

## Synthesis of Functionalized Bisarylacetylene Derivatives from Acetylene Gas Over Nano-sized Carbon Ball Supported Palladium Catalyst

Eul Kgun Yum,\* Jong Woo Son, Soo Kwang Kim, Sung Nam Kim, Kyung Mahn Kim,<sup>†</sup> and Chul Wee Lee<sup>‡</sup>

Department of Chemistry, Chungnam National University, Daejeon 305-764, Korea. \*E-mail: ekyum@cnu.ac.kr

<sup>†</sup>Advanced Material Division, KRICT, Daejeon 305-600, Korea

<sup>‡</sup>Green Chemistry Division, KRICT, Daejeon 305-600, Korea

Received April 13, 2010, Accepted May 28, 2010

**Key Words:** Bisarylacetylene, Acetylene, Carbon ball, Recycle, Palladium, Catalyst

Functionalized bisarylacetylenic compounds are valuable intermediates in organic synthesis of natural products, pharmaceuticals, synthetic agrochemicals, and molecular materials.<sup>1-3</sup> In particular, palladium-catalyzed cross-coupling between sp<sup>2</sup> hybridized carbon atoms and the terminal sp hybridized carbon atoms of acetylene has frequently been used to synthesize bisarylacetylene intermediates.<sup>3</sup> Although Sonogashira cross-coupling with substituted terminal acetylenes has been shown to be a powerful synthetic method for bisarylacetylenic compounds,<sup>4-6</sup> only a few literature sources have reported diarylation coupling reactions with acetylene gas.<sup>7-9</sup>

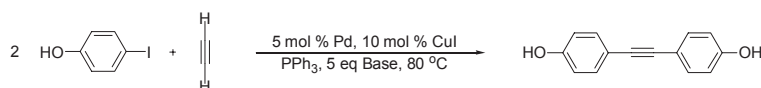
Recently, many reports have described nano-sized, semi-heterogeneous catalysts, the properties of which border between those of homogeneous and heterogeneous catalysts.<sup>10-12</sup> Separation of spent heterogeneous catalyst from a product mixture is easier than in the case of homogeneous systems. Heterogeneous catalysts also help to minimize waste derived from the reaction workup, thereby contributing to the development of green chemical processes. The most common strategy for preparing a heterogeneous catalyst involves using a solid support, such as metal oxide, carbon, silica, or various organic materials, with a catalytic metal.<sup>10</sup> Several studies have demon-

strated that both the production<sup>13</sup> and utilization of carbon nanomaterials show promise in catalytic organic reactions.<sup>4,14</sup>

Porous carbon-based nanomaterials are currently receiving a large degree of attention, and great progress has been made toward the synthesis of various shapes and sizes. Spherical carbon nanoparticles have been fabricated with a template-based synthesis.<sup>15</sup> These recently developed nano-sized carbon balls (NCBs) are an interesting material for use as a heterogeneous catalyst support. NCBs contain a hollow core and are mesoporous, ball-like structures with an average diameter of 500 nm, an average shell thickness of 40 - 50 nm, a specific surface area of at least 1,000 m<sup>2</sup>/g, and a total pore volume of about 0.9 cm<sup>3</sup>/g.<sup>16</sup> Due to the large surface area and pore volume, these materials make excellent substrates for adsorption-based applications.<sup>17</sup> However, the chemical inertness of NCBs limits their utilization in other potential applications such as those involving bioactive compounds and homogeneous catalysts.

Palladium-catalyzed heteroannulation has been studied on both internal and terminal acetylene with homogeneous and heterogeneous palladium catalysts.<sup>18-21</sup> NCBs may be useful as palladium-supporting materials for the preparation of heterogeneous palladium catalysts for the synthesis of functionalized

**Table 1.** Optimization of reaction parameters for the diarylation of acetylene gas with a Pd(NO<sub>3</sub>)<sub>2</sub>·2H<sub>2</sub>O-NCB catalyst



