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# Water-Soluble Single-Nano Carbon Particles: Fullerenol and Its Derivatives

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## 1. Introduction

Since its discovery in 1985, fullerene has been extensively investigated as a unique, “dissolvable,” and “modifiable” nanocarbon material. The most representative fullerene,  $C_{60}$ , is a perfectly spherical molecule with a diameter of ca. 1 nm (0.7 nm when the distance between the furthest C–C bond is considered, and 1 nm when the  $\pi$ -orbitals are included). It has many interesting electronic and biological properties owing to its spherical  $\pi$ -conjugation. While fullerenes satisfactorily dissolve in aromatic solvents such as toluene and *o*-dichlorobenzene as well as in carbon disulfide, they dissolve poorly in most common solvents such as hexane, chloroform, diethyl ether, ethyl acetate, tetrahydrofuran (THF), acetone, acetonitrile, ethanol, and even in benzene. This limitation has been one of the important issues hindering their practical application, especially in the field of life sciences.

Although the single-crystal X-ray structural analysis of  $C_{60}$  has been successful, it is generally difficult to grow the crystal of fullerene derivatives. Such a poor crystallinity is because of the lack of molecular orientation and intermolecular interaction that are crucial for determining the molecular alignment in a crystal. The lack of molecular orientation and interaction is attributed to the unidirectional spherical shape of these derivatives, which is different from the shapes of other organic molecules such as cubic- or plate-shaped ones. For the same reason, the solid form of  $C_{60}$  is known to easily afford its nanoparticles with a top-down approach, in which the solid is reduced to small particles (as small as 20 nm) by applying mechanical forces; such particles can even be obtained by hand-grinding (Deguchi et al., 2006; Deguchi et al., 2010). These small nanocarbon particles, so-called  $nC_{60}$  (Oberdörster, 2004; Brant et al., 2005) or nano- $C_{60}$  (Fortner et al., 2005), can be dispersed even in neutral water, and they remain dispersed for a long time, especially in the presence of humic acid (Chen & Elimelech, 2007; Isaacson & Bouchard, 2010). On the other hand, the aggregate of fullerene can be easily obtained by a bottom-up approach in many solvents such as benzene (Ying et al., 1994), benzonitrile (Nath et al., 1998), *N*-methylpyrrolidone (Yevlampieva et al., 2002; Kyzyma et al., 2010), and *o*-dichlorobenzene (Gun'kin & Loginova, 2006). The nanoparticle formation and aggregation behavior are among the outstanding features of fullerene in terms of both its practical application and the safe use of nanomaterials.

Polyhydroxylated fullerenes, so-called fullerenols or fullerols, are a class of fullerenes that has many hydroxyl groups, formed by the chemical modification of covalent C–O bonds,

on their spherical surfaces. The chemical formula  $C_{60}(OH)_n$  represents an average structure that consists of a mixture of fullerenols having different number of hydroxyl groups, each with its own regioisomer. The solubility of a fullerene molecule is dependent on the number of hydroxyl groups introduced; i.e., the low-degree hydroxylated fullerenols  $C_{60}(OH)_{10-12}$  (Chiang et al., 1994) can dissolve in some polar solvents, e.g., THF, dimethylformamide (DMF), and dimethyl sulfoxide (DMSO), and the medium-degree fullerenols  $C_{60}(OH)_{16}$  (Wang et al., 2005) and  $C_{60}(OH)_{20-24}$  (Li et al., 1993) are reported to dissolve even in water. However, these later fullerenols may be contaminated with Na salt because of the reagents used in synthesis, resulting in compositions with the formula  $Na^+_n[C_{60}Ox(OH)_y]^{n-}$  and exhibiting high water solubility in spite of their small number of hydroxyl groups (Husebo et al., 2004). In contrast, the high-degree hydroxylated fullerenols  $C_{60}(OH)_{36}$  and  $C_{60}(OH)_{44}$ , which are synthesized without using any Na salt, are completely water soluble by as much as 17 and 65 mg/mL, respectively (Kokubo et al., 2008; Kokubo et al., 2010). Particle size analysis revealed that the high-degree fullerenols exhibited high dispersion properties at a molecular level (ca. 1 nm, which is as large as the molecular diameter). The behavior of water-soluble carbon particles in the single-nano region (1–10 nm) is less well understood in terms of their chemical and physical properties.

This chapter focuses on the methods of synthesizing fullerenols, provides examples of applications, and describes the particle-size measurements of the high-degree fullerenols as water-soluble single-nano carbon particles.

