NOTES

Preparation of Chitosan Derivatives. Synthesis of *N*-Schiff Base Type and *N*-Secondary Amino Type Chitosan-Crown Ethers

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Chitin, obtained mainly from the cuticle of a marine crustacean, has recently aroused great interest in industrial and medical applications, owing to its specific structures and properties. Chitosan, which is a linear polymer of (1→4)-linked-2-amino-2-deoxy-D-glucopyranose easily derived from chitin by *N*-deacetylation, appears more useful than chitin, since it has both hydroxyl and amino groups that can be modified easily. Many research groups have reported on the preparation of chitosan derivatives.^{1,2} Attempts have been made to use chitosan for hemodialysis membranes,³ biocompatible materials,⁴ biodegradable sutures,⁵ and artificial skin substitutes.⁶ Although many chitosan derivatives have been prepared,^{7,8} the preparations of chitosan-crown ethers have not been reported yet.

At first, we prepared 4'-formyl benzo-15-crown-5 and 4'-formyl benzo-18-crown-6. The *N*-Schiff base type chitosan-crown ethers were obtained by the reaction of chitosan, and then the *N*-secondary amino type chitosan-crown ethers were prepared by the reaction of the *N*-Schiff base type chitosan-crown ethers with sodium borohydride.

As they have particular molecular structure, crown ethers have good complex selectivity for many metal ions. Because chitosan crown ethers have the structures and corresponding properties of both chitosan and crown ethers compounds, they have wide range of application prospect for the separation and concentration of heavy or precious mental ions.

EXPERIMENTAL

Materials

Chitosan, whose deacetylation was calculated to be 80% from amino content, was prepared by *N*-deacetylation of chitin from shrimpshells and was used after through 200 mesh sieve.

All inorganic compounds were of reagent grade and all solvents and available organic materials were commercial products used without purification.

3,4-Dihydroxy benzaldehyde was purchased from the First Chemical Factory in Shanghai (China).

Dichloro-ethers were prepared by this general method reported before.^{9,10} The yields were usually good.

4'-Formyl benzo-15-crown-5 and 4'-formyl benzo-18-crown-6 were prepared by the same procedure as described before.¹¹

Characterization

Elemental analysis was conducted on Perkin-Elmer automatic instrument, Infrared spectra were measured on a Nicolet 5DX FT-IR spectrophotometer, wide-angle X-ray diffraction patterns were recorded with a film camera using nickel-filtered Cu-*K*_α radiation produced by a Rigaku (D/MAX, 111A) diffractometer; Solid-state ¹³C NMR was conducted using BROKER MSL-400 model NMR machines, proton and carbon frequencies were 400 MHz and 100 MHz, respectively.

Preparation of Chitosan-Crown Ethers

Figure 1 shows the synthetic routes of chitosan-crown

Figure 1. Reaction scheme for the synthesis of chitosan derivatives (I–IV): The *N*-Schiff base type chitosan-crown ethers (*n* = 1 for crown ether, I; *n* = 2 for crown ether, II) and the *N*-secondary amino type chitosan-crown ethers (*n* = 1 for crown ether, III; *n* = 2 for crown ether, IV).

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ethers (I–IV).

Preparation of *N*-Schiff Base Type Benzo-15-Crown-5 Chitosan (I). Powdered chitosan (1.5 g) was dissolved in 100 ml of 10 wt% acetic acid and diluted with ethanol. 3.0 g 4'-formyl benzo-5-crown-5, dissolved in 20 ml ethanol, were slowly dropped into the chitosan solution under nitrogen. The mixture was refluxed with good agitation for 24 h to obtain a sticky solution, which was stored in an oven at 80°C for several hours to gain 4.0 g light brown solid, and then the product was washed thoroughly by Soxhlet's extraction with ethanol to remove any unreacted 4'-formyl benzo-15-crown-5 and dried to give **I** (89%).

Preparation of *N*-Schiff Base Type Benzo-18-Crown-6 Chitosan (II). This compound was prepared from 4'-formyl benzo-18-crown-6 and chitosan by the same procedure as described for **I**. The product was obtained in 80% yields.

Preparation of *N*-Secondary Amino Type Benzo-15-Crown-5 Chitosan (III). Following the procedure of **I**, a sticky solution was obtained and 1.0 g sodium borohydride dissolved in 20 ml ethanol was slowly dropped in the solution. The mixture was refluxed for another 6 h and dried to obtain a faint yellow solid. The product was successively washed by Soxhlet's extraction with ethanol to remove any unreacted 4'-formyl benzo-15-crown-5 and sodium borohydride, dried to give **III** (90%).

Preparation of *N*-Secondary Amino Type Benzo-18-Crown-6 Chitosan (IV). This compound was prepared from 4'-formyl benzo-18-crown-6, chitosan and sodium borohydride by the same procedure as described for **III**. The product was obtained in 82% yield.

