 9.60: found C, 47.87; H, 5.43; N, 3.89; S, 9.48).

If the product was not precipitated with water, the reaction mixture was dialyzed, concentrated and freeze-dried. Then, the obtained powder was dried *in vacuo*.

2.3.2. Chitin-4-(methylamino)butylate. Chitin (0.50 g, 2.46×10^{-3} mol) was dissolved in 5% (w/w) LiCl/NMP (45 ml). To the chitin solution, pyridine (1.4 ml, 1.70×10^{-2} mol) and then a solution of tosyl chloride (3.4 g, 1.78×10^{-2} mol) in NMP (5 ml) was added. The reaction was performed at 10°C for 24 hr. After this period, the polymer was precipitated into acetone and filtered off.

The product (0.55 g) was dissolved in water (100 ml) and stirred at 25°C for 24 hr. Then the mixture was dialyzed, concentrated and freeze-dried. Then the white powder was dried *in vacuo* (yield 0.54 g, DS 0.17; anal. calc. for C, 45.23; H, 6.17; N, 6.77: found C, 45.54; H, 6.26; N, 6.77).

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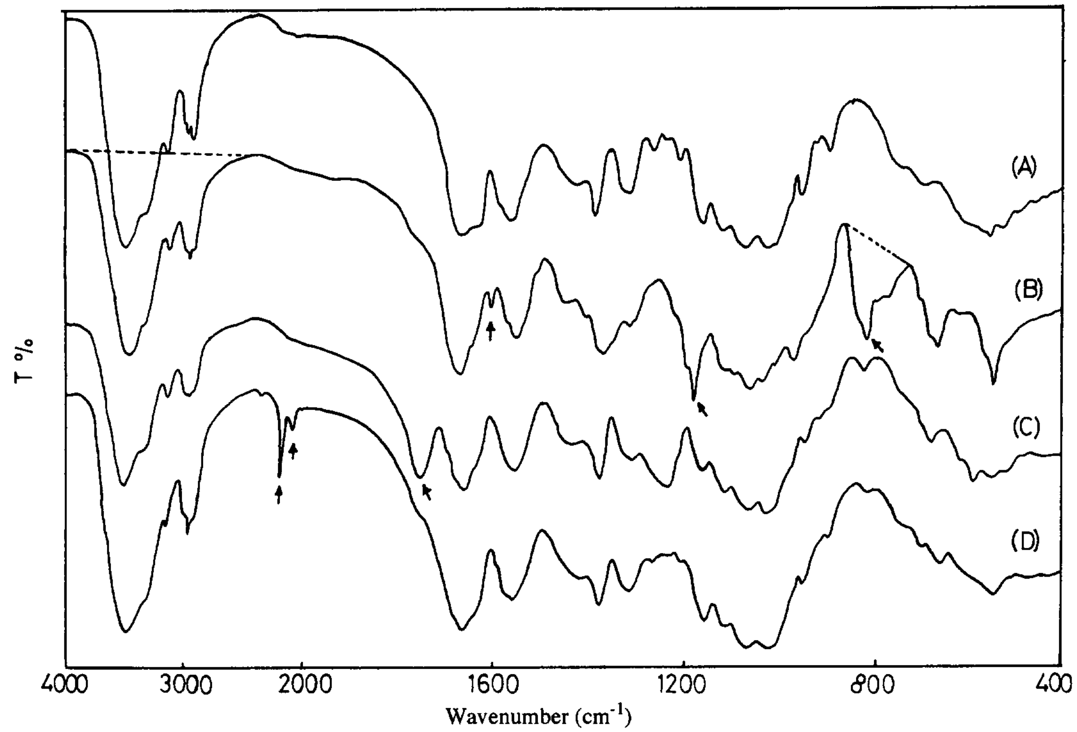


Fig. 1. i.r. spectra. (A) Chitin, (B) tosyl-chitin (DS 0.90), (C) tosyl-chitin (DS 0.10), (D) SCN-chitin (DS 0.42).

