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## COMMUNICATION

## Surfactant-free single-nano-sized colloidal Cu nanoparticles for use as an active catalyst in Ullmann-coupling reaction<sup>†</sup>

Yuto Isomura,<sup>a</sup> Takashi Narushima,<sup>b</sup> Hideya Kawasaki,<sup>a</sup> Tetsu Yonezawa<sup>b</sup> and Yasushi Obora\*<sup>a</sup>

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Surfactant-free, single-nano-sized copper nanoparticles (Cu NPs) (size: about 2 nm) were prepared by the DMF reduction method. The Cu NPs showed high catalytic activity (with a turnover number (TON) of up to  $2.2 \times 10^4$ ) in Ullmann-type cross-coupling of aryl halides with phenols under ligand-free conditions.

The interest and use of transition metal nanoparticles (NPs) (diameter ~100 nm) has shown an exponential growth in the past few years.<sup>1</sup> In particular, transition metal NPs have become a very important class of catalysts owing to their inherently large surface area, being different from that of the bulk metal.<sup>1</sup> To date, various synthetic methods of colloidal metal NPs have been developed and used as catalysts in chemical transformations.<sup>1b,c</sup> Such metal NPs are prone to lose reactivity in their bulk metal form; therefore, several stabilizers such as functionalized polymers,<sup>2</sup> dendrimers,<sup>3</sup> inorganic solids,<sup>4</sup> ligands,<sup>5</sup> and ionic surfactants<sup>6</sup> are generally prerequisites to prevent aggregation of the metal NPs in these preparations.

On the other hand, the use of precious metals limits the attractiveness in industrial applications owing to their high cost. As an alternative, Cu is widely used industrially and is an inexpensive metal, and considerable efforts have been devoted to explore its use in catalysis.<sup>7</sup> For instance, Cu-catalyzed arylation of phenols (Ullmann condensation) is an important organic transformation.<sup>8</sup> However, these examples generally require large Cu loadings (5–20 mol%) and are highly dependent on the use of pyridine- or phosphine-type ligands to achieve high catalytic activity. The employment of nano-particulate Cu catalysts represents a much more recent research trend. Various exploitable methods exist for the synthesis of Cu NPs and their reactions.<sup>81,m,p-r,9</sup> These Cu nanoparticle catalysts are attractive both from economic and industrial points of view, as compared to those of the precious metals.

Reflecting on these studies using an inexpensive Cu-catalyzed reaction, we became aware of the necessity of investigating *catalytically active* support/ligand/surfactant-free single-nano-sized Cu nanoparticles in a cross-coupling reaction.

More recently, we have studied the surfactant-free solution synthesis of noble-metal (Au, Pt and Pd) nanoclusters (NCs) (diameter 1–1.5 nm) using the DMF reduction method.<sup>10</sup> We found that the use of colloidal Pd NCs exhibits in highly catalytic cross-coupling reactions because of the ultra-small sizes and the surfactant free-active surfaces.<sup>10c</sup> The Pd NCs had a high turnover number, up to  $6.0 \times 10^8$  was achieved. Inspired by these studies on these noble metal NCs as active catalysts, we report the solution synthesis of surfactant-free, single-nano-sized Cu NPs (size: about 2 nm) using the DMF reduction method. We first found that the tiny Cu NPs showed high catalytic activity under unusual ligand-free conditions in Ullmann-type O-arylation reactions.

The Cu NPs can be prepared simply according to the following one-step reaction. A solution of 15  $\mu$ L of 0.1 M aqueous CuCl<sub>2</sub> was added to 15 mL of DMF at 140 °C; the DMF solution was heated under reflux at 140 °C for 8 h.

The transmission electron microscopy (TEM) image of the Cu NPs shows numerous nanoparticles of size approximately 2 nm (Fig. 1, left). The high-magnification TEM image of Cu NPs shows that the crystal lattice fringes are 0.2 nm apart, which agrees with the *d* value of the (111) planes of the metallic Cu crystal (see ESI†). Dynamic Light Scattering (DLS) measurement of the Cu NPs reveals that the average diameter of the Cu NPs is around 2 nm (Fig. 1), which is in good agreement with the HRTEM image. The resulting light-yellow solution was photoluminescent and the maximum emission wavelength was around 420 nm for UV excitation at 350 nm



**Fig. 1** Left: HRTEM image of DMF-protected Cu NPs. Bar length: 5 nm. Right: DLS spectrum of Cu NPs.

<sup>&</sup>lt;sup>a</sup> Department of Chemistry and Materials Engineering, Faculty of Chemistry, Materials and Bioengineering, Kansai University, Suita, Osaka 564-8680, Japan. E-mail: obora@kansai-u.ac.jp; Fax: +81-6-6339-4026; Tel: +81-6-6368-0876