## 2. Synthesis of fullerenols

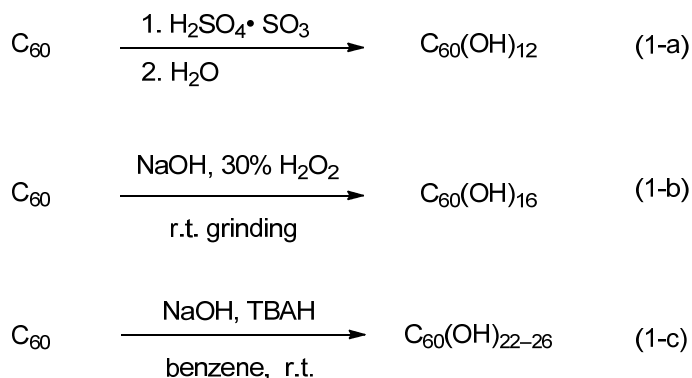
### 2.1 Hydroxylation of fullerene

Various types of fullerenols having different number of hydroxyl groups have been synthesized so far because of their promising water solubility and the expected bioactivities. In general, the structure of fullerenols is qualitatively identified by infrared spectroscopy as having a characteristic broad  $\nu O-H$  band, along with three broad peaks assigned for  $\nu C=C$ ,  $\delta_s C-O-H$ , and  $\nu C-O$ . The number of hydroxyl groups introduced is quantitatively determined by either elemental analysis or X-ray photoelectron spectroscopy (XPS). Such a quantitative analysis is founded on the hypothesis that the addend of a fullerene is composed of only hydroxyl group.

One of the most well-known fullerenols,  $C_{60}(OH)_{12}$ , was synthesized by L. Y. Chiang using oleum ( $H_2SO_4 SO_3$ ), followed by the hydrolysis of the intermediate cyclosulfated fullerene (Scheme 1a) (Chiang et al., 1994). The compound is soluble in an alkaline solution and some polar solvents such as THF and DMSO, but it is not soluble in neutral water because it has few hydroxyl groups. L. Y. Chiang also studied its antioxidant activity toward a superoxide, a reactive oxygen species (Chiang et al., 1995). Some other related methods of accessing the lower-degree fullerenols have been reported (Zhang et al., 2010).

The most frequently used method for synthesizing the medium-degree fullereneol  $C_{60}(OH)_{22-26}$  is the one reported by J. Li et al. (Scheme 1b) (Li et al., 1993). This method employs sodium hydroxide (NaOH) as a hydroxylation reagent, and molecular oxygen is required to neutralize the intermediate fullerene anion, which is formed by the attack of -

OH to  $C_{60}$ , in order to induce the successive attack of -OH. The fullerenols  $C_{60}(\text{OH})_{22-26}$ , as well as  $C_{60}(\text{OH})_{16}$  synthesized by a similar method using NaOH and  $\text{H}_2\text{O}_2$  (Scheme 1c) (Wang et al., 2005), exhibits sufficient solubility in neutral water. The fullereneol has also been known to have many bioactivities, including antioxidant activity similar to pristine  $C_{60}$  (Bosi et al., 2003; Bakry et al., 2007; Partha & Conyers, 2009). However, the practical use of these types of fullereneols might be restricted because of their unfavorable contamination by  $\text{Na}^+$  ions, which are inevitably introduced during treatment with NaOH, and the purification is rather difficult except when done by repeated gel column chromatography (Husebo et al., 2004). The relatively higher water solubility than that expected, given the number of hydroxyl groups, is reasonably explained by the corrected chemical formula  $\text{Na}^+_n[\text{C}_{60}\text{O}_x(\text{OH})_y]^{n-}$ . Such a Na salt form is attributed to the weak acidity of the phenolic O-H of the low-degree fullereneols, in contrast to the alcoholic O-H of the high-degree fullereneols. Therefore, there is a demand for the development of new, facile, and scalable methods for synthesizing highly water-soluble and pure fullereneols.

