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Synthesis of 1,1-diaryl ethylenes by Cu-catalyzed arene C–H addition to aryl acetylenes

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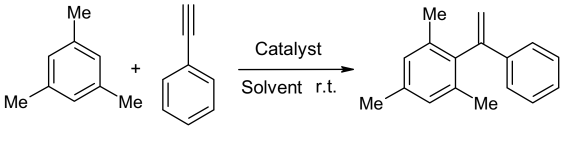
ABSTRACT

An unprecedented copper-catalyzed C–H addition of arenes to aryl acetylenes provides a facile route to 1,1-diaryl ethylenes in moderate to excellent yields. Arylboronic acids were likewise used along with aryl acetylenes in generating 1,1-diaryl ethylene.

Developing reliable methods for catalytic C–H functionalization has been a long-term goal in synthetic organic chemistry. For example, the catalytic addition of arene C–H bonds to unsaturated substrates continues to be a subject of interest for synthetic chemists.[1] Palladium complexes are known to catalyze arene C–H addition to simple alkenes and alkynes and provide various valuable synthetic intermediates in an atom-economical manner.[2,6] A few late-transition-metal complexes, including those containing Ru,[3] Rh,[4] Ir,[5] and Au,[7] have also been shown to catalyze these transformations, many of the systems requiring activated substrates or forcing conditions. However, to the best of our knowledge, there is no report on the Cu-catalyzed arene C–H additions to aryl acetylenes. Herein, we report a novel reagent system for arene C–H addition to aryl acetylenes, which facilitates a useful new synthesis of 1,1-diaryl ethylenes from aryl acetylenes.

The reaction of mesitylene and phenyl acetylene was initially investigated under Fujiwara's C–H activation conditions,[8] where Pd was replaced by Cu in TFA. To our delight, a 10% yield of the desired product was obtained by employing 2 mmol of mesitylene, 1 mmol of phenyl acetylene, and 0.1 mmol of $Cu(OTf)_2$ in 2 mL of TFA at room temperature for 24 h (Table 1, entry 1). The addition of either THF, nitrobenzene or DMSO had little effect on the reaction (Table 1, entries 2–4). One possible explanation for the ineffectiveness of additives could be the impediment of the ligand



Scheme 1. Cu-catalyzed reaction of mesitylene and phenyl acetylene.

Table 1
Optimization of reaction parameters[a]

Entry	Catalyst	Solvent + additive[b]	% Yield[c]
1	10% $Cu(OTf)_2$	TFA	10
2	10% $Cu(OTf)_2$	TFA + THF	11
3	10% $Cu(OTf)_2$	TFA + nitrobenzene	10
4	10% $Cu(OTf)_2$	TFA + DMSO	13
5	10% $Cu(OTf)_2$	TMSA	87 (80)
6	20% $Cu(OTf)_2$	TMSA	89 (83)
7	–	TMSA	0
8	$AlCl_3$	TMSA	0
9	$TiCl_4$	TMSA	0
10	$Cu(OAc)_2$	TMSA	0
11	CuI	TMSA	0

[a] All reactions were run by employing 2.0 mmol of mesitylene, 1.0 mmol of phenyl acetylene, and 0.10 mmol of $Cu(OTf)_2$ in 2 mL of TMSA at room temperature for 24 h, followed by hydrolysis.
[b] The equivalents of additive are based on phenyl acetylene.
[c] GC yields; yield of products obtained by column chromatography are reported in parentheses.

