

Immobilized CuO Hollow Nanospheres Catalyzed Alkyne-Azide Cycloadditions

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An approach for gram-scale synthesis of uniform Cu_2O nanocubes by a one-pot polyol process was used. The CuO hollow nanostructures were prepared by adding aqueous ammonia solutions with Cu_2O nanocube colloidal solutions. CuO hollow nanospheres on acetylene black (CuO/AB), were synthesized and used for the catalytic [3+2] cycloaddition of azides with terminal alkynes to provide products in good yields with high regioselectivity. The CuO/AB was readily separated by centrifugation and could be reused ten times under the present reaction conditions without any loss of catalytic activity. Transition metals loaded onto acetylene black are useful reagents for a wide variety of organic transformations. Moreover, these heterogeneous systems are promising industrial catalysts.

Keywords: Copper Oxide, Acetylene Black, Charcoal, Heterogeneous, Catalyst, Click Reaction.

IP: 130.63.0.29 On: Sat, 06 Dec 2014 14:24:55 Copyright: American Scientific Publishers

1. INTRODUCTION

The impossibility in recovering and recycling homogesneous catalysts is a task of great economic and environmental importance in the chemical and pharmaceutical industries, especially when expensive and/or toxic heavy metal complexes are employed.¹ The development of catalysts anchored to solid supports has been one of the areas of most intense research activity over the past years. Immobilization of homogeneous catalysts onto various insoluble supports, carbon black,² activated carbon,³ carbon nanotubes,⁴ carbon film,⁵ C60,⁶ acetylene-black(AB),⁷ charcoal,⁸ polymer,⁹ alumina,¹⁰ porous silica materials with high surface areas,¹¹ or onto soluble supports,¹² are usually the methods of choice since the immobilized catalysts can be easily recovered via simple filtration after the reaction (Scheme 1). A drawback of homogeneous catalysis is the impossibility of catalyst recovery and recycling. Immobilization of the catalysts onto an insoluble matrix can provides a simple solution to this problem. The possibility of recovering and recycling catalysts, which are often expensive, bring with it positive effects from an economical and environmental point of view. A further benefit is the ease of product isolation and purification.¹³ Moreover, these heterogeneous systems are promising industrial catalysts. For example, commercially available Pd/C is frequently used in debenzylation, hydrogenation, and C–C bond-formation reactions in the laboratory and industry and has recently been developed as a catalysts for coupling, hydrosilylation, and cycloaddition reactions, respectively.

This paper studies the click reaction using CuO on acetylene black based on the strength of these heterogeneous catalysts. Special attention was given to acetylene black out of the above-mentioned solid supports. Acetylene black is a special type of carbon black formed by an exothermic decomposition of acetylene and is characterized by the highest degree of aggregation and crystalline orientation when compared with all types of carbon black. The carbon content is approximately 99.9%. Acetylene black must not be confused with the carbon black produced as a by-product during the production of acetylene in the electric arc process. Acetylene black is widely used in battery systems possessing excellent electric conductivity, large specific surface areas and strong adsorptive abilities, as well as in supports.¹⁴

Click chemistry is a chemical philosophy introduced in 2001 by Sharpless, and is important in understanding the behavior of low-weight molecules.¹⁵ Click chemistry

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Scheme 1. Immobilization of homogeneous catalysts on various supports.

has had a substantial impact on organic synthesis, drug discovery, and biological applications.¹⁶ The formation of a triazole-containing carbon-heteroatom bonds through Huisen [3+2] cycloadditions is a representative example of a click reaction. The desired triazole-forming cycloaddition typically requires high temperatures and usually results in a mixture of the 1,4 and 1,5 regioisomers (Eq. (1)).

$$R^{1}-N_{3}+=R^{2}-R^{2}-R^{1}-N_{N}+R^{1}-N_{N}+R^{2}-R^{$$

2. EXPERIMENTAL PROCEDURE

2.1. General Remarks

Reagents were purchased from Aldrich Chemical Co. and Strem Chemical Co. and used as received. Reaction products were analyzed by ¹H-NMR. ¹H-NMR with spectra obtained on a Varian Mercury Plus (300 MHz). Chemical shift values were recorded as parts per million relative to tetramethylsilane as an internal standard, unless otherwise indicated, and coupling constants in Hertz. Reaction products were assigned by comparison with the literature value of known compounds. The CuO and CuO nanoparticles immobilized on acetylene black were characterized by TEM (Philips F20 Tecnai operated at 200 kV, KAIST). Samples were prepared by placing a few drops of the corresponding colloidal solution on carbon-coated copper grids (Ted Pellar, Inc). The X-ray powder diffraction (XRD) patterns were recorded on a Rigaku D/MAX-RB (12 kW) diffractometer. The copper loading amounts were measured by inductively coupled plasma-atomic emission spectrometry (ICP-AES).