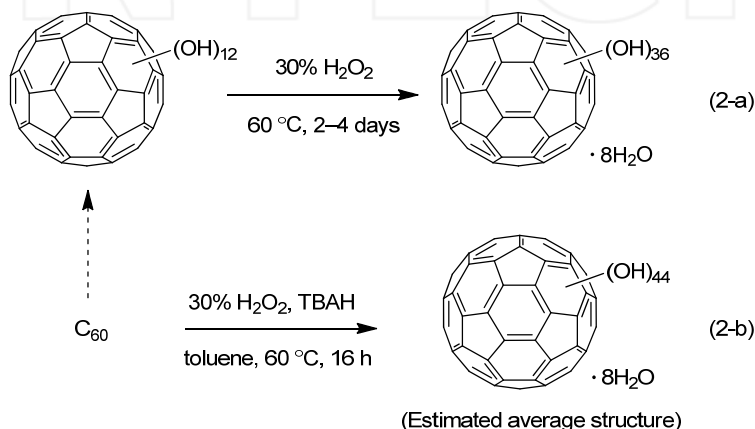


Scheme 1. Synthesis of low- and medium-degree fullereneols

## 2.2 Highly polyhydroxylated fullereneols

To avoid contamination by  $\text{Na}^+$  ions, we examined the use of hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) as a hydroxylation reagent instead of NaOH. Thus, we have found a new and facile approach for synthesizing high-degree fullereneols that have high water solubility without using any Na salts (Kokubo et al., 2008). The reddish brown suspension of fullereneol  $C_{60}(\text{OH})_{12}$  in 30% aqueous  $\text{H}_2\text{O}_2$  was stirred vigorously at 60 °C under air until it turned to a transparent yellow solution, which occurred within 2–4 days (Scheme 2a). To this solution, a mixture of 2-propanol, diethyl ether, and hexane as an antisolvent was added to afford a yellowish brown to milky white precipitation of the desirable high-degree fullereneol  $C_{60}(\text{OH})_{36} \cdot 8\text{H}_2\text{O}$ . A longer reaction time of up to two weeks gave the similar but more water-soluble fullereneol  $C_{60}(\text{OH})_{40} \cdot 9\text{H}_2\text{O}$ .

This new approach using  $\text{H}_2\text{O}_2$  to synthesize high-degree fullerlenols was useful; however, the starting material was limited to  $\text{C}_{60}(\text{OH})_{12}$  and was not applicable to pristine  $\text{C}_{60}$ . We then improved the method in order to provide a facile, one-step method for synthesizing fullerlenol from pristine  $\text{C}_{60}$ ; we added an  $\text{NH}_3$  aqueous solution to the  $\text{H}_2\text{O}_2$  aqueous solution to give similar water-soluble fullerlenols, although they contained some undesirable nitrogen-containing groups, along with hydroxyl groups (Matsubayashi et al., 2009). We further improved the method, synthesizing pure  $\text{C}_{60}(\text{OH})_{44} \cdot 8\text{H}_2\text{O}$  fullerlenol with no nitrogen in one step from pristine  $\text{C}_{60}$ . To the best of our knowledge, this fullerlenol has the largest number of hydroxyl groups per  $\text{C}_{60}$  among the fullerlenols reported so far; this fullerlenol was obtained by a two-phase synthesis in the presence of tetrabutylammonium hydroxide (TBAH) as a phase transfer catalyst (PTC) (Scheme 2b) (Kokubo et al., 2010). The fullerlenol exhibits a very high water solubility of up to 64.9 mg/mL.



Scheme 2. Synthesis of high-degree fullerlenols

### 2.3 Structural characterization

The structural characterization of the high-degree fullerlenols was conducted by infrared spectroscopy (Fig. 1). The spectra of the fullerlenols closely resembled each other, although their relative peak intensities differed somewhat, suggesting a difference in the number of introduced hydroxyl groups. Four characteristic broad bands were observed at 1080, 1370, 1620, and 3400  $\text{cm}^{-1}$  and were assigned to  $\nu\text{C-O}$ ,  $\delta_s\text{C-O-H}$ ,  $\nu\text{C=C}$ , and  $\nu\text{O-H}$ , respectively. A small shoulder peak at 1720  $\text{cm}^{-1}$  may imply the existence of a carboxylic acid group,  $\text{O=C-OH}$ , which might have formed by the further oxidation of a hydroxyl group associated with C-C bond cleavage of the fullerene nucleus. However, such partial oxidation must not be crucial because the generally strong  $\text{C=O}$  absorption is much smaller than the other generally weak or medium  $\text{C=C}$  or  $\text{C-O}$  absorptions, which is consistent with the results of the elemental analysis.

The quantitative analysis to determine the number of hydroxyl groups was conducted by elemental analysis. As shown in Table 1, the average structure of the high-degree fullereneol  $C_{60}(OH)_{44} \cdot 8H_2O$  would be deduced to be  $C_{60}(OH)_{52}$  if just the results of elemental analysis was used. However, the largest reported number of substituents in one  $C_{60}$  moiety is  $C_{60}F_{48}$  (Tuinman et al., 1992; Troyanov et al., 2010), and thus  $C_{60}(OH)_{52}$  is unlikely to be formed due to the enormous strain energy. On the other hand, it is known that the tightly entrapped water molecules, the secondary bound water, in highly hydroxylated fullerenols cannot be dissociated by the usual method of heating the fullerenols to about 120–150 °C. Therefore, water content measurements using thermogravimetric analysis was conducted (Figure 2). With a water content of 9.4 wt%, as shown in Table 1, the average structure of fullereneol was deduced to be  $C_{60}(OH)_{44} \cdot 8H_2O$ , using both elemental analysis and water content measurements.