Entry	Pd Source	Base (5 eq)	Ligand (mol %)	Solvent	Time (h)	Yield (%)
1	Pd(NO <sub>3</sub> ) <sub>2</sub> ·2H <sub>2</sub> O-NCB	Et <sub>3</sub> N	none	Acetone	12	-
2	"	Et <sub>3</sub> N	10	Acetone	12	22
3	"	Et <sub>3</sub> N	20	Acetone	12	38
4	"	Et <sub>3</sub> N	20	Acetone:H <sub>2</sub> O (3:1)	12	68
5	Pd(NO <sub>3</sub> ) <sub>2</sub> ·2H <sub>2</sub> O	Et <sub>3</sub> N	20	Acetone	12	62
6	Pd(II)-NaY	Et <sub>3</sub> N	20	Acetone	12	-
7	Pd/C	Et <sub>3</sub> N	20	Acetone	12	-
8	Pd/C	DBU	20	Dioxane:H <sub>2</sub> O (3:1)	12	48
9	Pd(PPh <sub>3</sub> ) <sub>4</sub>	Et <sub>3</sub> N	20	Acetone	12	52
10	Pd(PPh <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub>	Et <sub>3</sub> N	20	Acetone	12	45
11	Pd(NO <sub>3</sub> ) <sub>2</sub> ·2H <sub>2</sub> O-NCB	DBU	20	Dioxane	24	41
12	"	DBU	20	Dioxane:H <sub>2</sub> O (3:1)	8	83
13	"	Et <sub>3</sub> N	20	Dioxane:H <sub>2</sub> O (3:1)	12	51
14	"	Piperidine	20	Dioxane:H <sub>2</sub> O (3:1)	12	37

bisarylacetylene derivatives with acetylene gas.

The current study describes the preparation of bisarylacetylene compounds with acetylene gas using a NCB-supported heterogeneous palladium catalyst. The reusability of the catalyst is also discussed.

### Results and Discussion

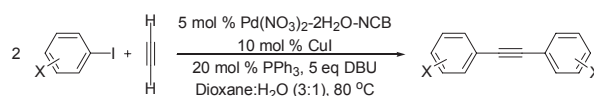
NCBs used in the present study were prepared according to a previously reported procedure and characterized by SEM.<sup>16</sup> The reaction of 4-iodophenol and acetylene gas was investigated as a model diarylation reaction with a 5.0 wt % Pd-loaded NCB catalyst. Reaction conditions were optimized by varying the Pd catalyst, base, ligand, and solvent as shown in Table 1. The reaction of Pd(NO<sub>3</sub>)<sub>2</sub>-2H<sub>2</sub>O-NCB catalyst with a PPh<sub>3</sub> ligand gave a better yield than the reaction without PPh<sub>3</sub> in acetone (entries 1-3). The same reaction was also performed in a 3:1 acetone:water mixture, producing a 68% yield of biarylated acetylene after 12 hours (entry 4). To compare catalytic activity, different Pd species were examined with Et<sub>3</sub>N base and 20% PPh<sub>3</sub> in acetone. The reaction using Pd(II)-NaY and did not result in acetylene diarylation (entry 6). Reactions with Pd(NO<sub>3</sub>)<sub>2</sub>-2H<sub>2</sub>O, Pd(PPh<sub>3</sub>)<sub>4</sub>, or Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> provided moderate yields of bisarylacetylene (entries 5, 9, and 10, respectively). Reactions performed with various organic bases in a 3:1 dioxane:H<sub>2</sub>O mixture were also evaluated (entries 12-14). The reaction with DBU provided an excellent yield of the desired product without any side products. Furthermore, the Pd(NO<sub>3</sub>)<sub>2</sub>-2H<sub>2</sub>O-NCB catalyst exhibited both a high catalytic activity and a high stability in aqueous solvent systems. These results suggest that the Pd(NO<sub>3</sub>)<sub>2</sub>-2H<sub>2</sub>O-NCB catalyst is very effective at absorbing acetylene gas from aqueous solvents.

The reaction of various substituted aromatic iodide compounds with acetylene gas was evaluated under the optimized reaction conditions shown in Table 1. The results are summarized in Table 2. Reactions with hydroxyl-substituted aryl iodides provided the corresponding hydroxyl-substituted bisarylacetylenes in good to excellent yields without any polymerized product (entries 2-4). Reactions incorporating electron-donating (CH<sub>3</sub>, NH<sub>2</sub>, entries 1 and 5) or electron-withdrawing groups (CO<sub>2</sub>Et, NO<sub>2</sub>, Br, entries 6, 7 and 8) substituted on the aryl iodide gave good to excellent yields of the desired products. These results demonstrated that excellent yields of bisarylated acetylenes can be obtained from a variety of substituted aryl halides using a heterogeneous palladium catalyst.

