Cross-Coupling

International Edition: DOI: 10.1002/anie.201601351
German Edition: DOI: 10.1002/ange.201601351

Nickel-Catalyzed Difluoroalkylation of (Hetero)Arylborons with Unactivated 1-Bromo-1,1-difluoroalkanes

*Yu-Lan Xiao[+], Qiao-Qiao Min[+], Chang Xu, Ruo-Wen Wang, and Xingang Zhang**

Abstract: *A nickel-catalyzed cross-coupling between (hetero)-arylborons and unactivated 1-bromo-1,1-difluoroalkanes has been developed. The use of two ligands (a bidentate bipyridine-based ligand, 4,4′-ditBu-bpy, and a monodentate pyridine-based ligand, DMAP) offers a highly efficient nickel-based catalytic system to prepare difluoroalkylated arenes which have important applications in medicinal chemistry.*

Difluoroalkylated arenes, in which a methylene group (CH_2) is replaced by its difluorinated counterpart (CF_2) at the metabolically labile benzylic position, constitute a distinct class of fluorinated compounds in medicinal chemistry because of the unique properties of CF_2 which can enhance the acidity of its neighboring group and dramatically improve the metabolic stability of biologically active compounds.[1] As a result, the incorporation of a CF_2 group into organic compounds at benzylic positions has become one of the useful strategies for modification of biologically active compounds (Figure 1).[2] For example, application of this strategy led to a difluorinated nitric oxide synthase (NOS) inhibitor (**I**) for chronic neurodegenerative pathologies with improved oral bioactivity compared to its parent compound.[2a] A remarkably improved metabolic stability of urea transporter B (UT-B) inhibitor (**II**), used for edema, has also resulted from replacement of benzylic CH_2 with CF_2.[2b] The most common method to access difluoroalkylated arenes (Ar-CF_2-alkyl), in which the difluorocarbon is substituted by an alkyl group, relies on the deoxygenative fluorination of a ketone with aminosulfur trifluorides, such as diethylaminosulfur trifluoride (DAST) or its derivatives.[3] However, such a process is restricted by its poor functional-group compatibility. To date, examples of efficient synthesis of Ar-CF_2-alkyl are very limited.[4] Recently, the direct fluorination of benzylic C–H bonds to prepare difluoroalkylated arenes has been reported.[5] Despite the importance of this method, it cannot selectively introduce the difluoroalkyl groups at any desired position on an aromatic ring. In particular, this strategy is not suitable for late-stage difluoroalkylation of complex molecules because of the limited availability of benzylic precursors. Therefore, developing efficient and mild methods to synthesize Ar-CF_2-alkyl is appealing, and would provide a useful instrument for drug discovery and development.

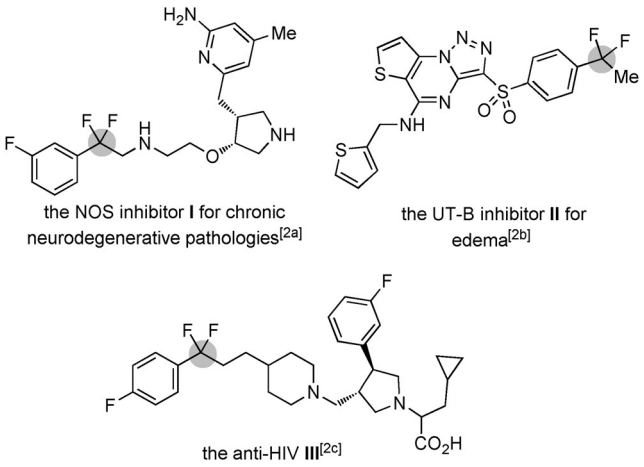


Figure 1. Representative biologically active molecules containing difluoroalkyl arene moieties.

