

# CHEMISTRY OF MATERIALS

VOLUME 16, NUMBER 8

APRIL 20, 2004

© Copyright 2004 by the American Chemical Society

## Communications

### One-Pot Reaction to Synthesize Water-Soluble Magnetite Nanocrystals

Zhen Li, Hui Chen, Haobo Bao, and Mingyuan Gao\*

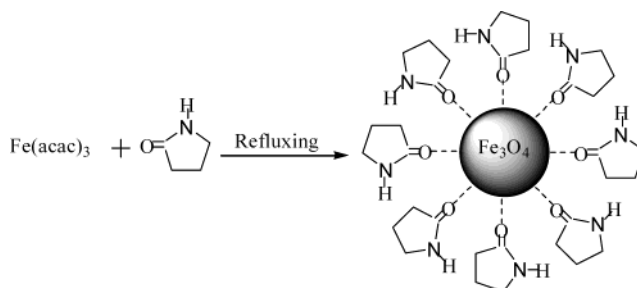
Key Laboratory of Colloid, Interface Science and Chemical Thermodynamics, Molecular Science Center, Institute of Chemistry, Chinese Academy of Sciences, Zhong Guan Cun, Bei Yi Jie 2, Beijing 100080, China

Received December 18, 2003

Revised Manuscript Received January 14, 2004

Magnetic nanoparticles have been widely studied because of their potential applications in biomedical fields such as biomolecular separation,<sup>1</sup> target-drug delivery,<sup>2</sup> cancer diagnosis and treatment,<sup>3</sup> DNA separation and detection sequencing of oligonucleotides,<sup>4</sup> and magnetic resonance imaging.<sup>5</sup> Among magnetic particles, iron oxides ( $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_3\text{O}_4$ ) have been extensively investigated. Different synthetic techniques such as coprecipitation and microemulsion methods,<sup>6,7</sup> ultra-

### Scheme 1. Synthetic Route of Water-Soluble Magnetite Nanocrystals



sound irradiation,<sup>8</sup> and laser pyrolysis techniques,<sup>9</sup> have been developed for producing particles smaller than 20 nm. However, the relatively poor size uniformity and crystallinity of nanoparticles obtained strongly affect their magnetic properties. Very recently, an alternative method has been developed to synthesize high-quality magnetic nanocrystals by thermal decomposition of different types of iron precursors such as  $\text{FeCuP}_3$ , ferric triacetylacetonate ( $\text{Fe}(\text{acac})_3$ ), and  $\text{Fe}(\text{CO})_5$ .<sup>10–12</sup> Alivisatos' group reported preparation of monodispersed maghemite by decomposition of  $\text{FeCuP}_3$  in the presence of octylamine and trioctylamine.<sup>10</sup> By a similar method, Sun et al. succeeded in synthesis of monodispersed magnetite nanoparticles using  $\text{Fe}(\text{acac})_3$  as starting material.<sup>11</sup> Hyeon and co-workers demonstrated that decomposition of  $\text{Fe}(\text{CO})_5$  followed by oxidation can also

\* To whom correspondence should be addressed. Phone: 0086-10-62625212. Fax: 0086-10-82613214. E-mail: gaomy@iccas.ac.cn.

(1) (a) Wilhelm, C.; Gazeau, F.; Bacri, J. C. *Eur. Biophys. J.* **2002**, *31*, 118. (b) Perez, J. M.; Simeone, F. J.; Saeki, Y.; Josephson, L.; Weissleder, R. *J. Am. Chem. Soc.* **2003**, *125*, 10192. (c) Fan, J. D.; Lu, J. G.; Xu, R. S.; Jiang, R.; Gao, Y. *J. Colloid Interface Sci.* **2003**, *266*, 215.

(2) Gupta, P. K.; Hung, C. T.; Lam, F. C.; Perrier, D. G. *Int. J. Pharm.* **1988**, *43*, 167.

