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Note

Chitin xanthate and some xanthate ester derivatives

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A viscous orange-red aqueous solution of *O*-(sodium thio)thiocarbonyl cellulose (sodium cellulose xanthate) is well known as "viscose", which is an intermediate for the manufacture of rayon and cellophane [1–3]. *O*-(Sodium thio)thiocarbonyl starch (sodium starch xanthate) is also known [4]. Chitin and chitosan structurally resemble cellulose and are widely distributed as the main structural components in cuticles of crustaceans, insects, and mollusks, and in cell walls of microorganisms. Noguchi et al. [5] first reported *O*-(sodium thio)thiocarbonyl chitin [sodium chitin xanthate (**2**) (Fig. 1)] without detailed analytical data and attempted to use it for the preparation of chitin fibers and for a composite with cellulose. Since then, almost no studies have dealt with **2** and its derivatives. Compound **2** is a key intermediate for the preparation of novel composites or blended materials with other organic and inorganic compounds. For analysis of the chemical structure of **2**, which is quite unstable, it is desirable to convert it into stable derivatives. We now report the preparation and structural analysis of **2** by preparing its *O*-(benzylthio)thiocarbonyl and *O*-(alkylthio)thiocarbonyl derivatives.

In earlier methods [6–10] for the preparation of "alkaline chitin" (**1**), natural chitin was treated repeatedly with concentrated NaOH, resulting in an inefficient use of the alkaline solution. Recently, we found that *N*-acetylchitosan xerogel (a regenerated chitin) [11,12] was an excellent starting material for the preparation of **1** (alkaline *N*-acetylchitosan), because the xerogel has intramolecular hydrogen bonds weaker than natural chitin, resulting in easy solubilization into 14% aq NaOH, with little waste of the concentrated alkaline solution.

Compound **1**, in 14% aq NaOH, was treated with carbon disulfide (40 mol equiv NAc) to afford a viscous orange-red solution of **2**, which was unstable in EtOH, in MeOH, and in aq acetic acid, giving *N*-acetylchitosan. The chemical structure of **2**

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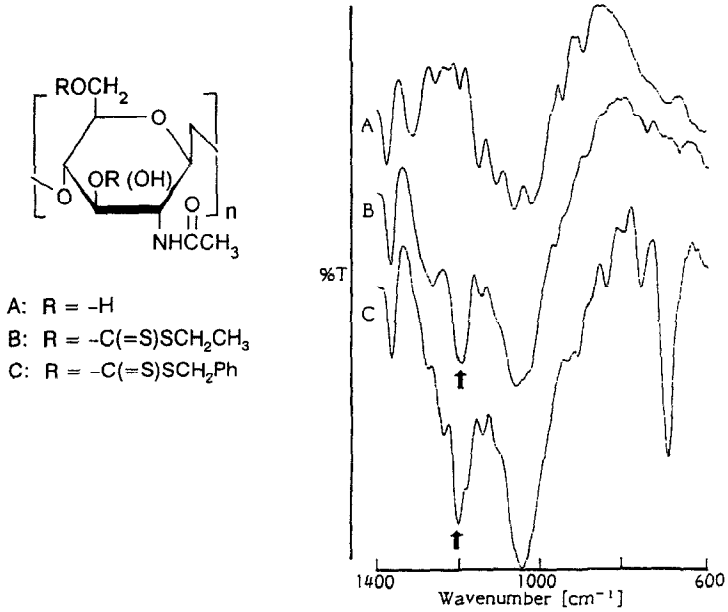


Fig. 1. FTIR spectra in the range of 144–600 cm^{-1} of *N*-acetylchitosan (A, **1**), *O*-(ethylthio)thiocarbonyl (B, **5**) and *O*-(benzylthio)thiocarbonyl (C, **3**) derivatives of *N*-acetylchitosan (**1**).

was analyzed by preparing a series of its derivatives. Compound **2** was treated with benzyl bromide, methyl iodide, ethyl bromide, *n*-propyl chloride, and *n*-butyl chloride under cooling to afford, as white, amorphous products in 71–89% yield, respectively: *O*-(benzylthio)thiocarbonyl (**3**, ds 1.1–1.6); *O*-(methylthio)thiocarbonyl (**4**, ds 1.5); *O*-(ethylthio)thiocarbonyl (**5**, ds 1.3); *O*-(*n*-propylthio)thiocarbonyl (**6**, ds 1.0); and *O*-(*n*-butylthio)thiocarbonyl (**7**, ds 1.8) derivatives of *N*-acetylchitosan. Initially, all of these products gave an orange-red color, but their repeated washing with MeOH gave rise to white, amorphous products. The products were treated with acetic anhydride in MeOH at room temperature for complete *N*-acetylation. The ds of 1.1–1.8 for the benzylthio and alkylthio groups, which was calculated from the elemental analysis data, indicates that the thiocarbonyl groups are present at C-6 and at C-3, since the ds for NAc at C-2 is 1.0. Therefore, the chitin xanthate has the structure of 3,6-*O*-(sodium thio)thiocarbonyl *N*-acetylchitosan. Compounds **3**–**7** were shown to swell only in *N*,*N*-dimethylformamide–5% LiCl, in *N*,*N*-dimethylacetamide–5% LiCl, and in 1-methyl-2-pyrolidone–5% LiCl, and were insoluble in 14% aq NaOH, water, MeOH, and EtOH.