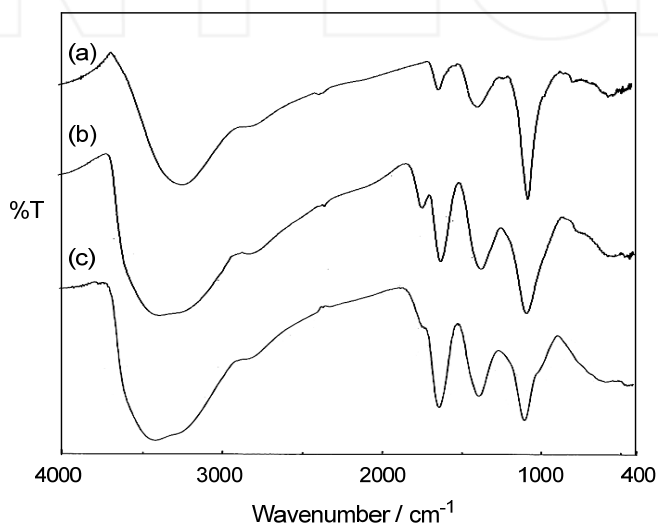


Fig. 1. IR spectra of (a)  $C_{60}(OH)_{12}$ , (b)  $C_{60}(OH)_{36} \cdot 8H_2O$ , and (c) purified  $C_{60}(OH)_{44} \cdot 8H_2O$ .

Average structure	Elemental analysis (%) Found (Calcd) <sup>a</sup>	Water content (wt%) <sup>a,b</sup>	Solubility (mg/mL) <sup>c</sup>
$C_{60}(OH)_{36} \cdot 8H_2O$	C: 48.06, H:3.61 (C: 48.79, H:3.54)	8.9 (9.7)	17.5
$(C_{60}(OH)_{44})$	(C: 49.06, H:3.02)	(0)	
$C_{60}(OH)_{44} \cdot 8H_2O$	C: 44.68, H:3.56 (C: 44.70, H:3.75)	9.4 (8.9)	64.9
$(C_{60}(OH)_{52})$	(C: 44.90, H:3.27)	(0)	

<sup>a</sup>Values in parentheses are calculated data. <sup>b</sup>Determined by TGA. <sup>c</sup>At 25 °C in neutral water (pH = 7).

Table 1. Average structure and water solubility of high-degree fullerenols

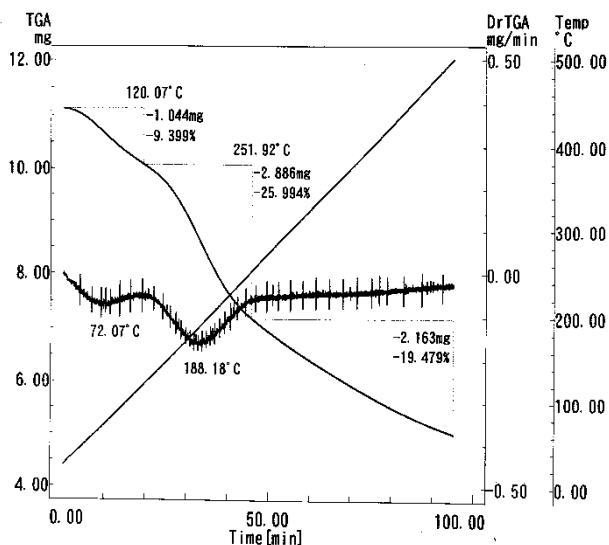
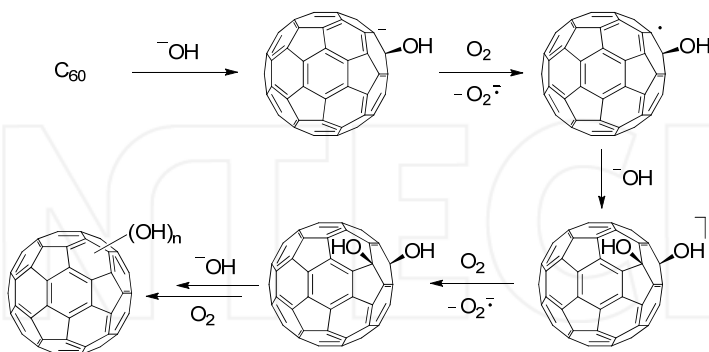


Fig. 2. Thermogravimetric analysis of fullereneol  $C_{60}(OH)_{44} \cdot 8H_2O$  under  $N_2$  flow.

## 2.4 Reaction mechanism

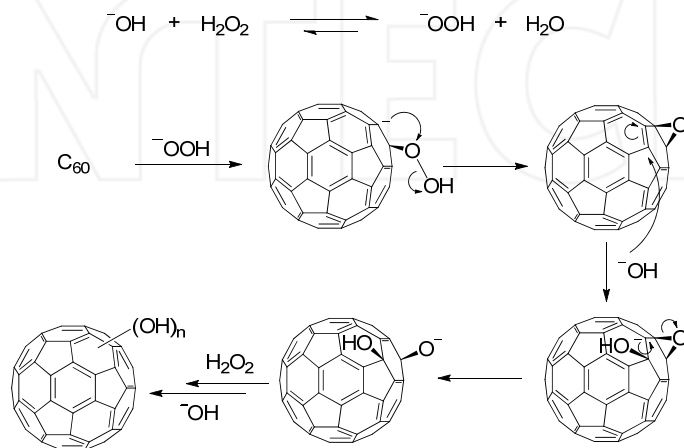
Possible reaction mechanisms for the formation of fullereneols are illustrated in Schemes 3 and 4. For the reaction using NaOH, the attack of  $-OH$  to  $C_{60}$  followed by the oxidation with molecular oxygen via one electron transfer from the  $C_{60}$  anion gives the hydroxylated  $C_{60}$ . The successive attack of  $-OH$  and repeated oxidation finally gives the medium-degree fullereneol (Scheme 3) (Husebo et al., 2004).