(3) Jordan, A.; Scholz, R.; Maier-Hauff, K.; Johannsen, M.; Wust, P.; Nadobny, J.; Schirra, H.; Schmidt, H.; Deger, S.; Loening, S.; Lanksch, W.; Felix, R. *J. Magn. Magn. Mater.* **2001**, *225*, 118.

(4) (a) Doyle, P. S.; Bibette, J.; Bancaud, A.; Viovy, J. L. *Science* **2002**, *295*, 2237. (b) Josephson, L.; Perez, J. M.; Weissleder, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 3204.

(5) Bulte, J. W. M.; Brooks, R. A. In *Scientific and Clinical Applications of Magnetic Carriers*; Häfeli, U., Schütt, W., Teller, J., Zborowski, M., Eds.; Plenum Press: New York and London, 1997; p 527.

(6) Harris, L. A.; Goff, J. D.; Carmichael, A. Y.; Riffle, J. S.; Harburn, J. J.; Pierre, T. G. S.; Saunders, M. *Chem. Mater.* **2003**, *15*, 1367.

(7) Mann, S.; Sparks, H. C.; Board, R. G. *Adv. Microb. Physiol.* **1990**, *31*, 125.

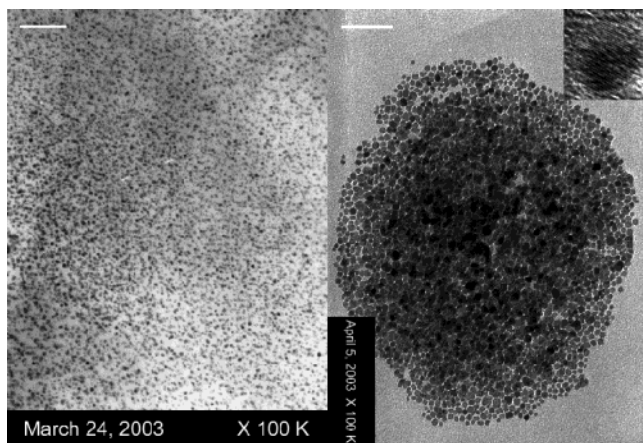
(8) Kumar, R. V.; Koltypin, Y.; Xu, X. N.; Yeshurun, Y.; Gedanken, A.; Felner, I. *J. Appl. Phys.* **2001**, *89*, 6324.

(9) Veintemillas-Verdaguer, S.; Bomati-Miguel, O.; Morales, M. P. *Scr. Mater.* **2002**, *47*, 589.

(10) Rockenberger, J.; Scher, E. C.; Alivisatos, P. A. *J. Am. Chem. Soc.* **1999**, *121*, 11595.

(11) Sun, S. H.; Zeng, H. *J. Am. Chem. Soc.* **2002**, *124*, 8204.

(12) Hyeon, T.; Lee, S. S.; Park, J.; Chung, Y.; Na, H. B. *J. Am. Chem. Soc.* **2001**, *123*, 12798.



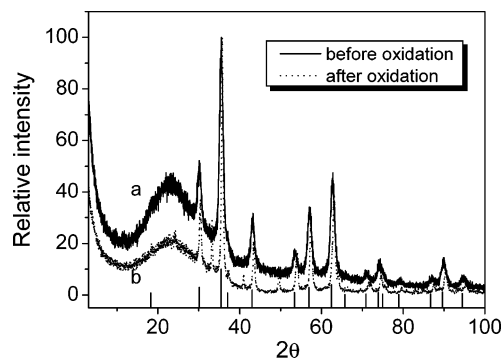
**Figure 1.** TEM images of 5- and 11-nm magnetite nanoparticles. In the right-hand photo a HRTEM image of a selected magnetic nanocrystal is inserted. TEM images were obtained on a JEOL-2010 microscope; the scale bar corresponds to 100 nm.

lead to high quality maghemite nanoparticles.<sup>12</sup> However, the direct products of the above-mentioned approaches are organic-soluble, which to some extent limits their use in the biomedical fields, especially for in vivo applications. Therefore, it is very important to further develop the thermal decomposition method to directly synthesize water-soluble magnetic nanoparticles by using strong polar molecules to modify the magnetic nanoparticles.