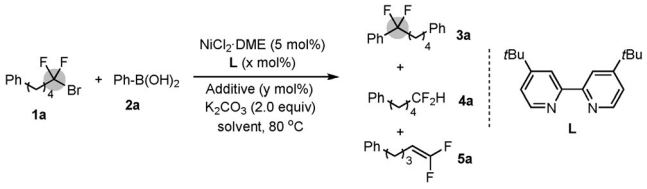
Considering the ready availability of 1-bromo-1,1-difluoroalkanes[6] and arylmetals, we envisioned that the transition-metal-catalyzed difluoroalkylation of arylboronic acids with unactivated 1-bromo-1,1-difluoroalkanes would be a straightforward and facile access to Ar-CF_2-alkyl compounds. Although examples of transition-metal-catalyzed difluoroalkylation of aromatics have been reported, all of the difluoroalkylating reagents (XCF_2R^1) used for the reported reactions require a π-system to activate the XCF_2R^1 (R^1 = π-system).[7,8] Very recently, a nickel-catalyzed Suzuki-cross coupling of unactivated 1-halo-1-fluoroalkanes (XFCH-Alkyl, X = Cl, Br, I) for the synthesis of secondary alkyl fluorides was reported by Gandelman and co-workers.[9] However, to the best of our knowledge, the use of unactivated XCF_2R^1 (R^1 = alkyl) to prepare Ar-CF_2-akyl compounds through such a strategy has not been reported and remains a challenge[9,10] because of the difficulties in the oxidative addition and in suppressing β-hydride elimination and dehalogenation.[11] Additionally, the competitive defluorination reaction is also another hurdle to realizing such a reaction.[12] In this study, we describe the discovery, development of the reaction which meets these challenges.

Inspired by our previous work on nickel-catalyzed difluoroalkylation of arylboronic acids with functionalized difluoroalkyl bromides (XCF_2R^1, R^1 = π-system),[8c] initially, we focused our efforts on the cross-coupling of phenylboronic acid (**2a**) with (5-bromo-5,5-difluoropentyl)benzene[6a] (**1a**) in the presence of $NiCl_2$·DME (5 mol%), with bipyridine (bpy) as a ligand (Table 1). It was found that 19% yield of the product **3a** along with the hydrodebrominated **4a** (3% yield)

[*] Y.-L. Xiao,[+] Q.-Q. Min,[+] C. Xu, Dr. R.-W. Wang, Prof. Dr. X. Zhang
Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences
345 Lingling Lu, Shanghai 200032 (China)
E-mail: xgzhang@mail.sioc.ac.cn
[+] These authors contributed equally to this work.

Supporting information for this article can be found under: http://dx.doi.org/10.1002/anie.201601351.

Table 1: Representative results for the optimization of the nickel-catalyzed cross-coupling of **1a** with **2a**.[a]

