Ligand-Free Copper-Catalyzed Cross-Coupling Reaction of Alkynes with Aryl Iodides and Vinyl Halides

Wan-Ting Tsai, Yun-Yung Lin, Yi-An Chen, Chin-Fa Lee*

Department of Chemistry, National Chung Hsing University, Taichung, Taiwan 402, R. O. C.
Fax +886(4)22862547; E-mail: cfalee@dragon.nchu.edu.tw

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Abstract: A copper-catalyzed cross-coupling reaction of alkynes with aryl iodides is described. The system tolerates a broad range of functional groups and enables the sterically demanding substrates presented during the catalysis with only 5–10 mol% of Cu_2O as the catalyst.

Key words: copper, cross-coupling, Sonogashira reaction, ligand-free, aryl iodide, vinyl halide

Functional alkynes and enynes are important compounds in organic synthesis[1,2] and organic materials.[3] The Sonogashira cross-coupling reaction employs a catalytic combination of palladium and copper salts as the most popular method for preparing such internal alkynes by reaction of aryl and vinyl halides with terminal alkynes.[1–4] Recently, copper has been used as a sole metal source in combination with appropriate ligands for the Sonogashira-type reaction owing to the low cost of the copper salts.[5–14] Ligands such as Ph_3P,[5–7] *N*,*N*-dimethylglycine,[8] ethylenediamine,[9] 1,4-diazabicyclo[2.2.2]octane,[10] pyrimidine,[11] 1,3-diphenylpropane-1,3-dione,[12] *N*,*N*-dimethylethylenediamine,[13] and others[14] have been reported. Some ligands, however, are expensive and require time-consuming syntheses. Mao reported the ligand-free iron–copper co-catalyzed coupling reaction of terminal alkynes with aryl iodides,[15] however, the scope of this system is limited to aryl alkynes. Furthermore, this catalytic system requires 30 mol% of $Fe(acac)_3$ and 10 mol% of CuI. Rothenberg et al. revealed that the copper clusters are active species for promoting the Sonogashira-type reaction, however, only phenylacetylene was involved in their system.[16] Biffis reported that CuO on alumina could be used as a catalyst for the same purpose, however, low yields were observed for alkyl alkynes.[17] Recently, Yuan et al. reported that CuO nanoparticles can also catalyze the coupling of alkynes with aryl iodides; however, the reactions were carried out at 160 °C, and only one alkyl alkyne was explored in this protocol.[18] Although in 2010, Novák and coworkers reported that trace amount of palladium is a key for the copper-catalyzed Sonogashira reaction.[19] Bolm et al. have demonstrated that the $[Cu(DMEDA)_2]Cl_2–H_2O$ complex can serve as a catalyst in combination of Cs_2CO_3 as a base in dioxane in this area. They have proposed the mechanism for the copper-catalyzed Sonogashira reaction. Importantly, the purity of reagents and copper sources have also been examined by ICP-MS technique in this report (with 4 ppb of palladium).[20] Very recently, Mao and coworkers have also reported that $[Cu(acac)_2]–H_2O$ is an active catalyst for the same propose. All reagents including $[Cu(acac)_2]–H_2O$, aryl halides, alkynes, K_2CO_3, and DMSO have been measured by ICP-MS, and no palladium was detected.[20] These results strongly suggest that copper can serve as the sole metal for the coupling of alkynes with aryl halides without palladium. Notably, the ligand is important in Bolm and Mao's systems.[20,21] Thus, it is desirable to develop a simpler system which employs copper as a catalyst in the absence of ligand. As part of our ongoing interests in this area,[22] herein we report that commercially available Cu_2O can be utilized as a catalyst for the copper-catalyzed cross-coupling reaction of aryl iodides and vinyl halides with alkynes in the absence of additional ligand. This system shows good functional-group compatibility with unprotected amines, bromo, chloro, and heterocyclic groups. Moreover, di-*ortho*-substituted aryl iodides with sterically demanding groups also work with alkynes, giving the corresponding internal alkynes in good yields.