The reusability of the Pd(NO<sub>3</sub>)<sub>2</sub>-2H<sub>2</sub>O-NCB catalyst was also evaluated. The used catalyst was filtered out of the reaction mixture, washed with water and ethanol, and dried with air at room temperature. The recycled catalyst was used five times for the same reaction, adding 10% CuI and 20% PPh<sub>3</sub> to each reaction without regenerating the catalyst. The results are summarized in Table 3. The recycled catalyst showed a high degree of catalytic reusability for the diarylation of acetylene over all five reaction cycles, requiring only longer reaction times to obtain yields comparable to those of the freshly prepared catalyst.

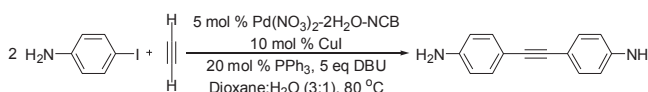
In conclusion, NCB-supported palladium catalysts exhibited excellent catalytic activity with a variety of substituted aryl

**Table 2.** Synthesis of functionalized bisarylacetylenes using a Pd(NO<sub>3</sub>)<sub>2</sub>-2H<sub>2</sub>O-NCB catalyst.



Entry	X	Reaction time (h)	Product yield (%)
1	4-CH <sub>3</sub>	12	75
2	4-CH <sub>2</sub> OH	10	85
3	3-OH	10	81
4	4-OH,3-CH <sub>3</sub>	10	62
5	4-NH <sub>2</sub>	15	92
6	4-CO <sub>2</sub> CH <sub>3</sub>	24	88
7	3-NO <sub>2</sub>	12	85
8	4-Br	12	89

**Table 3.** The reaction of 4-iodoaniline with acetylene gas using recycled Pd(NO<sub>3</sub>)<sub>2</sub>-2H<sub>2</sub>O-NCB catalyst.



Entry	Pd(NO <sub>3</sub> ) <sub>2</sub> -2H <sub>2</sub> O-NCB	Reaction time (h)	Yield (%)
1	Fresh	8	92
2	1st recycled	12	89
3	2nd recycled	18	88
4	3rd recycled	24	85
5	4th recycled	24	83
6	5th recycled	24	80

iodides under mild reaction conditions. The Pd(NO<sub>3</sub>)<sub>2</sub>-2H<sub>2</sub>O-NCB catalyst was easily recovered and exhibited a high degree of reusability in synthesis of functionalized bisarylacetylene derivatives in aqueous solvents. Given these results, the NCB-supported palladium catalyst shows considerable promise for use in a variety of organic reactions.

### Experimental Section

**Equipment.** Melting points were determined using a Thermo Scientific Electrothermal 9100 melting point apparatus. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a JEOL JNM-AL400 Spectrometer (400 MHz for <sup>1</sup>H and 100 MHz for <sup>13</sup>C).

**Preparation of Pd(NO<sub>3</sub>)<sub>2</sub>-2H<sub>2</sub>O-NCB catalyst.** NCB was synthesized as described previously.<sup>16</sup> The 5 wt % of Pd/NCB was prepared as follows: a homogeneous slurry composed of 1 g NCB and 100 mL of 3.0 × 10<sup>-3</sup> M aqueous Pd(NO<sub>3</sub>)<sub>2</sub>·2.5H<sub>2</sub>O (Kojima, Japan) was heated to dryness in a rotary evaporator at 70 °C. The metal content in the solid powder was determined using an inductively coupled plasma (ICP) spectrometer (J.Y. Ultima C, Jobin Yvon).

**General synthetic procedure.** A mixture of NCB (nanosized carbon balls)-supported Pd(NO<sub>3</sub>)<sub>2</sub>-2H<sub>2</sub>O-NCB (0.025 mmol), 4-hydroxyphenyliodide (0.44 g, 2.0 mmol), CuI (10 mol %), 20% PPh<sub>3</sub>, and DBU (5 equivalents) was dissolved in 4 mL of a 3:1 ratio of dioxane:H<sub>2</sub>O mixture in a two-necked round-bottom flask. The resulting mixture was stirred for 30 minutes at