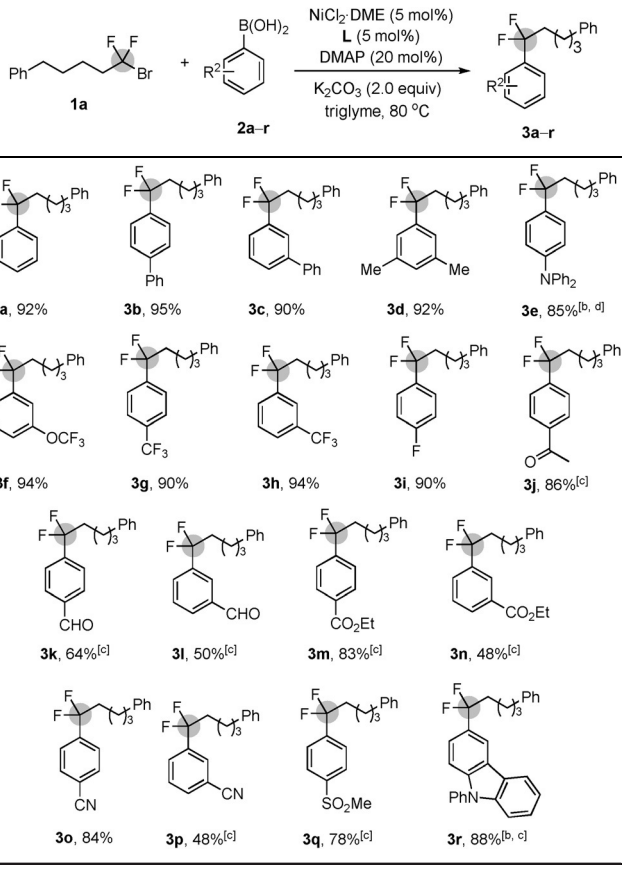


Entry	L (mol%)	Solvent	Additive (mol%)	Yield [%][b] 3a	4a	1a
1	bpy (5)	1,4-dioxane	–	19	3	69
2	bpy (5)	triglyme	–	43	6	51
3	**L** (5)	triglyme	–	52	6	38
4	**L** (5)	triglyme	Py (10)	80	6	12
5	**L** (5)	triglyme	4-MeOPy (10)	86	6	6
6	**L** (5)	triglyme	DMAP (10)	94	5	0
7	**L** (5)	triglyme	4-CF_3Py (10)	55	5	35
8	**L** (5)	triglyme	DMAP (20)	94 (92)	2	–
9[c]	L (5)	triglyme	DMAP (20)	n.r.		
10	–	triglyme	DMAP (20)	n.r.		

[a] Reaction conditions (unless otherwise specified): **1a** (0.3 mmol, 1.0 equiv), **2a** (1.5 equiv), solvent (2 mL), 12 h. [b] Determined by ^{19}F NMR spectroscopy using fluorobenzene as an internal standard. Value within parentheses is the yield of the isolated product. [c] Reaction was carried out in the absence of $NiCl_2$·DME, 12 h. DME = 1,2-dimethoxyethane.

and unreacted **1a** (69% yield) were obtained (entry 1). But the β-hydride elimination product (**5a**) was not observed.[13] To improve the reaction efficiency further, we examined a range of solvents, nickel catalysts, ligands, and bases (for details, see the Supporting Information). Ethereal solvents have a beneficial effect on the reaction, and triglyme was the best choice, thus providing **3a** in 43% yield (entry 2). Among the tested ligands, the use of the bipyridine-based ligand 4,4′-di*t*Bu-bpy (**L**) improved the yield of **3a** to 52% (entry 3), but **4a** (6% yield) and **1a** (38% yield) were still observed under these reaction conditions. This outcome is probably a result of the low reactivity of **1a**. We envisioned that if we used another tunable ligand to increase electron density at the nickel center, it would be feasible to accelerate the oxidative addition step and improve the yield of **3a** further. Apparently, with this combined ligand system [(2 + 1) a bidentate ligand plus a monodentate ligand], it would be easy to modulate the electronic and steric properties of the nickel center without tedious preparation of complicated ligands. Accordingly, different pyridine derivatives were tested (entries 4–8). As expected, the electronic nature of pyridine dramatically influenced the reaction efficiency, and electron-rich 4-MeOPy afforded a higher yield of **3a** (86%), as compared to that obtained with the electron-deficient 4-CF_3Py (55%; entries 5 and 7). To our delight, a highest yield (94%) was produced with the more electron-rich 4-(*N*,*N*-dimethylamino)pyridine (DMAP) as a co-ligand (entry 6). The use of 20 mol% of DMAP is required because of the reproducibility of the reaction (entry 8). The absence of either the nickel catalyst or ligand resulted in no product (entries 9 and 10), thus demonstrating that the $NiCl_2$·DME/**L** does play an essential role in promoting the catalytic cycle.