2.2. General Procedure for [3+2] Cycloaddition of Azides with Terminal Alkynes

In a 10 mL pressure tube Schlenk was placed 33.0 mg of CuO hollow nanospheres on acetylene black (CuO/AB), benzyl azide (0.1 mL, 0.84 mmol), phenylacetylene (0.13 mL, 1.18 mmol) and 2.5 mL H_2O/t -BuOH (1.7 mL:0.8 mL). The reaction mixture was stirred at 50 °C. After 5 h, the CuO/AB was recovered by centrifugation and the clean solution analyzed by 300 MHz NMR.

2.3. Synthesis of CuO Hollow Nanospheres

The CuO hollow nanospheres were synthesized by a controlled oxidation reaction of Cu₂O nanocubes. Typically, Cu₂O nanocubes were prepared by a polyol process in 1,5-pentanediol (PD, Aldrich, 96%) in the presence of poly(vinyl pyrrolidone) (PVP, Aldrich, $M_w = 55,000$). The PVP (5.3 g) dissolved in 45.0 mL of 1,5-pentanediol (PD, Aldrich, 96%), was slowly heated to 240° under a nitrogen atmosphere. Then, 4.0 mmol of Cu(acac)₂ (STREM, 98%), dissolved in 15 mL of PD, was injected into the hot PVP solution at 240 °C and the mixture allowed to stir for 15 min at the same temperature. The yellowish colloidal dispersion was cooled to room temperature and was precipitated by adding acetone followed by centrifugation at 8,000 rpm for 20 min. The precipitated Cu₂O particles were washed with ethanol several times and re-dispersed in ethanol. To obtain the CuO hollow nanospheres, an aqueous ammonia solution (2.0 mL, 3.7 M) was added into 25.0 mL of the Cu₂O cube dispersion in ethanol (16.0 mM with respect to the precursor concentration). The mixture was subjected to stirring at room temperature for 2 h. After the reaction, the final products were collected by centrifugation at 6,000 rpm for 20 min.

2.4. Immobilization of CuO Hollow Nanospheres on Acetylene Carbon Black (CuO/AB) and Charcoal (CuO/C)

The acetylene carbon black (STREM, 99.99%, 1.2 g) was mixed with 100 mL of the CuO hollow nanosphere dispersion in ethanol (17.0 mM), and the reaction mixture sonicated for 1 h at room temperature. After 1 h, the product CuO/AB was washed with ethanol several times and vacuum dried at room temperature. For the synthesis of CuO/C, the mixture solution of charcoal (0.8 g) and 50.0 mL of CuO hollow nanosphere dispersion in ethanol (50.0 mM) was refluxed for 4 h. After 4 h, the black suspension was cooled to room temperature and precipitated by centrifugation. The product CuO/C was washed with ethanol thoroughly and dried in a vacuum oven at room temperature.

3. RESULTS AND DISCUSSION

In the present study, an approach for gram-scale synthesis of uniform Cu_2O nanocubes by an one-pot polyol process was developed.¹⁷ The CuO hollow nanospheres were prepared by adding an aqueous ammonia solution to the Cu_2O nanocube colloidal solution. The CuO hollow nanospheres were immobilized onto acetylene black (AB) or charcoal. As such, these immobilized CuO hollow nanospheres overcame the issue of reuse.¹⁸

3.1. Catalyst Characterization

The Cu₂O nanocubes prepared by a polyol process were transformed into CuO hollow nanospheres by a controlled oxidation reaction using an aqueous ammonia solution. The addition of ammonia solution (2.0 mL, 3.7 M) into Cu₂O colloidal solution yielded CuO hollow nanospheres through a dissolution-precipitation process. The transmission electron microscopy (TEM) image in Figure 1(a) shows the regular hollow shape of the CuO particles. CuO hollow spheres were obtained as (103 ± 8) -nm-sized, highly monodisperse nanoparticles (Fig. 1(d)). The crystalline features of the hollow spheres are represented in the XRD data (Fig. 1(c)). The main peaks at $\theta = 35^{\circ}$ and 39° are assigned to the reflections of the (002)/(11-1)and (111)/(200) planes in the CuO phase (JCPDS No. 48-1548). The CuO hollow particles were immobilized on acetylene carbon black by simple sonication method at room temperature. The TEM image in Figure 1(b) shows that the immobilized CuO hollow spheres are well dispersed and isolated with approximately 100 nm in an average diameter, maintaining the original size and structure of CuO hollow spheres. The absolute amount of copper



Fig. 1. (a) TEM image, (c) XRD pattern, (d) size distribution diagrams of the CuO hollow nanospheres, and (b) TEM image of the CuO hollow nanospheres on acetylene black. The scale bars represent 200 nm.

metal on the acetylene black was determined by inductively coupled plasma-atomic emission spectroscopy (ICP-AES). The CuO hollow spheres on the acetylene black showed excellent activity towards a wide range of azides and acetylenes.