2.4. *Deoxy(thiocyanato)-chitin(SCN-chitin)*

Tosyl-chitin (0.20 g, DS 0.60) was dissolved in DMSO (10 ml) at 80°C for 20 min with stirring, then a solution of potassium thiocyanate (0.63 g, 6.49×10^{-3} mol) in DMSO (10 ml) was added to the reaction mixture. The reaction was conducted at 120°C for 3 hr with stirring. Then the reacted mixture was precipitated into acetone, filtered off and dried *in vacuo* (yield 0.12 g, DS 0.42; anal. calc. for C, 41.41; H, 5.46; N, 10.32: found C, 40.46; H, 5.03; N, 7.88.

2.5. *Analysis*

i.r. spectra were recorded with a Nihon-bunko A202 with the KBr method and film technique. X-ray diffraction diagrams were measured with a Rigaku Geiger-Flex instrument. Elemental analysis for sulfur and chlorine was carried out at Tokyo College of Pharmacy.

3. RESULTS AND DISCUSSION

3.1. *Preparation of tosyl-chitin*

The tosyl-chitin obtained was a white-yellow powder and became brown as DS increased. In spite of different reaction conditions, the yields of tosyl-chitin were all above 90%. Figure 1 shows the i.r. spectra of tosyl-chitin which has typical peaks at 810(C—O—S), 1180(SO_2) and 1600 (aromatic C=C)cm^{-1} arising from the tosyl-group. The absorbance ratio (D_{810}/D_{2891}) was determined by the baseline method as shown in Fig. 1 (2891 cm^{-1}, pyranose C—H). The relation between the absorbance ratio and DS by elemental analysis shows a linear dependence as presented in Fig. 2. The degree of tosylation was calculated with the following equation:

$$\text{degree of tosylation} = 0.56(D_{810}/D_{2891}) + 0.02.$$

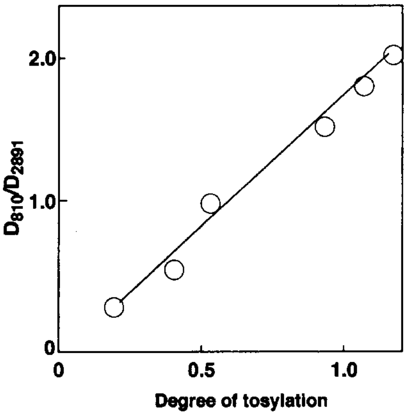
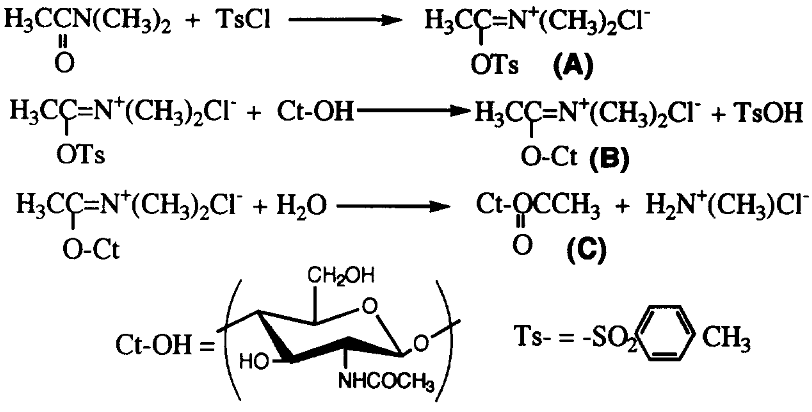


Fig. 2. Calibration line to determine the degree of tosylation.

