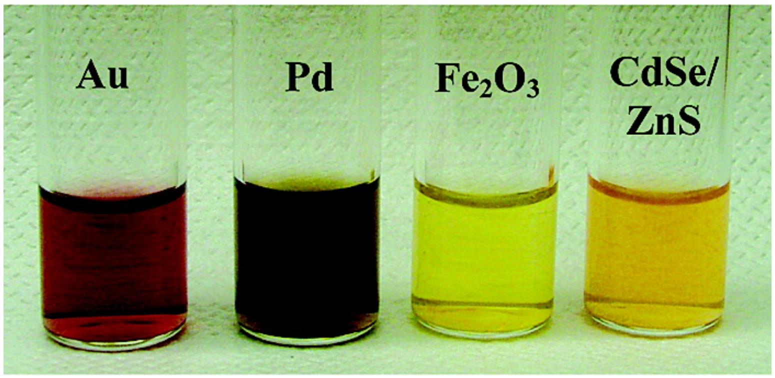
Communication

Phosphine Oxide Polymer for Water-Soluble Nanoparticles

Sang-Wook Kim, Sungjee Kim, Joseph B. Tracy, Alan Jasanoff, and Moungi G. Bawendi

J. Am. Chem. Soc., **2005**, 127 (13), 4556-4557• DOI: 10.1021/ja043577f • Publication Date (Web): 10 March 2005



Journal of the American Chemical Society is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

J|A|C|S
COMMUNICATIONS

Phosphine Oxide Polymer for Water-Soluble Nanoparticles

Sang-Wook Kim,† Sungjee Kim,† Joseph B. Tracy,† Alan Jasanoff,‡ and Moungi G. Bawendi*,†

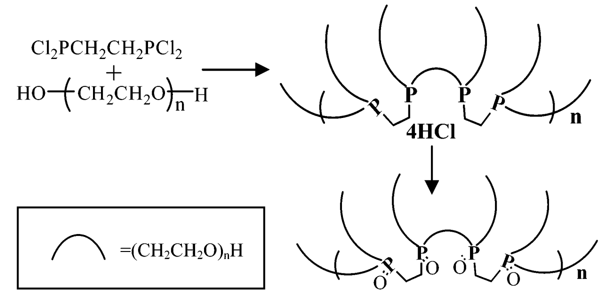
Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139, and
Whitehead Institute for Biomedical Research, 9 Cambridge Center, Cambridge, Massachusetts 02138

Received October 22, 2004; E-mail: mgb@mit.edu

Nanoparticles dispersed in water are useful for many applications. As examples, semiconductor quantum dots (QDs) are used as fluorescent tags in biology, magnetic Fe_2O_3 particles are used as contrast agents in magnetic resonance imaging (MRI), and Pd particles are used as green catalysts.[1] The easiest method to obtain nanoparticles in water is to prepare them directly in water using water-soluble surfactants or polymers. The size distributions of nanoparticles of Pd, Au, and metal oxides such as Fe_2O_3 or Fe_3O_4 that are prepared this way[2] are generally broad, however, and it is generally not possible to synthesize high-quality QDs directly in water. Many applications require uniform nanoparticles; there are many advantages of using particles with narrow size distributions because of their uniform physical and optical properties.

There are now many methods for preparing nanoparticles such as QDs, γ-Fe_2O_3, and Pd with narrow size distributions[3] using the decomposition of organometallic precursors in the presence of organic ligands, which renders them insoluble in water and precludes their use in biological applications without further processing. Ligand exchange procedures that allow the transfer of nanoparticles from organic solvents into water have therefore attracted considerable attention. To obtain water-soluble QDs, polymers, lipids, and thiol-based ligands including dithiols and thiol dendrimers have been used.[4] Various metallic nanoparticles have been dispersed in water using 4-(dimethyl-amino)pyridine.[5] Reports describing a method for dispersing Fe_2O_3 nanoparticles in water using α-cyclodextrin, and a general method for preparing water-dispersible nanoparticles using a polymer consisting of maleic anhydride were recently published.[6]

