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CuI-Catalyzed Suzuki−Miyaura and Sonogashira Cross-Coupling Reactions Using DABCO as Ligand

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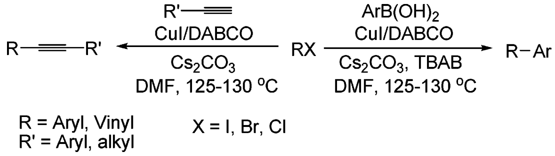

In the presence of TBAB, CuI-catalyzed Suzuki−Miyaura cross-coupling of vinyl halides and aryl halides with arylboronic acids was conducted smoothly to afford the corresponding diarylethenes and polyaryls in moderate to good yields using DABCO (1,4-diazabicyclo[2.2.2]octane) as the ligand. We also found that the inexpensive CuI/DABCO catalytic system was effective for Sonogashira cross-couplings of aryl halides and vinyl halides. A variety of aryl halides and vinyl halides including activated aryl chlorides underwent the coupling with terminal alkynes in moderate to excellent yields.

Introduction

Both the Suzuki−Miyaura and Sonogashira cross-coupling reactions have proven to be two important transformations, as the resulting biaryl and acetylenic products are extremely valuable intermediates in organic synthesis as well as important units found in a tremendous range of natural products and bioactive molecules.[1−3] The original and general Suzuki−Miyaura and Sonogashira coupling procedures involves the use of palladium−ligand (often a phosphine ligand) complexes as catalysts.[1] Nevertheless, the high price of Pd renders commercial processes based on Pd less attractive unless extremely active and/or recyclable catalysts are available. For these reasons, much recent attention has been attracted on employing less expensive transition metal catalyst complexes,[2,4−7] in particular, copper, to replace the palladium. However, only a few copper-catalyzed

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(1) For reviews, see: (a) Bringmann, G.; Walter, R.; Weirich, R. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 977−991. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483. (c) Diederich, F.; Stang, P. J. *Metal-Catalyzed Cross-coupling Reactions*; Wiley-VCH: Weinheim, 1998. (d) Miyaura, N. *Cross-Coupling Reaction*; Springer: Berlin, 2002. (e) Negishi, E. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Wiley−Interscience: New York, 2002. (f) Yong, B. S.; Nolan, S. P. *Chemtracts: Org. Chem.* **2003**, 205. (g) Tang, S.; Liang, Y.; Liu, W.-J.; Li, J.-H. *Chin. J. Org. Chem.* **2004**, *24*, 1133. (h) de Meijere, A.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley-VCH: Weinheim, 2004.

(2) For special reviews on copper-catalyzed cross-couplings, see: (a) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int Ed.* **2000**, *39*, 2632. (b) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (c) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400. (d) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337.

(3) (a) Viehe, H. G. *Chemistry of Acetylene*; Marcel Dekker: New York, 1969. (b) Bohlmann, F.; Burkhart, F. T.; Zero, C. *Naturally Occurring Acetylenes*; Academic Press: London and New York, 1973. (c) Trahanovsky, W. S. *Oxidation in Organic Chemistry*; Academic Press: New York and London, 1973; Vol. 5-B. (d) Hudlicky, M. *Oxidation in Organic Chemistry*, ACS Monograph 186; American Chemical Society: Washington DC, 1990. (e) Bringmann, G.; Gunther, C.; Ochse, M.; Schupp O.; and Tasler, S. In *Progress in the Chemistry of Organic Natural Products*; Herz, W., Falk, H., Kirby, G. W., Moore, R. E., Eds.; Springer: New York, 2001; Vol. 82, pp 1−293.

(4) For representative papers on the nickel-catalyzed Suzuki−Miyaura cross-coupling reaction, see: (a) Saito, S.; Ohtani, S.; Miyaura, N. *J. Org. Chem.* **1997**, *62*, 8024. (b) Zim, D.; Lando, V. R.; Dupond, J.; Monteiro, A. L. *Org. Lett.* **2001**, *3*, 3049. (c) Percec, V.; Golding, G. M.; Smidrkal, J.; Weichold, O. *J. Org. Chem.* **2004**, *69*, 3447.

