DOI 10.5012/bkcs.2010.31.12.3509

Cu_2O Nanocubes Catalyzed Difunctionalization Reaction of Vinyl Arenes with Cyclic Ethers

Jee Young Kim, Ji Chan Park,[†] Hyunjoon Song,[†] and Kang Hyun Park[*]

Department of Chemistry and Chemistry Institute of Functional Materials, Pusan National University, Pusan 609-735, Korea. [*]E-mail: chemistry@pusan.ac.kr

[†]Department of Chemistry, Korea Advanced Institute of Science and Technology, Daejeon 305-701, Korea

Received July 30, 2010, Accepted September 17, 2010

Key Words: Copper, Nanoparticle, C-H activation, Oxyalkyation, Vinyl arene

Metal nanoparticles whose sizes are between those of bulk and monomeric metal species have a wide range of applications; such nanoparticles are used in various electronic, optical, and magnetic devices as well as in the production of catalytic materials. Transition-metal nanoparticles are an important class of catalysts used in organic synthesis.[1] In recent years, significant improvements have been made to transition-metal-catalyzed C-C and C-H bond formation reactions.[2] In particular, functionalization of arenes *via* transition-metal catalysis, i.e., conversion of arenes to more valuable derivatives, has been identified as a very important reaction that can revolutionize the chemical industry.[3]

Extensive studies have been carried on the use of copper in organic synthesis because copper is a promising candidate for a highly efficient catalyst. Recently, remarkable improvements have been made to various copper-nanoparticle-catalyzed reactions such as the Ullmann reaction,[4] click reaction,[5] cross-coupling reactions,[6] cyclization reactions,[7] oxidation,[8] and oxyalkylation.[9] We have recently identified a very attractive alternative synthetic route to biaryl ethers. This synthetic route involves the reaction of an aryl halide with a phenol in the presence of Cu_2O nanocubes.[10] This process is simple and allows the formation of a diverse range of biaryl ethers in excellent yields. Another important advantage of this synthesis method is that the catalyst can be easily recycled without loss of activity and used as such without further purification.

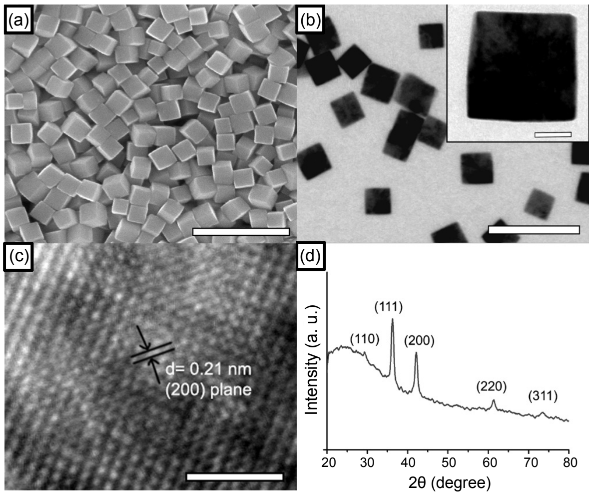
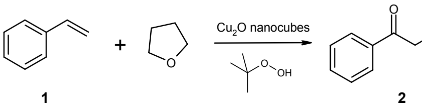


Figure 1. (a) SEM image, (b) TEM image, (c) HR-TEM image, (d) XRD pattern of the Cu_2O nanocubes. The scale bars represent (a) 200 nm and (b) 200 (inset = 20 nm) (c) 2 nm.

Herein, we report a novel difunctionalization of vinyl arenes; in this reaction, well-designed, uniform Cu_2O nanoparticles are used to catalyze the regioselective oxyalkylation of vinyl arenes under mild conditions.

Typically, Cu_2O nanocubes are synthesized *via* a one-pot polyol process using poly(vinyl pyrrolidone) (PVP) as a surfactant and 1,5-pentanediol (PD) as the reductant and solvent.[11] Figures 1a and 1b show the scanning electron microscopy (SEM) and transmission electron microscopy (TEM) images of the monodisperse cubic Cu_2O nanocubes (45.1 ± 3.1 nm), respectively. Figure 1c shows the high-resolution TEM (HRTEM) image of CuO single crystals. The lattice fringe images of a single metal core are continuous over all nanoparticle projections with the distance between neighboring fringes of 0.21 nm, which matches with that of (200) in the cubic Cu_2O phase. The X-ray diffraction (XRD) spectrum in Figure 1d shows the typical reflection patterns obtained for cuprite (JCPDS No. 77-0199).