<sup>&</sup>lt;sup>b</sup> Division of Materials Science and Engineering, Faculty of Engineering, Hokkaido University, Sapporo, Hokkaido 060-8628, Japan

<sup>&</sup>lt;sup>†</sup> Electronic supplementary information (ESI) available: Photoluminescence emission spectrum; XPS spectrum; experimental and characterization data and <sup>1</sup>H and <sup>13</sup>C NMR spectra for products **3a–3i**. See DOI: 10.1039/c2cc30975k

Table 1Cu-NPs-catalyzed Ullmann O-arylation of iodobenzene (1a)with 3,5-dimethyl phenol  $(2a)^a$ 



Entry	Solvent	$T/^{\circ}\mathrm{C}$	Yield $3a^{b}$ (%)	$TON^c$	
1	DMF	80	7	$7.0 \times 10^{-10}$	
2	DMF	110	>99(88)	$1.0 \times 10^{6}$	
3	DMF	140	88	$8.8 \times 10^{\circ}$	
4	MeCN	110	51	$5.1 \times 10^{-5}$	
5	NMP	110	12	$1.2 \times 10^{-1}$	
$6^d$	DMF	110	22	$2.2 \times 10^{\circ}$	
$7^e$	DMF	110	n.d.	—	

<sup>*a*</sup> Conditions: **1a** (1.5 mmol) was allowed to react with **2a** (1.0 mmol) in the presence of 1 mL of Cu NP catalyst solution (0.1 mM) and Cs<sub>2</sub>CO<sub>3</sub> (2.0 mmol) in solvent (1 mL) at T °C for 24 h. <sup>*b*</sup> GC yields based on **2a** used. The number in the parentheses shows the isolated yield. <sup>*c*</sup> TON = **3a** (mol)/Cu NPs (mol). <sup>*d*</sup> 1 mL of Cu NP catalyst solution (10  $\mu$ M) and **1a** (15 mmol) used. <sup>*e*</sup> Without Cu NPs.

because of the ultra-small sizes of around 2 nm (see ESI<sup>†</sup>).<sup>11</sup> The chemical composition of the Cu NPs was examined by X-ray photoelectron spectroscopy on a dried sample (see ESI<sup>†</sup>). The major contribution of the Cu  $2p_{3/2}$  peak (932.0 eV) is that associated with zerovalent copper<sup>12</sup> However, the minor shoulder peak with the smaller contribution at 934.4 eV is consistent with CuO,<sup>12</sup> suggesting the existence of a thin copper oxide layer around the particle surfaces.

The Cu NPs prepared by the DMF reduction method were evaluated as catalysts for arylation of phenols, which is an efficient catalytic method for aryl-oxygen bond formation in organic synthesis.<sup>8</sup> As shown in Table 1, the reaction conditions were optimized by using the reaction between iodobenzene (1a: 1.5 mmol) and 3,5-dimethylphenol (2a: 1.0 mmol) as the model reaction. For instance, Cu NPs ( $1 \times 10^{-2}$  mol% based on 2a used) in DMF were used at 80 °C, and the desired product 3a was obtained in only 7% yield (entry 1, Table 1). Then, when the reaction temperature was raised to 110 °C, quantitative yield and 88% isolated yield was achieved (entry 2). In this reaction, Cs<sub>2</sub>CO<sub>3</sub> was found to be a suitable base, whereas other bases such as Na<sub>2</sub>CO<sub>3</sub>, KOH, K<sub>3</sub>PO<sub>4</sub>, and NEt<sub>3</sub> totally inactivated the catalytic activity in this reaction under these conditions. Next, the solvent was evaporated under vacuum from a DMF solution of Cu NPs, and the residue was re-dissolved in other polar-solvents such as acetonitrile (MeCN) and N-methylpyrrolidone (NMP); then these solutions were used in the reaction. The reactions using MeCN and NMP were not effective and gave 3a in 51% and 12% yield, respectively (entries 4 and 5). Here, the conversions of 1a and 2a were low and remained unchanged. Therefore, DMF was considered to be the best solution as a solvent in this reaction. When the catalyst loading was decreased to  $1 \times 10^{-3}$  mol%, the highest turnover number (TON,  $2.2 \times 10^4$ ) was achieved in the presence of 15 mmol of 1a (entry 6). Needless to say, no reaction was induced in the absence of Cu NPs (entry 7). The present support/ligand/surfactant-free Cu NPs showed remarkable catalytic activity which showed almost an order of magnitude higher turnover number than Cu<sub>2</sub>O nanocube.<sup>8p</sup>

