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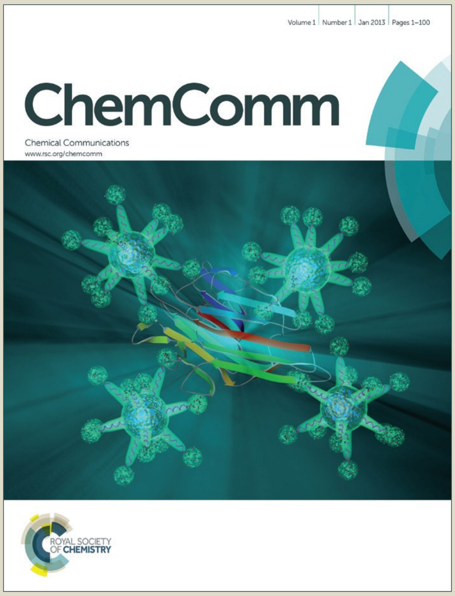

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Metal-Free Oxidative Cross-Coupling of Diazirines with Arylboronic Acids†

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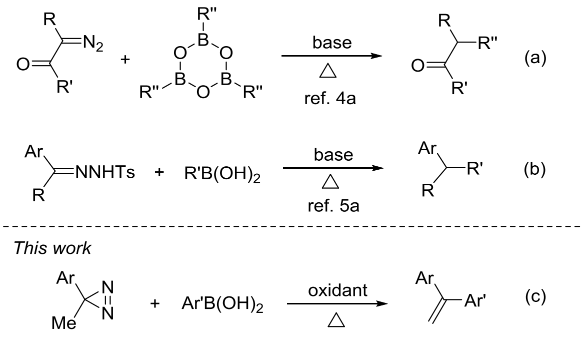
We report herein a metal-free cross-coupling of diazirines with arylboronic acids under oxidative conditions. The reaction affords a series of substituted olefins. It is proposed that the interaction between the nitrogen on diazirine with arylboronic acid plays a key role in this transformation.

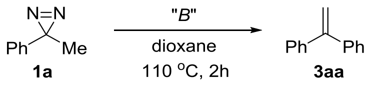
Among the various cross-coupling reactions, the reaction with arylboronic acids, namely Suzuki-Miyaura coupling, has found widespread applications both in academic researches and large-scale industrial applications.[1] On the other hand, the metal-free cross-coupling reactions have also become important because of the obvious advantages of avoiding the use of expensive transition metals.[2] In this context, a number of metal-free cross-couplings involving the reaction of organoboronic acids with diazo compounds have been developed.[3-6] In 2009, we reported the reaction of boroxines with α-dizaocarboyl compounds, which leads to the formation of α-arylated and α-vinylated carbonyl compounds (Scheme 1a).[4a] Subsequently, Barluenga and co-workers reported the metal-free reductive coupling of *N*-tosylhydrazone with arylboronic acids, affording a series of alkane products (Scheme 1b).[5a]

Diazirines are important precursors for generating carbene species,[7] which have been widely utilized as photoaffinity probes in biochemical research.[8,9] While the physical organic chemistry aspects of diazirines have been extensively studied over the decades, their applications in organic synthesis have not been significantly explored. We have recently reported the Pd(0)-catalyzed cross-coupling of diazirines with aryl halides,[10] in which diazirines are converted into the diazo compounds upon thermolysis. As the continuation of our interest in developing novel C-C bond forming methodologies based on diazo compounds and related compounds,[11] we report herein the first metal-free cross-coupling of diazirines with arylboronic acids under oxidative conditions (Scheme 1c). The reaction provides a straightforward access toward 1,1-diaryl-substituted olefins.



Scheme 1 Transition-metal-free cross-couplings of organoboron reagents

At the outset of the investigation, we explored the metal-free cross-coupling reaction of 3-methyl-3-phenyldiazirine **1a** and phenylboronic acid [$PhB(OH)_2$] (eq 1). The corresponding olefin **3aa** was obtained in 15% yield by heating the solution at 110 °C for 2 h. We also examined phenylboronate (PhBpin) and phenyl boroxine [$(PhBO)_3$]. The reaction with PhBpin gave no **3aa** while the reaction with $(PhBO)_3$ afforded **3aa** in 16%.