Initially, phenylacetylene (**1a**) and iodobenzene (**2a**) were chosen as the substrates to determine the optimal reaction conditions. The results are summarized in Table 1. To our delight, a 94% isolated yield was obtained when the reaction was carried out by using 5 mol% of Cu_2O as a catalyst[23] and Cs_2CO_3 as a base in DMF under ligand-free conditions (Table 1, entry 1). A lower yield was observed when the catalyst was decreased to 1.5 mol% (Table 1, entry 2). The control experiment showed that no product was formed when the reaction was performed without catalyst (Table 1, entry 3). Copper salts including CuI, CuO, $CuCl_2$, CuBr, and $Cu(OAc)_2$ (Table 1, entries 4–8, respectively) were tested, but Cu_2O was the best choice. Other bases (Table 1, entries 9–12) such as Na_2CO_3, K_2CO_3, K_3PO_4, and KO*t*-Bu could not provide satisfying results. The study of solvent effect (Table 1, entries 13–17) revealed that NMP is also suitable for this transformation; other solvents did not show good results. It was recognized that no product was obtained when the reactions were conducted under shorter reaction times (Table 1, entry 18) and lower temperatures (Table 1, entry 19).

We then explored the scope of this catalytic system to a variety of aryl alkynes and aryl iodides. As demonstrated in Table 2,[24] aryl alkynes bearing heterocyclic groups or unprotected amine and trifluoromethyl groups were cou-

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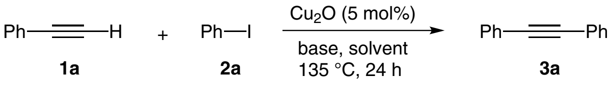
Table 1 Optimization of Copper-Catalyzed Coupling of Phenylacetylene with Iodobenzene[a]



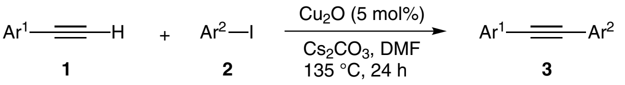
Entry	[Cu]	Base	Solvent	Yield (%)
1	Cu_2O	Cs_2CO_3	DMF	94
2	Cu_2O	Cs_2CO_3	DMF	80[b]
3	–	Cs_2CO_3	DMF	–[c]
4	CuI	Cs_2CO_3	DMF	80
5	CuO	Cs_2CO_3	DMF	31
6	$CuCl_2$	Cs_2CO_3	DMF	72
7	CuBr	Cs_2CO_3	DMF	84
8	$Cu(OAc)_2$	Cs_2CO_3	DMF	73
9	Cu_2O	Na_2CO_3	DMF	58
10	Cu_2O	K_2CO_3	DMF	45
11	Cu_2O	K_3PO_4	DMF	67
12	Cu_2O	KO*t*-Bu	DMF	–
13	Cu_2O	Cs_2CO_3	NMP	83
14	Cu_2O	Cs_2CO_3	DMSO	81
15	Cu_2O	Cs_2CO_3	dioxane	38
16	Cu_2O	Cs_2CO_3	DME	70
17	Cu_2O	Cs_2CO_3	DEF	92
18	Cu_2O	Cs_2CO_3	DMF	–[d]
19	Cu_2O	Cs_2CO_3	DMF	–[e]

[a] Reaction conditions unless otherwise stated: Cu_2O (0.05 mmol, 5.0 mol%), phenylacetylene (1.5 mmol), iodobenzene (1.0 mmol), base (2.0 mmol) in solvent (0.5 mL).
[b] Cu_2O: 1.5 mol%.
[c] No catalyst.
[d] Reaction time: 12 h.
[e] Reaction temperature: 120 °C.

pled smoothly with many aryl iodides, giving the internal alkynes in good to excellent yields. Notably, functional groups including unprotected amine (Table 2, entries 2 and 12), bromo (Table 2, entries 5 and 9), chloro (Table 2, entry 8), thiophene (Table 2, entry 11), and pyridine moiety (Table 2, entry 14) are tolerated under the reaction conditions employed. Moreover, the sterically demanding di-*ortho*-substituted aryl iodide, for example, 2-ethyl-6-methyliodobenzene was smoothly coupled with phenylacetylene to give **3h** in 93% yield (Table 2, entry 7).