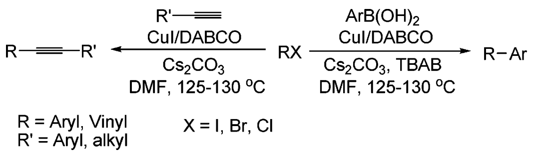
(5) For representative papers on the nickel-catalyzed Sonogashira cross-coupling reaction, see: (a) Wang, L.; Li, P.; Zhang, Y. *Chem. Commun.* **2004**, 514. (b) Beletskaya, I. P.; Latyshev, G. V.; Tsvetkov, A. V.; Lukashev, N. V. *Tetrahedron Lett.* **2003**, *44*, 5011.

(6) For papers on the copper-catalyzed Suzuki-Miyaura cross-coupling reaction, see: (a) Thathagar, M. B.; Beckers, J.; Rothenberg, G. *J. Am. Chem. Soc.* **2002**, *124*, 11858. (b) Thathagar, M. B.; Beckers, J.; Rothenberg, G. *Adv. Synth. Catal.* **2003**, *345*, 979.

(7) For papers on the Sonogashira cross-coupling reaction catalyzed by a catalytic amount of copper, see: (a) Okuro, K.; Furuune, M.; Enna, M.; Miura, M.; Nomura, M. *J. Org. Chem.* **1993**, *58*, 4716. (b) Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.* **2001**, *3*, 4315. (c) Thathagar, M. B.; Beckers, J.; Rothenberg, G. *Green Chem.* **2004**, *6*, 215. (d) Ma, D, Liu, F. *Chem. Commun.* **2004**, 1934. (e) Wang, Y. F.; Deng, W.; Liu, L.; Guo, Q. X. *Chin. Chem. Lett.* **2005**, *16*, 1197. (f) Saejueng, P.; Bates, C. G.; Venkataraman, D. *Synthesis* **2005**, 1706. (g) Xie, Y.-X.; Deng, C.-L.; Pi, S.-F.; Li, J.-H.; Yin, D.-L. *Chin. J. Chem.* **2006**, *24*, 1290.

10.1021/jo0623742 CCC: $37.00

SCHEME 1

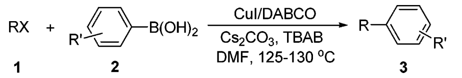


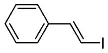
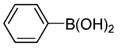
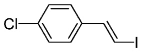
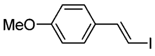
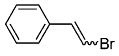
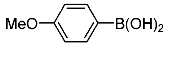
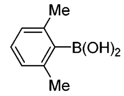
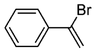
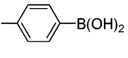
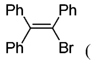
Suzuki−Miyaura and Sonogashira cross-coupling procedures exist.[2,6,7] In 2002, a pioneering work on the copper-catalyzed Suzuki−Miyaura coupling reaction was reported by Rothenberg and co-workers.[6] In the presence of copper or copper-based nanocolloids, a variety of aryl halides coupled with phenylboronic acid efficiently in moderate to excellent yields. Nevertheless, only the couplings of aryl iodides were investigated when the catalyst was copper alone.

Recently, copper (CuI or copper nanoclusters) has also emerged as a catalyst of choice partly for the Sonogashira cross-coupling reaction.[7] In 1993, Miura and co-workers reported the first catalytic Sonogashira cross-coupling between aryl iodides with terminal alkynes using CuI/PPh$_3$ as the catalytic system.[7a] Subsequently, Venkataraman and co-workers found that 1,10-phenanthroline was an effective ligand for the copper-catalyzed couplings of aryl iodides and vinyl iodides with terminal alkynes.[7b,f] Recently, Rothenberg applied copper nanoclusters in the reaction and extended the scope to the activated aromatic bromides without aid of any ligand.[7c] Ma and Liu have described that the deactivated aryl bromides could undergo the coupling smoothly using CuI as the catalyst and *N*,*N*-dimethylglycine as the ligand.[7d] Very recently, we found that pyrimidines, in particular 2-aminopyrimidine-4,6-diol, could promote the Cu(OAc)$_2$-catalyzed couplings between aryl halides and terminal alkynes under solvent-free and aerobic conditions, but only aryl iodides and the activated aryl bromides were suitable substrates.[7g] Although ethylenediamine combined with CuI was found to be an effective catalytic system for the couplings of aryl iodides and bromides, N^1,N^1,N^2,N^2-tetramethylethene-1,2-diamine, a tertiary amine, provided rather poor results.[7e] Our recent results showed that DABCO, another tertiary amine, was an efficient ligand for the cross-coupling reactions using palladium[8] or copper[9,10] as catalysts. Thus, we expected to extend the application of the ligand in other copper-catalyzed procedures. Indeed, DABCO was found to be an effective ligand for both the Suzuki and Sonogashira cross-coupling reactions.[12] Here, we wish to report our results in detail (Scheme 1).[10]