Table 2: Nickel-catalyzed difluoroalkylation of arylboronic acids **2** with **1a**.[a]

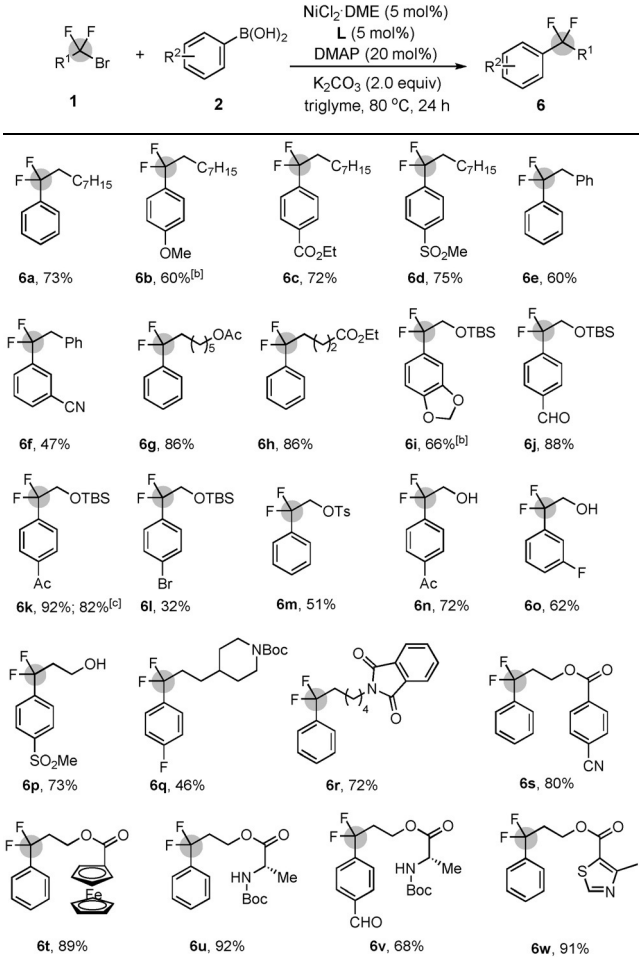


[a] Reaction conditions (unless otherwise specified): **1a** (0.6 mmol, 1.0 equiv), **2** (1.5–2.0 equiv), triglyme (4 mL), 12–24 h. All reported yields are those of the isolated products. [b] $NiCl_2$·DME (2.5 mol%), **L** (2.5 mol%), DMAP (10 mol%), 70°C, 24 h. [c] Reaction run for 48 h. [d] Yield determined by ^{19}F NMR spectroscopy. The compound **3e** is unstable upon purification with silica gel chromatography.

To ascertain the substrate scope of this method, a variety of arylboronic acids were investigated (Table 2). Overall, arylboronic acids bearing electron-donating or electron-withdrawing groups all underwent the reaction smoothly. Notably, in the case of 4-(diphenylamino)phenyl boronic acid (**2e**), only 2.5 mol% $NiCl_2$·DME/**L** was used, and provided the corresponding difluoroalkylated arene **3e** with high efficiency. Importantly, a variety of important functional groups, including base- and nucleophile-sensitive moieties, such as an enolizable ketone, formyl, alkoxycarbonyl, cyano, and methylsulfonyl groups, tolerated the reaction quite well (**3j–q**), thus providing good opportunities for downstream transformation without protection and deprotection steps. In addition, (9-phenyl-9*H*-carbazol-3-yl)boronic acid was also applicable to the reaction and provided **3r** in 88% yield. However, vinyl, benzyl, and aliphatic boronic acids were not suitable substrates, and will be the subject of future work.

In addition to demonstrating the substrate scope of this reaction, a variety of difluoroalkyl bromides (**1**) were examined. As shown in Table 3, 1-bromo-1,1-difluorononane (**1b**) and (2-bromo-2,2-difluoroethyl)benzene (**1c**) furnished the corresponding difluoroalkylated arenes with good yields

Table 3: Nickel-catalyzed difluoroalkylation of arylboronic acids **2** with **1**.[a]

