Organometallic Hollow Spheres

DOI: 10.1002/ange.201003101

Organometallic Hollow Spheres Bearing Bis(N-Heterocyclic Carbene)–Palladium Species: Catalytic Application in Three-Component Strecker Reactions**

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Recently, diverse micro- and submicroparticles have been designed and prepared for tailored applications in adsorbents, biomedical assays, and heterogeneous catalysis.[1] In addition to conventional inorganic particles, functional spheres can be formed by coordination-directed assembly of molecular building blocks.[2] In this case, unique molecule-based functionalities can be introduced into the spheres with a high density of molecular functional sites. For example, we reported formation of submicrospheres through a hapticity change of the [(η^6-hydroquinone)Rh(cod)]BF_4 (COD = 1,5-cyclooctadiene) building block, with successful application as catalysts for polymerization of phenylacetylene.[2b]

On the basis of structure, these molecular spherical materials can be divided into three classes: simple sphere, core/shell, and hollow sphere. Usually, the catalytic function of the spheres is related to the chemical properties of the surface, and the chemical species inside the spheres usually cannot participate. Thus, the core/shell structure is more appropriate to save materials costs by locating relatively inexpensive building blocks inside the spheres.[3] In this regard, we prepared organometallic spheres having a Mn–quinonoid core/Rh–quinonoid shell structure.[3b] Ultimately, in view of cost, a hollow shape with an empty inner space is more appropriate. However, direct formation of a molecular hollow sphere by coordination-directed assembly is quite difficult[4] and usually sequential synthetic steps are required with a designed template.[5] For example, Prussian blue hollow spheres were recently fabricated by using a block copolymer as template material.[5]

N-Heterocyclic carbene (NHC) ligands are currently very popular in organometallics.[6] The NHCs, generated by abstraction of the proton at the 2-position of 1,3-disubstituted imidazolium salts, show powerful coordination ability toward a wide range of metal ions. We have studied the synthesis of new functional materials based on NHC chemistry for diverse applications including heterogeneous catalysts and hydrogen storage materials.[7] Here we report the template-free synthesis of organometallic hollow spheres with concomitant formation of bis(NHC) Pd species and their catalytic applications in one-pot three-component reactions.

Usually, appropriate bases are required to generate NHC moieties by abstracting the proton at the 2-position of 1,3-disubstituted imidazolium salts.[6] However, some metal reagents have been known to react directly with imidazolium salts to form metal NHC species. For example, silver oxide[8] and copper oxide[9] can function as base and metal source. In addition, metal acetates such as palladium acetate can form metal NHC species by direct reaction with imidazolium salts.[10] Based on this chemistry, we designed a tetrahedral imidazolium building block for generating organometallic particles bearing metal NHC species through formation of 3D infinite networks of molecular building blocks (Scheme 1). One-dimensional main-chain metallopolymers have been prepared by using predesigned bis-phosphines or bis-NHC ligands.[11]

First, tetrakis(4-bromophenyl)methane was prepared from tetraphenylmethane by a literature method.[12] The four imidazolyl groups were then introduced by Ullmann-type coupling with copper catalysis. After screening several copper reagents, including the copper oxides, copper iodide showed the best reactivity. The resultant neutral tetrakis[4-(1-imidazolyl)phenyl]methane (**1**) was further treated with methyl iodide to form tetrahedral building block **2** having four imidazolium salts.

For preparation of organometallic hollow spheres (OMHS), building block **2** (0.5 equiv relative to Pd) was treated with palladium acetate in DMF (5 mL) at 110 °C. Gradually, a pale yellow precipitate was formed on the bottom of the glassware. After washing with DMF and dichloromethane and drying at 100 °C for 10 h under vacuum, the resultant solid was investigated by scanning electron microscopy (SEM). Figure 1 a shows a typical SEM image of the spherical particles. The average sphere size was calculated to (1.50 ± 0.15) μm by counting 544 particles (Figure 1 c). The negligible change in the size of the spheres when the solvent volume was changed from 5.0 to 20 mL implies that the particle size does not result from conventional kinetic effects in the growth process,[13] but rather from the solubility limitation of the particles. Interestingly, careful investigation of the SEM images of the spheres showed different contrast