3.2. Reaction Test

Research studies testing catalyst effectiveness have employed benzyl azide and phenylacetylene as the benchmark substrates. The cycloaddition reaction of benzyl azide (0.1 mL, 0.84 mmol) and phenylacetylene (0.13 mL, 1.18 mmol) with CuO/AB in H_2O/t -BuOH (1.7 mL:0.8 mL), off the shelf, afforded 1,4-disubstituted 1,2,3-triazoles as a single regioisomer. This CuO nanostructure catalyzed the reaction sequence that regiospecifically unites azides and terminal acetylenes to give only 1,4-disubstituted 1,2,3-triazoles.

As shown in Table I, the reaction was carried out at 25– 50 °C using benzyl azide and phenylacetylene as the benchmark substrate (Table I). The best results were obtained when *t*-BuOH was used as the solvent under mild, room temperature conditions.¹⁹ Improved results were possible with a solvent mixture of 2:1 rather than *t*-BuOH and H₂O independently, indicating that both solubility and hydroscopic properties are portant factors. First, no reaction occurred without a catalyst. When the Cu₂O nanocubes (5 mol%) were used, 1-benzyl-4-phenyl-1*H*-1,2,3-triazole was obtained in 100% conversion at 25 °C within 3 h (entry 2). When the CuO on AB (1 mol%) catalyst was used, less than a 1% yield was found under 25 °C for 3 h (entry 3). Furthermore, when 3 mol% of the catalyst was used, less than a 1% yield was achieved under the same

Table I. Optimization of click reaction catalyzed by various CuO NPs.

Entry	Cat (mol%)	Temp (°C)	Time (h)	Conv (%) ^a
1	Blank	50	5	7
2	CuO (5 mol%)	25	3	100
3	CuO on AB (1 mol%)	25	3	>1
4	CuO on AB (1 mol%)	50	5	22
5	CuO on AB (3 mol%)	25	5	>1
6	CuO on AB (3 mol%)	50	5	100
7	CuO on AB (3 mol%)	50	3	60
8	CuO on AB (3 mol%)	40	5	23
9	CuO on AB (3 mol%)	30	5	1.1
10	CuO on AB (3 mol%)	50	5	90
11	CuO on AB (5 mol%)	50	5	96
12	Recovered from # 6	50	5	100
13	Recovered from # 12	50	5	100
14	Recovered from # 13	50	5	100
15	Recovered from # 14	50	5	100
16	Recovered from # 15	50	5	100
17	Recovered from # 16	50	5	98
18	Recovered from # 17	50	5	100
19	Recovered from # 18	50	5	100
20	Recovered from # 19	50	5	100

^aDetermined by ¹H-NMR. Yields are based on the amount of benzyl azide used.

conditions (entry 5). In general, it was found that increasing the reaction temperature and time were an effective means of increasing conversion (22% for 50 °C, 5 h). Finally, the optimum reaction conditions were established: click reaction of benzyl azide (0.1 mL, 0.84 mmol) and phenylacetylene (0.13 mL, 1.18 m mol) with CuO on AB (26.0 mg, 3 mol%) in H₂O:*t*-BuOH(2:1) (2.5 mL) to afford 1,2,3triazole. In the case of using another heterogeneous catalyst (CuO on charcoal), 90% or 96% conversion was found under the same conditions (Table I, entries 10 and 11).

Remarkably, after the reaction, the CuO on AB were separated by centrifugation and reused ten times under the same reaction conditions without any catalytic activity loss. An inductively coupled plasma-mass spectrometry (ICP-AES) study showed that the copper that bled from the catalyst was negligible. These results confirm that the catalytic system presented here satisfies the conditions for heterogeneous catalysts of easy separation, recyclability, and persistence. As shown in Figure 2, the structure of the CuO hollow nanospheres on acetylene black (CuO/AB) remained unchanged after the reaction, demonstrating catalyst recyclability.