Table 1. Solubility of tosyl-chitin and SCN-chitin

Derivatives	DS	DMSO	DMF	DMAc	HMPA	CH_3Cl	H_2O	CH_3OH	HCOOH
Tosyl-chitin	0.10	±	±	±	+	±	±	±	+
Tosyl-chitin	0.52	+	±	+	+	±	−	−	+
Tosyl-chitin	1.09	+	+	+	+	±	−	−	+
SCN-chitin	0.42	+	+	+	−	±	−	−	+

+ : Soluble; − : insoluble; ± : swelled or partially soluble.



Scheme 1

The solubility of tosyl-chitin, as shown in Table 1, appeared to be much higher than that of the original chitin. The tosyl-chitin with DS above 0.5 became hydrophobic and was completely soluble in common polar organic solvents like DMSO and DMF. Even though DS was low, it was highly swelled with such solvents and water.

3.1.1. Effect of catalyst. Derivatization of cellulose utilizing LiCl/DMAc, side reactions often occurred because the reagent reacted with DMAc (solvolysis) [8, 11]. We examined first the tosylation of chitin with pyridine as catalyst. Even if a high concentration of pyridine and tosyl-chloride were used, DS was very low. From i.r. spectra, the peaks arising from tosyl groups are very weak, but strong peaks of O-acetyl group appear. These results suggest that solvolysis occurred.

Our proposed pathway is shown in Scheme 1. Via a Vilsmeier-Haak type reaction, an iminium salt (**A**) can react with a hydroxyl group instead of a tosyl group and produced charged iminium species [(**B**): chitin-N,N-dimethylacetamidiminium chloride]. Then (**B**) is easily hydrolyzed to an O-acetyl group (**C**). The degree of O-acetylation was 0.27 as determined by the Eberstadt method [12].

As shown in Table 2, tosylation was highly achieved with a strong base such as triethylamine and 4-dimethylaminopyridine, and the peaks of the O-acetyl group were not observed. But for a catalyst of low pKa, such as pyridine and N,N-dimethylaniline, DS was under 0.10. Thus, O-acetylation was reduced with these strong bases, when highly tosylated chitin would be obtained.

3.1.2. Effect of tosyl-chloride concentration. Figure 3 shows the relation between DS and the concentration of tosyl-chloride. DS increased with increasing tosyl-chloride, and leveled off about 20 M tosyl-chloride per pyranose unit (the maximum DS was 1.2).

The reason is that two hydroxyl groups of chitin have different reactivity. The C-6 hydroxyl group exchanged more easily by the tosyl-group than the

Table 2. Effect of base strength on tosylation

Catalyst	pKa	Degree of tosylation*
Triethylamine	10.65	0.86
4-Dimethylaminopyridine	9.70	0.58
Pyridine	5.25	0.10
N, N-dimethylaniline	5.15	0.02

*Determined by calibration line.
Chitin = 0.3 g, 5% (w/w) LiCl/DMAc 10 ml, [catalyst]/[pyranose] = 35 [tosyl-chloride]/[pyranose] = 12, 10 °C, 24 hr.

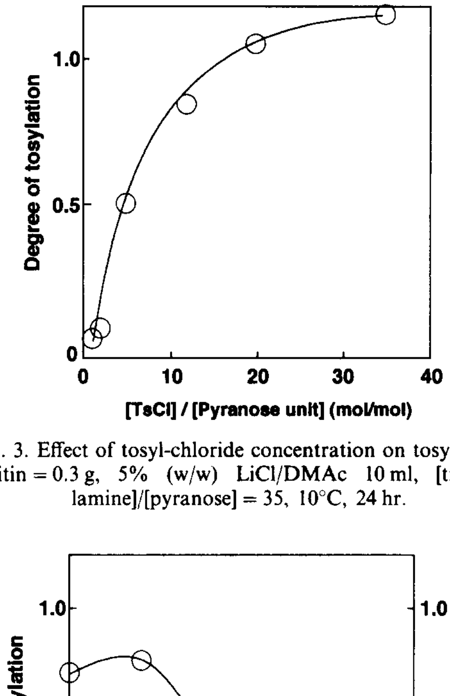


Fig. 3. Effect of tosyl-chloride concentration on tosylation. Chitin = 0.3 g, 5% (w/w) LiCl/DMAc 10 ml, [triethylamine]/[pyranose] = 35, 10°C, 24 hr.

