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Copper-Catalyzed Intermolecular Trifluoromethylarylation of Alkenes: Mutual Activation of Arylboronic Acid and CF_3^+ Reagent

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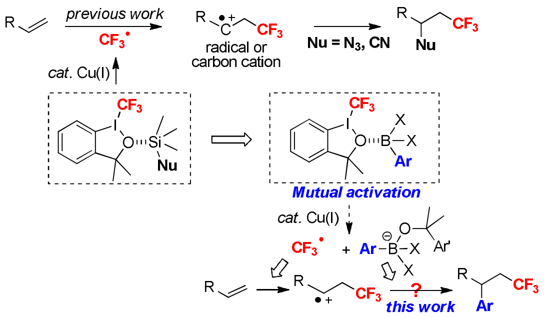
Supporting Information

ABSTRACT: A novel copper-catalyzed *intermolecular* trifluoromethylarylation of alkenes has been developed using less active ether type Togni's reagent under mild reaction condition. Various alkenes and diverse arylboronic acids are compatible with this reaction condition. Preliminary mechanistic studies revealed that a mutual activation process between arylboronic acid and CF_3^+ reagent are essential. In addition, the reaction possibly involves a rate-determining transmetallation, and the final aryl C-C bond is derived from reductive elimination of aryl(alkyl)Cu(III) intermediate.

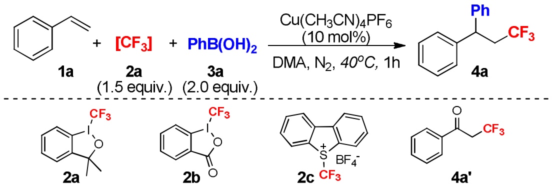
The rich variety of CF_3-containing molecules that occur as pharmaceuticals and agriculture chemicals has inspired considerable interests in the development of new methods for their synthesis.[1] Among them, direct introduction of CF_3 group into organic compounds is particularly attractive.[2] For instance, copper-catalyzed trifluoromethylation have received much attention for the synthesis of CF_3-containing aromatic and aliphatic compounds.[3,4] In 2012, our group reported the first *intramolecular* trifluoromethylarylation of activated alkenes using palladium catalyst to generate a series of CF_3-containing oxindole derivatives.[5] Later on, Sodeoka[6] demonstrated the similar transformation could be achieved using Cu(I)/Togni's reagent. Nevado[7] discovered a copper-catalyzed intramolecular trifluoromethylarylation of alkenes involving a 1,4-aryl migration and desulfonylation process. The related intramolecular 1,2-aryl migrations were also described by Wu[8a], Tu[8b] and Sodeoka.[8c] All those aryl transfer was proposed to undergo a radical process. We speculated that, if this arylation can be expanded to *intermolecular* fashion, a large number of vicinal CF_3- and aryl-containing aliphatic compounds could be easily obtained from various simple alkenes. However, related *intermolecular* reaction involving three or more components coupling is much more challenging and remains an underdeveloped process. Herein, we reported a novel copper-catalyzed *intermolecular* trifluoromethylarylation of alkenes using arylboronic acid as arylation reagent, in which *a mutual activation of arylboronic acid and CF_3^+ reagent was identified as essential step for this reaction*. More importantly, preliminary studies revealed that a rate-determining transmetallation was involved, and the final aryl C-C bond was derived from reductive elimination of aryl(alkyl)-Cu(III) intermediate, rather than previously suggested radical pathway.

Scheme 1. Intermolecualr Difunctionalization of Alkenes.