Results and Discussion

TABLE 1. Efficient CuI/DABCO-Catalyzed Suzuki−Miyaura Cross-Couplings of Vinyl Halides with Arylboronic Acids in the Presence of TBAB[a]



Entry	RX	ArB(OH)$_2$	Time (h)	Yield (%)[b]
1[c]	 (**1a**)	 (**2a**)	20	58 (**3aa**)
2	(**1a**)	(**2a**)	20	83 (**3aa**)
3[d]	(**1a**)	(**2a**)	20	63 (**3aa**)
4	 (**1b**)	(**2a**)	19	70 (**3ba**)
5	 (**1c**)	(**2a**)	20	95 (**3ca**)
6[e]	 (**1d**)	(**2a**)	18	67 (**3aa**)
7[f]	(**1d**)	 (**2b**)	18	50 (**3ca**)
8	(**1d**)	 (**2c**)	19	trace (**3dc**)
9	 (**1e**)	(**2a**)	20	77 (**3ea**)
10	(**1e**)	(**2b**)	20	51 (**3eb**)
11	(**1e**)	 (**2d**)	18	55 (**3ed**)
12	 (**1f**)	(**2a**)	24	trace (**3fa**)

[a] Unless otherwise indicated, the reaction conditions were as follows: **1** (0.3 mmol), **2** (0.4 mmol), CuI (10 mol %), DABCO (20 mol %), TBAB (1 equiv), and Cs$_2$CO$_3$ (2 equiv) in DMF (3 mL) at 125−130 °C. [b] Isolated yield. [c] Without TBAB. [d] Without DABCO. [e] Ratio of (*E*)-isomer/(*Z*)-isomer was 15:1 determined by GC−MS. [f] Ratio of (*E*)-isomer/(*Z*)-isomer was about 14:1 determined by GC−MS.

CuI/DABCO-Catalyzed Suzuki−Miyaura Cross-Coupling Reaction. In our preliminary communication,[10] couplings of aryl iodides and the activated aryl bromides with arylboronic acids catalyzed by catalytic amounts of CuI and DABCO were carried out smoothly in moderate to excellent yields. Although a stoichiometric amount of CuI together with TBAB was necessary for the couplings of the less activated aryl bromides, satisfactory yields were still obtained. Encouraged by the results, we decided to apply the CuI/DABCO system in coupling of vinyl halides with arylboronic acids. As shown in Table 1, treatment of 1-(2-iodovinyl)benzene (**1a**) with phenylboronic acid (**2a**), CuI, and DABCO in 20 h afforded the corresponding product **3aa** in a moderate yield (entry 1). We were happy to find that the yield of **3aa** was enhanced to 83% when 1 equiv of TBAB (*n*-Bu$_4$NBr) was added (entry 2). However, the yield of **3aa** was reduced to 63% in the absence of DABCO (entry 3). Under the standard reaction conditions, a variety of other vinyl halides **1b−e** underwent the coupling with arylboronic acids in moderate to good yields (entries 4−11). For example, the reactions of 1-(2-bromovinyl)benzene (**1d**) with arylboronic acids **2a** and **2b** were conducted smoothly to give the corresponding products **3aa** and **3ca** in 67% and 50% yields, respectively (entries 6 and 7). However, a trace amount of the target product was isolated from the coupling substrate **1d** with the bulky boronic acid **2c** (entry 8). It is noteworthy that 1-(1-bromovinyl)benzene (**1e**) can be coupled with boronic acids **2a**,