Scheme 1. Synthesis of PEG−Phosphine Oxide Polymer



Here we present an alternative method for bringing a variety of nanoparticles into water using easily synthesized polymers consisting of phosphine oxide and poly(ethylene glycol). The procedure for the synthesis of the polymers is shown in Scheme 1. (See Supporting Information for details.) There are two major steps: (1) polymerization of 1,2-bis(dichlorophosphino)ethane and poly(ethylene glycol) and (2) neutralization of HCl•phosphine salts that form during (1). The phosphines are oxidized to phosphine oxides during step (2). Figure 1 shows the ^{31}P NMR spectrum of the HCl•phosphine salts, phosphine oxide polymer, and Au•nanoparticles stabilized by polymer in water. A chemical shift of $\delta = 22$ ppm is observed for the HCl•phosphine salts, which shifts to $\delta = 27.6$ ppm for the phosphine oxide peaks. A comparison of the peak shifts of $\delta = 27.6$ ppm for the pure polymer and $\delta = 26$ ppm for the polymer-stablized Au nanoparticles in water suggests the formation of a weak Au•phosphine oxide complex. Shifting of the phosphine oxide peak is also observed with Fe_2O_3 nanoparticles. The best results were obtained using PEG (Mn-600). When PEG (Mn-200) was used, neutralization was not successful. The degree of polymerization is controlled by the stoichiometry of the phosphine and poly(ethylene glycol). We investigated polymers formed from ratios of 1:2, 1:3, and 1:10 phosphine:PEG. At a 1:2 ratio, all of the PEG hydroxyl groups have reacted, while at a 1:10 ratio, networks do not form. No particle transfer into the water is observed in either extreme case. Clear solutions of Au, γ-Fe_2O_3, Pd, and QD were obtained after filtration (Figure 2). When water is added during ligand exchange, an insoluble white precipitate forms, which is the original organic ligand that is displaced by the PEG−phosphine oxide polymer. A detailed procedure for the ligand exchange is described in the Supporting Information. The hydrodynamic radius is critically important for biological applications. For example, the preferred hydrodynamic radii are between 5 and 25 nm for mapping lymph nodes, and below 30 nm for cell injection.[7] Figure 3 shows the hydrodynamic radii of ~6 nm Au, ~ 8 nm Fe_2O_3, and ~6 nm QD nanoparticles in water using our polymer. A hydrodynamic radius of 15−25 nm is observed. The hydrodynamic radius of the nanoparticles is smaller than that of

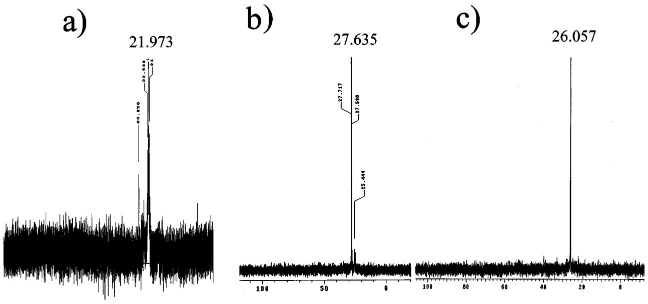


Figure 1. ^{31}P NMR spectrum of three different states of phosphines. (a) HCl phosphine salts, (b) phosphine oxide polymer, and (c) Au phosphine oxide polymer in water.

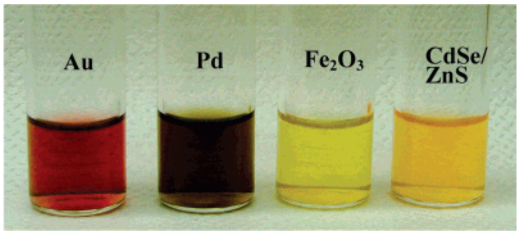


Figure 2. Photographs of nanoparticles dispersed in water.

---

† Massachusetts Institute of Technology.
‡ Whitehead Institute for Biomedical Research.

10.1021/ja043577f CCC: $30.25

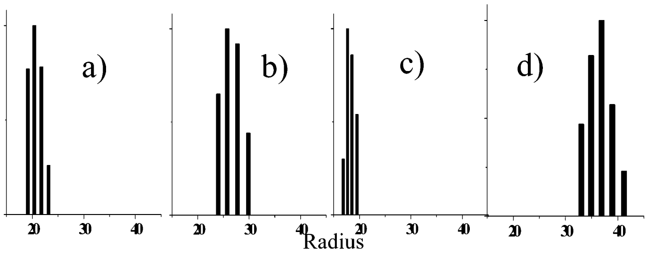


Figure 3. Hydrodynamic radius data of (a) Au, (b) Fe_2O_3, (c) CdSe/ZnS, (d) phosphine oxide gel in water.