In their IR spectra (Fig. 1), an absorption of –O–C(C=S)–S– at 1205–1221 cm^{-1} was characteristic of all the thiocarbonyl derivatives. An absorption for the monosubstitution of the benzyl group appeared at 700 cm^{-1} in the spectrum of **3**. In the ^{13}C CPMAS NMR spectra (Fig. 2), the ^{13}C-signal of the C=S in the thiocarbonyl group at 216.1–217.1 ppm was characteristic of all these compounds.

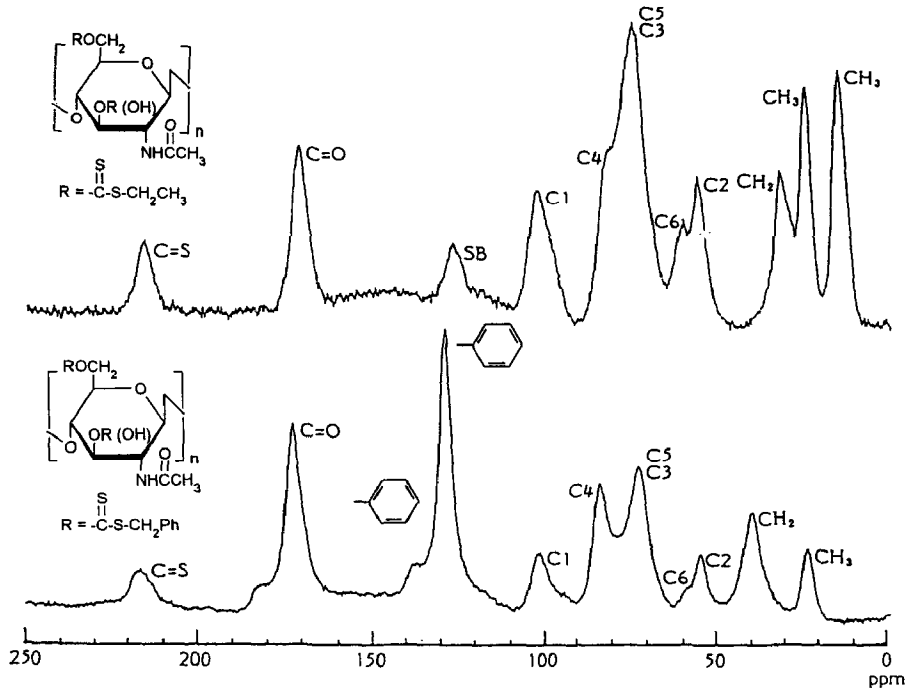
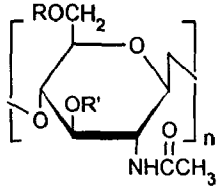


Fig. 2. ^{13}C CPMAS NMR spectra of *O*-(ethylthio)thiocarbonyl (upper trace, **5**) and *O*-(benzylthio)thiocarbonyl (lower trace, **3**) derivatives of *N*-acetylchitosan.

The ^{13}C-signals of the CH_2 and the CH_3 in the ethylthio group appeared at 32.4 and 15.1 ppm in the spectrum of **5**, while, in the spectrum of **3**, the ^{13}C signals of the phenyl group appeared at 135.2 and 192.4 ppm, and that of the CH_2 group in



1: R = R' = -H in 14% NaOH, "alkaline" *N*-acetylchitosan

2: R = -C(=S)S$^-$, Na$^+$; R' = -C(=S)S$^-$, Na$^+$ or -OH; sodium chitin xanthate

3: R = -C(=S)S-Bz, R' = -C(=S)S-Bz or -OH

4: R = -C(=S)S-Me, R' = -C(=S)S-Me or -OH

5: R = -C(=S)S-Et, R' = -C(=S)S-Et or -OH

6: R = -C(=S)S-Pr, R' = -C(=S)S-Pr or -OH

7: R = -C(=S)S-Bu, R' = -C(=S)S-Bu or -OH

the benzylthio functions appeared at 40.7 ppm. However, the ^{13}C-signals of C-1 through C-6, as well as the C=O and CH_3 of NAc, appeared at almost the same chemical shifts as those of *N*-acetylchitosan itself [13].