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(8) For papers on DABCO as the ligand for the palladium-catalyzed cross-coupling reactions, see: (a) Li, J.-H.; Liu, W.-J. *Org. Lett.* **2004**, *6*, 2809. (b) Li, J.-H.; Zhang, X.-D.; Xie, Y.-X. *Synthesis* **2005**, 804. (c) Li, J.-H.; Liu, W.-J.; Xie, Y.-X. *J. Org. Chem.* **2005**, *70*, 5409. (d) Li, J.-H.; Liang, Y.; Wang, D.-P.; Liu, W.-J.; Xie, Y.-X.; Yin, D.-L. *J. Org. Chem.* **2005**, *70*, 2832. (e) Li, J.-H.; Wang, D.-P.; Xie, Y.-X. *Synthesis* **2005**, 2193. (f) Li, J.-H.; Deng, C.-L.; Liu, W.-J.; Xie, Y.-X. *Synthesis* **2005**, 3039. (g) Li, J.-H.; Hu, X.-C.; Liang, Y.; Xie, Y.-X. *Tetrahedron* **2006**, *62*, 31. (h) Li, J.-H.; Zhu, Q.-M.; Xie, Y.-X. *Tetrahedron* **2006**, *62*, 10888. (i) Li, J.-H.; Hu, Q.-C.; Xie, Y.-X. *Tetrahedron Lett.* **2006**, *47*, 9239.

(9) For a paper on the use of the CuI/DABCO catalytic system for Heck reaction, see: Li, J.-H.; Wang, D.-P.; Xie, Y.-X. *Tetrahedron Lett.* **2005**, *46*, 4941.

(10) For a preliminary communication, see: Li, J.-H.; Wang, D.-P. *Eur. J. Org. Chem.* **2006**, 2063.

(11) The loading level of Pd is 6.27×10^{-5} mmol/mmol CuI, which was determined by means of an inductively coupled plasma-atomic emission spectrometer (ICP-AES).

(12) Stephens, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, 2*8*, 2163.

SCHEME 2

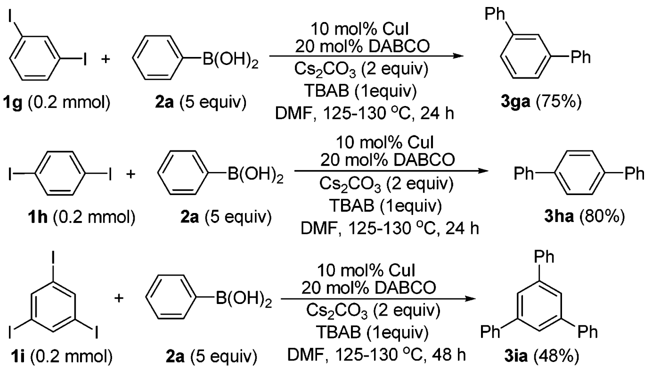
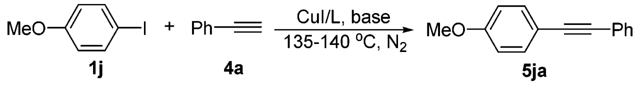


TABLE 2. CuI-Catalyzed Sonogashira Cross-Coupling Reaction of 1-Iodo-4-methoxybenzene (1j) with Phenylacetylene (4a)[a]



entry	ligand	base	solvent	time (h)	yield[b] (%)
1		K_2CO_3	DMF	12	trace
2[c]	DABCO	K_2CO_3	DMF	6	65
3	DABCO	K_2CO_3	DMF	6	95
4[d]	DABCO	K_2CO_3	DMF	6	96
5	Et_3N	K_2CO_3	DMF	12	45
6	TMEDA	K_2CO_3	DMF	6	56
7	HMPA	K_2CO_3	DMF	6	80
8	DABCO	K_2CO_3	MeCN	6	55
9[e]	DABCO	K_2CO_3	DMF	12	trace
10	DABCO	Cs_2CO_3	DMF	6	98
11	DABCO	Et_3N	DMF	6	61

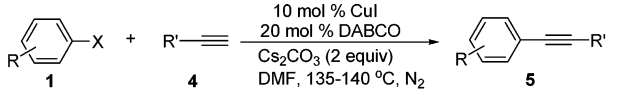
[a] Unless otherwise indicated, the reaction conditions were as follows: **1j** (0.5 mmol), **4a** (0.6 mmol), CuI (10 mol %), ligand (20 mol %), K_2CO_3 (2 equiv), and solvent (3 mL) at 135−140 °C under N_2. [b] Isolated yield. [c] DABCO (10 mol %). [d] DABCO (40 mol %). [e] At 100 °C. [f] Cs_2CO_3 (2 equiv) instead of K_2CO_3.