room temperature while purging with a nitrogen-filled balloon. The nitrogen balloon was replaced with an acetylene balloon, and after purging the flask with acetylene, the reaction mixture was sealed and stirred for 8 - 24 h at 80 °C. The reaction mixture was filtered through filter paper and the resulting solution was neutralized with 1 N HCl. The neutralized filtrate was then extracted with ethyl acetate (3 × 20 mL), washed with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>·5H<sub>2</sub>O and brine, dried over MgSO<sub>4</sub>, filtered, and concentrated. The product (**1**) was isolated with 83% yield *via* column chromatography on silica gel. mp 230 °C; <sup>1</sup>H NMR (acetone-*d*<sub>6</sub>, 400 MHz) δ 8.69 (2H, -OH), 7.34 (4H, Ar-H), 6.86 (4H, Ar-H), <sup>13</sup>C NMR (acetone-*d*<sub>6</sub>, 100 MHz) δ 88.3, 115.4, 116.4, 133.6, 158.4.

The following compounds were prepared by this general procedure.

**1,2-Bis[(4,4'-dimethyl)phenyl]ethyne (2):**<sup>5</sup> The reaction with 4-iodotoluene (0.44 g, 2.0 mmol) and acetylene gas provided product (**2**) with 75% yield as a solid. mp 129 °C; <sup>1</sup>H NMR (acetone-*d*<sub>6</sub>, 400 MHz) δ 7.40 (4H, Ar-H), 7.21 (4H, Ar-H), 2.34 (6H, Ar-CH<sub>3</sub>), <sup>13</sup>C NMR (acetone-*d*<sub>6</sub>, 100 MHz) δ 21.4, 89.5, 121.2, 130.1, 132.1, 139.3.

**1,2-Bis[(4,4'-dihydroxymethyl)phenyl]ethyne (3):** The reaction with 4-iodobenzylalcohol (0.468 g, 2 mmol) and acetylene gas provided product (**3**) with 85% as a solid. mp 198 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 7.50 (4H, Ar-H), 7.36 (4H, Ar-H), 5.28 (2H, -OH), 4.52 (4H, Ar-CH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) δ 62.5, 88.4, 115.5, 126.6, 130.9, 146.8.

**1,2-Bis[(3,3'-dihydroxy)phenyl]ethyne (4):** The reaction with 3-iodophenol (0.468 g, 2 mmol) and acetylene gas provided product (**4**) with 81% as a solid. mp 163 °C <sup>1</sup>H NMR (acetone-*d*<sub>6</sub>, 400 MHz) δ 8.61 (2H, -OH), 7.22 (2H, Ar-H), 7.01 (4H, Ar-H), 6.86 (2H, Ar-H), <sup>13</sup>C NMR (acetone-*d*<sub>6</sub>, 100 MHz) δ 89.5, 116.8, 118.7, 123.6, 124.9, 130.2, 158.1.

**4,4'-(Ethyne-1,2-diyl)bis(2-methylphenol) (5):** The reaction with 5-iodocresol (0.468 g, 2 mmol) and acetylene gas provided product (**5**) with 62% as a solid. mp 197 °C; <sup>1</sup>H NMR (acetone-*d*<sub>6</sub>, 400 MHz) δ 8.59 (2H, OH), 7.24 (2H, Ar-H), 7.16 (2H, ArH), 6.83 (2H, ArH), 2.21 (6H, Ar-CH<sub>3</sub>); <sup>13</sup>C NMR (acetone-*d*<sub>6</sub>, 100 MHz) δ 15.9, 88.3, 115.4, 115.6, 125.9, 130.9, 134.6, 156.4.

**4,4'-(Ethyne-1,2-diyl)diamine (6):**<sup>22</sup> The reaction with 4-iodoaniline and acetylene provided product (**6**) with 92% yield as a solid. mp 237 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 7.09 (4H d, ArH), 6.51 (4H, d, ArH), 5.37 (4H, s, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) δ 148.0, 131.6, 113.4, 112.7, 89.5.

**1,2-Bis(4-cabomethoxyphenyl)ethyne (7):**<sup>5</sup> The reaction with 4-iodo(methylbenzoate) and acetylene gas provided (**7**) with 89% as a solid. mp 220 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 8.02 (4H, m, ArH), 7.63 (4H, m, ArH), 3.93 (6H, s, -OCH<sub>3</sub>), <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 52.3, 91.3, 127.3, 129.6, 129.9, 131.6, 166.5.