Scheme 3. A possible reaction mechanism for medium-degree fullereneols using the NaOH method

In contrast, for the reaction using  $H_2O_2$ , the basic hydroxide ion from TBAH initially induces the hydroperoxide ion  $-OOH$  because of the slightly higher acidity of  $H_2O_2$  than that of  $H_2O$  (Scheme 4) (Wang et al., 2005; Kokubo et al., 2011). The  $-OOH$  thus formed attacks  $C_{60}$  to

give fullerene oxide  $C_{60}O$ , followed by the attack of  $-OH$  and protonation. The epoxidation process may be repeated to give  $C_{60}O_2$ ,  $C_{60}O_3$ , and so on (Tajima & Takeuchi, 2002), which are more susceptible than  $C_{60}O$  to the subsequent nucleophilic attack of  $-OH$  (or  $-OOH$ ) because of the higher strain. These fullerene oxide intermediates were detected in the reaction mixture by liquid chromatography-mass spectrometry (LC-MS) (APCI;  $m/z = 736$ ,  $752$ , and  $768$ ) and were proven to be the intermediates by their kinetic behavior. The role of the quaternary ammonium salt TBAH is that of the promotion of  $-OOH$  formation and its transfer from the hydrophilic aqueous phase to the hydrophobic fullereryl sites in the organic phase as PTC.



Scheme 4. Proposed reaction mechanism for high-degree fullerenols using the  $H_2O_2$  method

### 3. Measurement of particle size distribution

#### 3.1 Dynamic light scattering method

Although a fullereneol seems to completely dissolve in a solution, it may be aggregated in the nano-size region, as seen for many fullerene derivatives and some fullerenols (Mohan et al., 1998; Husebo et al., 2004; Brant et al., 2007; Chae et al., 2009; Su et al., 2010). The particle size of medium-degree fullereneol  $C_{60}(OH)_{24}$  in aqueous solution is reported as between ca. 20 and 450 nm depending on the measurement conditions. Even such a high number of hydroxyl groups results in the formation of aggregation due to the large hydrophobic and  $\pi$ - $\pi$  interactions between fullereryl cores.

In order to investigate the dispersant behavior, the particle size measurement of high-degree fullerenols in the 0.1 wt% aqueous solution was carried out using the common dynamic light scattering (DLS) method (Berne & Pecora, 1976). The narrow particle-size distributions around 1–2 nm in terms of the number of  $C_{60}(OH)_{36}$  and  $C_{60}(OH)_{44}$  molecules are essentially the same, indicating the highly dispersed nature of the fullerenols at a molecular level (Figure 3) (Kokubo et al., 2008; Kokubo et al., 2011). The average particle size of  $C_{60}(OH)_{44}$  was determined to be  $1.46 \pm 0.38$  nm ( $N = 8$ ). The particle size by intensity was not applicable to the fullereneol solution because of the interference from the intensity of contamination in the range of 60–130 nm.



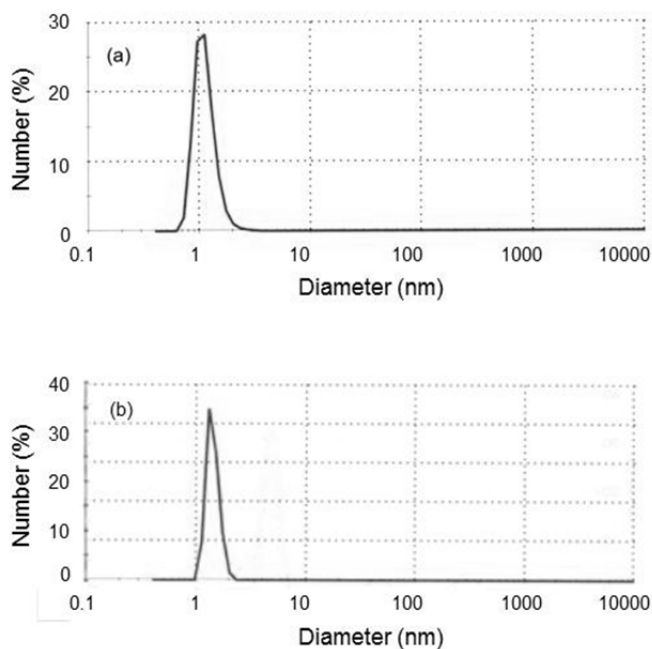


Fig. 3. DLS analysis of (a)  $C_{60}(OH)_{36}$  and (b)  $C_{60}(OH)_{44}$  in water (0.1 wt%) expressed by size distribution in number.