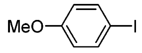
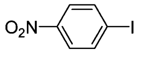
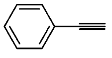
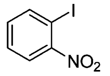
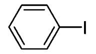
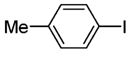
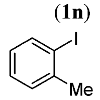
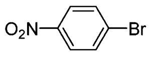
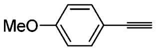
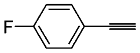
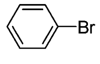
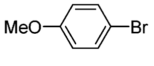
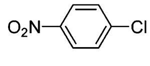
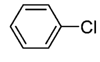
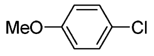
2b, and **2d**, respectively, in good yields (entries 9−11). Unfortunately, 1-bromo-1,2,2-triphenylethene (**1f**) was not a suitable substrate under the standard conditions (entry 12).

As demonstrated in Scheme 2, synthesis of polyaryls was then tested under the standard conditions. To our delight, diiodobenznes **1g**,**h** and triiodobenzene **1i** could selectively undergo the coupling with phenylboronic acid (**2a**) in moderate yields. In the presence of CuI, DABCO and TBAB, the reaction of 1,3-diiodobenzene (**1g**) or 1,4-diiodobenzene (**1h**) with **2a** provided the target products **3ga** and **3ha** in 75% and 80% yields, respectively. It was interesting to reveal that the coupling of 1,3,5-triiodomobenzene (**1i**) with **2a** was performed chemoselectively to afford the desired product **3ka** in a 48% yield.

CuI/DABCO-Catalyzed Sonogashira Cross-Coupling Reaction. Subsequently, we tried to apply the CuI/DABCO system in Sonogashira cross-coupling reaction, and the results are summarized in Tables 2 and 3 and Scheme 3. Initially, the catalytic activity of CuI/DABCO was tested in the Sonogashira reaction between 1-iodo-4-methoxybenzene (**1j**) and phenylacetylene (**4a**) (Table 1). It was found that the combination of CuI and DABCO was an effective catalytic system for the coupling of iodide **1j** with **4a**, and the amount of DABCO affected the reaction to some extent. Without the aid of any ligands, treatment of substrate **1j** with **4a**, CuI (10 mol %), and K_2CO_3 (2 equiv) afforded a trace amount of the corresponding coupled product **5ja**, whereas the yield of **5ja** was enhanced sharply to 95% when 20 mol % of DABCO was added (entries

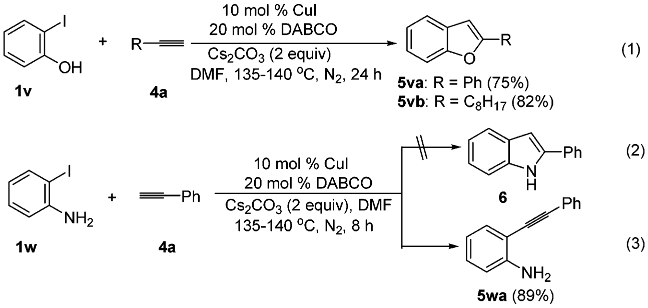
TABLE 3. CuI/DABCO-Catalyzed Sonogashira Cross-Coupling Reactions of Aryl Halides (1) with Terminal Alkynes (4)[a]



entry	ArX	Alkyne	time (h)	yield (%)[b]
1	 (**1j**)	$C_8H_{17}-\equiv$ (**4b**)	9	94 (**5jb**)
2	(**1j**)	$\equiv-CH_2OTHP$ (**4c**)	14	65 (**5jc**)
3	 (**1k**)	 (**4a**)	4	>99 (**5ka**)
4	(**1k**)	(**4b**)	4	>99 (**5kb**)
5	 (**1l**)	(**4a**)	12	73 (**5la**)
6	 (**1m**)	(**4a**)	10	94 (**5ma**)
7	 (**1n**)	(**4a**)	6	91 (**5na**)
8	(**1n**)	(**4b**)	6	96 (**5nb**)
9	 (**1o**)	(**4a**)	48	89 (**5oa**)
10	 (**1p**)	(**4a**)	8	95 (**5ka**)
11	(**1p**)	(**4b**)	24	85 (**5kb**)
12	(**1p**)	 (**4d**)	24	86 (**5pd**)
13	(**1p**)	 (**4e**)	15	88 (**5pe**)
14	 (**1q**)	(**4a**)	15	91 (**5ma**)
15	 (**1r**)	(**4a**)	10	97 (**5ja**)
16	(**1r**)	(**4b**)	25	65 (**5jb**)
17	 (**1s**)	(**4a**)	18	55 (**5ka**)
18[c]	(**1s**)	(**4a**)	12	92 (**5ka**)
19[c]	(**1s**)	(**4b**)	20	51 (**5kb**)
20[c]	 (**1t**)	(**4a**)	25	20 (**5ma**)
21[c]	 (**1u**)	(**4a**)	25	11 (**5ja**)