A low product yield was obtained when the above reaction conditions (5.0 mol% of catalyst) were applied to alkyl alkynes. However, satisfactory results can be achieved when the catalyst loading was increased from 5–10 mol%. The results are listed in Table 3: Alkyl alkynes **4** reacted

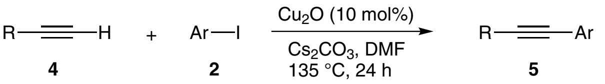
Table 2 Cu_2O-Catalyzed Cross-Coupling Reaction of Aryl Alkynes with Aryl Iodides[a]



Entry	Ar^1	Ar^2	Product **3**	Yield (%)
1	Ph	4-MeC_6H_4I	**3b**	94
2	Ph	$4\text{-H}_2NC_6H_4I$	**3c**	86
3	Ph	4-MeOC_6H_4I	**3d**	88
4	Ph	2-MeOC_6H_4I	**3e**	64
5	Ph	2-BrC_6H_4I	**3f**	81
6	Ph	2-MeC_6H_4I	**3g**	92
7	Ph	2-Et-6-MeC_6H_3I	**3h**	93
8	Ph	4-ClC_6H_4I	**3i**	93
9	Ph	4-BrC_6H_4I	**3j**	82
10	Ph	$(2,4,6\text{-trimethyl})C_6H_2I$	**3k**	85
11	3-thiophene	PhI	**3l**	71
12	$3\text{-H}_2NC_6H_4$	PhI	**3m**	59
13	$4\text{-F}_3CC_6H_4$	PhI	**3n**	70
14	Ph	3-iodopyridine	**3o**	75

[a] Reaction conditions unless otherwise stated: Cu_2O (0.05 mmol, 5 mol%), aryl alkyne (1.5 mmol), aryl iodide (1.0 mmol), Cs_2CO_3 (2.0 mmol) in DMF (0.5 mL).

Table 3 Cu_2O-Catalyzed Cross-Coupling Reaction of Alkyl Alkynes with Aryl Iodides[a]



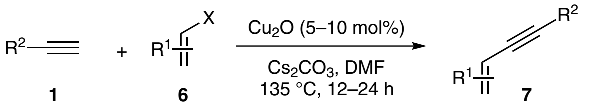
Entry	R	Ar	Product **5**	Yield (%)
1	$n\text{-C}_4H_9$	PhI	**5a**	74
2	$n\text{-C}_4H_9$	4-MeOC_6H_4I	**5b**	56
3	$n\text{-C}_4H_9$	4-BrC_6H_4I	**5c**	67
4	$n\text{-C}_4H_9$	4-MeC_6H_4I	**5d**	63
5	$n\text{-C}_4H_9$	2-iodopyridine	**5e**	43[b]
6	$n\text{-C}_4H_9$	2-MeC_6H_4I	**5f**	65[c]
7	$n\text{-C}_4H_9$	4-ClC_6H_4I	**5g**	48[b]
8	$n\text{-C}_8H_{17}$	PhI	**5h**	52
9	$n\text{-C}_8H_{17}$	4-MeOC_6H_4I	**5i**	47[b]
10	$n\text{-C}_8H_{17}$	2-MeC_6H_4I	**5j**	83[b]

[a] Conditions unless otherwise stated: Cu_2O (0.10 mmol, 10 mol%), alkyl alkyne (1.5 mmol), aryl iodide (1.0 mmol), Cs_2CO_3 (2.0 mmol) in DMF (0.5 mL).
[b] Reaction time: 48 h.
[c] Reaction time: 30 h.

with a variety of aryl iodides to afford the corresponding alkynes in moderate to good yields.