On the basis of the optimized reaction conditions, we expanded the scope of the reaction substrates, as shown in

**Table 2** Cu-NP-catalyzed Ullmann O-arylation of aryl halides (1)with various phenols  $(2)^a$ 

$$R^{1} \xrightarrow{K} X + HO \xrightarrow{Cat Cu NPs} R^{2} \xrightarrow{Cat Cu NPs} R^{1} \xrightarrow{K} O \xrightarrow{Cat Cu NPs} R^{2}$$

$$110 \ C, 24 h$$

$$3$$

			-			•	
Entry	Ar–X	1	Ar'–OH	2	$\operatorname{Yield}^{b}(\%)$		$\text{TON}^c (\times 10^3)$
$1^d$		1a	НО	2b	93(85)	3b	9.3
$2^d$		1a	HOLOMe	2c	85(81)	3c	8.5
3 <sup><i>d</i></sup>		1a	но	2d	71(65)	3d	7.1
4 <sup><i>d</i></sup>		1a	HO	2e	64(60)	3e	6.4
5 <sup><i>d</i></sup>		1a	HO	2f	70(66)	3f	7.0
6		1b	HO	2a	89(83)	3g	8.9
7	MeO	1c	HO	2a	87(80)	3h <sup>e</sup>	8.7
8	F <sub>3</sub> C	1d	HO	2a	90(75)	3i	9.0
9	⟨ <sup>S</sup> ⟩∕'	1e	HO	2a	n.d.	3j	_
10 <sup><i>d,f</i></sup>	Br	1f	HO	2a	93(85)	3a	9.3
11 <sup><i>d,f</i></sup>	Br	1f	но	2b	70(66)	3b	7.0
12 <sup><i>d,f</i></sup>	Br	1f	HO	2c	89(84)	3c	8.9

<sup>*a*</sup> Conditions: same as entry 2, Table 1. <sup>*b*</sup> GC yields based on **2** used. The numbers in the parentheses show the isolated yields. <sup>*c*</sup> TON = **3** (mol)/Cu NPs (mol). <sup>*d*</sup> Reaction temperature was 140 °C. <sup>*e*</sup> White solid: mp: 65–67 °C (Lit:<sup>8e</sup> 67 °C). <sup>*f*</sup> Bromobenzene (15 mmol) used.

Table 2. In the reaction of **1a** with various substituted phenols, the corresponding diaryl ethers were obtained in good to excellent yields (entries 1, 2 and 4–7, Table 2). Phenols bearing methyl (**2b**) and methoxy (**2c**) substituents provided arylation products in high yields (entries 1 and 2). Reaction of o- (**2d**), m- (**2e**), p-cresol (**2f**) gave the corresponding products (**3d**–**3f**) in good yields (entries 3–5). To further explore the scope of this reaction, several aryl halides were used (entries 6–12). The substrates bearing electron-donating and electron-withdrawing groups were tolerated as coupling partners (entries 6–8). The use of iodothiophene (**1e**) resulted in total

catalytic inactivity due to aggregation of the Cu NPs during the reaction course (entry 9). When the amount of bromobenzene (**1f**) was increased to 15 mmol, it also afforded arylation products in excellent yields (entries 10–12).

The reusability of the Cu NPs catalyst was examined under the conditions given in entry 2, Table 1. In the first cycle, the product **3a** was obtained in quantitative yield with complete conversion of **2a**. The resulting reaction mixture containing Cu NPs catalyst was subjected to reaction for the next catalytic sequence by adding **1a**, **2a** and Cs<sub>2</sub>CO<sub>3</sub>. The Cu NPs could be re-used as a catalyst for the coupling reaction at least three times.

However, the yield of 3a deteriorated after repeated use (51% and 18% after second and third re-uses, respectively).

In conclusion, we have developed Cu NPs with high surface area for effective utilization of metallic-resources in chemical transformations. The Cu NPs were firstly prepared by surfactantfree, DMF reduction methods, the particle size of which (about 2 nm) was estimated by HRTEM as well as DLS spectrum. These tiny Cu NPs served as an efficient catalyst in the crosscoupling reaction of aryl halides with phenols under low catalyst loading and ligand-free conditions.