[a] Reaction conditions: **1** (0.5 mmol), **4** (0.6 mmol), CuI (10 mol %), DABCO (20 mol %), Cs_2CO_3 (2 equiv), and DMF (3 mL) at 135−140 °C under N_2. [b] Isolated yield. [c] TBAB (1 equiv).

SCHEME 3



1 and 2). Identical results were observed when DABCO was further increased to 40 mol % (entry 4). Other tertiary amine ligands, such as Et_3N, TMEDA, and HMPA, were less effective than DABCO (entries 3 and 5−7). Another solvent, MeCN, was then examined, and it was less effective than DMF (entries 3 and 8). It is noteworthy that the reaction temperature plays a crucial role in the reaction. Trace amount of **5ja** was isolated when the reaction was conducted at 100 °C (entry 9). Finally, two other bases were evaluated (entries 10 and 11). Results identical to those of entry 3 were observed using Cs_2CO_3 as the base, but only a moderate yield of **5ja** was isolated when Et_3N, an organic base, was used.

As demonstrated in Table 2, CuI/DABCO as the catalytic system for the Sonogashira reactions of various aryl halides **1j−u** with alkynes **4a−e** proved exceptionally active. Treatment of aryl iodides **1j−o** with alkynes **4a−c**, 10 mol % of CuI, 20 mol % of DABCO, and 2 equiv of Cs_2CO_3 provided moderate to excellent yields (entries 1−9). Under the same reaction conditions, a number of aryl bromides were found to be quite reactive. In the presence of 10 mol % of CuI, 20 mol % of DABCO, and 2 equiv of Cs_2CO_3, the couplings of bromides **1p−r** with alkynes **4a**, **4b**, **4d**, and **4e** were carried out smoothly to afford the corresponding cross-coupled products in good yields (entries 10−16). For example, treatment of **1p** with alkynes **4a**, **4b**, **4d**, or **4e** gave the corresponding products **6ka**, **6kb**, **6pd**, and **6pe** in 95%, 85%, 86%, and 88% yields, respectively (entries 10−13). It is interesting to note that the CuI/DABCO catalytic system is also effective for the activated aryl chloride (**1s**). A moderate yield of the desirable product **5ka** was isolated from the reaction of substrate **1s** with **4a** performed under 10 mol % of CuI, 20 mol % of DABCO, and 2 equiv of Cs_2CO_3 (55% yield, entry 17). We also found that TBAB (n-Bu_4NBr) could promote the reaction. The yield of **5ka** was increased sharply to 92% when 1 equiv of TBAB was presented (entry 18). The reaction of **1s** with **4b** also proceeded smoothly to produce 51% yield of the corresponding product **5kb** under the same conditions (entry 19). However, the CuI/DABCO catalytic system was ineffective for the reaction of the other aryl chlorides **1t** and **1u** even in the presence of 1 equiv of TBAB (entries 20 and 21).

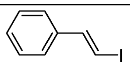
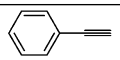
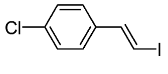
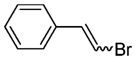
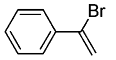
As shown in Scheme 3, coupling of 2-iodophenol (**1v**) with alkynes **4a** or **4b** gave the corresponding benzo[*b*]furans **5va** and **5vb** in the desired yields using CuI/DABCO as the catalytic system (eq 1 in Scheme 3).[9d] However, only 2-phenylethynylaniline (**5wa**) was observed in an 89% yield rather than 2-phenylindole (**6**) when 2-iodoaniline (**1w**) was reacted with **4a** (eqs 2 and 3).