This catalytic system is also applicable to the synthesis of enynes, and the results are summarized in Table 4. Alkyl vinyl iodides were reacted with alkyl and aryl alkynes to provide enynes in good to excellent yields in the presence of 5–10 mol% of Cu_2O (Table 4, entries 1–11). Interestingly, phenylacetylene was worked with bromostyrene to obtain the product **7m** in 67% yield (Table 4, entry 13). However, the alkyl vinyl bromide did not couple with alkyl and aryl alkynes in the present system.

Table 4 Cu_2O-Catalyzed Cross-Coupling Reaction of Alkynes with Vinyl Iodides and Bromide[a]



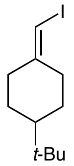
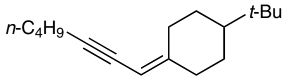
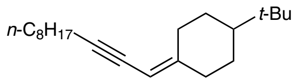
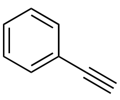
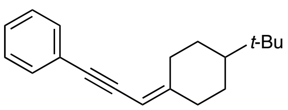
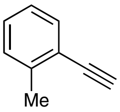
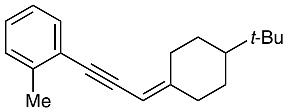
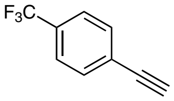
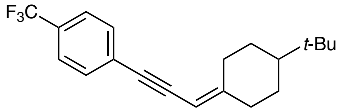
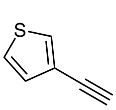
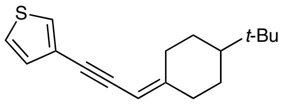
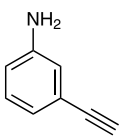
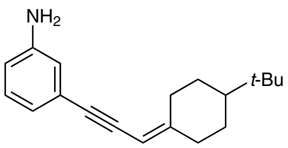
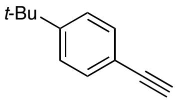
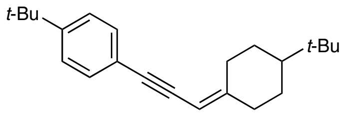
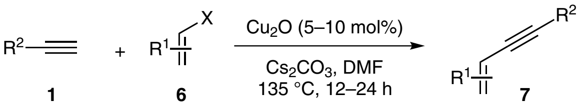
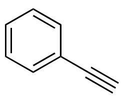
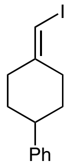
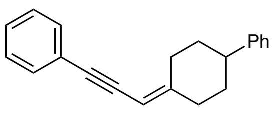
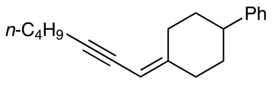
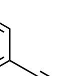
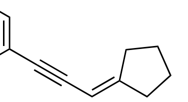
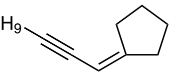
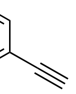
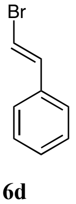
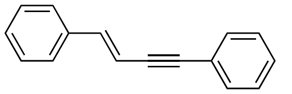
Entry	1	6	Product 7	Yield (%)
1	n-$C_4H_9C\equiv CH$	 **6a**	 **7a**	63
2	n-$C_8H_{17}C\equiv CH$	**6a**	 **7b**	64
3		**6a**	 **7c**	85
4		**6a**	 **7d**	51
5		**6a**	 **7e**	88
6		**6a**	 **7f**	53
7		**6a**	 **7g**	58
8		**6a**	 **7h**	81

Table 4 Cu_2O-Catalyzed Cross-Coupling Reaction of Alkynes with Vinyl Iodides and Bromide[a] (continued)



Entry	1	6	Product 7	Yield (%)
9		 **6b**	 **7i**	80
10	n-$C_4H_9C{\equiv}CH$	**6b**	 **7j**	50[b]
11		 **6c**	 **7k**	71
12	n-$C_4H_9C{\equiv}CH$	**6c**	 **7l**	42[b]
13		 **6d**	 **7m**	67[b,c]

[a] Reaction conditions unless otherwise stated: Cu_2O (0.025 mmol, 5 mol%), alkyne (0.75 mmol), vinyl halide (0.5 mmol), Cs_2CO_3 (1.0 mmol) in DMF (0.5 mL).