(1)

"*B*" = $Ph(OH)_2$, 15%; "*B*" = PhBpin, 0%; "*B*" = $(PhBO)_3$, 16%

With the initial results, we proceed to optimize the reaction conditions with phenylboronic acid **2a** (Table 1). First we screened the reaction temperature and solvents. We found that the yields could not be significantly improved (Table 1, entries 1-7). It was observed that only trace product could be obtained when the reaction was carried out under nitrogen atmosphere. We thus

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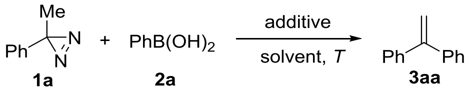
speculated that oxidants might play a role in the reaction. We then explored several oxidants, including 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), phenyliodine(III) diacetate (PIA), molecular oxygen and *p*-benzoquinone (BQ) (Table 1, entries 8-10). Among them, 1.2 equivalents of *p*-benzoquinone (BQ) afforded the product with best yield (Table 1, entry 11). With *p*-benzoquinone (BQ) as the oxidant, the optimal result was achieved by adjusting the ratio of **1a** to **2a** from 1:1.5 to 2:1 (Table 1, entries 12 and 13).

Table 1. Optimization of the reaction conditions[a]



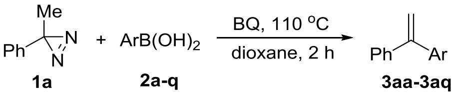
Entry	**1a**:**2a**	solvent	*T* (°C)	additive(equiv)	Yield[b](%)
1	1:1.5	dioxane	110	none	18
2	1:1.5	toluene	110	none	12
3	1:1.5	DCE	70	none	6
4	1:1.5	THF	80	none	--[c]
5	1:1.5	MeCN	80	none	--[c]
6	1:1.5	dioxane	90	none	10
7[d]	1:1.5	dioxane	90	none	--[c]
8	1:1.5	dioxane	110	DDQ (1.2)	18
9	1:1.5	dioxane	110	PIA (1.2)	23
10	1:1.5	dioxane	110	O_2 (1 atm)	26
11	1:1.5	dioxane	110	BQ (1.2)	54
12	1.5:1	dioxane	110	BQ (1.5)	66
13[e]	2:1	dioxane	110	BQ (2.0)	80

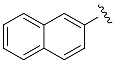
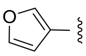
[a]Reaction conditions: **1a** (0.15 mmol), solvent (0.5 mL for entries 1-5; 0.2 mL for entries 6-13). [b]GC-MS yield with dodecane (0.15 mmol) as the internal standard. [c]Trace product was detected. [d]The reaction was carried out under N_2 atmosphere. [e]Reaction conditions: **1a** (0.15 mmol), dioxane (0.2 mL).

Under the optimized reaction conditions, the scope of substrates was then examined with diazirines **1a** and arylboronic acids **2a-q** (Table 2). All the reactions were completed within 2 hours, affording the corresponding olefins in moderate to excellent yields. For the arylboronic acids **2a-q**, the reactions showed good substrate scope as well as high functional group tolerance. The transformation could proceed smoothly with the arylboronic acids bearing both electron-withdrawing (entries 5-7, 11-13) and electron-donating substituents (entries 2-4). The reaction afforded good yields with *meta*- and *para*-substituted phenylboronic acids, but the yields diminished with *ortho*-substituted arylboronic acid (entry 8), presumably due to steric hindrance. The reaction also worked well with naphthalen-2-ylboronic acid (entry 16) and furan-3-ylboronic acid (entry 17). It is noteworthy that the halogen substituents tolerate the reaction (entries 5, 6, 12, 13 and 15), which is beneficial in the case when the subsequent transition-metal-catalyzed transformations is carried out.