1. Experimental

Materials.—Crab-shell chitosan (ds 0.1 for NAc; mol wt ~300 000) was a product of Tsuchiyoshi Company, Shimane, Japan. *N*-Acetylchitosan gel was prepared by *N*-acetylation of chitosan with acetic anhydride in 2% aq acetic acid–MeOH [11], followed by lyophilization to afford the xerogel.

Methods.—^{13}C CPMAS NMR spectra were recorded on a CMX 360 solid-state NMR spectrometer, IR spectra on a Jasco FTIR 5300 spectrometer, and specific rotations on a Jasco Dip-181 polarimeter. Elemental analyses were performed at the Microanalytical Center, Kyoto University, Kyoto.

A solution of "alkaline" N-acetylchitosan ["alkaline chitin," (1)]. —A finely powdered sample (> 80 mesh) of *N*-acetylchitosan xerogel (1.0 g) was swollen in 35% aq NaOH (20 mL) at 4°C for 20 h. The swollen mass was stirred with crushed ice, and the volume was adjusted to 50 mL. The mixture was stirred for a few h in an ice-bath to give a clear solution of 2% "alkaline" *N*-acetylchitosan in 14% aq NaOH; $[\alpha]_D^{24}$ –32° (*c* 2, 14% aq NaOH).

O-(Sodium thio)thiocarbonyl N-acetylchitosan [sodium chitin xanthate, (2)].—Chitin xanthate (**2a**). Carbon disulfide (3 mL) was added dropwise to a solution (10 mL) of **1** in 14% aq NaOH, which was prepared from *N*-acetylchitosan (0.2 g). The mixture was stirred at room temperature for 24 h to afford a viscous orange-red solution of **2a**.

Chitin xanthate (**2b**). Carbon disulfide (15 mL) was added dropwise to a solution (50 mL) of **1** in 14% aq NaOH, which was prepared from *N*-acetylchitosan (1.0 g), The mixture was stirred at room temperature for 24 h to afford a viscous orange-red solution of **2b**.

O-(Benzylthio)thiocarbonyl N-acetylchitosan (**3**).—Benzyl bromide [1.4 mL, 9 mol equiv to GlcNAc (Expt 1) or 4.3 mL, 35 mol equiv to GlcNAc (Expt 2)] was added to the solution of chitin xanthate **2a** in 14% aq NaOH (prepared in the foregoing section), with stirring and cooling in an ice-bath. An orange-red precipitate appeared within 30 min. The mixture was further stirred at room temperature overnight, and the resulting precipitate was filtered and washed with MeOH several times. For complete *N*-acetylation, suspension of the crude product in MeOH (100 mL) was stirred with acetic anhydride (0.3 mL) at room temperature for ~5 h. The product was collected by filtration, washed with MeOH, and dried.

In Expt 1, 0.30 g (76%) of the product [ds 1.10 for (benzylthio)thiocarbonyl] was isolated. ν_{max} (KBr): 1680 and 1516 (C=O and NH of NAc). 1211 [–O–C(=S)–S–], 700 (phenyl) cm^{-1}. Anal. Calcd for $[C_8H_{13}NO_5(C_8H_7S_2)_{1.10}(H)_{0.90} \cdot 0.35H_2O]_n$: C, 51.42; H, 5.21; N, 3.57; S, 17.98. Found: C, 51.13; H, 4.98; N, 3.59; S, 17.66.

In Expt 2, 0.38 g (84%) of the product [ds 1.55 for (benzylthio)thiocarbonyl] was isolated. ^{13}C CPMAS NMR: δ 217.1 (C=S), 173.8 (C=O of NAc), 135.2 and 129.4

(phenyl), 102.3 (C-1), 84.6 (C-4), 73.1 (C-5 and C-3), 59.5 (C-6), 55.3 (C-2), 40.7 (CH_2 of benzylthio), 24.0 (CH_3 of NAc). ν_{max}(KBr): 1680 and 1516 (C=O and NH of NAc), 1211 [–O–C(=S)–S–], 700 (phenyl) cm^{-1}. Anal. Calcd for $[C_8H_{13}NO_5(C_8H_7S_2)_{1.55}(H)_{0.45}]_n$: C, 53.16; H, 4.88; N, 3.04; S, 21.57. Found: C, 53.47; H, 4.82; N, 2.91; S, 20.66.