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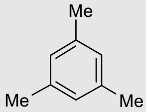
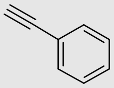
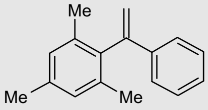
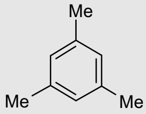
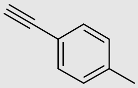
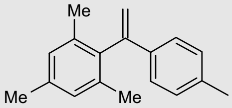
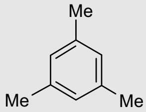
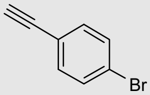
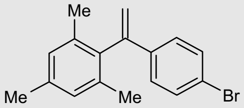
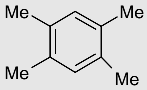
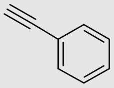
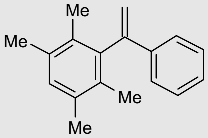
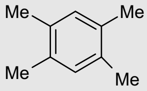
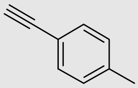
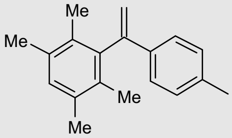
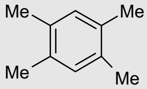
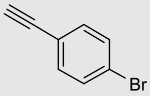
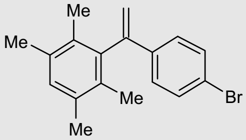
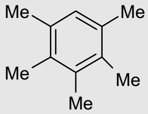
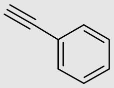
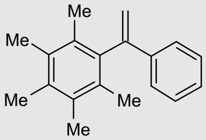
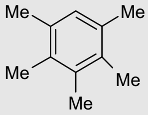
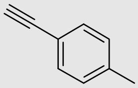
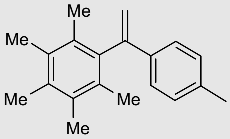
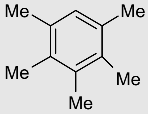
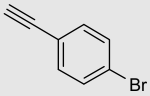
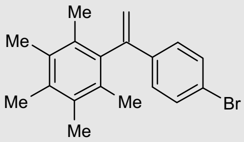
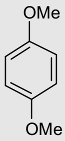
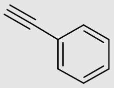
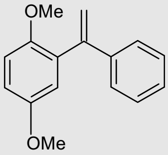
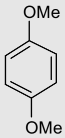
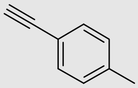
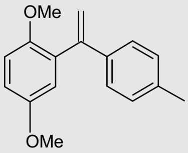
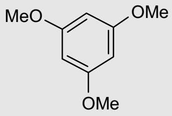
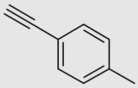
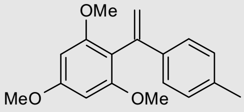
Table 2
Cu-catalyzed reaction of arenes and aryl acetylenes

Entry	Arene	Aryl acetylene	Product[a]	Yield (%)[b] (%)
1				80
2				84
3				78
4				86
5				89
6				80
7				85
8				88
9				80
10				77
11				82
12				81

[a] All reactions were run by employing 2.0 mmol of arene, 1.0 mmol of aryl acetylene, and 0.10 mmol of $Cu(OTf)_2$ in 2 mL of TMSA at room temperature for 20 h.[9]

[b] Isolated yields.

transfer mechanism. However, the use of trifluoromethane sulfonic acid (TMSA) instead of TFA assisted an increase in the yield up to 80% (Table 1, entry 5). No observable change in the yield was noticed even after increasing the amount of catalyst up to 20 mol % (compare Table 1, entries 5 and 6). A control reaction without the Cu(OTf)$_2$ catalyst failed to give the desired alkene (Table 1, entry 7). Lewis acids, such as $AlCl_3$ and $TiCl_4$ (Table 1, entries 8 and 9), as well as catalytic amounts of Cu(OAc)$_2$ and CuI were ineffective in catalyzing the reaction. (Table 1, entries 10 and 11) These results thus demonstrate the implicit role of the Cu(OTf)$_2$/TMSA combination as catalyst in the reaction. Under optimized reaction conditions (10 mol % of Cu(OTf)$_2$ and 2 mL of TMSA), a number of arenes and aryl acetylenes were successfully employed in the synthesis of alkenes (Table 2). Mesitylene was successfully employed for this reaction as the model substrate and several aryl acetylenes were tested. (Table 2, entries 1–3) Reaction proved to be highly regeoselective as 1,1-disubstituted ethylenes were obtained as the only product and no 1,2-disubstituted product was obtained (Table 3).

The coupling reaction was extended to 1,2,4,5-tetramethylbenzene and 1,2,3,4,5-pentamethylbenzene affording high yields of desired alkenes, (Table 2, entries 4–9). 1,4-Dimethoxy benzene and 1,3,5-trimethoxy benzene also participated in the reaction

