

# Pd-Catalyzed Stereoselective Carboperfluoroalkylation of Alkynes

Zhaodong Li, Andrés García-Domínguez, and Cristina Nevado\*

Department of Chemistry, University of Zurich, Winterthurerstrasse 190, CH 8057 Zurich, Switzerland

**S** Supporting Information

**ABSTRACT:** A Pd-catalyzed three component reaction involving terminal alkynes, boronic acids, and perfluoroalkyl iodides is presented here. Trisubstituted perfluoroalkenes can be obtained in a highly regio- and stereocontrolled manner by the simultaneous addition of both aryl and  $C_nF_m$  groups across the triple bond in a radical-mediated process. The reaction is operationally simple offering a broad scope and functional group tolerance.

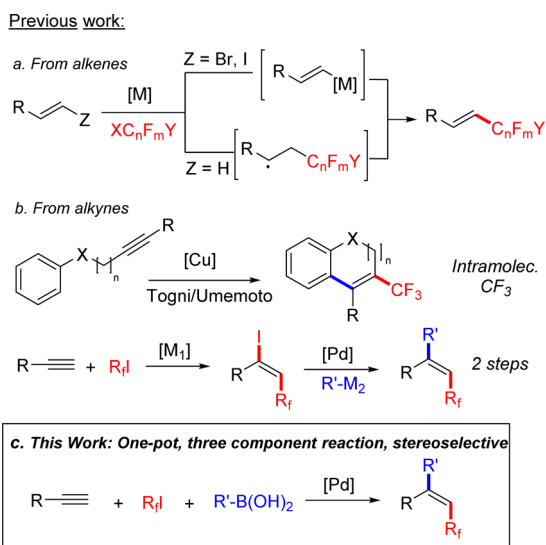
As a result of the unique solubility, cell permeability, and metabolic stability observed for organofluorine compounds,<sup>1</sup> the efficient introduction of fluoroalkyl motifs in commonly used building blocks has attracted increasing attention.<sup>2</sup> In contrast to the recent significant progress in the fluoroalkylation of aromatic compounds,<sup>3</sup> efficient methods to access fluoroalkylated alkenes are less abundant. Common strategies include transition-metal-mediated cross-coupling reactions of fluoroalkyl species with alkenyl halides as well as fluoroalkyl radical addition and elimination reactions on alkenes (Scheme 1a).<sup>4</sup> More straightforward approaches enabling additional functionalization have been explored with alkynes as starting materials, and thus the hydro-,<sup>5</sup> oxy-,<sup>6</sup> amino-trifluoromethylation<sup>7</sup> as well as the iodo-perfluoroalkylation<sup>8</sup> of alkynes have been recently reported.<sup>9</sup> Carbotrifluoromethylation

to simultaneously construct C–C and C(sp<sup>2</sup>)–C<sub>n</sub>F<sub>m</sub> bonds across the C≡C bond have also been explored, but the portfolio of these reactions is still limited to intramolecular settings.<sup>10,11</sup> Alternatively, multistep processes involving first an alkyne iodoperfluoroalkylation followed by classical Pd-catalyzed cross couplings have also been described to produce trisubstituted perfluoroalkenes (Scheme 1b).<sup>8a–c</sup> Most of the above-mentioned processes either require the preparation of alkenyl halides and/or fluoroalkyl radical precursors, which can be time-consuming and tedious, or rely on the use of electrophilic CF<sub>3</sub> sources such as Togni or Umemoto reagents,<sup>12</sup> which are expensive or require multistep synthesis. Furthermore, functionalization of alkynes via transition-metal-catalyzed multicomponent reactions has been studied extensively, although, with few exceptions,<sup>13</sup> multistep protocols using sensitive, highly reactive metal species are required, and thus competitive homo- and/or cross-coupling reactions are present in these transformations.<sup>14</sup> Thus, driven by our interest in radical reactions and fluorine chemistry,<sup>15</sup> we decided to explore the possibility of a one-pot intermolecular carboperfluoroalkylation reaction with alkynes as starting materials. Herein, we disclose a novel Pd-catalyzed three component reaction in which two new C–C bonds are simultaneously formed by addition of perfluoroalkyl halides and boronic acids to alkynes producing trisubstituted perfluoroalkenes in a highly regio- and stereoselective manner (Scheme 1c).