O-*(Methylthio)thiocarbonyl* N-*acetylchitosan* (**4**)—Methyl iodide (2.7 mL, 36 mol equiv to GlcNAc) was added to the solution of chitin xanthate **2a** in 14% aq NaOH (prepared in the foregoing section), with stirring and cooling in an ice-bath to give an orange-red precipitate within 30 min. The mixture was further stirred at room temperature overnight. The resulting precipitate was treated with acetic anhydride as described above, collected by filtration, and washed with MeOH to give a white precipitate (0.3 g, 80%). ^{13}C CPMAS NMR data: δ 216.6 (C=S), 172.1 (C=O of NAc), 102.8 (C-1), 83.0 (C-4), 75.2 (C-5 and C-3), 61.1 (C-6), 56.4 (C-2), 32.4 (CH_2), 24.0 (CH_3 of NAc), 20.9 (CH_3 of methylthio). ν_{max} (KBr): 1668 and 1529 (C=O and NH of NAc), 1211 [–O–C(=S)–S–] cm^{-1}. Anal. Calcd for $[C_8H_{13}NO_5(C_2H_3S_2)_{1.51}(H)_{0.49} \cdot 0.26H_2O]_n$: C, 38.47; H, 4.84; N, 4.09; S, 28.14. Found: C, 38.28; H, 4.59; N, 4.01; S, 27.90.

O-*(Ethylthio)thiocarbonyl* N-*acetylchitosan* (**5**).—Ethyl iodide (12 mL, 22 mol equiv to GlcNAc) was added to the solution of chitin xanthate **2b** in 14% aq NaOH (prepared in the foregoing section), with stirring and cooling in an ice-bath to give an orange-red precipitate within a few h. The mixture was further stirred at room temperature overnight and treated with acetic anhydride for *N*-acetylation as described above. The precipitate was collected by filtration, washed with MeOH to afford a white, amorphous product (1.48 g, 88%). ^{13}C CPMAS NMR: δ 216.1 (C=S), 171.7 (C=O of NAc), 102.8 (C-1), 82.5 (C-4), 74.1 (C-5 and C-3), 60.5 (C-6), 55.8 (C-2), 32.4 (CH_2 of ethylthio), 25.1 (CH_3 of NAc), 15.1 (CH_3 of ethylthio). ν_{max} (KBr): 1668 and 1527 (C=O and NH of NAc), 1207 [–O–C(C=S)–S–] cm^{-1}. Anal. Calcd for $[C_8H_{13}NO_5(C_3H_5S_2)_{1.30}(H)_{0.70}]_n$: C, 41.75; H, 5.48; N, 4.11; S, 24.36. Found: C, 41.68; H, 5.21; N, 3.93; S, 24.19.

O-*(*n*-Propylthio)thiocarbonyl* N-*acetylchitosan* (**6**).—*n*-Propyl chloride (17.8 mL, 45 mol equiv to GlcNAc) was added to the solution of chitin xanthate **2b** in 14% aq NaOH (prepared in the foregoing section), with stirring and cooling in an ice-bath. The mixture was stirred at room temperature overnight to give an orange-red, viscous solution. The solution was diluted with water (~500 mL) to afford a precipitate, which was collected by filtration and washed with EtOH. Its suspension in MeOH was treated with acetic anhydride for complete *N*-acetylation as described above. The precipitate was collected by filtration and washed with MeOH to afford a white, amorphous product (1.48 g, 88%). ν_{max} (KBr): 1664 and 1545 (C=O and NH of NAc), 1205[(–O–C(=S)–S–] cm^{-1}. Anal. Calcd for $[C_8H_{13}NO_5(C_4H_7S_2)_{1.01}(H)_{0.99} \cdot 0.25H_2O]_n$: C, 44.20; H, 6.03; N, 4.30; S, 19.80. Found: C, 44.24; H, 5.96; N, 4.34; S, 19.76.

O-*(*n*-Butylthio)thiocarbonyl* N-*acetylchitosan* (**7**).—*n*-Butyl chloride (3.9 mL, 42 mol equiv to GlcNAc) was added to the solution of chitin xanthate **2a** in 14% aq NaOH (prepared in the foregoing section), with stirring and cooling in an ice-bath. The mixture was stirred at room temperature overnight to give an orange-red

viscous solution. The solution was diluted with water (~ 100 mL) to afford a precipitate, which was collected by filtration, and washed with EtOH. Its suspension in MeOH was treated with acetic anhydride for complete *N*-acetylation as described above. The precipitate was collected by filtration, and washed with MeOH to afford a white, amorphous product (0.27 g, 80%). ν_{max} (KBr): 1664 and 1548 (C=O and NH of NAc), 1213 [(–O–C(=S)–S–] cm^{-1}. Anal. Calcd for $[C_8H_{14}NO_5(C_5H_9S_2)_{0.81}(H)_{0.19} \cdot 0.13H_2O]_n$: C, 46.31; H, 6.32; N, 4.48; S, 16.60. Found: C, 46.22; H, 6.32; N, 4.50; S, 16.74.

2. Acknowledgments

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