On the basis of our group's recent success in developing intermolecular difunctionalizaiton of alkenes,[9] we found that TMSNu (Nu = N_3, CN) act as Lewis acid to activate the ether type *Togni*'s reagent (**2a**), and the final C-N and C-C bond formation was derived from an alkyl radical or carbon cation intermediate (top, Scheme 1). In addition, Szabó demonstrated that B_2pin_2 could accelerate the Cu-catalyzed trifluoromethylation of alkenes using Togni's reagent as CF_3 source.[4q, 9c] We envisioned that, similar to TMSNu, arylboronic reagent could also activate the CF_3^+ reagent **2a** to release a CF_3 radical in the presence of copper catalyst. Notably, the reaction could simultaneously generate an activated arylboronic reagent, which possibly reacts with above mentioned alkyl radical or carbon cation intermediate, or reacts with Cu catalyst to reach final C_{alkyl}-C_{aryl} bond forming (bottom, Scheme 1). If so, the three components intermolecular reaction might be expected. In order to test this hypothesis, initial studies were focused on the reaction of styrene **1a** with Togni's reagent **2a** and $PhB(OH)_2$ **3a** in the presence of copper catalyst. We are delighted to find that the desired trifluoromethylarylation product **4a** was indeed observed. After extensive screening of different reaction parameters, the optimized reaction condition was obtained to provide the desired product **4a** in 76% yield (entry 1, table 1). Some essential observations were listed as: (1) when

Table 1. Optimization of the Reaction Condition.[a,b]



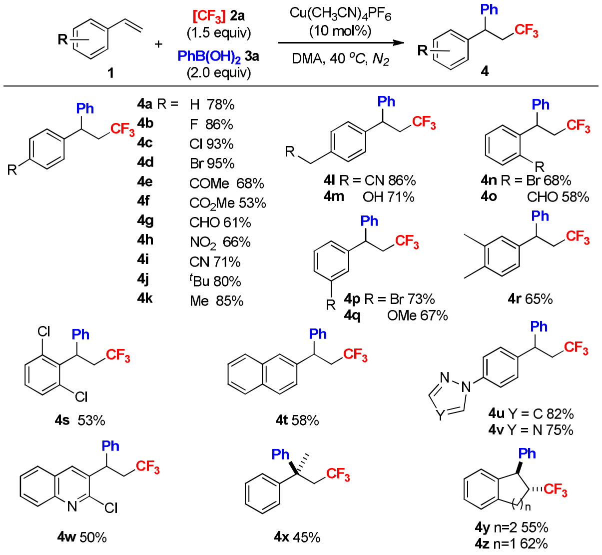
Entry	Reaction condition	Yield (**4a**)[b]
1	**Standard condition**	**76%**
2	**2a** was replaced by **2b** or **2c**	0
3	$PhB(OH)_2$ was replaced by $PhBF_3K$, PhBPin	0
4	$PhB(OH)_2$ was replaced by $PhSiMe_3$, $PhSnBu_3$	0
5	Reaction under Air	42% (21%)[c]
6	Reaction under O_2	13% (40%)[c]

[a] All the reactions were run at 0.1 mmol scale, . [b] Yield obtained by ^{19}F NMR with CF_3-DMA as internal standard. [c] Yield of side product **4a'**.

other CF_3^+ reagents **2b** and **2c** were employed, no reaction occurred (entry 2); (2) PhBPin and $PhBF_3K$ were inactive (etnry 3); (3) other type of arylmetallic reagents, such as $PhSnBu_3$ and $PhSiMe_3$, were failed to yield product **4a**, and the starting material was recovered quantitatively (entry 4); (4) both $[Cu(CH_3CN)_4]PF_6$ and $[Cu(CH_3CN)_4]BF_4$ were effective, but CuI and $Cu(OTf)_2$ exhibited lower reactivity, and no reaction occurred in the absence of copper catalyst (See SI); (5) slightly lower yield of **4a** was obtained under air, and a significant amount of side product **4a'** was observed; less **4a** and more **4a'** were given under dioxygen atmosphere (entries 5-6).