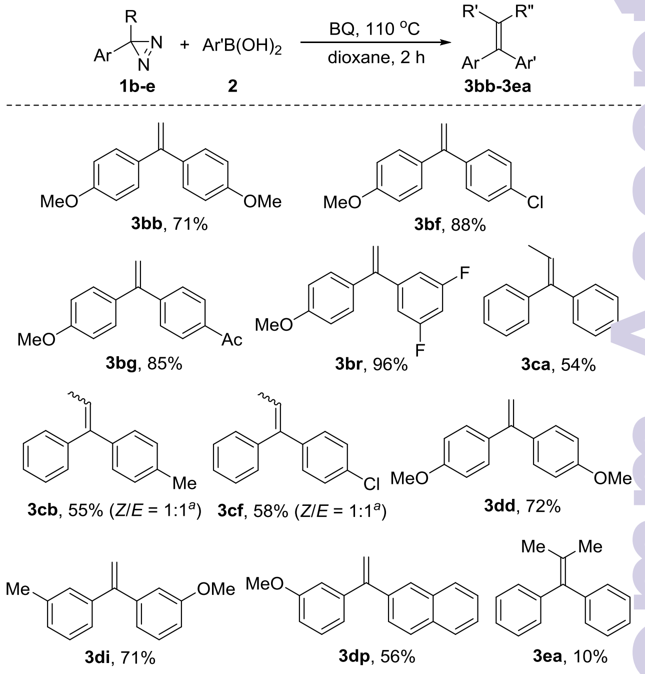
Next, the scope of diazirine substrates was investigated (Scheme 2). In these cases significant electronic effects were observed. The diazirine **1b** that bears electron-donating substituent showed higher reactivity and afforded the corresponding products in excellent yields (**3bb**-**3br**). Trisubstituted olefins were obtained in moderate yields by using the diazirine **1c** that bears an ethyl substituent (**3bb-3cf**). Finally, tetrasubstituted olefin could also be obtained by using diazirine **1e**, albeit in low yield (**3ea**).

Table 2. The substrate scope of arylboronic acids[a]



Entry	**2**, Ar =	Yield(%)[b]	Entry	**2**, Ar =	Yield(%)
1	**2a**, C_6H_5	**3aa**, 72%	11	**2k**, *p*-$F_3COC_6H_4$	**3ak**, 42%
2	**2b**, *p*-MeC_6H_4	**3ab**, 70%	12	**2l**, *m*-ClC_6H_4	**3al**, 50%
3	**2c**, *p*-$^t BuC_6H_4$	**3ac**, 64%	13	**2m**, *m*-BrC_6H_4	**3am**,17
4	**2d**, *p*-$MeOC_6H_4$	**3ad**, 57%	14	**2n**, *m,p*-$Me_2C_6H_3$	**3an**,62%
5	**2e**, *p*-BrC_6H_4	**3ae**, 73%	15	**2o**, *m,p*-$Br_2C_6H_3$	**3ao**,31
6	**2f**, *p*-ClC_6H_4	**3af**, 82%			
7	**2g**, *p*-AcC_6H_4	**3ag**, 27%	16	**2p**, 	**3ap**,
8	**2h**, *o*-MeC_6H_4	**3ah**, 34%			
9	**2i**, *m*-MeC_6H_4	**3ai**, 78%			
10	**2j**, *m*-$MeOC_6H_4$	**3ab**, 71%	17	**2q**, 	**3aq**, 58%

[a]Reaction conditions: **1a** (1.2 mmol), **2a-q** (0.6 mmol), BQ (1.2 equiv), dioxane (0.8 mL), oil bath 110 °C for 2 hours. [b]The yields refer to the isolated products.



Scheme 2 The Substrate Scope of Diazirine. Reaction conditions: **1b-e** (1.2 mmol), **2** (0.6 mmol), BQ (1.2 equiv), dioxane (0.8 mL), oil bath 110 °C for 2 hours. The yields refer to the isolated products. [a]Ratio was determined by ^1H NMR spectra.

A reaction mechanism for this metal-free coupling is speculated as shown in Scheme 3. As in the case of transition-metal-free coupling of *N*-tosylhydrazones with arylboronic acids reported by Barluenga and co-workers,[5a,6] the diazo intermediate may also be generated from the diazirine through thermal rearrangement.[7]

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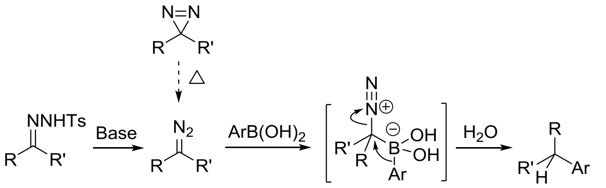
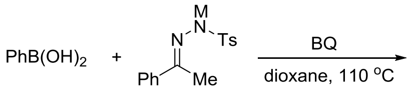
However, the reaction of diazo compound with arylboronic acid affords the product with C-C single bond formation, and no olefin product **3aa** could be observed for the reaction of phenylboronic acid **2a** with *N*-tosylhydrazone **4** (or its sodium salt **5**) in the presence of BQ (eq 2). Control experiments also indicated that **3aa** was not observed when 1,1-diphenylethane **6** was treated with BQ in dioxane at 100 °C (eq 3). These experiments support the conclusion that the coupling of diazirine with arylboronic acid follows a pathway that does not involve diazo intermediate.

