doi:10.1246/cl.2011.218
Published on the web February 5, 2011

A Simple *N*-Acyl-L-amino Acid Constructed Metal-complexed Organic Nanotube Having an Inner Diameter below 10 nm

Masaru Mukai, Masaru Aoyagi, Hiroyuki Minamikawa, Masumi Asakawa, Toshimi Shimizu, and Masaki Kogiso*
Nanotube Research Center (NTRC), National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba Central 5, 1-1-1 Higashi, Tsukuba, Ibaraki 305-8565

(Received November 5, 2010; CL-100932; E-mail: m-kogiso@aist.go.jp)

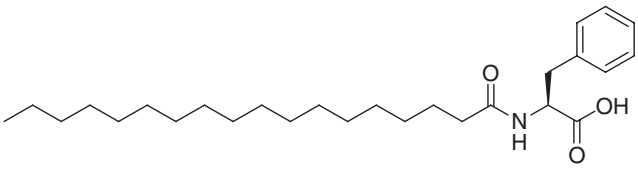
A novel metal-complexed organic nanotube (M–ONT) having an inner diameter below 10 nm was readily prepared from simple *N*-acyl-L-phenylalanine and nickel(II) ion.

Self-assembled organic nanotubes are attractive nanoarchitectures[1,2] since the hydrophilic hollow cylinders can act as vessels for nanomaterials,[3] templates for metal nanowires,[4] nanochannels for nanofluidic devices,[5] and carriers for drug delivery.[6] Both the rational functionalization of their surface properties and the control of their inner diameters are achieved by molecular design.[1] Although these morphological characteristics are important for effective and selective encapsulation of target guest substances into the hollow cylinders, it is still demanding to obtain organic nanotubes with desired surface properties and inner diameters simultaneously.[7,8]

Recently, we reported metal-complexed organic nanotubes (M–ONTs) using glycyl-glycine-containing peptide lipids.[9,10] These nanotubes are instantly formed by mixing two solutions of metal salt and the peptide lipid. The M–ONTs are expected to be useful as catalysts, adsorbents, and templates for metal–organic hybrid nanotubes.[11,12] However, the minimum inner diameter of M–ONTs (30 nm) is larger than those of organic nanotubes without metal ions (7 nm).[13] Small inner diameters, especially below 10 nm, are highly important, if considering applications such as carriers and separation materials for biological substrates like protein.[7] Thus, the development of M–ONTs with smaller diameters and control of surface properties from simple molecules is still challenging. In this paper, we report a novel M–ONT with an inner diameter below 10 nm using a simple designed lipid, *N*-octadecanoyl-L-phenylalanine (**1**) (Scheme 1). The simple *N*-acyl-L-amino acid also has an advantage of lower cost than dipeptides.

The lipid **1** was synthesized according to the literature.[14] The lipid **1** (1 mg, 2.3 µmol) was dispersed in aqueous NaOH (2.3 mM, 1 mL) with sonication. Drying of this solution resulted in sheet-like assemblies. Upon adding aqueous nickel(II) chloride solution (1 M, 2.3 µL), the lipid **1** self-assembled into a nanofibrous structure with length of over 1 µm, as shown in transmission-electron-microscopic (TEM) observation (Figure 1A). The nanofibrous structures were found to be nanotubes by high-magnification TEM observation (Figure 1B). The nanotubes were distinguishable from the nanofiber due to the penetration of a negative staining reagent, phosphotungstate, into the hollow cylinder. These ONTs have inner and outer diameters of 7–9 and 40–60 nm, respectively.

A similar nanostructure was also observable by scanning electron microscopy (SEM) without phosphotungstate, though it was unclear due to weakness against the electron beam. Energy dispersive X-ray (EDX) analysis of the nanotube showed peaks



Scheme 1. *N*-Octadecanoyl-L-phenylalanine (**1**).