The addition of *n*-perfluorobutyl iodide and 4-biphenylboronic acid to phenyl acetylene was selected as benchmark reaction (Table 1).<sup>16</sup> In the presence of 4 mol % of PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> and 2 equiv of K<sub>2</sub>CO<sub>3</sub> in THF, CH<sub>3</sub>CN, 1,4-dioxane, or acetone, only traces of the desired product were formed (Table 1, entry 1). Using dichloromethane as solvent, in the absence as well as in the presence of water, **1a** was obtained in moderate yields (Table 1, entries 2–3). Increasing the amount of the *n*-perfluorobutyl iodide resulted in an optimized 81% isolated yield for **1a**, which was obtained as a single regio- and stereoisomer (Table 1, entry 4). The replacement of water by other protic solvents as well as the change of base to Cs<sub>2</sub>CO<sub>3</sub> or catalyst to Pd(PPh<sub>3</sub>)<sub>4</sub> did not increase the yield of product **1a** either (Table 1, entries 5–8).

With the optimized reaction conditions in hand (Table 1, entry 4), we set out to explore the scope of this transformation. First, different aryl boronic acids were investigated in combination with phenyl acetylene (Table 2, top). Oxygen-based electron-donating groups in the aromatic ring were well tolerated and produced the corresponding difunctionalized products in excellent yields and complete regio- and stereoselectivity (**1a–d**). The presence of alkyl groups had also a

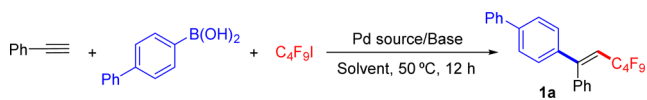
**Scheme 1. Comparison of Methods to Produce Perfluoroalkyl Alkenes**



Received: July 21, 2015

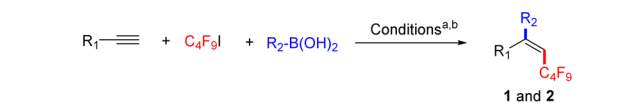
Published: August 26, 2015

Table 1. Optimization of the Reaction Conditions



entry <sup>a</sup>	catalyst (4 mol %)	solvent	base (2 equiv)	yield of 1a (%) <sup>d</sup>
1 <sup>a</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	THF, CH <sub>3</sub> CN, 1,4-dioxane, Me <sub>2</sub> CO	K <sub>2</sub> CO <sub>3</sub>	trace
2 <sup>a</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	DCM	K <sub>2</sub> CO <sub>3</sub>	57
3 <sup>a</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	DCM/H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	62
4 <sup>b</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	DCM/H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	85(81)
5 <sup>b</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	DCM/EtOH	K <sub>2</sub> CO <sub>3</sub>	50
6 <sup>b</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	DCM/H <sub>2</sub> O	Cs <sub>2</sub> CO <sub>3</sub>	73
7 <sup>b,c</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	DCM/H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	70
8 <sup>b</sup>	Pd(PPh <sub>3</sub> ) <sub>4</sub>	DCM/H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	70

<sup>a</sup>Conditions: phenyl acetylene (1 equiv), boronic acid (1.3 equiv), *n*-perfluorobutyl iodide (2 equiv), 0.2 M Solvent:H<sub>2</sub>O (5:1) if applied. <sup>b</sup>*n*-Perfluorobutyl iodide (3 equiv). <sup>c</sup>1 equiv of base. <sup>d</sup>Yield determined by <sup>1</sup>H NMR with *p*-nitroacetophenone as internal standard. In brackets: isolated yield after column chromatography.