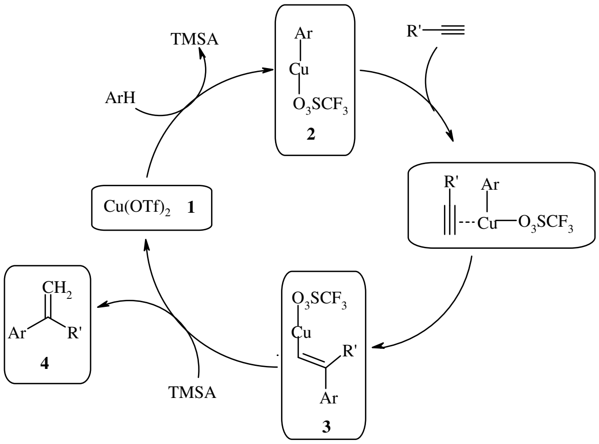
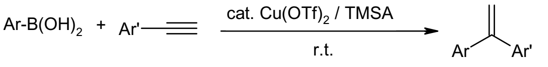
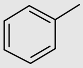
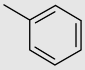
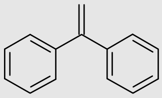
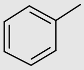
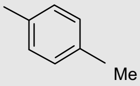
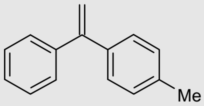
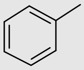
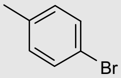
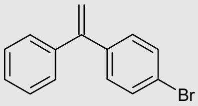
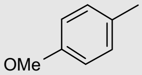
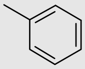
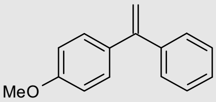
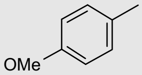
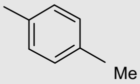
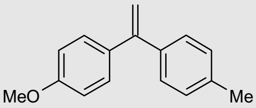
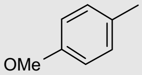
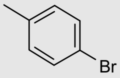
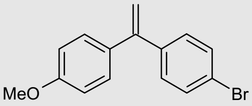
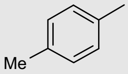
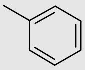
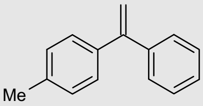
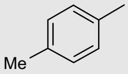
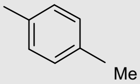
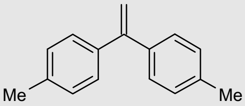
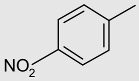
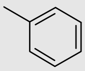
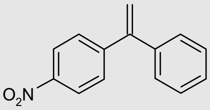


Figure 1. Plausible mechanism.



Scheme 2. Cu-catalyzed reaction of aryl acetylenes and arylboronic acids.

Table 3
Addition of arylboronic acids to aryl acetylenes

Entry	Ar	Ar′	Product[a]	Yield[b] (%)
1				72
2				75
3				73
4				70
5				85
6				80
7				88
8				82
9				45

[a] All reactions were run by employing 1.0 mmol of arylboronic acid, 5.0 mmol of aryl acetylene, and 0.10 mmol of Cu(OTf)$_2$ in 2 mL of TMSA at room temperature for 24 h.
[b] Isolated yields.

with equal ease. The desired alkenes were obtained in high yields, (Table 2, entries 10–12).

A plausible mechanism for the reaction involving the steps shown in Figure 1 could be (1) electrophilic metalation of the arene by the Cu(II) catalyst **1**, which generates arylcopper species **2**; (2) coordination of the acetylene to the Cu; (3) the intramolecular rearrangement of intermediate **2** to a transient vinyl copper species, **3;** and (4) protonation of **3** by TMSA, which affords the product alkene **4** and regenerates the Cu(II) catalyst (Scheme 1).

This mechanism suggests that the arylcopper species **2**, if generated by some other means, should also react under similar reaction conditions with aryl acetylenes.[2a] Indeed, we have found that arylboronic acids react under our optimized reaction conditions with phenyl acetylene to provide the corresponding 1,1-disubstituted alkene in high yield (Scheme 2). Most likely these reactions proceed by transmetalation between arylboronic acid and Cu(II) generating arylcopper species **2**, followed by the coordination of acetylene to **2**, which on subsequent rearrangement generates transient vinyl copper species **3** (Fig. 1). Several arylboronic acids were reacted with different aryl acetylenes to synthesize desired alkenes in high yields. In all the cases, formation of only 1,1-disubstituted ethylenes was observed.

$$\mathrm{ArB(OH)_2 + Cu(OTf)_2 \rightarrow ArCu(OTf)\ (\mathbf{2}) + (OH)_2{-}B{-}OTf}$$

Equation 1: Transmetalation.

In conclusion, we report an efficient metalation of aromatic C–H bonds at room temperature by Cu(II) species in trifluoromethane sulfonic acid (TMSA), leading to the addition of simple arenes to the C≡C bond. The addition to aryl alkynes exclusively affords the 1,1-diaryl ethylenes. The hydroarylation of alkynes has also been achieved by the reaction of arylboronic acids and aryl alkynes.