[b] Cu_2O (0.05 mmol, 10 mol%), 24 h.

[c] The starting 1-(2-bromovinyl)benzene (**6d**) contains ratio of $E/Z = 10:1$ (the ratio of E/Z was determined by GC–MS and ^1H NMR techniques). Only E-form product **7m** was detected.

In conclusion, we report that the commercially available Cu_2O is an active catalyst for the coupling of terminal alkynes with aryl iodides, vinyl iodides, and bromide without the necessity of additional ligand. A variety of functional groups such as unprotected amines, chloro, bromo, and heterocycles were tolerated by the reaction conditions. Moreover, highly sterically demanding substrates, for example, 2-ethyl-6-methyliodobenzene could be coupled with alkyne to provide the corresponding alkyne in good yield.

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References and Notes

(1) (a) Nicolaou, K. C.; Dai, W.-M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1387. (b) Grissom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453.

(2) Sonogashira, K. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley-Interscience: New York, **2002**, 493–529.

(3) (a) de Haro, T.; Nevado, C. *J. Am. Chem. Soc.* **2010**, *132*, 1512. (b) Panda, B.; Sarkar, T. K. *Tetrahedron Lett.* **2010**, *51*, 301. (c) Carril, M.; Correa, A.; Bolm, C. *Angew. Chem. Int. Ed.* **2008**, *47*, 4862.

(4) For reviews, see: (a) Heravi, M. M.; Sadjadi, S. *Tetrahedron* **2009**, *65*, 7761. (b) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874. (c) Doucet, H.; Hierso, J.-C. *Angew. Chem. Int. Ed.* **2007**, *46*, 834. (d) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442. (e) Negishi, E.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979. (f) Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176. (g) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem. Int. Ed.* **2000**, *39*, 2632. (h) Martin, R. E.; Diederich, F. *Angew. Chem. Int. Ed.* **1999**, *38*, 1350.

(5) Okuro, K.; Furuune, M.; Enna, M.; Miura, M.; Nomura, M. *J. Org. Chem.* **1993**, *58*, 4716.

(6) Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.* **2001**, *3*, 4315.

(7) Saejueng, P.; Bates, C. G.; Venkataraman, D. *Synthesis* **2005**, 1706.

(8) Ma, D.; Liu, F. *Chem. Commun.* **2004**, 1934.

(9) Wang, Y. F.; Deng, W.; Liu, L.; Guo, Q. X. *Chin. Chem. Lett.* **2005**, *16*, 1197.

(10) Li, J.-H.; Li, J.-L.; Wang, D.-P.; Pi, S.-F.; Xie, Y.-X.; Zhang, M.-B.; Hu, X.-C. *J. Org. Chem.* **2007**, *72*, 2053.

(11) Xie, Y.-X.; Deng, C.-L.; Pi, S.-F.; Li, J.-H.; Yin, D.-L. *Chin. J. Chem.* **2006**, *24*, 1290.

(12) Monnier, F.; Turtaut, F.; Duroure, L.; Taillefer, M. *Org. Lett.* **2008**, *10*, 3203.

(13) Zuidema, E.; Bolm, C. *Chem. Eur. J.* **2010**, *16*, 4181.