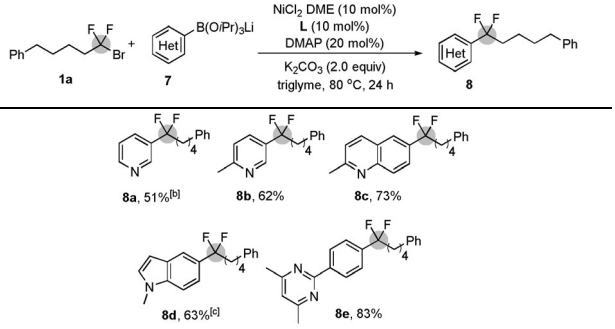


[a] Reaction conditions (unless otherwise specified): **1** (0.6 mmol, 1.0 equiv), **2** (1.5 equiv), triglyme (4 mL). All reported yields are those of the isolated products. [b] $NiCl_2$·DME (2.5 mol%), **L** (2.5 mol%), DMAP (10 mol%), 70°C, 24 h. [c] Reaction run on a gram scale. Boc = *tert*-butoxycarbonyl, TBS = *tert*-butyldimethylsilyl, Ts = 4-toluenesulfonyl.

(**6a–f**). Excellent functional-group compatibility was also observed for difluoroalkyl bromides. The substrates **1**, bearing important functional groups, such as enolizable alkoxycarbonyl, tosyloxy, hydroxy, amide, nitrile, ferrocenyl, and thiazole, all underwent the reactions smoothly (**6g**, **6h**, **6m–t**, **6w**). Remarkably, the successful formation of **6l** with an intact bromide also highlighted the advantage of the present reaction. The reaction also delivered the compounds **6o** and **6q**, which are key intermediates in the preparation of a nitric oxide synthase (NOS) inhibitor (**I**)[2a] and *anti*-HIV agent (**III**), respectively.[2c] Moreover, the amino-acid-containing difluoroalkyl bromide **1n** was a competent coupling partner and afforded **6u** and **6v** with good to high yields without erosion of the enantioselectivity (for details, see the Supporting Information). This fact is noteworthy, as the fluorinated amino acids and their derivatives have important applications in the chemical biology.

The reaction can also be extended to heteroarylboron compounds (Table 4). Initially, no product was obtained when

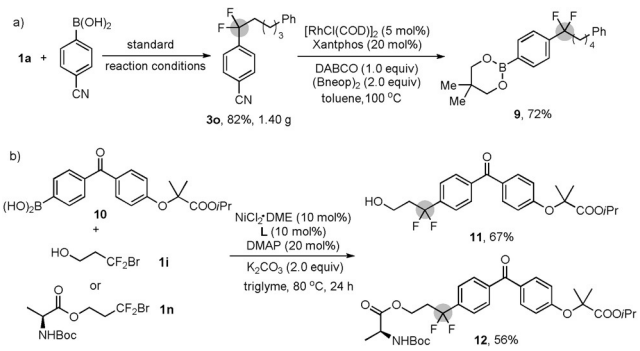
Table 4: Nickel-catalyzed difluoroalkylation of heteroarylborates **7** with **1a**.[a]



[a] Reaction conditions (unless otherwise specified): **1a** (0.3 mmol, 1.0 equiv), **7** (0.45 mmol, 1.5 equiv), triglyme (2 mL), 24 h. All reported yields are those of the isolated products. [b] $NiCl_2$·DME (15 mol%), **L** (15 mol%) and **7** (0.6 mmol, 2.0 equiv) were used. [c] [$NiCl_2$·DME] (15 mol%) and **L** (15 mol%) were used. The yield was determined by ^{19}F NMR spectroscopy because of the instability of **8d** upon purification using silica gel chromatography.

3-pyridylboronic acid (**7a′**) was used as a coupling partner. However, after extensive efforts, we found that switching **7a′** with lithium triisopropyl 3-pyridylborate (**7a**), which was previously demonstrated to be stable against protodeboronation,[14] afforded **8a** in 51% yield. Encouraged by these results, other heterarylborates, such as quinolone-, indole-, and pyrimidine-containing lithium triisopropyl borates were also examined and provided corresponding products in good yields (**8c–e**). Because heteroaromatics are a class of important structural motif in numerous pharmaceuticlas and agrochemicals, we view this transformation would be a useful instrument for drug discovery and development.