Table 2. Reaction Scope on Boronic Acid and Alkynes<sup>a</sup>


Scope Boronic Acid	R =	Yield (%)	Scope Alkyne	R <sub>1</sub>	R <sub>2</sub>	Yield (%)
4-Biphe-	<b>1a</b> , 81	3-thiophene	<b>1m</b> , 70	TIPS	4-Biphe-	<b>2k</b> , 40
<i>p</i> -OMe-C <sub>6</sub> H <sub>4</sub> -	<b>1b</b> , 77	<i>p</i> -Cl-C <sub>6</sub> H <sub>4</sub> -	<b>1n</b> , 80	<i>n</i> Bu	4-Biphe-	<b>2l</b> , 83 <sup>b</sup>
<i>m</i> -OMe-C <sub>6</sub> H <sub>4</sub> -	<b>1c</b> , 78	<i>o</i> -F-C <sub>6</sub> H <sub>4</sub> -	<b>1o</b> , 78	-(CH <sub>2</sub> ) <sub>3</sub> OBz	4-Biphe-	<b>2m</b> , 81 <sup>b</sup>
3,5-(OMe) <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> -	<b>1d</b> , 84 <sup>c</sup>	2,4-(F) <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> -	<b>1p</b> , 71	-(CH <sub>2</sub> ) <sub>3</sub> OBz	Ph	<b>2n</b> , 76 <sup>b</sup>
<i>p</i> -tBu-C <sub>6</sub> H <sub>4</sub> -	<b>1e</b> , 75	<i>p</i> -CO <sub>2</sub> Et-C <sub>6</sub> H <sub>4</sub> -	<b>1q</b> , 57	"	<i>p</i> -OMe-C <sub>6</sub> H <sub>4</sub> -	<b>2o</b> , 75 <sup>b</sup>
<i>o</i> -Me-C <sub>6</sub> H <sub>4</sub> -	<b>1f</b> , 79 <sup>c</sup>	<i>p</i> -CF <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> -	<b>1r</b> , 75 <sup>c</sup>	"	2,4-(F) <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> -	<b>2p</b> , 78 <sup>b</sup>
2,4-(Me) <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> -	<b>1g</b> , 80	<i>p</i> -Ac-C <sub>6</sub> H <sub>4</sub> -	<b>1s</b> , 50	"	<i>p</i> -tBu-C <sub>6</sub> H <sub>4</sub> -	<b>2q</b> , 70 <sup>b</sup>
Ph	<b>1h</b> , 67			"	<i>p</i> -OPr-C <sub>6</sub> H <sub>4</sub> -	<b>2r</b> , 82 <sup>b</sup>
Ph	<b>1h</b> , 70 <sup>d,e</sup>			"	<i>m</i> -Me-C <sub>6</sub> H <sub>4</sub> -	<b>2s</b> , 87 <sup>f</sup>
Ph	<b>1h</b> , 50 <sup>d,f</sup>			"		
2-Naphthyl	<b>1i</b> , 90					
( <i>E</i> )-cynamyl	<b>1j</b> , 48					
( <i>E</i> )-1-octenyl	<b>1k</b> , 45					
3-furyl	<b>1l</b> , 50					

<sup>a</sup>Optimized conditions, Table 1, entry 4. <sup>b</sup>Isolated yield after column chromatography. <sup>c</sup>Conditions: alkyne (1.5 equiv), boronic acid (1 equiv), and then as in Table 1, entry 4. <sup>d</sup><sup>1</sup>H NMR yield with *p*-nitroacetophenone as internal standard. <sup>e</sup>With PhBpin. <sup>f</sup>With PhBF<sub>3</sub>K. <sup>g</sup>75% yield in 2 mmol scale. <sup>h</sup>10:1 *E/Z* ratio determined by <sup>19</sup>F NMR. <sup>i</sup>6:1 *E/Z* ratio: 4-Biphe:4-Biphenyl.