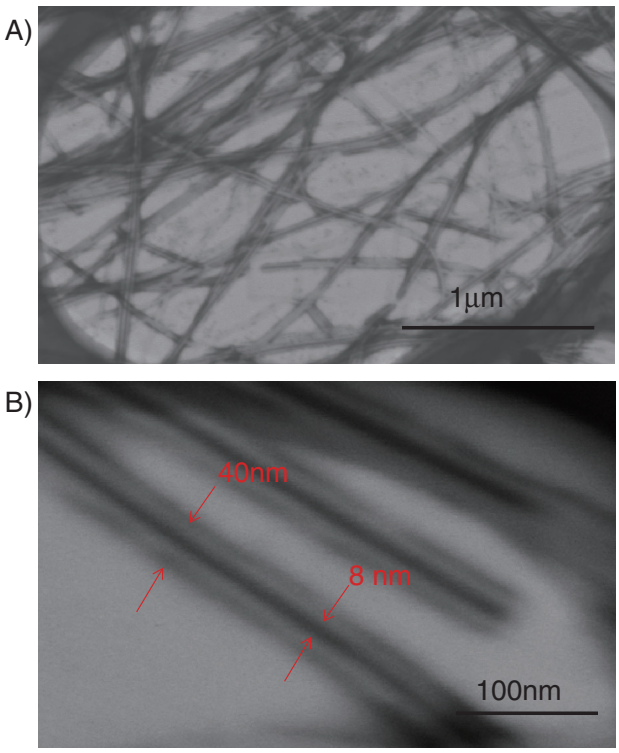


Figure 1. (A) TEM image of the nanotubes formed from **1** and Ni^{2+} ion and (B) its high-magnification image. Sample is negatively stained with phosphotungstate. Red arrows indicate an outer diameter and an inner diameter. Magnifications are (A) $\times 30 \times 10^3$ and (B) $\times 130 \times 10^3$, respectively.

at 7.47 and 8.26 keV, which are assignable to Ni (Figure 2). This indicates that the ONTs are formed from the lipid **1** and Ni ion.

X-ray diffraction (XRD) of the dried nanotubes is not highly resolved, but two diffractions around 2.58 and 5.16° are shown in the small-angle region (Figure 3). *d*-Spacing values were calculated to be 3.42 and 1.71 nm by Bragg's law. This indicates the tubular membranes are formed from 3.42 nm thick multilamellar bilayers. Since the extended molecular length of **1** is 2.6 nm, the bilayers are an interdigitated-membrane structure of

© 2011 The Chemical Society of Japan

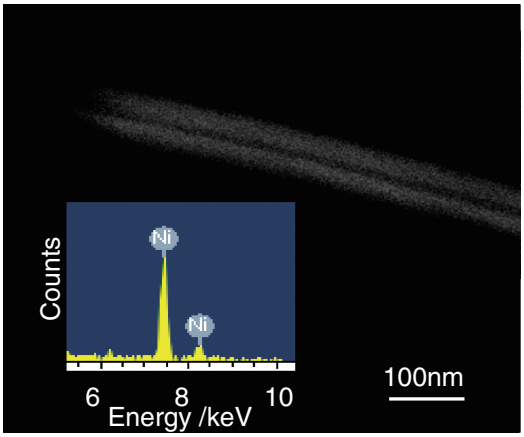


Figure 2. SEM image and EDX of Ni–ONT.

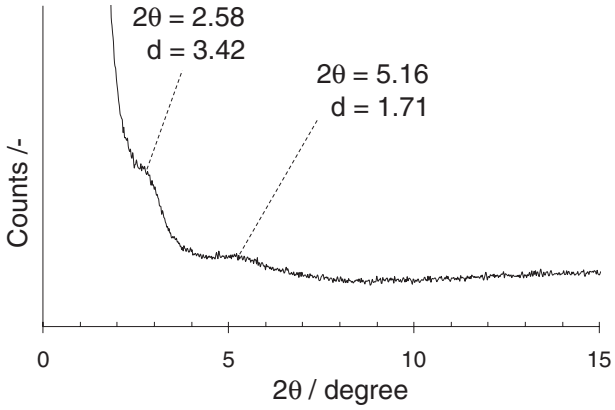


Figure 3. XRD of dried Ni–ONT.

the lipids. It suggests that the 5–8 bilayers construct the nanotube walls.

Figure 4 shows Fourier transform infrared (FT-IR) spectra of the peptide–lipid **1** and Ni–ONT. The lipid **1** shows the amide I and amide II bands at 1645 and 1550 cm^{-1}, indicating the hydrogen-bond network formation between the amide groups. On the contrary, FT-IR of Ni–ONT showed a broad band between 1500–1700 cm^{-1}. The amide I band was blue-shifted upon addition of Ni^{2+} ion, since the hydrogen-bond network became stronger by the addition of Ni^{2+} ions (Figure S1).[15] FT-IR analyses also evidenced that the carboxylate anion of the lipid **1** coordinates to Ni^{2+} ion. The lipid **1** shows an IR band assignable to C=O stretching vibration at 1724 cm^{-1}. Upon addition of NaOH and Ni^{2+} ion, a decrease in this band was observed though it did not disappear completely. In addition, a new band appeared below 1600 cm^{-1} which is assignable to COO^- coordinating to Ni^{2+} ion (Figure S1).[15] The amide I, II, and this new bands are included in the broad band between 1500–1700 cm^{-1}. After the addition of Ni^{2+} ion, a broad band is also observable between 3100–3600 cm^{-1}, indicating of the existence of water or hydroxide ion. These two broad bands closely resemble that of $[Ni^{2+}(\text{aspartate}^-)(OH^-)(H_2O)]$.[16] The broad bands and the remaining of COOH band suggest the existence of hydroxide ion in the Ni–ONT. The result of FT-IR analysis indicates that $[Ni^{2+}(\mathbf{1})(\mathbf{1}^-)(OH^-)(H_2O)]$ complex will