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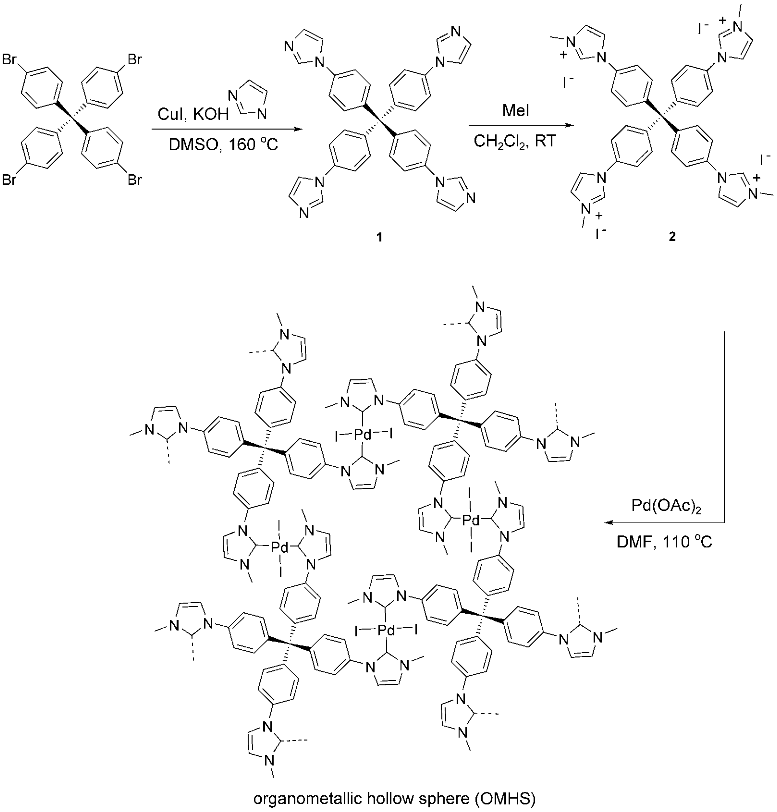
[**] This work was supported by grant NRF-2009-0084799 and the WCU program (R31-2008-000-10029-0) funded by MEST of Korea. H.Y.Y. thanks NRF-2009-0094024 (Priority Research Centers Program) for grants. H.J.K. acknowledges the Hydrogen Energy R&D Center, a 21st century Frontier R&D Program.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201003101.



Scheme 1. Formation of a 3D infinite network through NHC chemistry involving tetrahedral imidazolium building block **2**.

between the center and side parts of the spheres, which implies a hollow structure of the materials (Figure 1 a and Figure S1 in Supporting Information). Sometimes, open spheres showed empty inner spaces (inset of Figure 1 a) In addition, when the spheres were heated for several days, distorted spheres were observed (see representative image in the inset of Figure 1 a and Figure S2 in the Supporting Information) To clarify the structure, the spheres were microtomed after being embedded into epoxy resin, and the cut spheres showed an empty inner space. (Figure 1 b) For further investigation of the structural homogeneity of the materials, transmission electron microscopy (TEM) studies were conducted and showed vivid contrast difference in all images (at least 25) of spheres with bright core and dark shell (Figure S3 in the Supporting Information).

To acquire information on the chemical components of the hollow spheres, elemental analysis (EA) by combustion was conducted, which clearly supports the formation of the [(nhc)$_2$PdI$_2$] species. The observed contents of carbon (36.65), nitrogen (8.62), and hydrogen (2.85 wt %) in the hollow spheres matched well with the calculated values of for [{C$_{41}$H$_{36}$N$_8$Pd$_2$I$_4$}$_n$] (C 36.18, N 8.23, H 2.67 wt %). The iodide counteranions of building block **2** formed part of the ligand sphere in the {(nhc)$_2$Pd} species, a common observation in the synthesis of mono- and polymeric Pd NHC complexes from imidazolium halides and palladium acetate.[11,14] Elemental mapping by energy dispersive X-ray absorption spectroscopy (EDS) confirmed a homogeneous distribution of palladium and iodine (Figure 1 d). Again, the intensity of the mapped images showed the characteristic properties of a hollow structure with contrast between the interiors and walls of the spheres. The powder X-ray diffraction pattern (XRPD) of OMHS showed amorphous character. The thermal stability of the hollow spheres was investigated by thermogravimetric analysis (TGA), which showed them to be stable up to at least 250 °C (Figure 1 e).