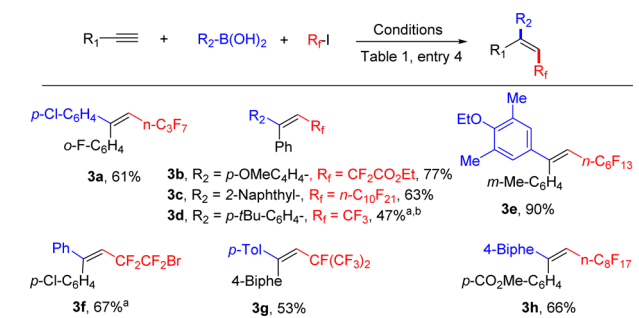
positive influence in the reaction outcome, even in the case of sterically demanding ortho-substituted substrates, as demonstrated by the high yields obtained for products **1e–g**. Not only phenyl boronic acid but also the corresponding pinacol ester and the potassium trifluoroborate proved to be amenable substrates under these conditions (**1h**). Naphthyl, cynamyl, and octenyl as well as heteroaryl boronic acid could be coupled in moderate to high yields (**1i–m**). Halogen groups (**1n–p**) were also well tolerated, whereas the presence of electron-withdrawing groups seems to limit the reaction efficiency as demonstrated in **1q–s**.

More elaborated boronic acids could also be successfully involved as shown by compounds **1t** and **1u**, respectively. In all studied cases, the products were obtained with perfect regio- and stereocontrol as single isomers.

The substitution pattern on the alkyne was explored next (Table 2, bottom). Using *p*-tert-butyl-phenyl boronic acid as partner, aryl alkynes bearing both electron-donating as well as electron-withdrawing groups were submitted to the standard reaction conditions providing the corresponding trisubstituted olefins in high yields and complete stereocontrol in favor of the *E* isomer (**2a–k**). The structure of **2h** could be confirmed by X-ray diffraction analysis.<sup>17</sup> The presence of a 2-thiophene or a bulky triisopropylsilyl group seemed to compromise the reaction efficiency (**2j**, **2k**). Alkyl-substituted alkynes proved to be suitable partners for the present difunctionalization reaction. Different boronic acids could be incorporated across a set of unactivated alkynes providing the corresponding trisubstituted alkenes in excellent yields and good levels of stereocontrol in favor of the thermodynamically favored *E*-olefin (**2l–s**).

Different perfluoroalkyl halides were also investigated as shown in Scheme 2. Except for trifluoromethyl and bulky

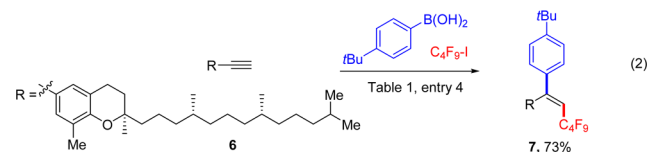
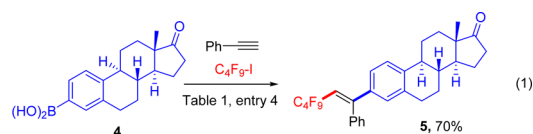
Scheme 2. Reaction Scope on Perfluoroalkyl Iodides



<sup>a</sup>Conditions: alkyne (1.5 equiv), boronic acid (1 equiv), and then as in Table 1, entry 4. <sup>b</sup>All compounds obtained as single isomers except **3d** which was isolated in a 11:1 *E/Z* ratio (determined by <sup>19</sup>F NMR). 4-Biphe:4-Biphenyl.

perfluoroisopropyl iodide (**3d** and **3g**), the corresponding arylperfluoroalkylated products (**3a–f**, **3h**) could be obtained in comparable yields to those reported in Table 2.

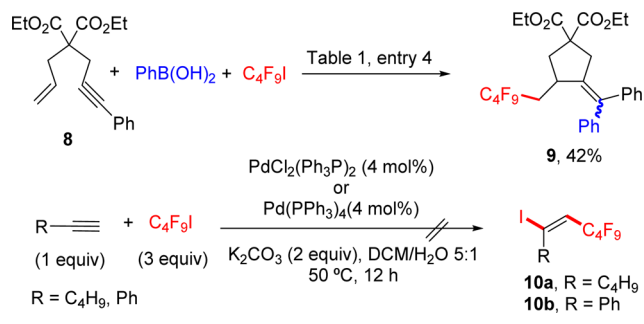
More elaborate substrates such as estrone-derived boronic acid **4** and alkyne  $\gamma$ -tocopherol-containing alkyne **6** could be successfully transformed into the corresponding carboperfluoroalkylated products **5** and **7**, respectively, in good yields eqs 1 and 2.<sup>18</sup>