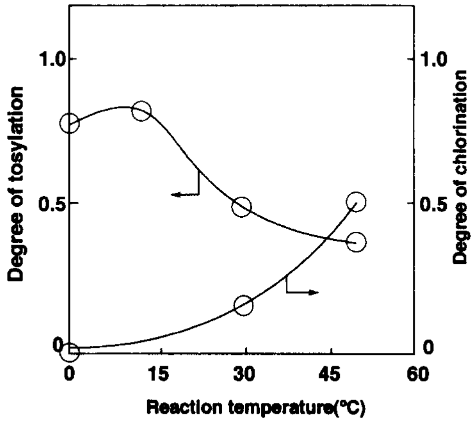
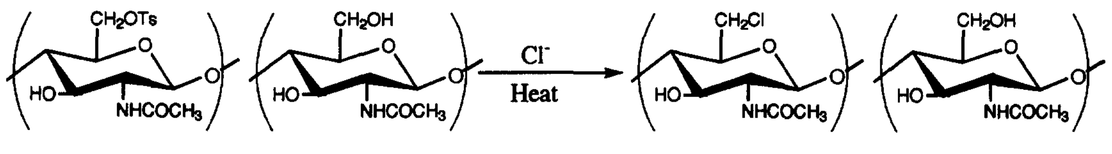


Fig. 4. Effect of reaction temperature on tosylation. Chitin = 0.3 g, 5% (w/w) LiCl/DMAc 10 ml, [triethylamine]/[pyranose] = 35, [tosyl-chloride]/[pyranose] = 35, 4 hr.



Scheme 2

C-3 hydroxyl group. Since an amino group is less nucleophilic than hydroxyl groups, N-tosylation occurs rarely. In the case of tosylation with alkali-chitin [9, 10] or acylation of chitin in trichloroacetic acid-dichloroethane solvent [13], the maximum DS values were also about 1.

3.1.3. Effect of reaction temperature. Many literature reports indicate that substitution reactions with tosyl-cellulose occur at high temperature. Figure 4 presents the relation between the reaction temperature and the degree of substitution. The degree of tosylation was maximum at 10°C, and then decreased at a higher temperature. The degree of chlorination increased with increasing reaction temperature. Above 50°C, chlorination was superior to tosylation. In all reaction conditions under 10°C, incorporation of chlorine was below 0.05.

As shown in Scheme 2, elevating the temperature led to displacement of tosyl group by chlorine ion and produced chlorodeoxychitin. This partially chlorinated tosyl-chitin prepared at 50°C was also soluble in methanol and could be cast as a transparent film.

3.1.4. Effect of reaction time. Next, the relation between the reaction time and DS was investigated. As shown in Fig. 5, DS increased rapidly to 0.8 within 4 hr and then increased very slowly. Though the reaction continued for 48 hr, DS reached only 1.17. This suggests that two hydroxyl groups have a different reactivity as described above.

3.1.5. Effect of lithium chloride concentration. Lithium chloride is necessary for chitin to dissolve in DMAc. Thus the relation between LiCl concentration in DMAc and DS was examined for a homogeneous reaction (Fig. 6).

Chitin cannot be soluble in DMAc, but its solubility in DMAc increases with an increasing amount of LiCl. In this case, the reaction system became more homogeneous. The result shows that the increase of DS depended on LiCl concentration. But above 10 wt% of LiCl, DS decreased again.

It was confirmed that LiCl and DMAc were coordinated with hydoxyl groups of chitin by ^{1}H-NMR studies [14, 15]. This would reduce hydrogen bonds between hydroxyl and acetamide groups. Therefore, an excess concentration of LiCl led to steric hindrance to yield tosyl-chitin with low DS.