In the presence of CuI and DABCO, the Sonogashira reactions of vinyl halides with terminal alkynes were also carried out smoothly in good yields, and the results are summarized in Table 4. The results indicated that TBAB was also required to improve the couplings of vinyl halides (entries 1 and 2). (*Z*)-1-(2-Iodovinyl)benzene (**1a**) was reacted with phenylactylene (**4a**), CuI, and DABCO to generate the corresponding product **5aa** in a 45% yield, whereas the yield of **5aa** was increased to 80% in the presence of TBAB. Under the same conditions, substrates **1b** and **1d** underwent coupling with alkynes in good yields (entries 3−5). Bromide **1d** coupled with **4a** or **4b**, for example, was conducted smoothly in 83% and 65% yields, respectively (entries 4 and 5). Unfortunately, coupling of another vinyl bromide **1e** with **4a** was unsuccessful (entry 6).

Three control reactions of substrate **1d** with phenylboronic acid **2a** were conducted to explore the mechanism of the present Suzuki−Miyaura cross-coupling (Scheme 4).[11] Although there are 6.27 × 10^{-5} mmol palladium species in per mmol the commercially available CuI (purity: 98%), the following results showed that the key catalyst is CuI. As demonstrated in Scheme 4, identical results were observed using 99.999% purity of CuI to those of the commercially available CuI (run 1). We then examined the Suzuki−Miyaura cross-coupling of substrate **1d** with **2a** using $Pd(OAc)_2$ as the catalyst alone. It was interesting to find that bromide **1d** performed the coupling with **2a**, $Pd(OAc)_2$ (0.7 mol %), DABCO (1.4 mol %), TBAB (1 equiv), and Cs_2CO_3 (2 equiv) at 125−130 °C in DMF (3 mL) for 5 h to provide the target product **3aa** in 80% yield (run 2). However, a rather low yield of **3aa** was isolated after 18 h at a loading of 0.0007 mol % Pd (the loading of Pd in 10 mol % CuI; run 3).

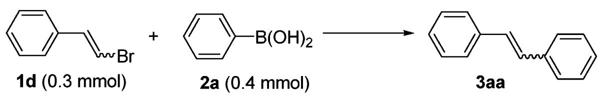
A working mechanism was proposed as outlined in Scheme 5 for the copper-catalyzed Suzuki cross-coupling reaction on the basis of the previously reported mechanism.[1,2,7,12] The reaction of intermediate **7**, a four-centered transition state proposed by Castro and Stephens,[12] with aryl halides or vinyl halides afforded intermediate **8**. Then transmetalation of intermediate **8** with arylboronic acid occurred to form intermediate **9**, followed by a reductive elimination of intermediate **9**, giving the coupled product **3** and regenerated the active copper(I) complex **7**. We deduced that mechanism of the present Sono-

TABLE 4. CuI/DABCO-Catalyzed Sonogashira Cross-Couplings of Vinyl Halides (1) with Terminal Alkynes (4) in the Presence of TBAB[a]

Entry	RX	ArB(OH)$_2$	Time (h)	Yield (%)[b]
1[c]	 (**1a**)	 (**4a**)	20	45 (**5aa**)
2	(**1a**)	(**4a**)	16	80 (**5aa**)
3	 (**1b**)	(**4a**)	19	73 (**5ba**)
4[d]	 (**1d**)	(**4a**)	16	83 (**5aa**)
5[e]	(**1d**)	$C_5H_{11}C{\equiv}CH$ (**4f**)	17	65 (**5db**)
6	 (**1e**)	(**4a**)	20	trace (**5ea**)

[a] Unless otherwise indicated, the reaction conditions were as follows: **1** (0.3 mmol), **4** (0.4 mmol), CuI (10 mol %), DABCO (20 mol %), TBAB (1 equiv), and Cs_2CO_3 (2 equiv) in DMF (3 mL) at 135−140 °C under N_2 atmosphere. [b] Isolated yield. [c] Without TBAB. [d] Ratio of (*E*)-isomer/(*Z*)-isomer was 15:1 determined by GC−MS. [e] Ratio of (*E*)-isomer/(*Z*)-isomer was 16:1 determined by GC−MS.