In our study, we first carried out a reaction between styrene **1** (1.6 mL, 13.9 mmol) and *tert*-butyl hydroperoxide (TBHP, 2.8 mL, 25.8 mmol) in tetrahydrofuran (THF, 10 mL) (Table 1). To ensure complete consumption of **1** in some of the reactions that did not go to completion, we decided to optimize the reaction conditions; for this purpose, we carried out a series of reactions by varying the air pressure, temperature, reaction time, and catalyst amount. As shown in Table 1, the best results were obtained when the reaction was carried out at high temperature or high pressure (Table 1, entries 1, 2, and 5). We carried out the aforesaid reactions at 100 - 130 °C. The rate of substrate conversion could be improved by further increasing the reaction temperature. The yield of 2-(tetrahydrofuran-2-yl) phenylethanone **2** was very poor when the reaction was carried out at 1 atm air pressure and 100 °C (Table 1, entry 9). On the basis these observations, we established the optimum reaction conditions. 1 (0.3 mL, 3.0 mmol) and Cu_2O nanocubes (2.0 mg, 1.4 mmol, 1.0 mol %) were added to THF (10.0 mL) in a 25-mL stainless-steel reactor. The mixture was stirred for 1 h at 130 °C and 3 atm air pressure. In the absence of TBHP, the reaction carried out using **1** gave very poor yields even under the optimum conditions (Table 1, entry 6). Hence, we concluded that both TBHP

Table 1. Oxyalkylation of styrene under aerobic conditions

Entry	Cat (mol %)	Air (atm)	Temp (^{o}C)	Time (h)	Yield (%)[a]
1	0.5 mol %	5	130	1	100 (68)
2	1 mol %	5	130	0.5	97 (81)
3	1 mol %	5	100	1	90 (83)
4	1 mol %	5	100	0.5	68 (40)
5	1 mol %	3	130	1	98 (75)
6	1 mol %	3	130	1	10 (7)[b]
7	1 mol %	3	100	1	50 (44)
8	1 mol %	1	130	1	86 (70)
9	1 mol %	1	100	1	33 (33)
10	CuBr	3	130	1	67 (62)

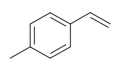
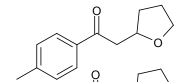
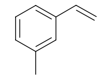
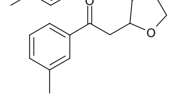
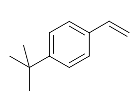
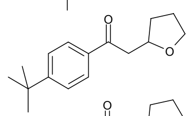
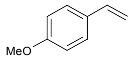
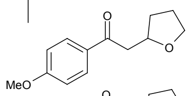
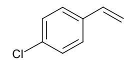
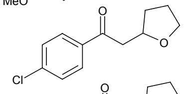
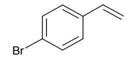
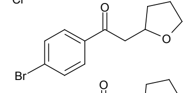
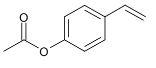
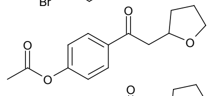
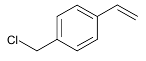
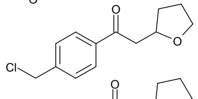
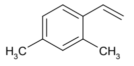
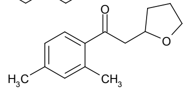
[a] Determined by ^{1}H-NMR. Yields are based on the amount of vinyl arene used. Yields in parentheses are isolated yields after column chromatography on silica. [b] Reaction undergoing in the absence of TBHP.

and Cu_2O nanocubes are essential for oxidative carbonyalkylation. Cu_2O nanocubes gave a 72% yield in the second run, which were recovered from the reaction of entry 5 *via* centrifugation. Unfortunately, the structure of the Cu_2O nanocubes changed after the reaction (TEM images are analyzed). This observation suggests that atomic leaching from the nanoparticles occurs during the reaction, which is considered to be the result of the high temperature that the reaction takes place.

The substrate scope of the Cu_2O-nanocube-catalyzed oxyalkylation of vinyl arenes is summarized in Table 2. From the table, it is clear that this reaction can be extended to a wide variety of substituted and unsubstituted vinyl arenes (Table 2, entries 1-8). Interestingly, the conversion yield was very low when vinyl arenes with a methyl group at the 2- and 4-positions were employed (Table 2, entry 9). The steric effect on the vinyl arene had a very weak effect on the reactivity. The desired products were isolated in good yield, i.e., the conversion rate was good, when the substrate had methyl groups at the 3- and 4-positions (Table 2, entries 1, and 2). The presence of electron-donating (methoxy) or electron-withdrawing (halogen and acetate) groups in the substrate influenced the product yield to a certain extent (Table 2, entries 4-7). The carbon-halogen bonds in the abovementioned electron-withdrawing groups were unaffected under the present reaction conditions. Unexpectedly high yields of the product were achieved when the electron-withdrawing group contained a halogen. Chloromethyl benzene afforded the expected product 1-(4-(chloromethyl)phenyl)-2-(tetrahydrofuran-2-yl)ethanone in 100% yield (entry 8).

