# PHYSICAL CONTROL OF NANODIAMOND BY CHEMICAL SURFACE CONTROL AIMING MEDICINAL APPLICATION

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## Abstract

The surface of nanodiamond with 30 nm in diameter was chemically controlled to be -H, $-NH_2$, $-OCOCH_3$ and -OH through gas- and liquid-phase reactions. These functionalized nanodiamonds show different aqueous solubilities which are highly influenced by the polarity of the functional groups on their large surface areas.

## Introduction

Although quantum dots[1] and carbon nanotubes[2] have been developed as promising fluorescent probes in modern biotechnology, they always have considerable concerns about cytotoxicity and photobleaching. Quite recently, however, nanodiamond powder has been reported to be successfully employed as a fluorescent probe with no photobleaching and low cytotoxicity. This clearly shows the potential of nanodiamond powder to biological and medicinal applications.[3]

On the other hand, chemical modification of the powdered diamond surface has been extensively investigated; hydrogenation,[4-7] oxidation,[5,7,8] fluorination,[5-7, 9-11] chlorination,[5,7, 12-16] alkylation,[6,12,13,17,18] amination,[5,6,14,15,19,20] esterification[21-23] silylation,[24] and so on. One of the main purposes of the surface modification is the control of the physical properties of the diamond powder by utilizing large specific surface area. Among a large number of the above-mentioned previous reports, however, only a few referred to the correlation of the surface structure with the physical properties; solubility,[6] hydrophilicity and -phobicity,[7, 25] and water repellency.[26] This is probably because the particle size of the diamonds is not small enough and/or the coverage of the functionalities is not enough to affect their physical properties.

In continuation of our effort to develop nanodiamond-based molecular imaging probes, we successfully controlled the chemical structure of nanodiamond powder and correlated the surface functionalities with water solubility of the nanodiamond powder.[27-29] The nanodiamond with polar functional groups showed the water solubility as high as 5.5 mg/ml, which is considered to be high enough for biological and even medicinal applications.

## Materials and Methods

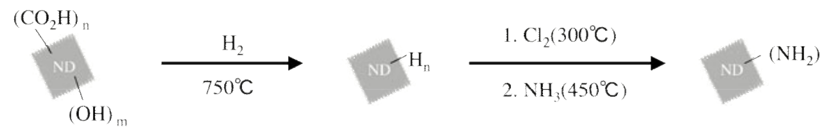
Nanodiamond powder with around 30 nm average diameter, designated as ND30, used for the surface modification was prepared by high temperature high pressure (HTHP) method followed by disintegration by ball milling and size separation. It is a gift from Tomei Diamond Co. Gas-phase reactions were carried out in electric furnace under gas flow. Liquid-phase reactions were preformed in glass wares under argon atmosphere.

The solubility of functionalized nanodiamonds were determined according to the following procedure; nanodiamond (120 mg) in distilled water (8 mL) was bath-sonicated at 20°C for 1 h and the resulting suspension was subjected to centrifugation at 18500 *g* for 10 min. The solubility was determined by the weight of the well-dried residue from 5 mL of the supernatant.

## Results and Discussion

### *Surface Chemical Control of Nanodiamonds*

Hydrogenation of ND30 was carried out according to the reported procedure for much larger size of diamond (500 nm in diameter).[4] In IR spectrum (Figure 1A), the absorption due to C-H stretching vibration was observed at 2900 $cm^{-1}$ without any other clear absorption such as O-H and C=O, indicating that most of polar functional groups were replaced by hydrogen. This is supported by the result of elemental analysis, which shows that the content of oxygen reduced to zero from 10.25% after the hydrogenation of ND30.




**Scheme 1.** Preparation of hydrogenated and aminated nanodiamonds

Thus prepared hydrogenated nanodiamond was aminated via successive gas-phase reactions with chlorine and ammonia as shown in Scheme 1.[16] The two newly observed absorptions at 3400 and 1650 $cm^{-1}$ in IR spectrum (Figure 1B) are assigned to N-H stretching and deformation vibrations, respectively. The content of nitrogen (0.80%) in elemental analysis (Table 1) also shows that some of the hydrogen atoms were replaced by amino groups.

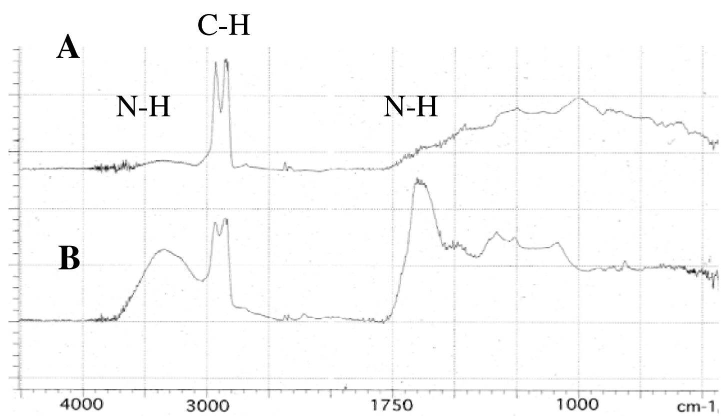



**Figure 1.** Infrared (IR) absorption spectra of hydrogenated (A) and aminated nanodiamonds (B).

Acetoxylation of hydrogenated nanodiamond was carried out in acetic acid in the presence of benzoyl peroxide as radical initiator at 75°C (Scheme 2).[21] The incorporation of acetoxyl group was confirmed by the three absorptions, 1700, 1350 and 1250 $cm^{-1}$, corresponding to C=O, $CH_3$ and CO-O, respectively, in IR spectrum (Figure 2A), and the content of oxygen (1.72%) in elemental analysis (Table 1).