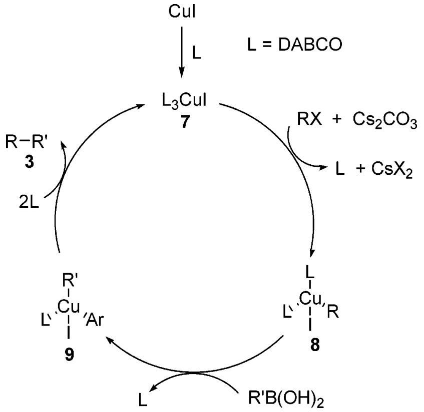
SCHEME 4



1d (0.3 mmol) **2a** (0.4 mmol) **3aa**

run	conditions	isolated yield
1	10 mol % CuI (99.999% metal), DABCO (20 mol %) TBAB (1 equiv), and Cs_2CO_3 (2 equiv) in DMF (3 mL) at 125-130 °C for 18 h	68%
2	0.7 mol % $Pd(OAc)_2$, DABCO (1.4 mol %) TBAB (1 equiv), and Cs_2CO_3 (2 equiv) in DMF (3 mL) at 125-130 °C for 5 h	80%
3	0.0007 mol % $Pd(OAc)_2$, DABCO (0.0014 mol %) TBAB (1 equiv), and Cs_2CO_3 (2 equiv) in DMF (3 mL) at 125-130 °C for 18 h	9%

SCHEME 5



gashira cross-coupling is similar to Miura's mechanism. Study of the accurate mechanism is in progress.

Conclusion

In summary, an inexpensive and highly efficient CuI/DABCO system for the cross-coupling reactions of aryl halides and vinyl halides with arylboronic acids or terminal alkynes has been developed. Compared with previous reports, several interesting features are apparent on the basis of the present results, including the following: (1) The catalytic system is efficient and general for a variety of aryl halides and vinyl halides. (2) Several functional groups, such as amino, methoxy, and fluoro groups, could be tolerated well. (3) The inexpensive CuI/DABCO system emerged as an attractive alternative to the palladium/ligand catalyst systems. Further efforts to extend the application of the system in other coupling transformations are underway in our laboratory.

Experimental Section

Typical Experimental Procedure for the CuI/DABCO-Catalyzed Suzuki-Type Cross-Coupling Reactions. A mixture of vinyl or aryl halide **1** (the indicated amount), boronic acid **2** (the indicated amount), CuI (10 mol %), DABCO (20 mol %), Cs_2CO_3 (2.0 equiv), TBAB (1 equiv), and DMF (3 mL) in a Schlenk tube was stirred under N_2 at 125−130 °C (oil bar temperature) for the desired time (indicated in Table 1 and Schemes 2 and 4) until complete consumption of starting material as monitored by TLC. After the mixture was filtered and evaporated, the residue was purified by flash column chromatography (hexane or hexane/ethyl acetate) to afford the corresponding coupled products.

Typical Experimental Procedure for the CuI/DABCO-Catalyzed Sonogashira-Type Cross-Coupling Reactions. A mixture of aryl halide 1 (the indicated amount), alkyne 4 (the indicated amount), CuI (10 mol %), DABCO (20 mol %), Cs_2CO_3 (2.0 equiv), and DMF (3 mL) in a Schlenk tube was stirred under N_2 at 135−140 °C (oil bar temperature) for the desired time (indicated in Tables 2 and 3 and Scheme 3) until complete consumption of starting material as monitored by TLC. After the mixture was filtered and evaporated, the residue was purified by flash column chromatography (hexane or hexane /ethyl acetate) to afford the corresponding coupled products.

2-Octylbenzofuran (**5vb**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, $J = 8.0$ Hz, 1H), 7.41 (d, $J = 8.4$ Hz, 1H), 7.22−7.15 (m, 2H), 6.37 (s, 1H), 2.76 (t, $J = 7.6$ Hz, 2H), 1.77−1.70 (m, 2H), 1.41−1.27 (m, 10H), 0.88 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 154.6, 129.0, 123.0, 122.3, 120.1, 110.7, 101.7, 31.8, 29.3, 29.2, 28.4, 27.7, 22.7, 14.1; LRMS (EI, 70 eV) *m*/*z* 230 (M^+, 64), 187 (11), 173 (8), 145 (13), 131 (100); HRMS (EI) for $C_{16}H_{22}O$ (M^+) calcd 230.1680, found 230.1678.

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Supporting Information Available: Analytical data and spectra (^{1}H and ^{13}C NMR) for all products **3** and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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