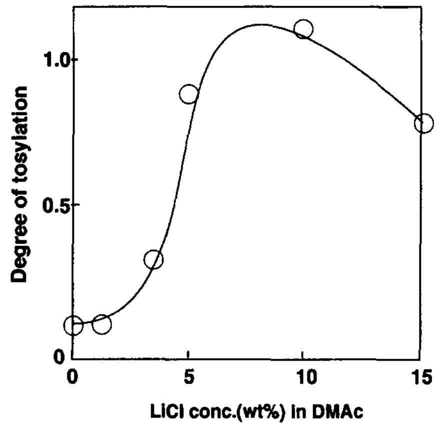


Fig. 6. Effect of lithium chloride concentration on tosylation. Chitin = 0.3 g, LiCl/DMAc 10 ml, [triethylamine]/[pyranose] = 35, [tosyl-chloride]/[pyranose] = 35, 10°C, 24 hr.

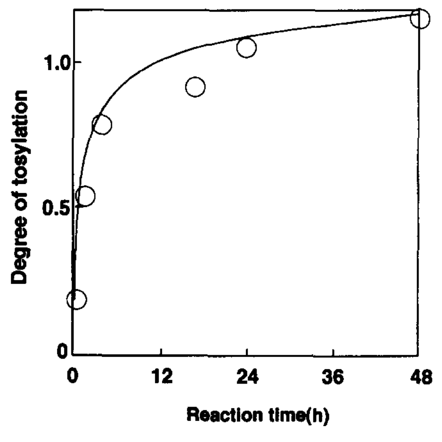


Fig. 5. Effect of reaction time on tosylation. Chitin = 0.3 g, 5% (w/w) LiCl/DMAc 10 ml, [triethylamine]/[pyranose] = 35, [tosyl-chloride]/[pyranose] = 35, 10°C.

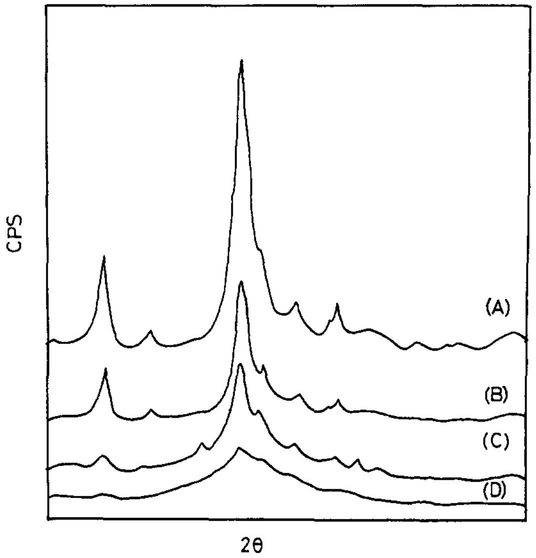
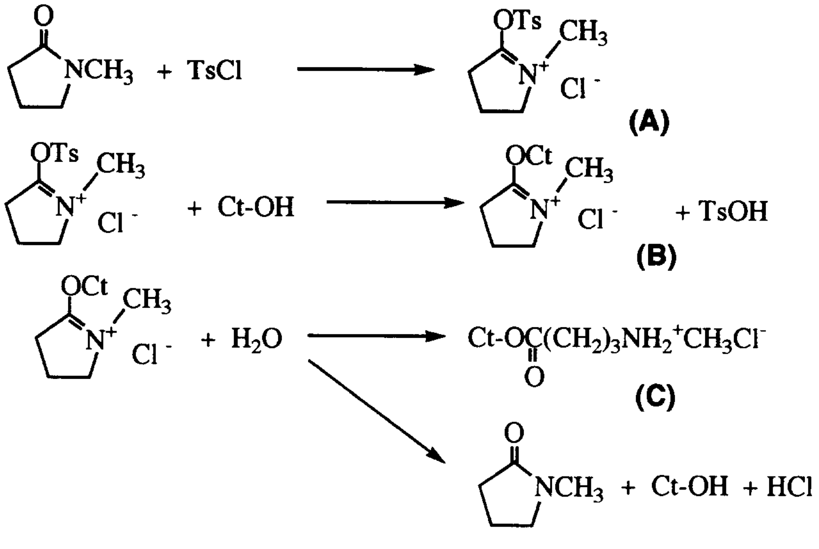
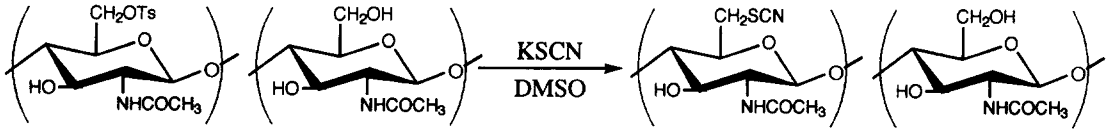