With the optimized reaction conditions in hand, the substrate scope of the styrenes was firstly examined and the results were summarized in Table 2. A variety of styrenes bearing mono-substitutents on aryl ring were initially surveyed. Both electron-donating and electron-withdrawing groups were compatible for this transformation, and various functional groups, such as halogen, ester, nitro, nitrile, aldehyde, ketone and hydroxyl group, were tolerated to give desired products **4a-4q** in moderate to excellent yields. For the styrenes with disubstitutents on the aryl ring, including 2,6-dichlorostyrene, the reactions were proceeded smoothly to generate **4r-4s** in moderate yields. The reaction of 2-vinylnaphthalene delivered **4t** in 58% yield**.** The styrenes containing heterocycles were also suitable to produce products **4u-4w** in satisfactory yields. Compared with monosubstituted styrenes, 1,1-disubstituted styrenes exhibited slightly lower reactivity to give product **4x** in 45% yield. However, the cyclic styrenes exhibited good reactivities to give products **4y** and **4z** as a single isomer in moderate yields.

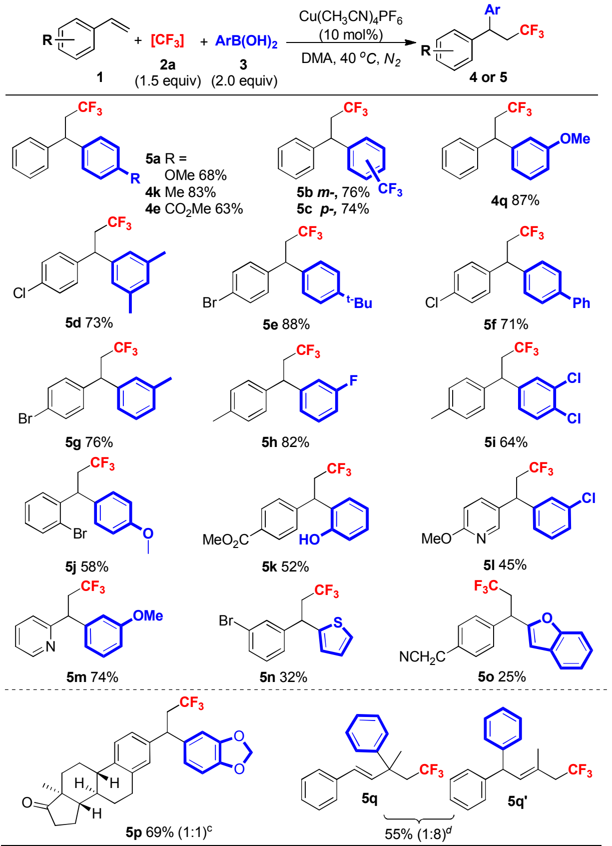
Table 2. Substrate Scope of Styrene.[a,b]



[a] All the reactions were conducted in 0.2 mmol scale. [b] Isolated yield.

Inspired by above results, we turned our attention to investigate the reactivity of diverse arylboronic acids (Table 3). To our delight, a range of arylboronic acids were suitable to react with various styrenes, and a series of function group, such as ether, ester, halides and CF_3, could survive to give the desired products **5a-5m, 4k,4e** and **4q** in good to excellent yields. Notably, the reaction of $2\text{-}OHC_6H_4B(OH)_2$ proceeded smoothly to produce **5k** in moderate yield. In addition, the reaction of (hetero)-$ArB(OH)_2$ also provided products **5n-5o** in *albeit* low yields. Finally, estrone derivative was also employed to the reaction condition to deliver product **5p** in 69% yield. And a conjugated diene substrate was also compatible with this transformation to give regioisomers **5q** and **5q'** in 55% yield with good regioselectivity (1:8 ratio).

Table 3. Substrate Scope of other Arylboronic Acids.[a,b]



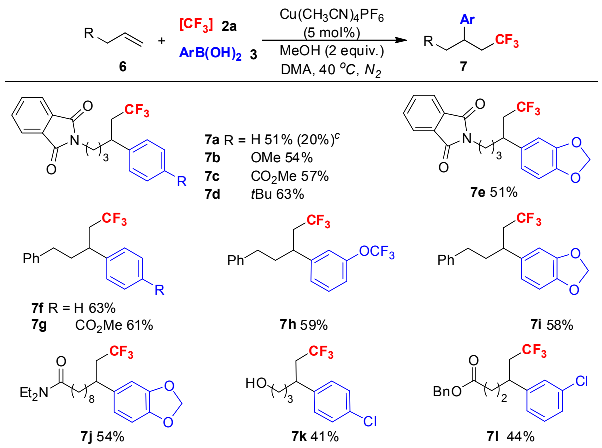
[a] All the reactions were conducted in 0.2 mmol scale. [b] Isolated yield. [c] Diastereoselectivity. [d] Regioselectivity.