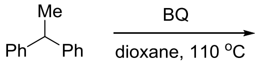


Scheme 3 A proposed reaction mechanism involving diazo intermediate



4, M = H, K$_2$CO$_3$; **5**, M = Na

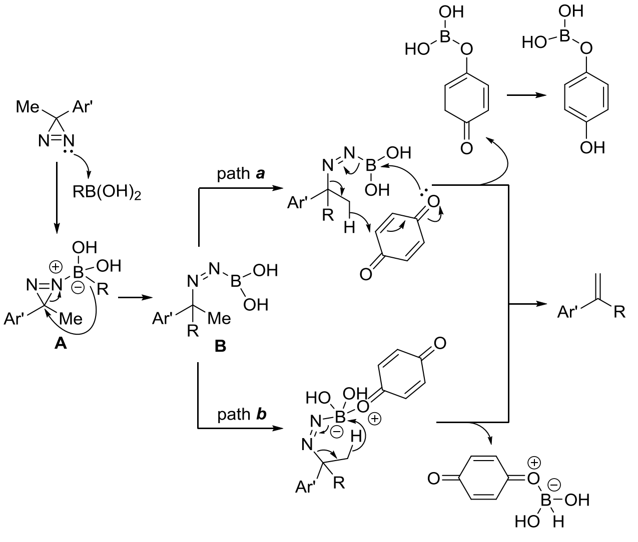
3aa, 0%



6

3aa, 0%

Thus, an alternative reaction mechanism is proposed as shown in Scheme 4. The reaction is initiated by nucleophilic attack of the nitrogen of the diazirine to the boron of arylboronic acid, generating intermediate **A**. Subsequently, migration of the aryl group from boron to the carbon of the three-membered ring generates intermediate **B**, with simultaneous ring opening. The intermediate **B** is then oxidized with hydrogen shift assisted by BQ through path ***a*** or path ***b*** to afford the final product and hydroquinone, which was detected by GC-MS. Further investigations are necessary to verify this mechanistic proposal.



Scheme 4 The proposed reaction mechanism

In summary, we have reported herein a novel C-C bond form reaction of diazirines and arylboronic acids under metal-fre conditions. The substrate scope and functional group tolerance this reaction are good and the operation procedure is simple. T reaction thus constitutes a straightforward access toward 1, diaryl-substituted olefins.[12]