(14) For more selected examples, see: (a) Hosseinzadeh, R.; Mohadjerani, M.; Tavakoli, R. *Synth. Commun.* **2010**, *40*, 282. (b) Thakur, K. G.; Jaseer, E. A.; Naidu, A. B.; Sekar, G. *Tetrahedron Lett.* **2009**, *50*, 2865. (c) Guan, J. T.; Yu, G.-A.; Chen, L.; Weng, T. Q.; Yuan, J. J.; Liu, S. H. *Appl. Organomet. Chem.* **2009**, *23*, 75. (d) Mao, J.; Guo, J.; Ji, S.-J. *J. Mol. Catal. A: Chem.* **2008**, *284*, 85. (e) Tang, B.-X.; Wang, F.; Li, J.-H.; Xie, Y.-X.; Zhang, M.-B. *J. Org. Chem.* **2007**, *72*, 6294. (f) Colacino, E.; Daïch, L.; Martinez, J.; Lamaty, F. *Synlett* **2007**, 1279. (g) Thathagar, M. B.; Beckers, J.; Rothenberg, G. *Green Chem.* **2004**, *6*, 215. (h) Liu, Y.; Yang, J.; Bao, W. *Eur. J. Org. Chem.* **2009**, 5317. (i) Xie, X.; Xu, X. B.; Li, H. F.; Xu, X. L.; Yang, J. Y.; Li, Y. Z. *Adv. Synth. Catal.* **2009**, *351*, 1263. (j) Wu, M.; Mao, J.; Guo, J.; Ji, S. *Eur. J. Org. Chem.* **2008**, 4050. (k) Bates, C. G.; Saejueng, P.; Venkataraman, D. *Org. Lett.* **2004**, *6*, 1441. (l) Okuro, K.; Furuune, M.; Enna, M.; Miura, M.; Nomura, M. *J. Org. Chem.* **1993**, *58*, 4716. (m) Okuro, K.; Furuune, M.; Miura, M.; Nomura, M. *Tetrahedron Lett.* **1992**, *33*, 5363.

(15) Mao, J.; Xie, G.; Wu, M.; Guo, J.; Jia, S. *Adv. Synth. Catal.* **2008**, *350*, 2477.

(16) Thathagar, M. B.; Beckers, J.; Rothenberg, G. *Green Chem.* **2004**, *6*, 215.

(17) Biffis, A.; Scattolin, E.; Ravasio, N.; Zaccheria, F. *Tetrahedron Lett.* **2007**, *48*, 8761.

(18) Yuan, Y.; Zhu, H.; Zhao, D.; Zhang, L. *Synthesis* **2011**, 1792.

(19) Gonda, Z.; Tolnai, G. L.; Novák, Z. *Chem. Eur. J.* **2010**, *16*, 11822.

(20) Zou, L.-H.; Johansson, A. J.; Zuidema, E.; Bolm, C. *Chem. Eur. J.* **2013**, *19*, 8144.

(21) Li, T.; Qu, X.; Xie, G.; Mao, J. *Chem. Asian J.* **2011**, *6*, 1325.

(22) (a) Tsai, W.-T.; Lin, Y.-Y.; Wang, Y.-J.; Lee, C.-F. *Synthesis* **2012**, *44*, 1507. (b) Lin, Y.-Y.; Wang, Y.-J.; Cheng, J.-H.; Lee, C.-F. *Synlett* **2012**, *23*, 930. (c) Lin, C.-H.; Wang, Y.-J.; Lee, C.-F. *Eur. J. Org. Chem.* **2010**, 4368.

(23) ICP-MS analysis showed 2 ppb of palladium in Cu_2O; no palladium has been detected in Cs_2CO_3 and phenylacetylene.

(24) **General Procedure for the Synthesis of Compounds 3a–e**
A sealable vial equipped with a magnetic stir bar was charged with Cs_2CO_3 (652 mg, 2.0 mmol) and Cu_2O (7.0 mg, 0.05 mmol) under a nitrogen atmosphere. The aperture of the vial was then covered with a rubber septum. Under a nitrogen atmosphere, aryl alkyne **1** (1.5 mmol), aryl iodide **2** (1.0 mmol), and DMF (0.5 mL) were added by syringe. The septum was then replaced by a screw cap containing a Teflon-coated septum, and the reaction vessel was placed at 135 °C. After stirring at this temperature for 24 h, the heterogeneous mixture was cooled to r.t. and diluted with EtOAc (20 mL). The resulting solution was filtered through a pad of silica gel, then washed with EtOAc (20 mL), and concentrated to give the crude material which was then purified by column chromatography on silica gel to yield alkyne **3**.