Fig. 7. X-ray diffraction diagrams. (A) chitin, (B) tosyl-chitin (DS 0.10), (C) tosyl-chitin (DS 0.52) and (D) tosyl-chitin (DS 1.17).



Scheme 3



Scheme 4

3.1.6. Tosylation in LiCl/NMP solvent. LiCl/NMP similar to LiCl/DMAc is also known to be a chitin solvent. Using triethylamine and 4-dimethylaminopyridine, tosylation was successfully achieved in a similar manner to LiCl/DMAc. But with pyridine catalyst in this solvent, chitin-4(methylamino) butylate was obtained. This derivative had no tosyl-groups and the degree of 4-(methylamino)butyl group was 0.17. The considered reaction pathway is shown in Scheme 3. The solvolysis of tosyl-chloride by NMP occurred to yield an iminium salt (**A**) that reacted with a hydroxyl group of chitin. This cyclic–iminium–chitin derivative (**B**) was easily hydrolyzed to give chitin-4(methylamino) butylate (**C**). Another route would regenerate NMP and underivatized chitin [16]. The derivative (**A**) had high solubility not only in DMSO and DMF but also in water.

3.1.7. Crystallinity of tosyl-chitin. Figure 7 shows X-ray diffraction diagrams of tosyl-chitin. The crystallinity of tosyl-chitin drastically decreased with an increase of DS. The reason is that the tosyl-group is sufficiently bulky in contrast to the hydroxyl group.

3.2. Preparation of SCN-chitin

Because tosyl-chitin has high solubility, it may become a good intermediate for further chemical modifications. Tosyl-chitin is completely soluble in DMSO. Therefore, by treating with potassium thiocyanate in an homogeneous solution, a deoxy(thiocyanato) group easily substituted a tosyl group as shown in Scheme 4. The SCN-chitin obtained was a yellow powdery product and the yield based on tosyl-chitin was about 70–85%. In the case of the derivatization from tosyl-chitin with DS 0.60, the degree of SCN-groups was determined by elemental analysis to be 0.42. This substitution reaction proceeded at a high temperature above 80°C. At a lower temperature, a tosyl group was not substituted completely. i.r. spectra (Fig. 1) showed that SCN-chitin had no absorption of tosyl groups but the new peak arising from SCN groups appeared at $2270\,\mathrm{cm}^{-1}$. It indicates that most of the tosyl groups were displaced by SCN groups. The peak at $2170\,\mathrm{cm}^{-1}$ is attributed to the isothiocyanate group (C=N=S), that also appeared in the case of deoxy(thiocyanato) cellulose [17]. SCN-chitin was more soluble than tosyl-chitin (Table 2); therefore, SCN-chitin proved to be valuable for subsequent derivatization. Now, we are examining various reaction conditions for preparation of SCN-chitin in detail and also the graft copolymerization of vinyl monomer onto it. The results will be soon reported.

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