To confirm the chemical structure of the hollow spheres, solid-state ^{13}C NMR spectroscopic studies were conducted. As shown in Figure 2 b, all peaks were clearly assignable to the carbon atoms in the expected structure with help of a model compound (see below). The ^{13}C NMR peaks from the methyl and methylene groups, the different benzene rings, and the imidazole ring appeared at 39, 64, and 124–147 ppm. In particular, the ^{13}C NMR peak for carbene carbon appeared at 168 ppm, which matches well with known values (167–169 ppm) in [(nhc)$_2$PdI$_2$] complexes.[15] In addition, a model compound was prepared by treating 1-methyl-3-(4-tolyl)imidazolium iodide (Figure 2 a) with palladium acetate in DMF at 110 °C for one day to

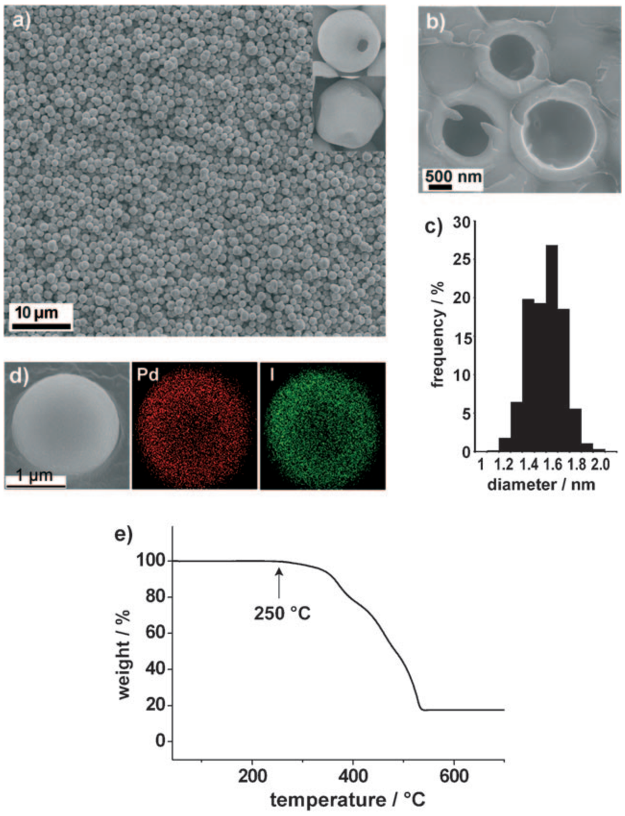


Figure 1. a) Typical SEM image of organometallic hollow spheres (OMHS) bearing {(nhc)$_2$Pd} species (inset: selected open and distorted spheres); b) SEM image of microtomed spheres; c) size distribution diagram; d) EDS elemental-mapping images of hollow spheres; e) TGA curve of OMHS.

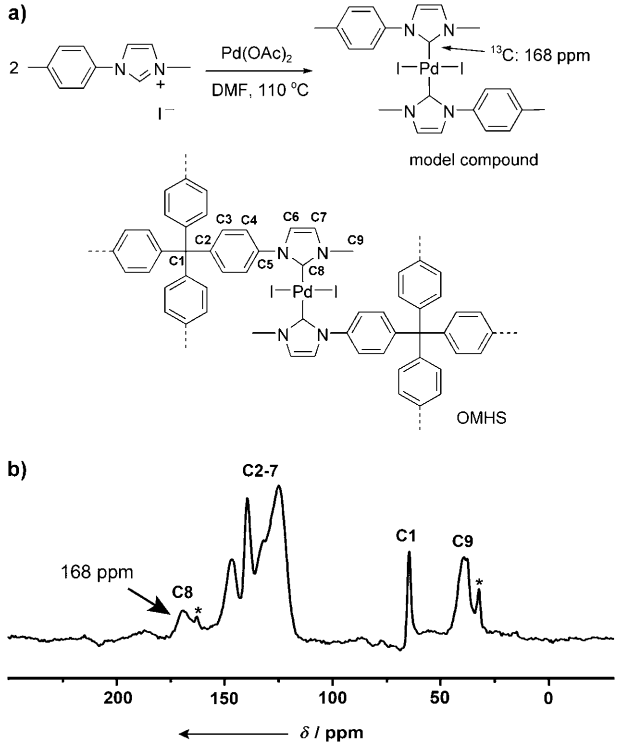


Figure 2. A model compound (a) and solid-phase ^{13}C NMR spectrum of OMHS (b). Peaks indicated by asterisks correspond to DMF.