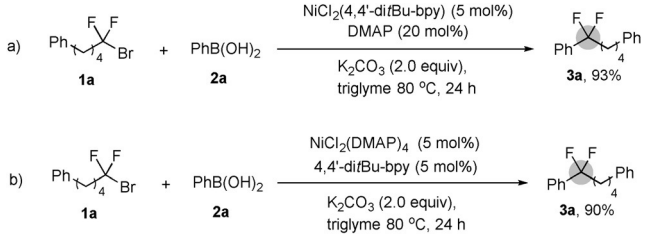
It is also possible to prepare difluoroalkylated arenes on a gram scale. As shown in Table 3 and Scheme 1 a, good yields were provided for the gram-scale synthesis of **6k** and **3o**, respectively, thus offering a reliable and practical access to highly functionalized difluoroalkylated arenes. Importantly, **3o** can be easily transformed into the aryl borate **9**,[15] thus providing good possibilities for the synthesis of complex fluorinated molecules. To demonstrate the importance and utility of this method, the late-stage difluoroalkylation of Fenofibrate®, a drug against cardiovascular disease,[16] was



Scheme 1. Synthesis of difluoroalkylated arenes for biologically active molecules.

successfully performed (Scheme 1b), thus featuring the applicability of this protocol in medicinal chemistry.

To establish whether DMAP serves as a co-ligand to coordinate to the nickel complex and thus facilitate the catalytic cycle, a nickel complex [$NiCl_2$(4,4′-di*t*Bu-bpy)] (**13**) was prepared.[17] When the reaction of **2a** with **1a** was carried out in the presence of **13**, DMAP, and K_2CO_3 in triglyme at 80 °C, a comparable yield of **3a** was provided (Scheme 2a). A similar finding was also observed by using [$NiCl_2(DMAP)_4$] (**14**) as a precatalyst and 4,4′-di*t*Bu-bpy as a ligand (Scheme 2b). Thus, these results demonstrated that DMAP can function as a co-ligand to facilitate the nickel-based catalytic cycle, and the combined ligands (4,4′-di*t*Bu-bpy + DMAP) offered a highly efficient nickel-based catalytic system for the preparation of Ar-CF_2-alkyl compounds, which are important in medicinal chemistry.



Scheme 2. The role of DMAP.

To probe whether a difluoroalkyl radical exists in the reaction, radical clock experiments and the EPR study of the reaction of **1a** with a spin-trapping agent, phenyl *tert*-butyl nitrone (PBN), in the presence of **2a** were all conducted and demonstrated that a free difluoroalkyl radical was involved in the reaction (for details, see the Supporting Information). Although the exact mechanism of the current reaction is unclear, on the basis of above results and previous reports,[18] a Ni^{I}/Ni^{III} catalytic cycle is proposed. The reaction begins with the transmetalation between arylboronic acid and [$Ni^{I}L_n$](**A**), which was supposed to be generated by comproportionation of in situ generated Ni^0 and the remaining Ni^{II} species.[18c,19] Subsequently, the resulting arylnickel complex [Ar-$Ni^{I}L_n$] (**B**) reacts with **1** by a SET pathway to produce the arylnickel(difluoroalkyl) complex [(Ar)(alkyl-CF_2)$Ni^{III}L_nX$] (**C**), which undergoes reductive elimination to produce final product and regenerate [Ni^{I}] simultaneously.[20]

In conclusion, we have demonstrated the first example of a nickel-catalyzed cross-coupling of (hetero)arylborons with unactivated 1-bromo-1,1-difluoroalkanes. The reaction proceeds under mild reaction conditions with high efficiency and excellent functional-group compatibility. The use of combined ligands (4,4′-di*t*Bu-bpy + DMAP) makes it possible to employ a wide range of unactivated 1-bromo-1,1-difluoroalkanes as coupling partners, even substrates containing either a hydroxy or bromide group. The significant features of this protocol are that it employs a low-cost nickel catalyst, is synthetically straightforward, and can be used for late-stage difluoroalkylation of biologically active molecules. Furthermore, the resulting difluoroalkylated arenes can also serve as key intermediates for the synthesis of biologically relevant compounds. We believe that this method will not only provide a useful instrument for drug discovery and development, but also prompt research in transition-metal-catalyzed fluoroalkylation reactions with unactivated halofluoroalkanes. Further studies to develop derivative reactions are underway in our laboratory and will be reported in due course.