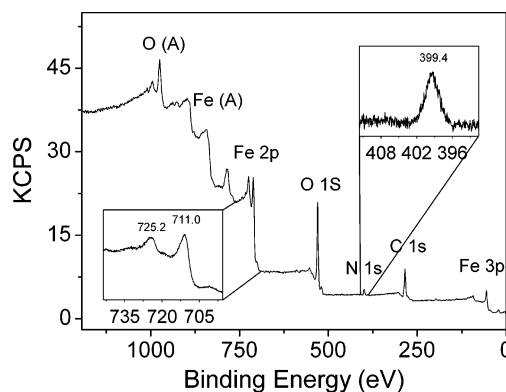
In this communication, we report a one-pot reaction to achieve water-soluble iron oxide nanocrystals by thermal decomposition of  $\text{Fe}(\text{acac})_3$  in 2-pyrrolidone (Scheme 1) and results of surface coordination of the magnetic nanocrystals obtained. In the one-pot reaction, 2-pyrrolidone was chosen as solvent and stabilizer because it has strong polarity, a high boiling point, and coordination capacity with transition metal ions.<sup>13</sup>

A typical synthesis yielding iron oxide nanoparticles with 5-nm particle diameter is described as follows. A 20-mL portion of 2-pyrrolidone solution containing 2.0 mmol  $\text{Fe}(\text{acac})_3$  was first purged with nitrogen to remove oxygen and then heated. After being refluxed for 10 min, the reaction system was cooled to room temperature. Addition of methanol into the 2-pyrrolidone solution resulted in a dark-brown precipitate which was washed with acetone for several times and then dried. The final black powder was proven to be soluble in water and 2-pyrrolidone. Figure 1 (left) shows TEM images of the nanoparticles obtained. Their average diameter is  $5 \pm 1.2$  nm.

To prepare larger particles, the seed-mediated growth method was adopted as described elsewhere.<sup>11</sup> By controlling the quantity of seeds as well as refluxing time, the particle size can effectively be tuned. Here we present only one set of larger-size particles, obtained by using the 5-nm iron oxide nanoparticles as seeds, as an example to show the effectiveness of the growth method. Figure 1 (right) presents the images of larger particles of  $11 \pm 2.5$  nm obtained. Typically, 20 mg of 5-nm particles was added into 20 mL of 2-pyrrolidone



**Figure 2.** Powder X-ray diffractograms of 11-nm magnetite nanoparticles before (a) and after (b) oxidation. Diffractograms were collected on a Regaku D/Max-2500 diffractometer under  $\text{Cu K}\alpha$  radiation ( $\lambda = 1.54056 \text{ \AA}$ ). Bottom: JCPDS card (19-0629) data for magnetite.



**Figure 3.** X-ray photoelectron spectra of 5-nm magnetite nanoparticles. The insets are expanded spectra of Fe 2p and N 1s. XPS spectra were recorded by using a VG ESCALAB 220i-XL spectrometer with an Al  $\text{K}\alpha$  monochromatic X-ray source.

containing 0.2 mmol  $\text{Fe}(\text{acac})_3$ . The mixture was refluxed for 40 min to get the larger nanoparticles mentioned above. The insert in Figure 1 is a high-resolution TEM (HRTEM) image of a larger particle selected from the right panel of the figure. The clear crystalline structure demonstrates that the iron oxide particles are nanocrystals. The lattice plane distance is  $4.83 \text{ \AA}$  and corresponds to the [111] lattice plane of magnetite. The crystalline structure was further determined by powder X-ray diffraction (XRD) as shown in Figure 2. The positions and relative intensities of all diffraction peaks in Figure 2a match well with those from the JCPDS card (19-0629) for magnetite (Table 1). The average particle size calculated using Scherrer's formula is about 10.8 nm, which is quite close to the TEM result for the larger particles. The crystallographic form of the ferric oxide nanocrystals obtained was also verified by its structural transformation to maghemite upon oxidation at  $250 \text{ }^\circ\text{C}$ . Noticeable changes in the diffraction peak positions are shown in Figure 2b, in addition to newly developed diffractions after the 11-nm magnetite nanocrystals are oxidized. The resulted diffraction pattern matches very well with the crystal structure of maghemite.