Next investigation was focused on the reaction of unactivated alkenes. When aliphatic alkene **6a** and **2a** were treated under above optimized reaction condition, however, the desired product **7a** was obtained in low yield (around 20% yield) and poor reproducibility. With further screening of reaction condition, we are delight to find that addition of water or alcohol could significantly promote trifluoromethylarylation reaction and give a reproducible yield. In addition, copper catalyst could be lowered down to 5 mol %. MeOH was proven to be the best additive to provide product **7a** in moderate yield (51%). With the modified reaction condition, a series of unactivated alkenes **6** with various $ArB(OH)_2$ **3** could be transformed to the desired products **7a-7l** in satisfactory yields (Table 4). It should be noted that the side reaction of allylic C-H trifluoromethylation was hard to inhibit, and the related products were observed in 10-20% yields.[10]

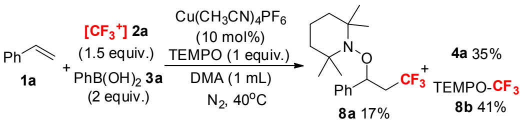
In order to rationalize reaction pathway, preliminary mechanistic studies were surveyed. Firstly, addition of TEMPO could significantly inhibit the trifluoromethylarylation reaction, and oxytrifluoromethylated product **8a** and TEMPO-CF_3 adduct **8b** were observed (eq 1). In addition, both reactions of *Z*-**9** and *E*-**9** afforded product **10** with the same diastereoselectivity (5:1) in *albeit* low yields (eq 2). These results indicated that a CF_3 radical was involved in the reaction, and a benzyl radical species was generated through the addition of CF_3 radical to alkenes.[11]

Secondly, compared to the standard reaction condition, *Togni*'s reagent **2a** was inert in the absence $ArB(OH)_2$.[12] Thus, it

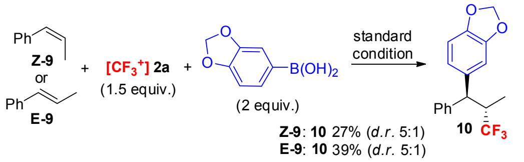
Table 4. Substrate Scope of Unactivated Alkenes.[a,b]



[a]All the reactions were conducted in 0.2 mmol scale. [b]Isolated yield. [c]without MeOH.



(1)



(2)

is possible that **2a** was activated by ArB(OH)$_2$ **3**,[13] then reacted with Cu(I) to generate CF$_3$ radical species. Observation of only one CF$_3$ signal in the mixture of **2a** and **3a** (at -10°C) suggested a fast equilibrium was existed between **2a** with **3a** and **int.I** (**2a• 3a**). In addition, the CF$_3$ signal gradually shifted to down field and broadened with increase the amount of PhB(OH)$_2$ (Fig 1, middle). Furthermore, the interaction of *electron-poor* arylboronic acid (*EP*-AA **3r**, Fig 1, left) with **2a** was stronger than that of *electron-rich* arylboronic acid (*ER*-AA **3c**, Fig 1, right), which means Togni's reagent **2a** with *EP*-AA should be more reactive with Cu(I) than *ER*-AA.