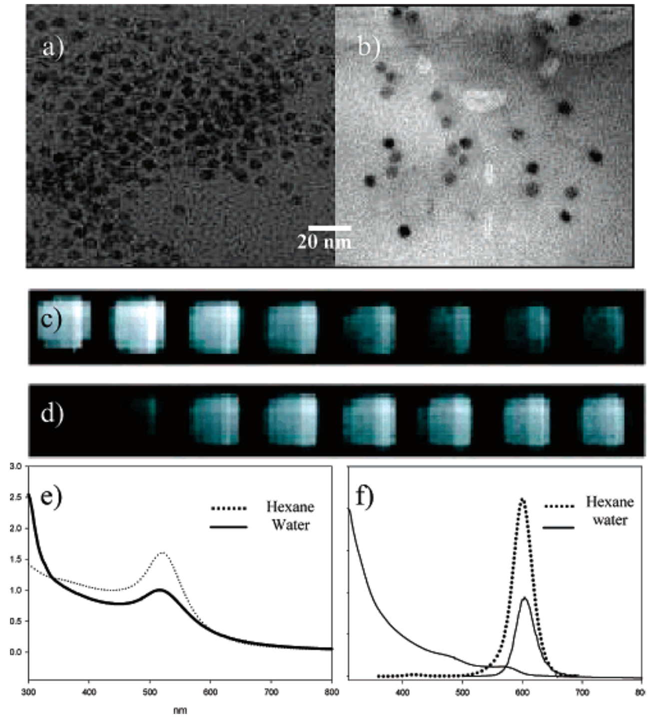


Figure 4. TEM images of Fe_2O_3 in hexane (a) and water (b); T_1 weighting ($T_R = 100$ ms, $T_E = 3$ ms) (c) and T_2 weighting $T_R = 1$ s, $T_E = 41$ ms) (d) in MRI image of Fe_2O_3 in water; UV spectra of Au NPs (e); absorbance and photoluminescence spectra of CdSe/ZnS QDs (f).

the phosphine oxide gel by itself as the gel apparently becomes more compact when associated with the nanoparticles.

The important physical properties of the nanoparticles are unchanged when they are brought into water. Panels a and b of Figure 4 show TEM images of γ-Fe_2O_3 in hexane and water, respectively. Figure 4c shows a T_1-weighted magnetic resonance (MR) image of serially diluted solutions of phosphine-coated γ-Fe_2O_3 nanoparticles in PBS buffer. Figure 4d shows a T_2-weighted scan of the same concentration series. High T_1-weighted and low T_2-weighted signal intensities at high iron concentrations indicate that the phosphine-stabilized γ-Fe_2O_3 particles are potent T_1 and T_2 relaxation agents, comparable to previously reported iron oxide MR contrast agents.[8] Figure 4e shows that the optical absorption spectrum of Au nanoparticles shows the same 525 nm surface plasmon resonance in water and in hexane. Figure 4f shows the absorption and photoluminescence (PL) spectra of CdSe/ZnS quantum dots. The peak positions of the PL are the same in hexane and water. Quantum yields of 15−20% are reproducibly observed in water, roughly half that of the original CdSe/ZnS quantum dots (34%) in organic solvent.

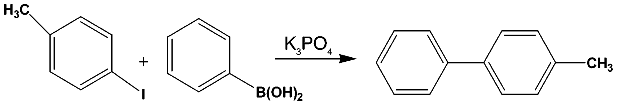


Figure 5. Suzuki coupling reaction using Pd nanoparticles.

Palladium is the most important catalyst for carbon−carbon bond formation, of which Suzuki, Heck, and Stille coupling are examples. Water-dispersible Pd nanoparticles offer an opportunity here for green chemistry. The reactivity of aqueous Pd nanoparticless was investigated using the Suzuki coupling reaction (Figure 5). When 4-iodotoluene and phenylboronic acid were reacted in the presence of 2 mol % water-dispersed Pd nanoparticles, a 97% yield of the product was obtained. In the second recycle reaction, the yield decreased to 65%, which is comparable to the reactivity of the second recycle reaction in organic solvent (71%). A small amount of black aggregate was also observed, as in organic solvent systems. We have not investigated the potential biological applications but expect that PEG−phosphine oxide gel-stabilized nanoparticles could be used for biomedical imaging of lymph nodes because the hydrodynamic radii are 15−20 nm.