Control experiments were also designed to interrogate the reaction mechanism. Addition of TEMPO, BHT, or 1,4-dinitrobenzene to the reaction mixture suppressed, or sub-

stantially compromised, product formation.<sup>16</sup> The reaction of enyne **8** seems to support a radical-mediated process, in which addition of C<sub>4</sub>F<sub>9</sub> to the more reactive alkene moiety takes place followed by cyclization and trapping of the resulting vinyl radical to give **9** (Scheme 3, top). In this reaction, vinyl iodides could

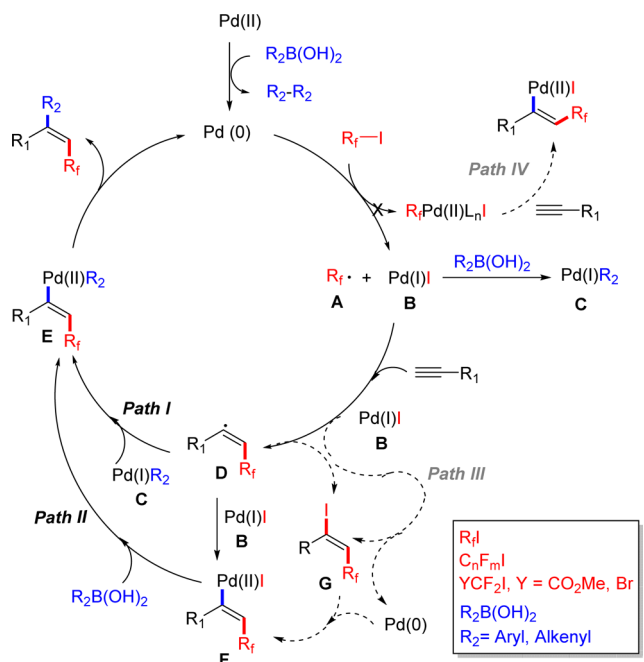
### Scheme 3. Control Experiments



also be detected,<sup>16</sup> prompting us to carry out the reactions of 1-hexyne and phenyl acetylene in the absence of boronic acid in order to check whether iodoperfluoroalkylation products **10a,b** could be produced under our standard conditions. As shown in the second half of Scheme 3, neither PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> nor Pd(PPh<sub>3</sub>)<sub>4</sub> as catalysts managed to produce significant amounts of **10**, thus questioning vinyl iodides as effective intermediates in these transformations.

Although multiple scenarios can be envisaged, based on these and additional control experiments,<sup>16</sup> we propose the following mechanism for these transformations. Palladium not only is a good cross-coupling catalyst<sup>20</sup> but has also been successfully used as a single electron donor.<sup>21</sup> As depicted in Scheme 4, the electrophilic perfluoroalkyl radical **A** can be formed by reaction of Pd(0) (generated in situ with the aid of boronic acid)<sup>22</sup> with Rf-I.<sup>23,24</sup> The perfluoroalkyl radical could add intermolecularly to the C≡C affording vinyl radical **D**. The subsequent recombination with either Pd(I)R<sub>2</sub> (**C**) or Pd(I)I (**B**) (paths I and II,

### Scheme 4. Proposed Reaction Mechanism



respectively) would finally give the key palladium species **E**, which undergoes reductive elimination to produce the corresponding fluoroalkylated alkenes while regenerating Pd(0). Alternatively, a third pathway can be proposed involving the formation of the corresponding iodoperfluoroalkyl alkenes **G** as potential reaction intermediates in these transformations (path III). However, the reactions shown at the bottom of Scheme 3 disfavor this hypothesis. The selectivity in favor of the *E* isomer also rules out a reaction mechanism involving the direct perfluoroalkyl palladation of the alkyne via putative R<sub>f</sub>-Pd(II)-I intermediate (path IV), in line with the highly unreactive nature toward unsaturated moieties reported for these complexes.<sup>23</sup> As such, the high stereoselectivity can be explained based on the less steric demand of a fast-interconverting *E/Z* vinyl radical **D**<sup>25</sup> for recombination with an external radical from the opposite side to that in which the perfluoroalkyl group has been incorporated.