Thirdly, we moved our attention to the mechanism of final C-C bond formation. The electronic effect of arylboronic acids and styrenes were evaluated under the standard condition at 25 ℃. As shown in Fig 2A, *ER*-AA (R = OMe, Me) presented faster reaction rate than that of *EP*-AA (R = Cl, CO$_2$Me). However, no significant electronic effect of styrenes was observed with much small Hammett ρ-value (-0.087, Fig 2B). In addition, *the reaction rate exhibited the saturation dependence on the concentration of PhB(OH)$_2$ and the zero-order dependence on styrene.*[10] Those observations implied that addition of CF$_3$ radical to styrenes should be a fast step to generate a alkyl radical **int.III**, and this species should be involved after the rate-determining step. While ArB(OH)$_2$ should be involved in the rate-determining step or before.

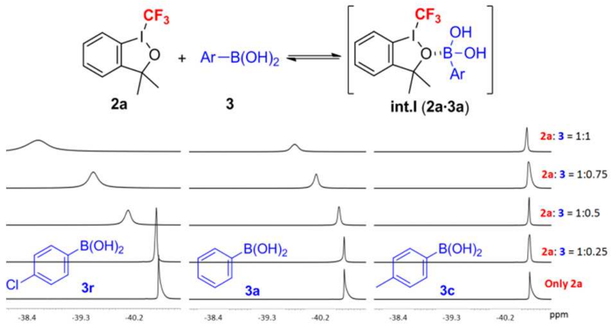


Fig 1. The reactions of **3** and **2a** monitored by ^{19}F-NMR.

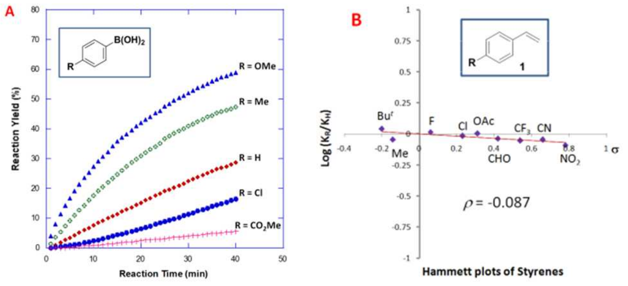
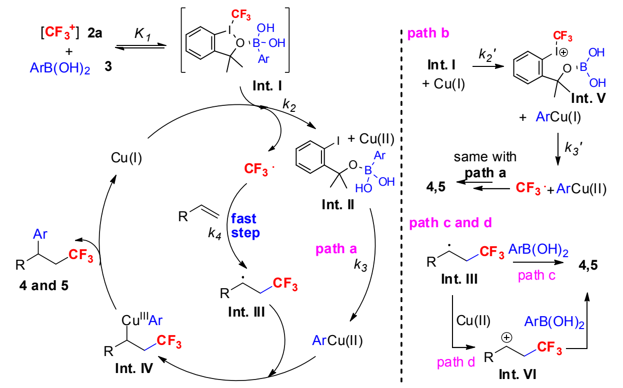


Fig 2. Electron effect of arylboronic acids and styrenes: (A) time course of diverse ArB(OH)$_2$; (B) Hammett plots of styrenes.

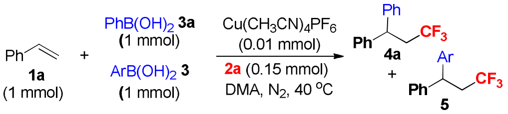
As our originally proposed, if the final C-C bond formation was derived from the intermediate of benzyl radical (**int.III**) or benzyl carbon cation (**int.VI**) with ArB(OH)$_2$ (see path c and d in Scheme 2), the reaction should involve a rate-determining CF$_3$ radical forming step. If so, the reaction of *EP*-AA should be faster since its adduct **int.I** is more reactive (see Fig 1), which is opposite with the result in Fig 2A. Thus, these observations concluded that path c and d (Scheme 2) is less likely.

Scheme 2. Proposed Mechanism.