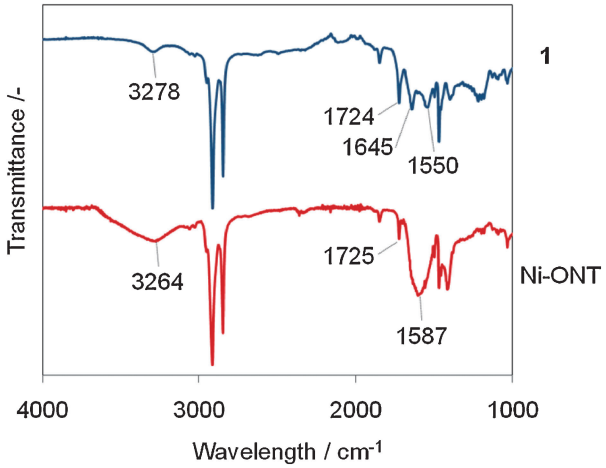


Figure 4. FT-IR spectra of peptide–lipid **1** and Ni–ONT.

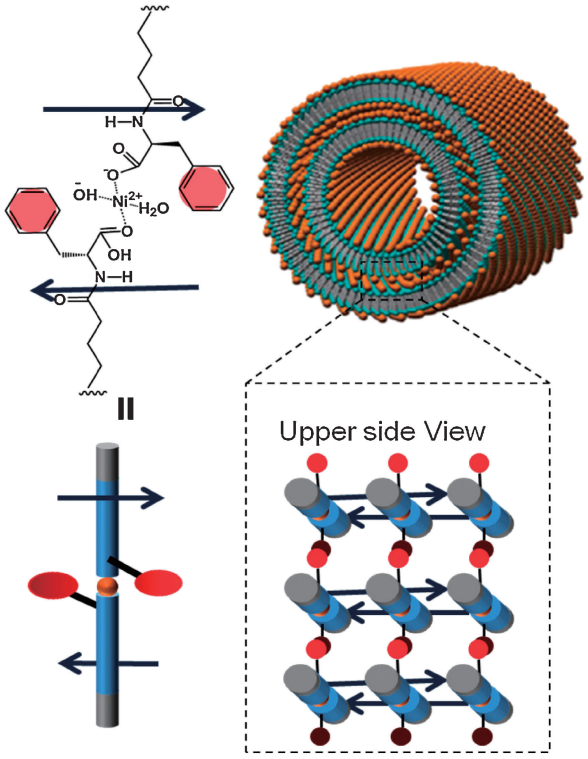


Figure 5. A schematic model of the metal-complexed organic nanotube and its interactions in the membrane.

construct the Ni–ONT. The elemental analysis of the dried nanotube supports this type of metal complex, showing the composition of one Ni^{2+} ion, two lipid molecules, and one counter anion.

Figure 5 shows a schematic model of the M–ONT. Two lipid molecules and one Ni^{2+} ion form a metal complex between the bilayers. When the amide groups form hydrogen-bonds one-dimensionally (blue arrows), side-chain phenyl groups (red circles) exist perpendicularly to the direction of the hydrogen bonds. In the membrane formation, these phenyl groups will form side-by-side π–π interaction. Unfortunately, π–π interaction could not be confirmed by UV–vis spectra since the light

 © 2011 The Chemical Society of Japan

scattering is very strong in the nanotube dispersion. But we observed that *N*-octadecanoyl-L-alanine did not form any tubular morphology. It suggests π–π interaction between L-phenylalanine residues plays an indispensable role in the spontaneous nanotube formation from the lipid **1**. Some authors have reported that the π–π interaction is important for the tubular structure in cases of phenylalanine-based organic nanotubes.[17]

Some peptide derivatives with large hydrophobic side chains, like Phe, Tyr, Trp, Leu, and Val, are known to form nanotubular structures.[18] More than two amino acids have been necessary for nanotube formation to date. In this study, lipid **1** with only one phenylalanine was able to form nanotubes. Both metal complexation and hydrophobic interaction between alkyl chains will make up for the lack of hydrophobic side chain. In addition, the chirality of L-phenylalanine can induce a twisted alignment between neighboring lipids in a right- or left-handed manner. It can result in a spontaneous curvature in the membranes.