Furthermore, in the case of using various terminal alkynes, good results were achieved (Table II). Hydroxy-substituted alkynes such as propargyl alcohol, 2-methyl-3-butyn-2-ol, and 1-phenyl-2-propyn-1-ol also gave the expected adducts of (1-benzyltriazol-4-yl)methanol, 2-(1-benzyl-1H-1,2,3-triazol-4-yl)propan-2-ol, and (1-benzyl-1H-1,2,3-triazol-4-yl)(phenyl)methanol as a single regioisomer in good to high yields (Table II, entries I, II, and III.). Acetylenes conjugated with an ester group,

Table II. [3+2] Cycloaddition of benzyl azides with terminal alkynes in the presence of CuO hollow nanospheres.



Fig. 2. TEM images of CuO/AB, before (a) and after the fifth cycle. (b) The scale bars represent 100 nm.

Entry	Alkyne	Product	Conv (%) ^a
1	,он	N ^{≠N} N Ph	100
2	=-/_	N ^{=N} N Ph	100
3		Ph N=N OH	100
4	<u></u>	Ph	72
5	≡ Ph	Ph	100
6	── CO ₂ Et		100
7	<u>—</u> Со ₂ Ме	Ph N=N CO ₂ Me Ph	100
8	──TMS	N N N Ph	45
9	<u> </u> с,н,	N ^N →C _i H ₉	94
10	<u> </u>	Ph	87

such as methyl propargyl ether and phenyl propargyl ether, reacted without incident with the benzyl azide. The corresponding triazoles 1-benzyl-4-(methoxymethyl)-1H-1,2,3-triazole and 1-benzyl-4-(phenoxymethyl)-1H-1,2,3-triazole were obtained in high yields (Table II, entries 4 and 5). The reaction with alkynes containing electron-withdrawing substituents such as ethyl propiolate and methyl propiolate gave distinctively high yields (Table II, entries 6 and 7). The reactions with aliphatic alkynes such as ethynyltrimethylsilane, 1-hexyne, and 1-octyne, were relatively sluggish (Table II, entries 8, 9, and 10).

In a second series of experiments, various azides bearing different groups were submitted to phenylacetylene (Table III). When the phenyl group was directly linked to the reactive azide, phenyl azide or its analogue with a *p*-Cl, Ph-O group gave expected 1,4-diphenyl-1H-1,2,3-triazole, 1-(4-Chlorophenyl)-4-phenyl-1H-1,2,3-triazole, and 1-(4-phenoxyphenyl)-4-phenyl-1H-1,2,3-triazole as single regioisomers with 100% conversion yield (Table III,

Table III. [3+2] Cycloaddition of various azides with phenylacetylene in the presence of CuO hollow nanospheres.



entries 1, 2, and 3). In some case, electrondonating or -withdrawing groups on the benzyl azides greatly affected reactivity. Electron-withdrawing groups disfavoured the reaction, with lower obtained yields. Within these groups, fluorine and nitrogen dioxide exhibited the largest effect (Table III, entries 4 and 5). Interestingly, the result showed low conversion yield when the methoxy group, one of the electron-donating groups, was located on para and meta position while 100% conversion yield was shown when it is located on ortho position. As in the other series (Table III, entries 1 versus 10), electronic effects of azides were more pronounced and they significantly altering the reactivity. For instance, it is highly reactive when azides are bonded directly to the phenyl group while only a low conversion yield is observed when it is indirectly bonded as in (2-azidoethyl)benzene. Indeed, ethyl 2-azidoacetate was obtained in high yields without any problem (Table III, entry 6). Nevertheless, a single regioisomer was still produced and the substitution and yields of the isolated products remained excellent.

4. CONCLUSION

In summary, oxidation of Cu_2O nanocubes has been controlled to yield CuO hollow nanospheres through a sequential dissolution-precipitation process. As expected, CuO hollow nanospheres on acetylene black (CuO/AB) have been used for the catalytic [3+2] cycloaddition of azides with terminal alkynes to provide products in good yields with high regioselectivity. The CuO/AB was readily separated by centrifugation and could be reused ten times under the present reaction conditions without any loss in catalytic activity. Transition metals loaded onto acetylene black are useful reagents for a wide variety of organic transformations. Moreover, these heterogeneous systems are promising industrial catalysts.

Acknowledgments: This study was supported by the Research Fund Program of Research Institute for Basic Science, Pusan National University, Korea, 2009, Project No. RIBS-PNU-2009-108.

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Received: 26 November 2009. Accepted: 27 November 2009.

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