Based on above analysis, an alternative pathway involving ArCu(II) species was proposed to address the final C-C bond formation (path a and b in Scheme 2): Treatment of activated CF$_3^+$ speceis **int.I** by Cu(I) catalyst to release CF$_3$ radical, the reaction simultaneously generated a new activated arylbronoic acid **int.II** and a Cu(II) species, which could undergo transmetallation to give a ArCu(II) species (path a). Then, the ArCu(II) could be oxidized by alkyl radical **int.III** to yield a Cu(III) species **int.IV**,[14] which delivers the final product through reductive elimination.[15] Due to the saturation dependence on the concentration of PhB(OH)$_2$ and the independence on styrene, transmetallation (path a) should be involved as a rate-determining step.[16,17] In addition, another possible pathway involves an initial transmetallation to give ArCu(I) and **int.V**, then ArCu(I) was oxidized by **int.V** to yield ArCu(II) and release CF$_3$ radical (path b), which can be also used to well address above observations.

For the case of path a, the reaction of **int.I** of *EP*-AA with Cu(I) (k_2) is faster, but following transmetallation step (k_3) is favored for the *ER*-AA;[16b] In contrast, both two steps (k_2' and k_3') are favored for the *ER*-AA in path b. In order to differentiate these two possibility, the competing experiments were conducted, and no significantly different reaction rate of *EP*-AA and *ER*-AA was observed (eq 3), which is obviously different from individual reactions (Figure 2A). The possible reason is that the concentration of **int.II** of *EP*-AA is higher than that of *ER*-AA, but the transmetallation of *ER*-AA (k_3) is faster than *EP*-AA. Thus, the k_3[**int.II**] value of *EP*-AA is reasonably close with the *ER*-AA, resulting the similar yields of **4a** and **5** in one pot reaction. *This observation is more consistent with the path a, and against the path b.*[18]



(3)

Ar = *p*-RC$_6$H$_4$	R = OMe	Me	Cl	CF$_3$	CO$_2$Me
ratio (**5**:**4a**)	1:1.3	1:0.92	1:1.2	1:0.91	1:1.3

In summary, we have developed a novel copper-catalyzed intermolecular trifluoromethylarylation of alkenes under mild reaction condition. Diverse alkenes and arylboronic acids were compatible to the reaction condition for the efficient synthesis of CF_3-containing diarylmethane derivatives efficiently. Preliminary mechanistic studies revealed the mutual activation process between arylboronic acid and the CF_3^+ reagent is vital to generate initial CF_3 radical. And transmetallation of $ArB(OH)_2$ to Cu(II) was involved as a key step, and the final C-C bond formation is derived from a Cu(III) species. Further application and more mechanistic investigation of this process are in progress.

Supporting Information

Synthetic procedures, characterization, mechanistic study data and additional data. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

(1) (a) Smart, B. E. *Chem. Rev.* **1996**, *96*, 1555. (b) Filler, R.; Kobayashi, Y. *Biomedicinal Aspects of Fluorine Chemistry*; Elsevier: Amsterdam, 1982. (c) Welch, J. T.; Eswarakrishman, S. Eds. *Fluorine in Bioorganic Chemistry*; Wiley: New York, 1991. (d) Banks, R. E.; Smart,B. E.; Tatlow, J. C. Eds. *Organofluorine Chemistry*: Principles and Commercial Applications; Plenum Press: New York, 1994. (e) Purser, S.; Moore, P. R.; Swallow, S., Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320.

(2) For reviews for trifluoromethylation, see: (a) Schlosser, M. Angew. *Chem. Int. Ed.* **2006**, *45*, 5432. (b) Ma, J.-A.; Cahard, D. *J. Fluorine Chem.* **2007**, *128*, 975. (c) Ma, J.-A.; Cahard, D. *Chem. Rev.* **2008**, *108*, PR1. (d) Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475. (e) Studer, A. *Angew. Chem. Int. Ed.* **2012**, *51*, 8950.

(3) (a) Chen, P.; Liu G. *Synthesis* **2013**, *45*, 2919. (b) Ye, Y.; Sanford, M. S. *Synlett* **2012**, *23*, 2005. (c) Liu, T.; Shen, Q. *Eur. J. Org. Chem.* **2012**, *34*, 6679. (d) Wu, X.-F.; Neumann, H.; Beller, M. *Chem.–Asian. J.* **2012**, *7*, 1744.