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## Notes and references

- 1 (a) Metal Nonoclusters in Catalysis and Materials Science; The Issue of Size Control, ed. B. Corain, G. Schmid and N. Toshima, Elsevier, 2007; (b) Nanoparticles and Catalysis, ed. D. Astruc, Wiley-VCH, Weinheim, Germany, 2008; (c) Selective Nanocatalysts and Nanoscience, eds. A. Zecchina, S. Bordiga and E. Groppo, Wiley-VCH, Weinheim, Germany, 2011.
- K. Okamoto, R. Akiyama, H. Yoshida, T. Yoshida and S. Kobayashi, J. Am. Chem. Soc., 2005, 127, 2125;
   (b) R. Narayanan and M. A. El-Sayed, Langmuir, 2005, 21, 2027; (c) H. Oyamada, R. Akiyama, H. Hagio, T. Naito and S. Kobayashi, Chem. Commun., 2006, 4297; (d) Y. Gao, C.-A. Chen, H.-M. Gau, J. A. Bailey, E. Akhadov, D. Williams and H.-L. Wang, Chem. Mater., 2008, 20, 2839; (e) R. Xing, Y. Liu, H. Wu, X. Li, M. He and P. Wu, Chem. Commun., 2008, 6297; (f) G. Wei, W. Zhang, F. Wen, Y. Wang and M. Zhang, J. Phys. Chem. C, 2008, 112, 10827; (g) I. Pastoriza-Santos and L. M. Liz-Marza'n, Adv. Funct. Mater., 2009, 19, 1; (h) D. Srimani, A. Bej and A. Sarkar, J. Org. Chem., 2010, 75, 4296.
- G. R. Newkome, E. He and C. N. Moorefield, *Chem. Rev.*, 1999, **99**, 1689; (b) E. H. Rahim, F. S. Kamounah, J. Frederiksen and J. B. Christensen, *Nano Lett.*, 2001, **1**, 499; (c) K. Yamamoto, M. Higuchi, S. Shiki, M. Tsuruta and H. Chiba, *Nature*, 2002, **415**, 509; (d) K. R. Gopidas, J. K. Whitesell and M. Anne Fox, *Nano Lett.*, 2003, **3**, 1757; (e) M. Pittelkow, K. Moth-Poulsen, U. Boas and J. B. Christensen, *Langmuir*, 2003, **19**, 7682; (f) C. Ornelas, J. R. Aranzaes, L. Salmon and D. Astruc, *Chem.-Eur. J.*, 2008, **14**, 50; (g) T. Mizugaki, T. Kibata, K. Ota,