As mentioned above, the dried as-synthesized nanocrystal powder can be redissolved in water and 2-pyrrolidone. It has been demonstrated that 2-pyrrolidone can coordinate with copper(II), cobalt(II), and nickel(II) via carbonyl group.<sup>13</sup> In addition, 2-pyridone can also

(13) (a) Shukla, P. R.; Bhargava, J. *J. Indian Chem. Soc.* **1983**, *60*, 788. (b) Goodgame, D. M. L.; Williams, D. J.; Winpenny, R. E. P. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 6. 1044.

**Table 1. Comparison of *d*-Spacing Values of the Synthesized Iron Oxide Nanocrystals (Before and After Oxidation) with Standard JCPDS Fe<sub>3</sub>O<sub>4</sub> and  $\gamma$ -Fe<sub>2</sub>O<sub>3</sub> Data**

11-nm iron oxide nanocrystals (before oxidation)	Fe <sub>3</sub> O <sub>4</sub>	11-nm iron oxide nanocrystals (after oxidation)	$\gamma$ -Fe <sub>2</sub> O <sub>3</sub>
2.953	2.967	2.942	2.953
2.527	2.532	2.693	2.643
2.094	2.099	2.508	2.517
1.706	1.714	2.200	2.232
1.610	1.615	2.080	2.088
1.479	1.484	1.836	1.822
1.274	1.280	1.694	1.704
1.089	1.093	1.605	1.607
		1.473	1.475
		1.451	1.453
		1.269	1.273
		1.085	1.087

coordinate with iron(III) ion through carbonyl group alone.<sup>14</sup> The FTIR measurements reveal that the vibrational band of C=O shifts from 1686 cm<sup>-1</sup> for pure 2-pyrrolidone to 1634 cm<sup>-1</sup> for the current magnetite nanocrystals, which indicates that the O from C=O coordinates with Fe on the surface of the magnetite nanocrystals.<sup>13</sup> To further confirm this coordination, X-ray photoelectron spectroscopy (XPS) was used to prove the coordination between the nitrogen from 2-pyrrolidone and magnetite nanoparticles. Figure 3 presents the XPS spectra of 5-nm magnetite nanoparticles prepared in 2-pyrrolidone. The photoelectron peaks at 711.0 and 725.2 eV are the characteristic doublets of Fe 2p<sub>3/2</sub> and Fe 2p<sub>1/2</sub> from iron oxide.<sup>15</sup> It is well-known that the binding energy of N 1s will shift to lower value by 1–3 eV when nitrogen is bound to metals, due to a transfer of electron density from nitrogen to metals.<sup>16</sup> Therefore, the peak position of N1s centered at 399.4 eV indicates that the nitrogen from the amide group in 2-pyrrolidone does not coordinate with the magnetite nanocrystals,<sup>16b,17</sup> which supports that 2-pyrrolidone coordinates with the magnetite nanocrystals only via O from the carbonyl group.

The atomic ratio between Fe and N in the nanocrystals is determined to be 3.37 by XPS. This suggests that there are roughly 370 2-pyrrolidone molecules forming a layer on the surface of a 5-nm magnetite particle. Thermogravimetric analysis (TGA) also supports this result. The 2-pyrrolidone layer forming on the surface of magnetite nanocrystals renders not only stability but also solubility to the magnetite nanocrystals.