**1,2-Bis(3-nitrophenyl)ethyne (8):** The reaction with 3-nitrobenzene and acetylene gas provided (**8**) with 85% as a solid. mp 168 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 8.42 (2H, m, ArH),

8.23 (2H, m, ArH), 7.87 (2H, m, ArH), 7.59 (2H, m, ArH), <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 89.1, 123.7, 124.0, 126.6, 129.6, 137.3, 148.2.

**1,2-Bis(4-bromophenyl)ethyne (9):**<sup>5</sup> The reaction with 1-bromo-4-iodobenzene and acetylene gas provided product (**9**) with 89% as a solid. mp 186 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.49 (4H, d, ArH), 7.38 (4H, d, ArH); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 89.4, 121.9, 122.8, 131.7, 133.0.

**Acknowledgments.** This work was supported by a grant from the Fundamental R&D Program for Core Technology of Materials funded by the Ministry of Knowledge Economy, Republic of Korea.

## References

1. Blaszczyk, A.; Chadim, M.; Hanisch, C.; Mayor, M. *Eur. J. Org. Chem.* **2006**, 3809.
2. Gadzikwa, T.; Zeng, B.-S.; Hupp, J. T.; Nguyen, S. T. *Chem. Commun.* **2008**, 3672.
3. Negishi, E.; de Meijere, A. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Vol. 1, Wiley-interscience, John Wiley & Sons, Inc.: pp 493-549.
4. Doucet, H.; Hierso, J.-C. *Angew. Chem. Int. Ed.* **2007**, *46*, 834 and reference therein.
5. Mio, M. J.; Kopel, L. C.; Braun, J. B.; Gadzikwa, T. L.; Hull, K. L.; Brisbois, R. G.; Markworth, C. J.; Grieco, P. A. *Org. Lett.* **2002**, *4*, 3199.
6. Finke, A. D.; Elleby, E. C.; Boyd, M. J.; Weissman, H.; More, J. F. *J. Org. Chem.* **2009**, *74*, 8897.
7. Li, C.-J.; Chen, D.-L.; Costello, C. W. *Organic Process Research & Development* **1997**, *1*, 325.
8. Pal, M.; Kundu, N. G. *J. Chem. Soc., Perkin Trans. I* **1995**, 449.
9. Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *50*, 4467.
10. Astruc, D.; Lu, F.; Aranzaes, J. R. *Angew. Chem. Int. Ed.* **2005**, *44*, 7852 and reference therein.
11. Tomas, J. M.; Raja, R.; Lewis, D. W. *Angew. Chem. Int. Ed.* **2005**, *44*, 6456.
12. Corma, A.; Garcia, H. *Topics in Catalyst* **2008**, *48*, 8-31.
13. Nakagawa, K.; Oda, H.; Yamashita, A.; Okamoto, M.; Sato, Y.; Gamo, H.; Nishitani-gamo, M.; Ogawa, K.; Ando, T. *J. Mater. Sci.* **2009**, *44*, 221.
14. Narayanan, R.; El-Sayed, M. A. *Journal of Catalysis* **2005**, *234*, 348-355.
15. Yu, J.-S.; Kang, S.; Yoon, B.; Chai, G. *J. Am. Chem. Soc.* **2002**, *124*, 9382.
16. Lee, J. K.; Han, S. Y.; Park, S.-K.; Park, Y.-K.; Lee, C. W. *Korean J. Chem. Eng.* **2005**, *22*, 42-45.
17. Liu, Z.-X.; Park, J.-N.; Abdi, S. H. R.; Park, S.-K.; Park, Y.-K.; Lee, C. W. *Topics in Catalysis* **2006**, *39*, 221.
18. Park, S. S.; Choi, J. K.; Yum, E. K.; Ha, D.-C. *Tetrahedron Lett.* **1998**, *39*, 627.
19. Chi, S. M.; Choi, J. K.; Yum, E. K.; Chi, D. Y. *Tetrahedron Lett.* **2000**, *41*, 919.
20. Kang, S. K.; Park, S. S.; Kim, S. S.; Choi, J. K.; Yum, E. K. *Tetrahedron Lett.* **1999**, *40*, 4379.
21. Hong, K. B.; Lee, C. W.; Yum, E. K. *Tetrahedron Lett.* **2004**, *45*, 693.
22. Deeming, A. J.; Hogarth, G.; Lee, M.; Saha, M.; Redmond, S. P.; Phetmung, H.; Orpen, A. G. *Inorg. Chim. Acta* **2000**, *309*, 109.