(4) For recent copper catalyzed trifluoromethylation of alkenes, see: (a) Parsons, A. T.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2011**, *50*, 9120. (b) Xu, J.; Fu, Y.; Luo, D.; Jiang, Y.; Xiao, B.; Liu, Z.; Gong, T.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 15300. (c) Wang, X.; Ye, Y.; Zhang, S.; Feng, J.; Xu, Y.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2011**, *133*, 16410. (d) Shimizu, R.; Egami, H.; Hamashima, Y.; Sodeoka, M. *Angew. Chem. Int. Ed.* **2012**, *51*, 4577. (e) Mizuta, S.; Galicia-López, O.; Engle, K. M.; Verhoog, S.; Wheelhouse, K.; Rassias, G.; Gouverneur, V. *Chem. Eur. J.* **2012**, *18*, 8583. (f) Janson, P. G.; Ghoneim, I.; Ilchenko, N. O.; Szabó, K. J. *Org. Lett.* **2012**, *14*, 2882. (g) Shimizu, R.; Egami,H.; Hamashima, Y.; Sodeoka, M. *Angew. Chem. Int. Ed.* **2012**, *51*, 4577. (h) Li, Y.; Studer. A. *Angew. Chem. Int. Ed.* **2012**, *51*, 8221. (i) Yasu, Y.; Koike, T.; Akita, M. *Angew. Chem. Int. Ed.* **2012**, *51*, 9567. (j) Zhu, R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2012**, *134*, 12462. (k) Zhu, R.; Buckwald, S. L. *Angew. Chem. Int. Ed.* **2013**, *52*, 12655. (l) Feng, C.; Loh, T.-P. *Chem. Sci.* **2012**, *3*, 3458. (m) Mizuta, S.; Verhoog, S.; Engle, K. M.; Khotavivattana, K. M.; O'Duill, M.; Wheelhouse, K.; Rassias, G.; Médebielle, M.; Gouverneur, V. *J. Am. Chem. Soc.* **2013**, *135*, 2505. (n) Wu, X.; Chu, L.; Qing, F. *Angew. Chem. Int. Ed.* **2013**, *52*, 2198. (o) Egami, H.; Kawamura, S.; Miyazaki, A.; Sodeoka, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 7841. (p) Feng, C.; Loh, T.-P. *Angew. Chem. Int. Ed.* **2013**, *52*, 12414. (q) Ilchenko, N. O.; Janson, P. G.; Szabó, K. J.*Chem. Comm.* **2013**, *49*, 6614.

(5) Mu, X.; Wu, T.; Wang, H.-Y.; Guo, Y.-L.; Liu, G. *J. Am. Chem. Soc.* **2012**, *134,* 878.

(6) (a) Egami, H.; Shimizu, R.; Sodeoka, M. *J. Fluorine Chem.* **2013**, *152*, 51. (b) Egami, H.; Shimizu, R.; Kawamura, S.;Sodeoka, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 4000.

(7) (a) Kong, W.; Casimiro, M.; Fuentes, N.; Merino, E.; Nevado, C. *Angew. Chem. Int. Ed.* **2013**, *52*, 13086. (b) Kong, W.; Casimiro, M.; Merino, E.; Nevado, C. *J. Am. Chem. Soc.* **2013**, *135,* 14480.

(8) (a) Liu, X.; Xiong, F.; Huang, X.; Xu, L.; Li, P.; Wu, X. *Angew. Chem.* **2013**, *125*, 7100; *Angew. Chem. Int. Ed.* **2013**, *52*, 6962. (b) Chen, Z.-M.; Bai, W.; Wang, S.-H.; Yang, B.-M. Tu, Y.-Q.; Zhang, F.-M. *Angew. Chem.* **2013**, *125*, 9963; *Angew. Chem. Int. Ed.* **2013**, *52*, 9781. (c) Egami, H.; Shimizu,R.; Usui, Y.; Sodeoka, M. *Chem. Commun.* **2013**, *49*, 73465.