T. Mitudome, K. Ebitani, K. Jitsukawa and K. Kaneda, *Chem. Lett.*, 2009, 1118.

- 4 (a) B. Yoon and C. M. Wai, J. Am. Chem. Soc., 2005, 127, 17174;
   (b) Z. Zhang and Z. Wang, J. Org. Chem., 2006, 71, 7485;
   (c) T. Mitsudome, K. Nose, K. Mori, T. Mizugaki, K. Ebitani, K. Jitsukawa and K. Kaneda, Angew. Chem., Int. Ed., 2007, 46, 3288; (d) V. K. Kanuru, S. M. Humphrey, J. M. W. Kyffin, D. A. Jefferson, J. W. Burton, M. Armbrüster and R. M. Lambert, Dalton Trans., 2009, 7602.
- 5 J. L. Bolliger, O. Blacque and C. M. Frech, *Chem.-Eur. J.*, 2008, **14**, 7969.
- 6 (a) G. Zhang, H. Zhou, J. Hu, M. Liu and Y. Kuang, *Green Chem.*, 2009, **11**, 1428; (b) J. Huang, T. Jiang, H. Gao, B. Han, Z. Liu, W. Wu, Y. Chang and G. Zhao, *Angew. Chem.*, *Int. Ed.*, 2004, **43**, 1397.
- 7 (a) Catalysis Without Precious Metals, ed. R. M. Bullock, Wiley-VCH, Weinheim, Germany, 2010; (b) G. Evano, N. Blanchard and M. Toumi, Chem. Rev., 2008, 108, 3054; (c) H. Rao and H. Fu, Synlett, 2011, 745.
- 8 (a) F. Ullmann, Ber. Dtsch. Chem. Ges., 1904, 37, 853; (b) F. Ullmann and P. Sponagel, Ber. Dtsch. Chem. Ges., 1905, 38, 2211; (c) E. Buck, Z. J. Song, D. Tschaen, P. G. Dormer, R. P. Volante and P. J. Reider, Org. Lett., 2002, 4, 1623; (d) D. Ma and Q. Cai, Org. Lett., 2003, 5, 3799; (e) H. J. Cristau, P. P. Cellier, S. Hamada, J.-F. Spindler and M. Taillefer, Org. Lett., 2004, 6, 913; (f) Y.-J. Chem and H.-H. Chen, Org. Lett., 2006, 8, 5609; (g) H. Rao, Y. Jin, H. Fu, Y. Jiang and Y. Zhao, Chem.-Eur. J., 2006, 12, 3636; (h) Q. Cai, B. Zou and D. Ma, Angew. Chem., Int. Ed., 2006, 45, 1276; (i) R. A. Altman and S. L. Buchwald, Org. Lett., 2007, 9, 643; (j) B. H. Lipshutz, J. B. Unger and B. R. Taft, Org. Lett., 2007, 9, 1089; (k) X. Lv and W. Bao, J. Org. Chem., 2007, 72, 3863; (l) M. Kidwai, N. K. Mishra, V. Bansal, A. Kumar and S. Mozumdar, Tetrahedron Lett., 2007, 48, 8883; (m) J. Zhang, Z. Zhang, Y. Wang, X. Zheng and Z. Wang, Eur. J. Org. Chem., 2008, 5112; (n) F. Monnier and M. Taillefer, Angew. Chem., Int. Ed., 2009, 48, 6954; (o) A. B. Naidu, A. Jaseer and G. Sekar, J. Org. Chem., 2009, 74, 3675; (p) J. Y. Kim, J. C. Park, A. Kim, A. Y. Kim, H. J. Lee, H. Song and K. H. Park, Eur. J. Inorg. Chem., 2009, 4219; (q) V. Engels, F. Benaskar, N. Patil, E. V. Rebrov, V. Hessel, L. A. Hulsof, D. A. Jefferson, J. A. J. M. Vekemans, S. Karwal, J. C. Schouten and A. E. H. Wheatley, Org. Process. Res. Dev., 2010, 14, 644; (r) F. Benaskar, V. Engels, N. Patil, E. V. Rebov, J. Meuldijk, V. Hessel, L. A. Hulshof, D. A. Jefferson, J. C. Schouten and A. E. H. Wheatley, Tetrahedron Lett., 2010, 51, 248; (s) H. Yang, C. Xi, Z. Miao and R. Chen, Eur. J. Org. Chem., 2011, 3353.
- (a) H. A. Orgueira, D. Fokas, Y. Isome, P. C. M. Chan and C. M. Baldino, *Tetrahedron Lett.*, 2005, 46, 2911; (b) L. D. Pachon, J. H. van Maarseveen and G. Rothenberg, *Adv. Synth. Catal.*, 2005, 347, 811; (c) G. Molteni, C. L. Bianchi, G. Marinoni, N. Santo and A. Ponti, *New J. Chem.*, 2006, 30, 1137; (d) M. L. Kantam, V. S. Jaya, B. Sreedhar, M. M. Rao and B. M. Choudary, *J. Mol. Catal. A: Chem.*, 2006, 256, 273; (e) A. Sarkar, T. Mukherjee and S. Kapoor, *J. Phys. Chem. C*, 2008, 112, 3334; (f) F. Alonso, Y. Moglie, G. Radivoy and M. Yus, *Tetrahedron Lett.*, 2009, 50, 2358; (g) E. A. Karakhanov, A. L. Maximov, Y. S. Kardasheva, V. A. Skorkin, S. V. Kardashev, V. V. Predeina, M. Y. Talanova, E. Lurie-Luke, J. A. Seeley and S. L. Cron, *Appl. Catal., A*, 2010, 385, 62; (h) S. J. Ahmadi, S. Sadjadi, M. Hosseinpour and M. Abdollahi, *Monatsh. Chem.*, 2011, 142, 801.
- 10 (a) H. Kawasaki, H. Yamamoto, H. Fujimori, R. Arakawa, Y. Iwasaki and M. Inada, *Langmuir*, 2010, 26, 5926; (b) H. Kawasaki, H. Yamamoto, H. Fujimori, R. Arakawa, M. Inada and Y. Iwasaki, *Chem. Commun.*, 2010, 46, 3759; (c) M. Hyotanishi, Y. Isomura, H. Yamamoto, H. Kawasaki and Y. Obora, *Chem. Commun.*, 2011, 47, 5750.
- 11 H. Kawasaki, Y. Kosaka, Y. Myoujin, T. Narushima, T. Yonezawa and R. Arakawa, *Chem. Commun.*, 2011, **47**, 7740.
- 12 J. J. Brege, C. E. Hamilton, C. A. Crouse and A. R. Barron, *Nano Lett.*, 2009, 6, 2239.