### 3.2 Induced grating method

Recently, the induced grating (IG) method was developed to improve the reproducibility of particle size measurements, especially in the single-nano region (Wada et al., 2006). DLS measurements provide the diffusion coefficient  $D$ , which is converted to the diameter by monitoring the fluctuations in scattering intensity due to the Brownian motion of particles. However, because the efficiency of DLS is proportional to the sixth power of the particle diameter (Kerker, 1969), the detection sensitivity strongly depends on the particle size and thus the presence of impurities. The IG method also determines the diffusion coefficient  $D$  given by the following Einstein–Stokes equation:

$$D = \frac{k_B T}{3\pi\eta d}$$

where  $k_B$  is the Boltzmann's constant,  $T$  is the temperature in Kelvin,  $\eta$  is the viscosity of the medium, and  $d$  is the diameter of the particles. When the radio frequency voltage is turned off, the diffraction light intensity  $I$  begins to decrease according to the following equation:

$$I = I_0 \exp(-2Dq^2 t)$$

where  $I_0$  is the initial intensity and  $q$  is the value of  $2\pi$  divided by the pitch of the grating. However, the measurement also includes an activation procedure induced by dielectrophoresis to form a particle grating (Pohl, 1978). Dielectrophoresis first generates a

periodic density modulation of the particles, which are then relaxed to a diffuse state until they reach a steady state. Thus, the diffraction light is less affected by the presence of impurities as compared with DLS.

We therefore also conducted particle size measurements of high-degree fullerenols using the IG method (Kokubo et al., 2011). In the diffusion region, sufficient photointensity was observed for the  $C_{60}(OH)_{44}$  aqueous solution (0.1 wt%) and the logarithmic value of the relative photointensity correlated well linearly with the time scale (Fig. 4).

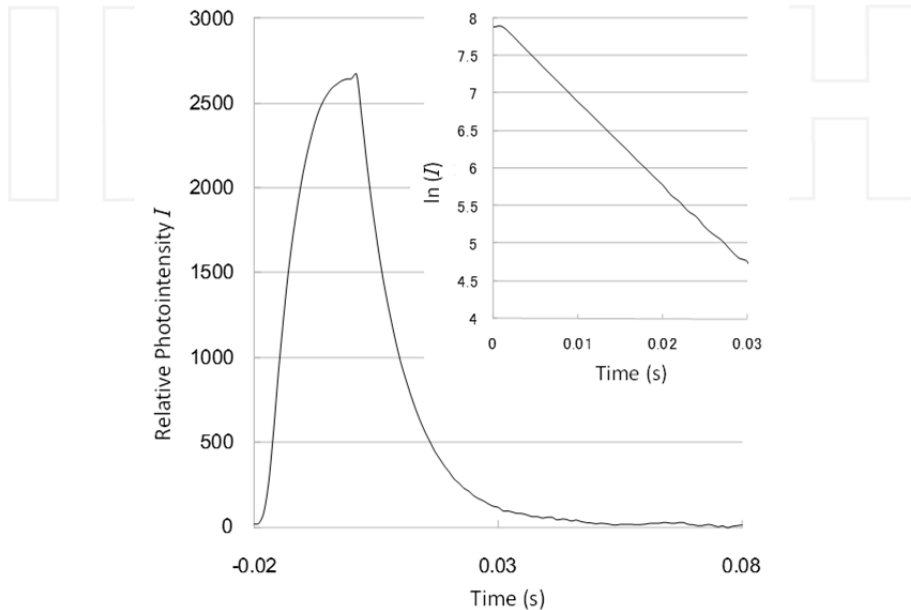


Fig. 4. Time course of relative photointensity  $I$  of  $C_{60}(OH)_{44}$  aqueous solution (0.1 wt%) measured by the IG method.

The particle size distribution was narrow, in the range of 0.7–1 nm, and the average particle size was determined to be  $0.806 \pm 0.022$  nm ( $N = 8$ ), which was fairly consistent with the DLS results (Fig. 5). Therefore, it was confirmed that the high-degree fullerenols have high dispersion properties in water on a molecular level around their diameter of ca. 1 nm. It is remarkable that the reproducibility of the data measured over eight runs was 10 times higher for the IG method than for the DLS method.

### 3.3 Other methods

The particle size measurements by the DLS and IG methods were verified by a scanning probe microscope (SPM, Kokubo et al., 2011). We directly measured the particle size of the fullerenol as a function of protrusion height observed on a mica plate on which a highly diluted aqueous solution of fullerenol was applied and dried. As shown in Fig. 6, the protrusions were clearly observed as scattered spots, whereas a mica plate without the

fullerenol treatment, used as a control, did not show any spots at all. From the height of eight spots, the average particle size was determined to be  $1.03 \pm 0.28$  nm ( $N = 8$ ).