In conclusion, we have developed a phosphine oxide gel using bis(dichlorophosphino)ethane and poly(ethylene glycol) that can be used to transfer various nanoparticles from organic solvents to water. These aqueous nanoparticles have physical properties and reactivities comparable to those in organic solvent.

Acknowledgment. This work was supported by the post-doctoral fellowship program of the Korea Science & Engineering Foundation, the U.S. National Science Foundation-Materials Research Science and Engineering Center program under grant DMR-9808941, the U.S. National Institutes of Health grant R33 EB-00673, and by the Institute for Collaborative Biotechnologies through grant DAAD19-03-D-0004 from the U.S. Army Research Office.

Supporting Information Available: Experimental details of synthetic procedure of phosphine oxide gel, ligands exchange. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Dubertret, B.; Skourides, P.; Norris, D.; Noireaux, V.; Brivanlou, A.; Libchaber, A. *Science* **2002**, *298*, 1759−1762. (b) Perez, J. M.; Josephson, L.; O'Loughlin, T.; Hogemann, D.; Weissleder, R. *Nat. Biotechnol.* **2002**, *20*, 816−820. (c) Li, Y.; Hong, X. M.; Collard, D. M.; El-Sayed, M. A. *Org. Lett.* **2000**, *2*, 2385−2388.

(2) (a) Teranish, T.; Miyake, M. *Chem. Mater.* **1998**, *10*, 594−600. (b) Enustun, B. V.; Turkevich, J. *J. Am. Chem. Soc.* **1963**, *85*, 3317−3328. (c) Kang, Y. S.; Risbud, S.; Rabolt, J. F.; Stroeve, P. *Chem. Mater.* **1996**, *8*, 2209−2211.

(3) (a) Murray, C. B.; Norris, D. J.; Bawendi, M. G. *J. Am. Chem. Soc.* **1993**, *115*, 8706−8715. (b) Hyeon, T.; Lee, S. S.; Park, J.; Chung, Y.; Na, H. B. *J. Am. Chem. Soc.* **2001**, *123*, 12798−12801. (c) Kim, S.-W.; Park, J.; Jang, Y.; Chung, Y.; Hwang, S.; Hyeon, T. *Nano Lett.* **2003**, *3*, 1289−1291.

(4) (a) Bruchez, J. M.; Moronne, M.; Gin, P.; Weiss, S.; Alivisatos, A. P. *Science* **1998**, *281*, 2013−2016. (b) Chan, W. C. W.; Nie, S. *Science* **1998**, *281*, 2016−2018. (c) Mattoussi, H.; Mauro, J. M.; Goldman, E. R.; Anderson, G. P.; Sundar, V. C.; Mikulec, F. V.; Bawendi, M. G. *J. Am. Chem. Soc.* **2000**, *122*, 12142−12150. (d) Wang, Y. A.; Li, J. J.; Chen, H. Y.; Peng, X. G. *J. Am. Chem. Soc.* **2002**, *124*, 2293−2298.

(5) Gittins, D. I.; Caruso, F. *Angew. Chem., Int. Ed.* **2001**, *40*, 3001−3004.

(6) (a) Wang, Y.; Wong, J. F.; Teng, X.; Lin, X. G.; Yang, H. *Nano Lett.* **2003**, *3*, 1555−1559. (b) Pellegrino, T.; Manna, L.; Kudera, S.; Liedl, T.; Koktysh, D.; Rogach, A. L.; Keller, S.; Radler, J.; Natile, G.; Parak, W. J. *Nano Lett.* **2004**, *4*, 703−707

(7) Seksek, O.; Biwersi, J.; Verkman, A. S. *J. Cell. Biol.* **1997**, *138*, 131−142.

(8) Shen, T.; Weissleder, R.; Papisov, M.; Bogdanov, A., Jr.; Brady, T. *J. Magn. Reson. Med.* **1993**, *29*, 599−604.

JA043577F