**Table 1.** Elemental analysis of nanodiamonds with various functional groups on their surface.

| Functional group | C (%) | H (%) | N(%) | O (%) |
|---|---|---|---|---|
| OH, $CO_2H$ | 87.58 | 0.74 | 0.40 | 10.25 |
| H | 98.53 | 0.77 | 0 | 0 |
| $NH_2$ | 96.79 | 0.79 | 0.80 | - |
| $OCOCH_3$ | 97.05 | 0.95 | 0 | 1.72 |
| OH | 93.20 | 1.21 | 0 | 1.33 |

The acetoxyl group was hydrolyzed in aqueous NaOH solution at 80°C to give nanodiamond with hydroxyl group. In IR spectrum (Figure 2B), all the absorptions due to acetoxyl group were disappeared and that corresponding to O-H stretching appeared. In addition, the content of oxygen in elemental analysis (Table 1) reduced from 1.72% to 1.33%. These results clearly show the hydrolysis of aceoxyl group to generate hydroxy group.

### *Aqueous Solubility of the Functionalized Nanodiamonds*

The aqueous solubility of the functionalized nanodiamonds was determined as shown in Figure 3. While the solubility of hydrogenated nanodiamond was only 0.34 mg/mL, nanodiamonds with polar functionalities, amino, acetoxyl and hydroxy groups, exhibited more than 10 times larger solubility to water. This is a clear quantitative example to show that the control of physical property, solubility in this case, was achieved by chemical functionalization of the surface in nanodiamond.


## Acknowledgement

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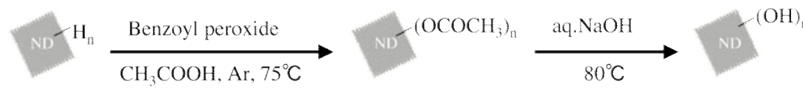


**Scheme 2.** Preparation of acetoxylated and hydroxylated nanodiamonds.

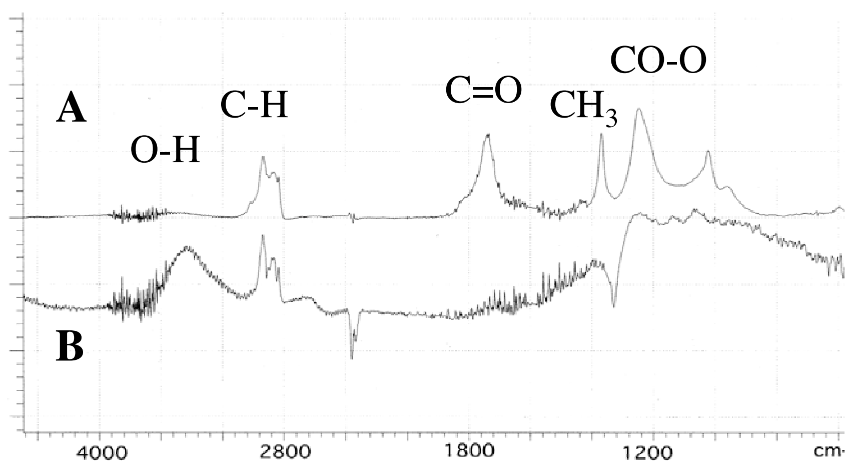


**Figure 2.** Infrared (IR) absorption spectra of acetoxylated (A) and hydroxylated nanodiamonds (B).

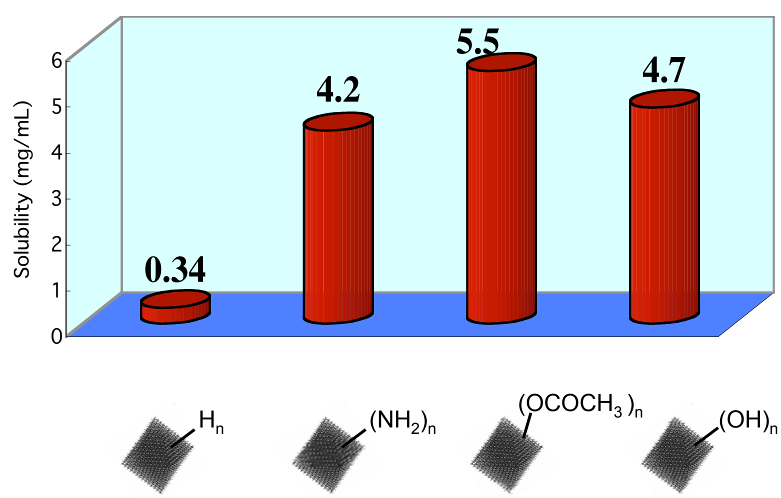


**Figure 3.** Aqueous solubility of nanodiamonds with various functionality.

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