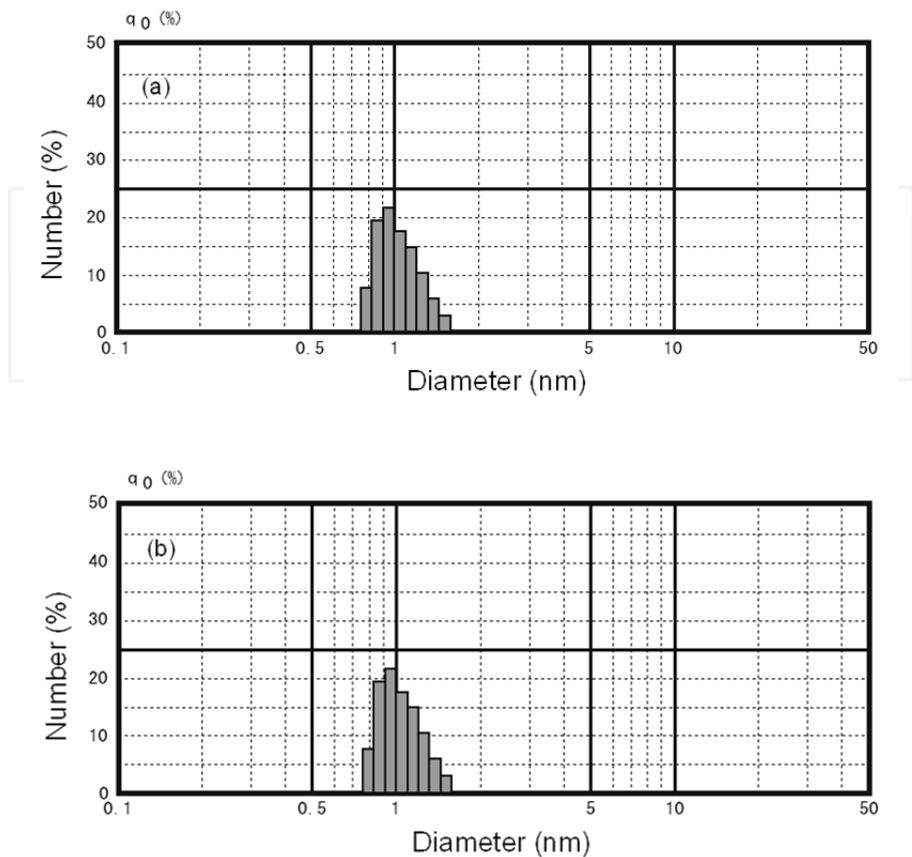


Fig. 5. IG analysis of (a)  $C_{60}(OH)_{36}$  and (b)  $C_{60}(OH)_{44}$  in water (0.1 wt%) expressed by size distribution in number.

The size distribution of fullerenols has also been investigated using flow field-flow fractionation (FFF) technique (Assemi et al., 2010) and transmission electron microscopy (TEM) (Wang et al., 2010). The FFF is an elution technique that analyzes ensembles of the sample that have a similar property and produces a size distribution rather than an average size. They found that the size of medium-degree fullerenol  $C_{60}(OH)_{24}$  nanoparticles was ranging from about 1.8 nm (0.001 M NaCl) to 6.7 nm (0.1 M NaCl). However, this result is in contrast to some DLS data that reports sizes on the order of 100 nanometers for fullerenol nanoparticles. This is because of the fact that the impurities and the large aggregation are separated from the monodispersed fraction eluting from the FFF channel. The TEM observation revealed that the aggregation form of the low-degree fullerenol  $C_{60}(OH)_{12}(ONa)_2$  in the solution with a particle size of 50–250 nm.

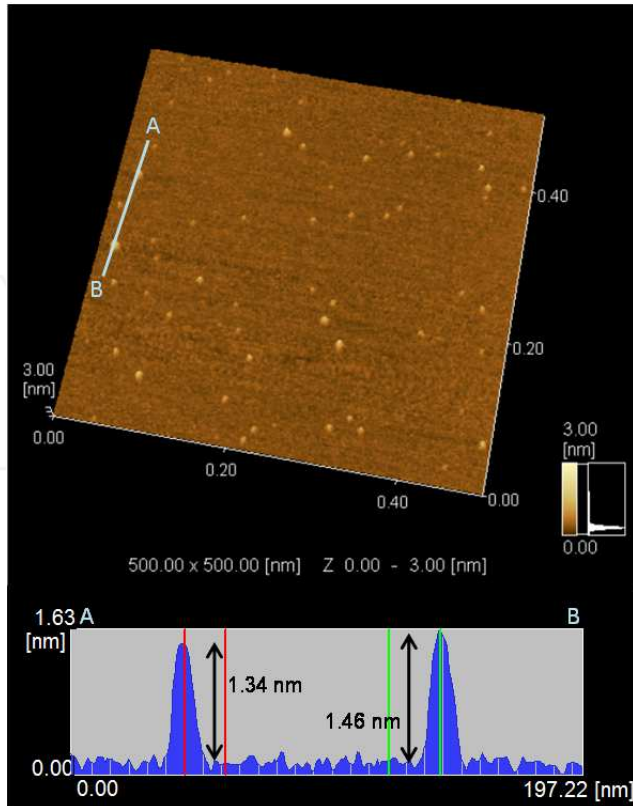


Fig. 6. SPM analysis of  $C_{60}(OH)_{36}$  applied as a diluted solution and dried on a mica plate.