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References and notes

1. For selective reviews, see: (a) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879; (b) Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507; (c) Kakiuchi, F.; Chatani, N. *Adv. Synth. Catal.* **2003**, *345*, 1077.
2. For selective examples, see: (a) Zhou, C.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 2302; (b) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2002**, *124*, 1586; (c) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731. and references cited therein.
3. (a) Lail, M.; Arrowood, B. N.; Gunnoe, T. B. *J. Am. Chem. Soc.* **2003**, *125*, 7506; (b) Youn, S. W.; Pastine, S. J.; Sames, D. *Org. Lett.* **2004**, *6*, 581; (c) Kakiuchi, F.; Murai, S. *Acc. Chem. Res.* **2002**, *35*, 826.
4. (a) Lenges, C. P.; Brookhart, M. *J.Am. Chem. Soc.* **1999**, *121*, 6616; (b) Thalji, R. K.; Ahrendt, K. A.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2001**, *123*, 9692.
5. (a) Matsumoto, T.; Taube, D. J.; Periana, R. A.; Taube, H.; Yoshida, H. *J. Am. Chem. Soc.* **2000**, *122*, 7414; (b) Dorta, R.; Togni, A. *Chem. Commun.* **2003**, *760*.
6. (a) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1996**, *118*, 6305; (b) Tsukada, N.; Mitsuboshi, T.; Setoguchi, H.; Inoue, Y. *J. Am. Chem. Soc.* **2003**, *125*, 12102.
7. (a) Reetz, M.; Sommer, K. *Eur. J. Org. Chem.* **2003**, 3485; (b) Mamane, V.; Hannen, P.; Fürstner, A. *Chem. Eur. J.* **2004**, *10*, 4556.
8. (a) Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992; (b) Jia, C.; Lu, W.; Oyamada, J.; Kitamura, T.; Matsuda, K.; Irie, M.; Fujiwara, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7252; (c) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633. and references cited therein.
9. Typical experimental procedure

   Reaction of arenes and aryl acetylenes: The arene (2.0 mmol), the aryl acetylene (1.0 mmol), $Cu(OTf)_2$ (0.10 mmol), and TMSA (2 mL) were stirred at room temperature for 20 h. Water (20 mL) was added to the reaction mixture and was extracted with diethyl ether (3 × 15 mL). The combined organic layers were treated with saturated $NaHCO_3$ solution and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to obtain a 1,1-diaryl ethylene product. The crude product was purified by chromatography on a silica gel column.

   The reaction of arylboronic acids and aryl acetylenes: The arylboronic acid (1.0 mmol), the aryl acetylene (5.0 mmol), $Cu(OTf)_2$ (0.10 mmol), and TMSA (2 mL) were stirred at room temperature for 24 h. Water (20 mL) was added to the reaction mixture and was extracted with diethyl ether (3 × 15 mL). The combined organic layers were treated with saturated $NaHCO_3$ solution and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to obtain a 1,1-diaryl ethylene product. The crude product was purified by chromatography on a silica gel column.

   Spectral data of compounds

   1,3,5-Trimethyl-2-(1-phenyl-vinyl)-benzene (Table 1, entry 1) colorless oil; ^1H NMR (300 MHz, $CDCl_3$) δ 2.10 (s, 6H), 2.31 (s, 3H), 5.08 (s, 1H), 5.94 (s, 1H), 6.90 (s, 2H), 7.23–7.28 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.08, 21.03, 114.50, 125.81, 127.52, 128.10, 128.39, 136.11, 136.38, 138.16, 139.54, 146.86; MS (EI) m/z (rel. intensity) 222 (M^+, 44), 207 (100), 192 (81), 178 (08), 165 (11), 152 (05), 128 (11), 115 (12), 96 (11), 77 (10).

   1,2,3,4,5-Pentamethyl-6-(1-phenyl-vinyl)-benzene (Table 1, entry 7) white solid; ^1H NMR (300 MHz, $CDCl_3$) δ 2.10 (s, 6H), 2.16 (s, 3H), 2.26 (s, 6H), 5.06 (s, 1H), 5.96 (s, 1H), 7.23– 7.28 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.89, 16.56, 17.87, 20.54, 114.29, 126.00, 127.43, 128.35, 128.94, 132.28 132.33, 133.71, 139.99, 148.63; MS (EI) m/z (rel. intensity) 250 (M^+, 46), 235 (78), 220 (100), 205 (18), 189 (07), 178 (09), 165 (09),141 (06), 128 (06), 110 (09), 96 (09), 77 (08).