In summary, a simple, functional-group tolerant, Pd-catalyzed three component reaction of terminal alkynes with boronic acids and perfluoroalkyl iodides is reported. This method, involving the simultaneous addition of both aryl/alkenyl and perfluoroalkyl group across the alkyne, streamlines the access to perfluoroalkylated trisubstituted alkenes in a highly regio- and stereo-controlled manner in what seems to be a radical-mediated process with broad scope and wide synthetic applicability.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b07432.

Compound synthesis and characterization (PDF)  
 Crystallographic data (CIF)

## ■ AUTHOR INFORMATION

### Corresponding Author

\*cristina.nevado@chem.uzh.ch

### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

We thank the European Research Council (ERC Starting grant agreement no. 307948), the Swiss National Science Foundation (200020\_146853), and the Novartis Post-Doctoral program for financial support. We thank Prof. Dr. Anthony Linden for the X-ray crystal structure determination of **2h** and Dr. Estibaliz Merino for her support in the initial stages of the project.

## ■ REFERENCES

- (1) For selected reviews, see: (a) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881. (b) O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308. (c) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320.
- (2) (a) Umemoto, T. *Chem. Rev.* **1996**, *96*, 1757. (b) Prakash, G. K. S.; Yudin, A. K. *Chem. Rev.* **1997**, *97*, 757. (c) Ma, J.-A.; Cahard, D. *Chem. Rev.* **2004**, *104*, 6119. (d) Liang, T.; Neumann, C. N.; Ritter, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 8214.
- (3) For selected reviews, see: (a) Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature* **2011**, *473*, 470. (b) Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475. (c) Besset, T.; Schneider, C.; Cahard, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 5048.
- (4) For selected examples, see: (a) Taguchi, T.; Kitagawa, O.; Morikawa, T.; Nishiwaki, T.; Uehara, H.; Endo, H.; Kobayashi, Y. *Tetrahedron Lett.* **1986**, *27*, 6103. (b) Sato, K.; Kawata, R.; Ama, F.; Omate, M.; Ando, A.; Kumadaki, I. *Chem. Pharm. Bull.* **1999**, *47*, 1013.