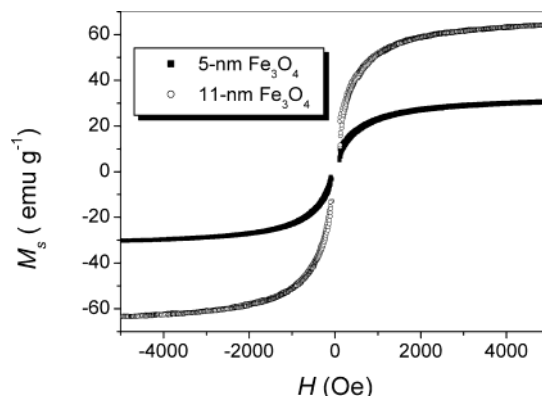
(14) Goodgame, D. M. L.; Williams, D. J.; Winpenny, R. E. P. *Inorg. Chim. Acta* **1989**, *166*, 159.

(15) (a) Teng, X. W.; Black, D.; Watkins, N. J.; Gao, Y. L.; Yang, H. *Nano Lett.* **2003**, *2*, 261. (b) McIntyre, N. S.; Zetaruk, D. G. *Anal. Chem.* **1977**, *49*, 1521.

(16) (a) Wu, J. B.; Lin, Y. F.; Wang, J.; Chang, P. J.; Tasi, C. P.; Lu, C. C.; Chiu, H. T.; Yang, Y. W. *Inorg. Chem.* **2003**, *42*, 4516. (b) Charlier, J.; Cousty, J.; Xie, Z. X.; Poulenec, V. L.; Bureau, C. *Surf. Interface Anal.* **2000**, *30*, 283.

(17) Moulder, J. F.; Stickle, W. F.; Sobol, P. E.; Bomben, K. D. *Handbook of X-ray Photoelectron Spectroscopy*; Physical Electronics: Eden Prairie, MN, 1995.

(18) (a) Vestal, R.; Zhang, Z. J. *J. Am. Chem. Soc.* **2003**, *125*, 9828. (b) Morales, M. P.; Veintemillas-Verdaguer, S.; Montero, M. I.; Serna, C. J.; Roig, A.; Casas, L.; Martinez, B.; Sandiumenge, F. *Chem. Mater.* **1999**, *11*, 3058.



**Figure 4.** Room-temperature magnetization curves of obtained magnetite nanocrystals. Black squares: 5-nm magnetite nanocrystals; hollow circles: 11-nm magnetite nanocrystals.

The magnetic properties of the magnetite nanoparticles were investigated with a vibrating sample magnetometer (VSM). Figure 4 shows the room-temperature magnetization of as-prepared magnetite nanocrystals. Both 5- and 11-nm magnetite nanocrystals exhibit the superparamagnetic characteristics. Their saturation magnetizations are 31 and 65 emu/g, respectively. The difference in saturation magnetization of our samples should be mainly attributed to the differences in particle size. In addition, saturation magnetizations of our samples are lower than those of similarly sized nanoparticles prepared by other methods,<sup>11</sup> which might be caused by the surface spin canting effects since strong polar 2-pyrrolidone was used instead of oleic acid.<sup>18</sup>

In summary, we report a novel synthetic approach for preparing water-soluble magnetite nanocrystals by thermal decomposition of Fe(acac)<sub>3</sub> in 2-pyrrolidone. The experimental results reveal that 2-pyrrolidone not only serves as a media for high-temperature reaction, but also involves surface coordination which renders the magnetite nanocrystals water-soluble and the colloidal solution stable. The magnetic properties of obtained magnetite nanocrystals are size dependent. Although the current synthetic approach is a small modification to the thermal decomposition method, it is very meaningful because it allows us to directly produce high-quality water-soluble magnetic nanocrystals, which is very important for applications of magnetic nanocrystals in biomedical fields. Our more recent results prove that the surface of the magnetite nanocrystals can also be modified by other functional molecules, such as amino acid and poly(ethylene glycol) if they are present during the formation of the Fe<sub>3</sub>O<sub>4</sub> nanocrystals. This makes the current synthetic approach applicable for producing versatile water-soluble magnetite nanocrystals. Details on further surface modification will be published in our next paper.

**Acknowledgment.** We thank Prof. S.-K. Yan for his assistance with TEM measurements. Funding was provided by an 863 project (2002AA302201) and NSFC projects (20225313, 90206024, 90201006).

CM035346Y