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Notes and references

1 For reviews, see: (a) A. Suzuki, *Acc. Chem. Res.,* 1982, **15**, 178; (b) Miyaura and A. Suzuki, *Chem. Rev.,* 1995, **95**, 2457; (c) A. Suzuki, *Metal-Catalyzed Cross-Coupling Reactions*; F. Diederich and P. J. Star Eds.; Wiley-VCH: Weinheim, 1998; pp 49-97; (d) N. Miyaura, *Top. Curr. Chem.,* 2002, **219**, 11; (e) N. Miyaura, *J. Organomet. Chem.,* 2002, 54; (f) T. Ishiyama and N. Miyaura, *Chem. Rec.,* 2004, **3**, 271; (g) Miyaura, *Bull. Chem. Soc. Jpn.,* 2008, **81**, 1535; (h) A. Suzuki, *An Chem. Int. Ed.,* 2011, **50**, 6722.
2 For a recent review, see: C.-L. Sun and Z.-J. Shi, *Chem. Rev.,* 2014, **114**, 9219.
3 For reviews, see: (a) H. Li, Y. Zhang and J. Wang, *Synthesis,* 2013, **4** 3090; (b) S. Roscales and A. G. Csákÿ *Chem. Soc. Rev.,* 2014, **43**, 8215.
4 (a) C. Peng, W. Zhang, G. Yan and J. Wang, *Org. Lett.*, 2009, **11**, 166; (b) P. K. Elkin, V. V. Levin, A. D. Dilman, M. I. Struchkova, P. A. Belyakov, D. E. Arkhipov, A. A. Korlyukov and V. A. Tartakovsky, *Tetrahedron* 2011, **52**, 5259; (c) G. Wu, Y. Deng, C. Wu, Y. Zhang and J. Wan *Angew. Chem. Int. Ed.,* 2014, **53**, 10510.
5 (a) J. Barluenga, M. Tomás-Gamasa, F. Aznar and C. Valdés, *Nat. Che* 2009, **1**, 494; (b) M. C. Pérez-Aguilar and C. Valdés, *Angew. Chem. In Ed.*, 2012, **51**, 5953; (c) D. M. Allwood, D. C. Blakemore, A. D. Brov and S. V. Ley, *J. Org. Chem.,* 2014, **79**, 328.
6 For a photochemically promoted reaction, see: K. Ito, H. Tamashima, N. Iwasawa and H. Kusama, *J. Am. Chem. Soc.,* 2011, **133**, 3716.
7 For reviews, see: (a) R. A. Moss, *Acc. Chem. Res.,* 2006, **39**, 267 and th references therein; (b) M. T. H. Liu, Ed. *Chemistry of Diazirines;* C Press: Boca Raton, Florida, 1987; (c) R. A. Moss, *J. Phys. Org. Chem.,* 2010, **23**, 293.
8 For a review, see: J. Das, *Chem. Rev.,* 2011, **111**, 4405.
9 For selected reports, see: (a) T. Mayer and M. E. Maier, *Eur. J. Org. Chem.,* 2007, 4711; (b) N. S. Kumar and R. N. Young, *Bioorg. Med. Chem.,* 2009, **17**, 5388; (c) G. Chee, J. C. Yalowich, A. Bodner, X. W and B. B. Hasinoff, *Bioorg. Med. Chem.,* 2010, **18**, 830; (d) Hashimoto, K. Furukawa, T. Tomohiro and Y. Hatanaka, *Chem. Phar Bull.,* 2010, **58**, 405; (e) J. A. Stewart, B. F. Piligian, S. R. Rundell and M. Swarts, *Chem. Commun.,* 2015, **51**, DOI: 10.1039/c5cc07536j.
10 X. Zhao, G. Wu, Y. Zhang and J. Wang, *Org. Lett.,* 2010, **12**, 5580.
11 For reviews, see: (a) Q. Xiao, Y. Zhang and J. Wang, *Acc. Chem. Re* 2013, **46**, 236; (b) Y. Xia, Y. Zhang and J. Wang, *ACS Catal.,* 2013, 2586; (c) Z. Liu and J. Wang, *J. Org. Chem.,* 2013, **78**, 10024; (d) F. Hu, Xia, C. Ma, Y. Zhang and J. Wang, *Chem. Commun.*, 2015, **51**, 7986.
12 For selected recent reports on the synthesis of 1,1-diaryl-substitute olefins, see: (a) A. Hamze, A. Giraud, S. Messaoudi, O. Provot, F. Peyrat, J. Bignon, J. M. Liu, J. Wdzieczak-Bakala, S. Thoret, J. Dubo J.-D. Brion and M. Alami, *ChemMedChem* 2009, **4**, 1912; (b) A. Hamze, Damien, O. Provot, J.-D. Brion and M. Alami, *J. Org. Chem.*, 2009, **7** 1337; (c) X. Zhao, J. Jing, K. Lu, Y. Zhang and J. Wang, *Chem. Commu* 2010, **46**, 1724; (d) A. Hamze, J.-D. Brion and M. Alami, *Org. Lett.*, 20 2, **14**, 2782 and the references therein; (e) M. Roche, A. Hamze, O. Prov J.-D. Brion and M. Alami, *J. Org. Chem.*, 2013, **78**, 445; (f) M. Roche, M. Salim, J. Bignon, H. Levaique, J.-D. Brion, M. Alami and A. Hazme, *Org. Chem.*, 2015, **80**, 6715; (g) H, Tan, I. Houpis, R. Liu, Y. Wang and Z. Chen, *Org. Lett.*, 2015, **17**, 3548.