- (c) Schwaebe, M. K.; McCarthy, J. R.; Whitten, J. P. *Tetrahedron Lett.* **2000**, *41*, 791. (d) Fier, P. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2012**, *134*, 5524. (e) Prakash, G. K. S.; Ganesh, S. K.; Jones, J.-P.; Kulkarni, A.; Masood, K.; Swabeck, J. K.; Olah, G. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 12090. For radical methods, see: (f) Sato, K.; Omote, M.; Ando, A.; Kumadaki, I. *J. Fluorine Chem.* **2004**, *125*, 509. (g) Murakami, S.; Ishii, H.; Tajima, T.; Fuchigami, T. *Tetrahedron* **2006**, *62*, 3761. (h) Li, Y.; Liu, J.; Zhang, L.; Zhu, L.; Hu, J. *J. Org. Chem.* **2007**, *72*, 5824. (i) Yu, C.; Iqbal, N.; Park, S.; Cho, E. *J. Chem. Commun.* **2014**, *50*, 12884. (j) For a novel Pd-catalyzed Heck-type reaction of fluoroalkyl bromides, see: Feng, Z.; Min, Q.-Q.; Zhao, H.-Y.; Gu, J.-W.; Zhang, X. *Angew. Chem., Int. Ed.* **2015**, *54*, 1270.
- (5) (a) Kitazume, T.; Ishikawa, N. *J. Am. Chem. Soc.* **1985**, *107*, 5186. (b) Mizuta, S.; Verhoog, S.; Engle, K. M.; Khotavivattana, T.; O'Duill, M.; Wheelhouse, K.; Rassias, G.; Médebielle, M.; Gouverneur, V. *J. Am. Chem. Soc.* **2013**, *135*, 2505. (c) Choi, S.; Kim, Y. J.; Kim, S. M.; Yang, J. W.; Kim, S. W.; Cho, E. *J. Nat. Commun.* **2014**, *5*, 4881. (d) Iqbal, N.; Jung, J.; Park, S.; Cho, E. *J. Angew. Chem., Int. Ed.* **2014**, *53*, 539.
- (6) (a) Janson, P. G.; Ghoneim, I.; Ilchenko, N. O.; Szabó, K. *J. Org. Lett.* **2012**, *14*, 2882. (b) Egami, H.; Shimizu, R.; Kawamura, S.; Sodeoka, M. *Tetrahedron Lett.* **2012**, *53*, 5503.
- (7) (a) Ge, G.-C.; Huang, X.-J.; Ding, C.-H.; Wan, S.-L.; Dai, L.-X.; Hou, X.-L. *Chem. Commun.* **2014**, *50*, 3048. (b) Wang, F.; Zhu, N.; Chen, P.; Ye, J.; Liu, G. *Angew. Chem., Int. Ed.* **2015**, *54*, 9356.
- (8) (a) Jennings, M. P.; Cork, E. A.; Ramachandran, P. V. *J. Org. Chem.* **2000**, *65*, 8763. (b) Li, Y.; Li, H.; Hu, J. *Tetrahedron* **2009**, *65*, 478. (c) Xu, T.; Cheung, C. W.; Hu, X. *Angew. Chem., Int. Ed.* **2014**, *53*, 4910. (d) Wallentin, C.-J.; Nguyen, J. D.; Finkbeiner, P.; Stephenson, C. R. *J. Am. Chem. Soc.* **2012**, *134*, 8875 See also ref 5d.
- (9) For reviews on alkyne perfluoroalkylations, see: (a) Besset, T.; Poisson, T.; Pannecoucke, X. *Chem. - Eur. J.* **2014**, *20*, 16830. (b) Gao, P.; Song, X.-R.; Liu, X.-Y.; Liang, Y.-M. *Chem. - Eur. J.* **2015**, *21*, 7648.
- (10) Gao, P.; Shen, Y.-W.; Fang, R.; Hao, X.-H.; Qiu, Z.-H.; Yang, F.; Yan, X.-B.; Wang, Q.; Gong, X.-J.; Liu, X.-Y.; Liang, Y.-M. *Angew. Chem., Int. Ed.* **2014**, *53*, 7629.
- (11) (a) Li, Y. W.; Lu, Y.; Qiu, G.; Ding, Q. *Org. Lett.* **2014**, *16*, 4240. (b) Xu, J.; Wang, Y.-L.; Gong, T.-J.; Fu, Y. *Chem. Commun.* **2014**, *50*, 12915. (c) Ji, Y.-L.; Lin, J.-H.; Xiao, J.-X.; Gu, Y.-C. *Org. Chem. Front.* **2014**, *1*, 1280. (d) Wang, Y.; Jiang, M.; Liu, J.-T. *Chem. - Eur. J.* **2014**, *20*, 15315. (e) Hua, H.-L.; He, Y.-T.; Qiu, Y.-F.; Li, Y.-X.; Song, B.; Gao, P.; Song, X.-R.; Guo, D.-H.; Liu, X.-Y.; Liang, Y.-M. *Chem. - Eur. J.* **2015**, *21*, 1468.
- (12) (a) Eisenberger, P.; Gischig, S.; Togni, A. *Chem. - Eur. J.* **2006**, *12*, 2579. (b) Umemoto, T.; Ishihara, S. *J. Am. Chem. Soc.* **1993**, *115*, 2156.