(9) (a)Wang, F.; Qi, X.; Liang, Z.; Chen, P.; Liu, G. *Angew.Chem., Int. Ed.* **2014**, *53,* 1881. (b) Liang, Z.; Wang, F.; Chen, P.; Liu, G. *J. Fluorine. Chem.* **2014**, doi: 10.1016/j.jfluchem.2014.04.004. (c) Ilchenko, N. O.; Janson, P. G.; Szabó, K. J. *J. Org. Chem.* **2013**, *78*, 11087. b) He, Y.-T.; Li, L.-H.; Yang, Y.-F.; Zhou, Z.-Z.; Hua, H.-L.; Liu, X.-Y.; Liang, Y.-M. *Org. Lett.* **2014**, *16*, 270.

(10) For details, see the Supporting Information (SI).

(11) For the side product **4a'** generation (entries 5-6, table 1) from benzyl radical species and dioxygen, see: Deb, A.; Manna, S.; Modak, A.; Patra, T.; Maity, S.; Maiti, D. *Angew. Chem. Int. Ed.* **2013**, *52*, 9747.

(12) In the absence of arylboronic acid, no trifluoromethylation of alkenes was occurred, and CF_3^+ reagent **2a** was quantitatively recovered.

(13) No significant interaction between ester type Togni's reagent **2b** with **3a** was observed. For details, see SI.

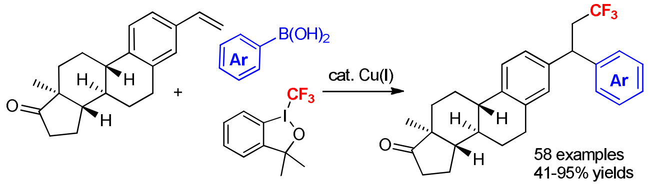
(14) The oxidation of Cu(II) by alkyl radical to give Cu(III) was also proposed, see: (a) Ye, Y.; Sanford, M. S. *J. Am. Chem. Soc.* **2012**, *134*, 9034. (b) Tran, B. L.; Li, B.; Driess, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 2555.

(15) The reductive elimination of Cu(III) to form C-C bond, see: (a) Wang, Z.-L.; Zhao, L.; Wang, M.-X. *Chem. Commun.* **2012**, *48*, 9418. (b) Wang, Z.-L.; Zhao, L.; Wang, M.-X. *Org. Lett.* **2012**, *48*, 9418.

(16) The slow transmetallation of $ArB(OH)_2$ to Cu(II) was also reported by Stahl, see: (a) King, A. E.; Brunold, T. C.; Stahl, S. S. *J. Am. Chem. Soc.* **2009**, *131*, 5044. And the transmetallation of *ER*-AA with Cu(II) exhibits faster rate than that of *EP*-AA, see: (b) King, A. E.; Ryland, B. L.; Brunold, T. C.; Stahl, S. S. *Organometallics* **2012**, *31*, 7948.

(17) The reaction rate was increased by addition of MeOH. It is possible that addition of MeOH could accelerate transmetallation step, see SI.

(18) Reviewer raised an possible alternative pathway, which involves a initial oxidation of Cu(I) by **int.I** to give a $Cu^{III}CF_3$, and subsequently undergoes a rate-determining transmetallation with $ArB(OH)_2$. The formed $ArCu^{III}CF_3$ complex could further release $ArCu^{II}$ and CF_3 radical, which latter could react with alkenes to generate alkyl radical, and recombine with ArCu(II) to generate **int.IV.** For more details of this mechanism, see ref. 9c and the SI.



Advantage:
- *three components coupling*
- *mutual activation of CF_3^+ and $ArB(OH)_2$*
- *broad substrated scope of alkenes and $ArB(OH)_2$*
- *a novel mechanistic pathway for C_{aryl}-C_{alkyl} forming*