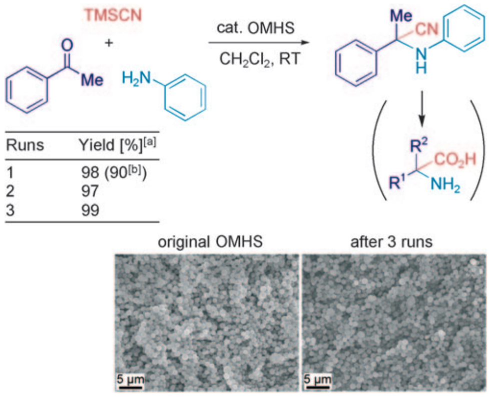


Figure 3. Top: OMHS-catalyzed (4.0 mol% Pd relative to acetophenone) three-component Strecker reaction at room temperature for 10 h between acetophenone (1.0 mmol), aniline (1.1 mmol), and trimethylsilyl cyanide (TMSCN, 2.0 mmol). [a] Conversion. [b] Yield of isolated product. Bottom: SEM images of OMHS before and after catalysis.

give the corresponding [(nhc)$_2$PdI$_2$] complex, which was fully characterized by ^{1}H and ^{13}C NMR spectroscopy and high-resolution mass spectrometry.[16] As expected, the ^{13}C NMR peak of the carbene carbon atom of the model compound appeared at $\delta = 168$ ppm.

According to time-dependent TEM studies, the hollow core was gradually formed from a nonhollow sphere during the reaction. We speculate that formation of a more compact network during the ripening process generates the hollow structure, as observed in template-free synthesis of metal oxide or metal chalcogenide hollow spheres in materials science[17] (Figure S4 in the Supporting Information).

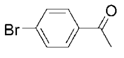
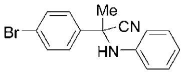
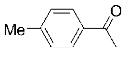
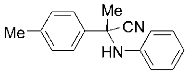
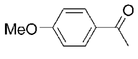
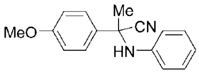
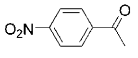
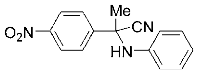
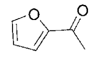
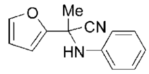
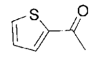
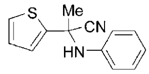
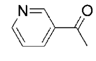
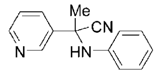
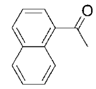
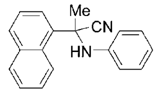
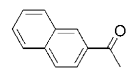
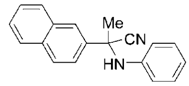
Recently, diverse metal NHC complexes have been prepared and applied as catalysts in various organic transformations.[6] The unique coordination abilities of the NHC-based ligands are responsible for their unprecedented stability and catalytic reactivity. Among them, Pd NHC complexes attract special attention as catalysts in C−C and C−N bond formation.[18] Considering the existence of Pd NHC species and the atom-economical hollow structure, we applied OMHS as a heterogeneous catalyst.

Among the diverse reactions, the three-component Strecker reaction attracted our attention.[19] The Strecker reaction, forming α-amino nitriles by reaction of an amine, a cyanide source, and an aldehyde or ketone, is especially useful for the synthesis of α-amino acid derivatives, even on an industrial scale (Figure 3). Although this reaction has attracted continuous attention, the Pd NHC catalysts were only reported recently.[20] Moreover, as far as we are aware, no heterogeneous systems based on metal NHC complexes have been reported for this reaction. Most studies on the one-pot three-component Strecker reaction focus on aldehydes, and efficient systems for ketones are still lacking. Hence, in this study, we focused on the one-pot Strecker reaction of ketones.

As shown in Figure 3, OMHS (4.0 mol% Pd relative to substrate) showed excellent activity in the one-pot Strecker reaction of acetophenone with aniline at room temperature. In a control experiment without catalyst, no conversion of acetophenone occurred. The catalysts were easily isolated by centrifugation and reused without loss of the original shape and catalytic activity for three successive runs. We speculate that excellent maintenance of the structure and catalytic activities may originate from the low reaction temperature and relatively simple Lewis acidic function of the catalysts (see Figure S5 in Supporting Information for SEM image of recovered OMHS).