- (13) (a) Zhang, X.; Larock, R. C. *Tetrahedron* **2010**, *66*, 4265. (b) Tetsuya, S.; Shinji, O. *Angew. Chem., Int. Ed.* **2004**, *43*, 5063. (c) Xue, F.; Zhao, J.; Hor, T. S. A.; Hayashi, T. *J. Am. Chem. Soc.* **2015**, *137*, 3189. (d) Monks, B. M.; Cook, S. P. *J. Am. Chem. Soc.* **2012**, *134*, 15297.
- (14) For selected examples, see: (a) Shirakawa, E.; Yamagami, T.; Kimura, T.; Yamaguchi, S.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 17164. (b) Shirakawa, E.; Ikeda, D.; Masui, S.; Yoshida, M.; Hayashi, T. *J. Am. Chem. Soc.* **2012**, *134*, 272. (c) Murakami, K.; Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2007**, *9*, 1569. (d) Stuedemann, T.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 93. (e) Murakami, K.; Yorimitsu, H.; Oshima, K. *Chem. - Eur. J.* **2010**, *16*, 7688. (f) Tan, B.-H.; Dong, J.; Yoshikai, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 9610.
- (15) (a) Kong, W.; Casimiro, M.; Merino, E.; Nevado, C. *J. Am. Chem. Soc.* **2013**, *135*, 14480. (b) Kong, W.; Feige, P.; De Haro, T.; Nevado, C. *Angew. Chem., Int. Ed.* **2013**, *52*, 2469. (c) Kong, W.; Casimiro, M.; Fuentes, N.; Merino, E.; Nevado, C. *Angew. Chem., Int. Ed.* **2013**, *52*, 13086. (d) Kong, W.; Merino, E.; Nevado, C. *Angew. Chem., Int. Ed.* **2014**, *53*, 5078. (e) Fuentes, N.; Kong, W.; Fernández-Sánchez, L.; Merino, E.; Nevado, C. *J. Am. Chem. Soc.* **2015**, *137*, 964. (f) Kong, W.; Fuentes, N.; García-Domínguez, A.; Merino, E.; Nevado, C. *Angew. Chem.* **2015**, *127*, 2517.
- (16) For additional experiments, see [Supporting Information](#).
- (17) X-ray diffraction analysis data for **2h** are available from the CCDC database: CCDC 1411445.
- (18) Reaction performed using 1 equiv of boronic acid and 1.5 equiv of alkyne.
- (19) Independently prepared perfluoroalkyl iodoalkenes **10a** and **10b** could be efficiently engaged in Pd-cross coupling reactions with boronic acids: as already shown in refs **8a–c**; see [SI](#).
- (20) For selected reviews, see (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147.
- (21) See ref **4j** and also: Mazzoti, A.; Campbell, M.; Tang, P.; Murphy, J.; Ritter, T. *J. Am. Chem. Soc.* **2013**, *135*, 14012.
- (22) Traces of biaryls stemming from homocoupling of the boronic acids could be detected in the crude reaction mixtures. See ref **16**.
- (23) (a) Chen, Q. Y.; Yang, Z.-Y. *Acta Chim. Sinica* **1985**, *43*, 1118. (b) Chen, Q.-Y.; Yang, Z.-Y.; Zhao, C.-X.; Qiu, Z.-M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 563. (c) Ishikara, T.; Kuroboshi, M.; Okada, Y. *Chem. Lett.* **1986**, 1895.
- (24) Although radical activation of Rf-I by carbonate bases has been recently proposed (see ref **8c** and also: (a) Aihara, Y.; Tobisu, M.; Fukumoto, Y.; Chatani, N. *J. Am. Chem. Soc.* **2014**, *136*, 15509. (b) Zhang, B.; Studer, A. *Org. Lett.* **2014**, *16*, 3990 no significant reactivity was observed in the present reactions in the absence of Pd (see ref **16**).
- (25) (a) Galli, C.; Guarnieri, A.; Koch, H.; Mencarelli, P.; Rappaport, Z. *J. Org. Chem.* **1997**, *62*, 4072. (b) Singer, L. A.; Chen, J. *Tetrahedron Lett.* **1969**, *10*, 4849. (c) Evans, P. A.; Manangan, T. *J. Org. Chem.* **2000**, *65*, 4523.