In conclusion, we demonstrated a first M–ONT with an inner diameter below 10 nm by using the simple *N*-acyl-L-amino acid **1**. Its inner hollow cylinder with a single nanometer size and a Ni^{2+}-coordinated surface appears promising for applications such as carriers and separating materials of biological substrates like DNA and protein.

References and Notes

1 Reviews: T. Shimizu, M. Masuda, H. Minamikawa, *Chem. Rev.* **2005**, *105*, 1401; X. Gao, H. Matsui, *Adv. Mater.* **2005**, *17*, 2037.

2 Y. Yamamoto, T. Fukushima, Y. Suna, N. Ishii, A. Saeki, S. Seki, S. Tagawa, M. Taniguchi, T. Kawai, T. Aida, *Science* **2006**, *314*, 1761; S. B. Lee, R. Koepsel, D. B. Stolz, H. E. Warriner, A. J. Russell, *J. Am. Chem. Soc.* **2004**, *126*, 13400; G. John, M. Mason, P. M. Ajayan, J. S. Dordick, *J. Am. Chem. Soc.* **2004**, *126*, 15012.

3 T. Shimizu, *J. Polym. Sci., Part A* **2006**, *44*, 5137; Y. Zhao, N. Mahaja, J. Fang, *Small* **2006**, *2*, 364.

4 O. Carny, D. E. Shalev, E. Gazit, *Nano Lett.* **2006**, *6*, 1594; B. Yang, S. Kamiya, K. Yoshida, T. Shimizu, *Chem. Commun.* **2004**, 500.

5 K. Sott, T. Lobovkina, L. Lizana, M. Tokarz, B. Bauer, Z. Konkoli, O. Orwar, *Nano Lett.* **2006**, *6*, 209.

6 U. Raviv, D. J. Needleman, Y. Li, H. P. Miller, L. Wilson, C. R. Safinya, *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 11167.

7 N. Kameta, H. Minamikawa, Y. Someya, H. Yui, M. Masuda, T. Shimizu, *Chem.—Eur. J.* **2010**, *16*, 4217.

8 N. Kameta, M. Masuda, H. Minamikawa, N. V. Goutev, J. A. Rim, J. H. Jung, T. Shimizu, *Adv. Mater.* **2005**, *17*, 2732.

9 M. Kogiso, Y. Zhou, T. Shimizu, *Adv. Mater.* **2007**, *19*, 242.

10 M. Kogiso, M. Aoyagi, M. Asakawa, T. Shimizu, *Chem. Lett.* **2010**, *39*, 822.

11 T. Chattopadhyay, M. Kogiso, M. Asakawa, T. Shimizu, M. Aoyagi, *Catal. Commun.* **2010**, *12*, 9.

12 Y. Zhou, M. Kogiso, M. Asakawa, S. Dong, R. Kiyama, T. Shimizu, *Adv. Mater.* **2009**, *21*, 1742.

13 N. Kameta, G. Mizuno, M. Masuda, H. Minamikawa, M. Kogiso, T. Shimizu, *Chem. Lett.* **2007**, *36*, 896.

14 A. Sivasamy, M. Krishnaveni, P. G. Rao, *J. Am. Oil Chem. Soc.* **2001**, *78*, 897.

15 Figures S1 is shown in Supporting Information which is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

16 O. V. Cabral, C. A. Téllez, S. T. Giannerini, J. Felcman, *Spectrochim. Acta, Part A* **2005**, *61*, 337.

17 C. H. Görbitz, *Chem. Commun.* **2006**, 2332; M. Z. Menzenski, I. A. Banerjee, *New J. Chem.* **2007**, *31*, 1674; C. Tang, A. M. Smith, R. F. Collins, R. V. Ulijn, A. Saiani, *Langmuir* **2009**, *25*, 9447.

18 S. Vauthey, S. Santoso, H. Gong, N. Watson, S. Zhang, *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 5355; C. Valéry, M. Paternostre, B. Robert, T. Gulik-Krzywicki, T. Narayanan, J.-C. Dedieu, G. Keller, M.-L. Torres, R. Cherif-Cheikh, P. Calvo, F. Artzner, *Proc. Natl. Acad. Sci. U.S.A.* **2003**, *100*, 10258; M. Reches, E. Gazit, *Science* **2003**, *300*, 625.

 © 2011 The Chemical Society of Japan