## 4. Application of fullerenols

### 4.1 Biochemical application

The water-soluble medium-degree fullerenols have been demonstrated to be useful as free-radical scavengers for the absorption of superoxide radicals generated by *in vitro* xanthine and xanthine oxidase in aqueous solution, suggesting potential use of fullerenols in biochemical or pharmaceutical applications (Chiang et al., 1995). Since then, much research has been devoted to studies on the antioxidant (Dugan et al., 1996; Djordjevic et al., 2004; Bogdanovic et al., 2008), antimicrobial (Aoshima et al., 2009), anti-cancer (Chaudhuri et al., 2009; Krishna et al., 2010), antitumor, and antimetastatic activities of medium-degree fullerenols (Jiao et al., 2010).

Recently, N. Miwa et al. reported the antioxidant activity (Kato et al., 2009) and related bioactivities (Saitoh et al., 2010; Saitoh et al., 2011) of high-degree fullerenols. Some reviews relevant to the biochemical application of fullerenes and fullerenols have also been reported (Nielsen et al., 2008; Rade et al., 2008; Partha & Conyers, 2009). Fullerenes are not considered to have highly significant acute toxicity and genotoxicity, although some toxicological

results have also been reported. In contrast, fullerlenols are considered to be less toxic than  $C_{60}$  due to the introduction of hydrophilic groups that reduce their cytotoxicity.

#### 4.2 Industrial application

Because of a 1 nm grain size, high water dispersibility on a molecular level and metal-free material, the high-degree fullerlenol has been proposed as a chemical mechanical polishing (CMP) slurry for use during planarization in the Cu damascene process for the fabrication of next-generation semiconductors. Y. Takaya et al. found that the Cu-surface roughness was improved from 20 to 0.6 nm root mean square (RMS) by using  $C_{60}(OH)_{36}$  as functional molecular abrasive grains to achieve better polishing performance than could be achieved using conventional processes (Takaya et al., 2009). The etching ability of  $C_{60}(OH)_{36}$  for a Cu surface evaluated in static etch was also found to be high in relation to the achievement of a highly planar surface by polishing experiment. Very recently, further XPS analysis and SEM observation revealed that the chemical effect of fullerlenol plays a key role in high polishing performance; i.e., the fullerlenol chemically reacted with the copper surface to form a complex brittle layer that was fragile enough to be removed by rubbing with a polishing pad (Takaya et al., 2011).

#### 4.3 Other applications

Other examples of applications using low- to medium-degree fullerlenols have been reported, such as polymer-based solar cells (Cao et al., 2001; Rincón et al., 2005), drug delivery and MRI contrast agents using endohedral metallofullerenol (Sitharaman et al., 2004), macromolecular materials and polymer nanocomposites (Goswami et al., 2003; Ouyang et al., 2004), proton conductors (Hinokuma et al., 2001; Maruyama et al., 2002), and electrodeposited films (Wang et al., 2010). Following these applications, water-soluble high-degree fullerlenols will open the new pathways for the new fullerlenol chemistry.

### 5. Summary

Fullerlenols are one of the most important and promising fullerene derivatives that can be easily synthesized with tunable properties by varying the number of hydroxyl groups introduced. Their water solubility, high dispersing nature as single-nano carbon particles, and varied biochemical properties are extremely attractive from the viewpoint of materials chemistry as well as life science applications. The analytical methods for particle size measurement of single-nano particles will continue to be improved by the further development of these kinds of nanocarbon materials.

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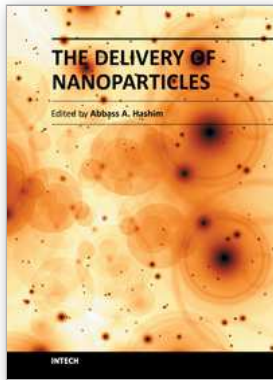
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## **The Delivery of Nanoparticles**

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Nanoparticle is a general challenge for today's technology and the near future observations of science. Nanoparticles cover mostly all types of sciences and manufacturing technologies. The properties of this particle are flying over today scientific barriers and have passed the limitations of conventional sciences. This is the reason why nanoparticles have been evaluated for the use in many fields. InTech publisher and the contributing authors of this book in nanoparticles are all overconfident to invite all scientists to read this new book. The book's potential was held until it was approached by the art of exploring the most advanced research in the field of nano-scale particles, preparation techniques and the way of reaching their destination. 25 reputable chapters were framed in this book and there were alienated into four altered sections; Toxic Nanoparticles, Drug Nanoparticles, Biological Activities and Nano-Technology.

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