Data for Five Representative Examples

Diphenylacetylene (3a)[25]
Following the general procedure, using Cs_2CO_3 (652 mg, 2.0 mmol) and Cu_2O (7.0 mg, 0.05 mmol) in DMF (0.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3a** as a white solid (168 mg, 94% yield); mp 58–59 °C (lit.[25] 60–61 °C). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.26$–7.41 (m, 6 H), 7.56–7.60 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 89.4, 123.2, 128.2, 128.3, 131.6$ ppm.

Phenyl-*p*-tolylacetylene (3b)[25]
Following the general procedure, using phenylacetylene (0.0167 mL, 1.5 mmol) and 4-iodotoluene (218 mg, 1.0 mmol), then purified by column chromatography (SiO_2, hexane) to provide **3b** as a white solid (181 mg, 94% yield); mp 69–70 °C (lit.[25] 71–72.5 °C). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.17$ (s, 3 H), 6.96–6.97 (m, 1 H), 6.14–6.16 (m, 2 H), 7.28–7.38 (m, 2 H), 7.37–7.39 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.5, 88.7, 89.5, 120.1, 123.4, 128.0, 128.3, 129.1, 131.5, 131.5, 138.4$ ppm.

4-(Phenylethynyl)aniline (3c)[19c]
Following the general procedure, using phenylacetylene (0.167 mL, 1.5 mmol) and 4-iodoaniline (218 mg, 1.0 mmol), then purified by column chromatography (SiO_2, hexane–EtOAc = 9:1) provide **3c** as a brown solid (166 mg, 86% yield); mp 123–124 °C (lit.[19c] 126–127 °C). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.75$ (br s, 2 H), 6.57 (d, $J = 8.0$ Hz, 2 H), 7.28–7.33 (m, 5 H), 7.48–7.50 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 87.3, 90.1, 112.5, 114.7, 123.8, 127.6, 128.2, 131.3, 132.9, 146.6$ ppm.

(4-Methoxyphenyl)phenylacetylene (3d)[25]
Following the general procedure, using phenylacetylene (0.083 mL, 0.75 mmol) and 4-iodoanisole (120 mg, 0.5 mmol), then purified by column chromatography (SiO_2, hexane–EtOAc = 10:1) to provide **3d** as a white solid (92 mg, 88% yield); mp 55–57 °C (lit.[25] 58–60 °C). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.75$ (s, 3 H), 6.83–6.85 (m, 2 H), 7.28–7.31 (m, 3 H), 7.44–7.52 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 55.1, 88.0, 89.4, 113.9, 115.3, 123.5, 127.9, 128.2, 131.4, 133.0, 159.6$ ppm.

2-(Phenylethynyl)anisole (3e)[19c]
Following the general procedure, using phenylacetylene (0.167 mL, 1.5 mmol) and 2-iodoanisole (0.130 mL, 1.0 mmol), then purified by column chromatography (SiO_2, hexane–EtOAc = 9:1) to provide **3e** as a yellow oil (132 mg, 64% yield). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.86$ (s, 3 H), 6.84–6.93 (m, 2 H), 7.24–7.33 (m, 4 H), 7.48–7.50 (m, 1 H), 7.54–7.57 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 55.7, 85.7, 93.3, 110.6, 112.3, 120.4, 123.5, 128.0, 128.2, 129.7, 131.5, 133.5, 159.9$ ppm.

(25) Li, P.; Wang, L.; Li, H. *Tetrahedron* **2005**, *61*, 8633.