RESULTS AND DISCUSSION

N-Schiff base type chitosan-crown ethers were light brown and the *N*-secondary amino type chitosan-crown ethers were yellow in color. All these chitosan derivatives did not dissolved in organic solvents such as dimethylsulfoxide (DMSO), chloroform, formamide, and dimethylformamide (DMF), but they were swollen in acetic acid solution.

Elemental Analysis

Table I shows the elemental analysis and degree of substitution (DS) of chitosan and chitosan derivatives. The nitrogen content of chitosan-crown ethers was much lower than that of chitosan. It was thought that the decrease was attributed to the presence of the Schiff base type or the secondary amino type benzo-crown ethers groups produced in the course of the reaction of chitosan with 4'-formyl benzo-crown ethers. It could also be seen N% of **III** was higher than that of **I**, it was because DS of **I** was higher than that of **III**.

Figure 2 shows the infrared spectra of chitosan and chitosan derivatives. Although marked differences were not observed in the IR spectra, characteristic peaks of C=N stretch vibration appeared at 1640 cm⁻¹ for **I** and **II**, owing to the presence of the Schiff base groups produced in the course of the reaction (from chitosan to chitosan-crown ethers). Nothing that these characteristic peaks disappeared in **III** and **IV**, which demonstrated

Table I. Results of elemental analysis of chitosan and chitosan-crowns ethers

	Chitosan	Chitosan-Crown ethers			
		I	II	III	IV
N%	6.53	3.69	3.29	3.76	3.28
H%	6.89	6.32	6.66	6.57	6.61
C%	37.85	45.85	49.08	44.47	40.91
DS%		43.49	49.62	42.42	49.77

Figure 2. FT-IR spectra of the chitosan (a) and chitosan-crown ethers **I** (b), **II** (c), **III** (d), and **IV** (e).

that the Schiff base groups were completely reduced after treatment with sodium borohydride. The four chitosan derivatives had the characteristic peaks of aromatic backbone vibration at 1510 cm⁻¹ and the characteristic peaks of aromatic C-H out of plane deformation at 930 cm⁻¹ and 750 cm⁻¹ because of the presence of phenyl groups. It was also seen that chitosan and chitosan derivatives (**I**–**IV**) have the characteristic peaks of pyranil vibration at 900 cm⁻¹ caused by the presence of the chitosan backbone chain.

X-Ray Diffraction Analysis

Figure 3 shows the wide-angle X-ray diffraction (WAXD) patterns of chitosan and chitosan derivatives. WAXD patterns of chitosan showed the characteristic peak at 2θ = 10° due to the presence of (001) and (100) and at 2θ = 20° caused by the presence of (101) and (011). Noting that the peak at 2θ = 10° disappeared in chitosan derivatives (**I**, **II**) or decreased in chitosan derivatives (**III**, **IV**) and the peak at 2θ = 20° decreased in all chitosan

Figure 3. X-Ray diffraction patterns of chitosan (a) and chitosan derivatives **I** (b), **II** (c), **III** (d), and **IV** (e).

Figure 4. Solid-state ^{13}C NMR spectra of chitosan (a) and chitosan-crown ethers **I** (b), **II** (c), **III** (d), and **IV** (e).

derivatives, for chitosan-crown ethers **I** and **II**, the intensity of the peak at $2\theta = 20^\circ$ decreased more than that of chitosan crown ethers **III** and **IV**. It was thought that the decrease in crystallinity of chitosan derivatives was attributed to deformation of the strong hydrogen bond in chitosan backbone chain as the amino groups

were substituted by 4'-formyl benzo-crown ethers. The four chitosan-crown ethers gave a low crystallinity indicating that they were considerably more amorphous than chitosan.

Solid-State ^{13}C NMR Analysis

Figure 4 shows solid-state ^{13}C NMR spectra for chitosan and chitosan derivatives. Similar to IR analysis, characteristic aromatic carbon appeared at 128 ppm in all chitosan derivatives. The characteristic peak of carbon in $\text{C}=\text{N}$ groups appeared at 151 ppm in chitosan-crown ethers **I** and **II**. Noting that these peaks did not appear in the spectra of chitosan and chitosan-crown ethers **III** and **IV**. Changes in intensity were also noticeable for carbon in CH_2 groups at 70 ppm, as a consequence of the presence of crown-ether groups in the chitosan-crown ethers.

CONCLUSIONS

N-Schiff base type chitosan-crown ethers (**I** and **II**) were synthesized *via* Schiff-base reaction between amino groups in chitosan and 4'-formyl benzo-crown ethers. After treatment with sodium borohydride, the Schiff-base was reduced to *N*-secondary amino type chitosan-crown ethers (**III** and **IV**). The physical and chemical properties of chitosan-crown ethers were greatly improved by incorporation of benzo-crown ethers groups in chitosan. They did not dissolve in general organic solvent and could be powdered easily, thus having also more useful than chitosan.

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