In conclusion, we synthesized uniform Cu_2O nanocubes on a gram scale. We used well-designed, uniform Cu_2O nanocubes for the catalytic oxyalkylation of various vinyl arenes and obtained the desired products in good yields and with high regioselectivity. The abovementioned process is simple and allows the formation of a diverse range of oxyalkylated vinyl arenes in excellent yields. The high chemical reactivity of the nanoparticles is an important factor that affects the yield of the reaction. This lab is currently examining the scope of this catalytic system using various shape and size Cu_2O nanocubes. Attempts to improve the catalytic activities and to study the role of the TBHP are in progress. On the basis of the present results, we state that transition-metal nanoparticles can be used as catalysts for a wide variety of organic transformations.

Table 2. Cu_2O nanocubes catalyzed oxyalkylation of the vinyl arene.[a]

Entry	Substrate	Product	Conv. (%)[b]
1			98
2			95
3			88
4			63
5			68
6			73
7			69
8			100
9			51

[a] Reaction conditions: styrene (13.9 mmol), catalyst (1 mol %, 2.0 mg, 1.4 mmol), solvent (10.0 mL) at 130 ^{o}C, 1h, 3 atm air. [b] Determined by ^{1}H-NMR. Yields are based on the amount of vinyl arene used.

Acknowledgments. This work was supported for 2 years by Pusan National University Research Grant.

References

1. (a) Dan, X.; Stoyan, B.; Zhaoping, L.; Jiye, F.; Nikolay, D. *Angew. Chem., Int. Ed.* **2009**, *49*, 1282. (b) McCarren, P. R.; Liu, P.; Cheong, P. H.-Y.; Jamison, T. F.; Houk, K. N. *J. Am. Chem. Soc.* **2009**, *131*, 6654. (c) Song, Y.-J.; Yoo, C. Y.; Hong, J.-T.; Kim, S.-J.; Son, S. U.; Jang. H.-Y. *Bull. Korean Chem. Soc.* **2008**, *29*, 1561.
2. (a) Hongjian, L.; Jingran, T.; Jess, E. J.; Lukasz, W.; Zhang, X. P. *Org. Lett.* **2010**, *12*, 1248. (b) Cheong, J. Y.;, Bae, H. J.; Baburaj, B.; Daniel T.; Mahn-Joo Kim, M.-J.; Rhee, Y. H. *Bull. Korean Chem. Soc.* **2009**, *30*, 1239. (c) Lee, H. R.; Jang, M.-S.; Song, Y.-J.; Jang, H.-Y. *Bull. Korean Chem. Soc.* **2009**, *30*, 327.
3. Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1683.
4. Son, S. U.; Park, I. K.; Park, J.-N.; Hyeon, T.-H. *Chem Commun.* **2004,** 778.
5. Kim, J. Y.; Park, J. C.; Kang H.-T.; Song, H.-J.; Park, K. H. *Chem. Commun.* **2010**, *46*, 439.
6. Diego, A.; Cayane, G. S.; Marcio, W. P.; Letiere, C. S.; Diego, D. S.; Oscar, E. D. R.; Antonio, L. B. *Tetrahedron Letters* **2009**, *50*, 6635.
7. Park, I. S.; Kwon, M. S.; Kim, Y.-K.; Lee, J. S.; Park, J. W. *Org. Lett.* **2008**, *10*, 497.
8. White, B.; Yin, M.; Hall, A.; Le, D.; Stolbov, S.; Rahman, T.; Turro, N.; O'Brien, S. *Nano Lett.* **2006**, *6*, 2905.
9. Kai, C.; Lehao, H.; Yuhong, Zhang. *Org. Lett.* **2009**, *11*, 2908.
10. Kim, J. Y.; Park, J. C.; Kim, A. R.; Kim, A. Y.; Lee, H. J.; Song, H.-J.; Park, K. H. *Eur. J. Inorg. Chem.* **2009**, 4219.
11. Seo, D.-H.; Park, J. C.; Song, H.-J. *J. Am. Chem. Soc.* **2006**, *128*, 14863.