Table 1 summarizes the catalytic activity of the hollow spheres toward a variety of ketones. In a recent report on one-pot three-component Strecker reactions catalyzed by homogeneous Pd NHC complexes, 3.0 mol% catalyst gave 86% conversion of 4-methoxyacetophenone in 24 h.[20] In contrast, the heterogeneous systems presented herein (4.0 mol% Pd) showed 92% conversion of 4-methoxyacetophenone in 10 h. As reported in the literature, the present catalytic system also showed significant functional-group dependency, possibly due to the coordination ability of the functional groups of the substrates.[19,20] In the case of 4-nitroacetophenone, 2-acetylthiophene, and 3-acetylpyridine, conversion of the substrate was almost completely or significantly suppressed. (Table 1, entries 4, 6, and 7) In sharp contrast to 2-acetylthiophene, 2-acetylfuran showed good conversion to the expected product (Table 1, entry 5). These observations strongly imply that the catalytic function of the hollow spheres originates from Lewis acidic activation of the ketone or imine through coordination of palladium. In the case of mono-acetyl naphthalenes, a significant steric effect was observed (Table 1, entries 8 and 9) Compared with 2-acetylnaphthalene, the conversion of 1-acetylnaphthalene was significantly suppressed.

Table 1: One-pot three component Strecker reactions of ketones catalyzed by OMHS.[a]

Entry	Ketone	Product	Yield [%][b]
1			96 (85)
2			95 (91)
3			92 (83)
4			3 (–)[c]
5			95 (89)
6			56 (44)
7			51 (50)
8			68 (65)
9			91 (86)

[a] Reaction conditions: 1.0 mmol substrate, 1.1 mmol aniline, 2.0 mmol TMSCN, cat. OMHS (4.0 mol% Pd relative to substrate), 2.0 mL CH_2Cl_2, 10 h, room temperature. [b] Determined by ^{1}H NMR spectroscopy; yields of isolated product are given in parentheses. [c] Nearly the same results were observed in repeated tests.

In conclusion, organometallic hollow spheres bearing $\{(nhc)_2Pd\}$ species were prepared for the first time by a template-free route using tetraimidazolium building blocks and palladium acetate. Their physical structure and properties were characterized by SEM, TEM, microtoming experiments, and TGA, and their chemical composition by EDS, solid-phase ^{13}C NMR spectroscopy and EA. The organometallic hollow spheres demonstrate excellent activities as heterogeneous catalysts in one-pot three-component Strecker reactions of ketones. We believe that this approach can be extended to the development of more diverse NHC-based heterogeneous catalysts.

Experimental Section

All SEM and EDS-mapped images were taken with an FE-SEM (JSM6700F). The TEM images were taken with a JEOL 2100F unit operated at 200 kV. Solid-phase ^{13}C NMR spectra were recorded on a 400 MHz Solid State Bruker DSX NMR spectrometer at Korea Basic Science Institute (Daegu). Elemental analysis was performed on a CE EA1110 instrument. TGA curve was obtained on a Seiko Exstar 7300. All ^{1}H NMR and ^{13}C NMR spectra for new compounds in the synthesis of the building block were recorded on Varian (300 MHz) spectrometers. Mass spectra of new compounds were obtained with a JEOL JMS 700 spectrometer.

Synthesis of OMHS: Building block **2** (50 mg, 0.043 mmol) was dissolved in DMF (5 mL) by sonication. Palladium acetate (19 mg, 0.085 mmol) was added and the reaction mixture heated at 110°C for 2 d. A pale yellow solid was formed and washed with DMF and methylene chloride. After drying at 100°C for 10 h under vacuum, OMHS (25 mg) was isolated in 43% yield (based on Pd). The detailed synthetic procedure for building block **2** is described in the Supporting Information.

Procedure for catalytic reactions: OMHS (27 mg, 0.040 mmol Pd), ketone (1.0 mmol), aniline (0.10 mL, 1.1 mmol), and TMSCN (0.27 mL, 2.0 mmol) were added to 2 mL of dichloromethane. The reaction mixture was stirred for 10 h at room temperature. After reaction, the catalyst was recovered by centrifugation and dichloromethane was removed by evaporation. The crude product was directly analyzed by ^{1}H NMR spectroscopy and purified by flash column chromatography.

Received: May 12, 2010
Revised: July 15, 2010

Keywords: carbene ligands · heterogeneous catalysis · hollow spheres · palladium · Strecker reaction

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