Acknowledgements

This work was financially supported by the National Basic Research Program of China (973 Program) (No. 2012CB821600 and 2015CB931900), the NSFC (21425208, 21421002, and 21332010), and SIOC.

Keywords: arenes · cross-coupling · fluorine · ligand design · nickel

How to cite: *Angew. Chem. Int. Ed.* **2016**, *55*, 5837–5841
Angew. Chem. **2016**, *128*, 5931–5935

[1] a) K. Muller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881; b) D. O'Hagan, *Chem. Soc. Rev.* **2008**, *37*, 308; c) C. Ni, L. Zhu, J. Hu, *Acta Chim. Sin.* **2015**, *73*, 90.

[2] a) F. Xue, H. Li, S. L. Delker, J. Fang, P. Martasek, L. J. Roman, T. L. Poulos, R. B. Silverman, *J. Am. Chem. Soc.* **2010**, *132*, 14229; b) M. O. Anderson, J. Zhang, Y. Liu, C. Yao, P.-W. Phuan, A. S. Verkman, *J. Med. Chem.* **2012**, *55*, 5942; c) C. L. Lynch, C. A. Willoughby, J. J. Hale, E. J. Holson, R. J. Budhu, A. L. Gentry, K. G. Rosauer, C. G. Caldwell, P. Chen, S. G. Mills, M. MacCoss, S. Berk, L. Chen, K. T. Chapman, L. Malkowitz, M. S. Springer, S. L. Gould, J. A. DeMartino, S. J. Siciliano, M. A. Cascieri, A. Carella, G. Carver, K. Holmes, W. A. Schleif, R. Danzeisen, D. Hazuda, J. Kessler, J. Lineberger, M. Millerc, E. A. Emini, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 119.

[3] a) W. J. Middleton, E. M. Bingham, *J. Org. Chem.* **1980**, *45*, 2883; b) G. S. Lal, G. P. Pez, R. J. Pesaresi, F. M. Prozonic, H. Cheng, *J. Org. Chem.* **1999**, *64*, 7048; c) D. Solas, R. L. Hale, D. V. Patel, *J. Org. Chem.* **1996**, *61*, 1537.

[4] For a radical-type direct difluoroalkylation of heteroarenes with sodium difluroalkylsulfinates, see: a) Q. Zhou, A. Ruffoni, R. Gianatassio, Y. Fujiwara, E. Sella, D. Shabat, P. S. Baran, *Angew. Chem. Int. Ed.* **2013**, *52*, 3949; *Angew. Chem.* **2013**, *125*, 4041. During our manuscript preparation, a radical Smiles rearrangement from a difluorobromo sulfonate was reported, but only the difluoroethanol motif can be introduced into heteroarenes and the substrate scope of arenes is limited. See : b) J. J. Douglas, H. Albright, M. J. Sevrin, K. P. Cole, C. R. J. Stephenson, *Angew. Chem. Int. Ed.* **2015**, *54*, 14898; *Angew. Chem.* **2015**, *127*, 15111.

[5] a) J.-B. Xia, C. Zhu, C. Chen, *J. Am. Chem. Soc.* **2013**, *135*, 17494; b) P. Xu, S. Guo, L. Wang, P. Tang, *Angew. Chem. Int. Ed.* **2014**, *53*, 5955; *Angew. Chem.* **2014**, *126*, 6065.

[6] 1-Bromo-1,1-difluoroalkanes (**1**) can be easily prepared from the reaction of olefines with CF_2Br_2. See: a) Q.-Y. Lin, X.-H. Xu, F.-L. Qing, *Org. Biomol. Chem.* **2015**, *13*, 8740; For other related papers, see: b) J. Gonzalez, C. J. Foti, S. Elsheimer, *J. Org. Chem.* **1991**, *56*, 4322; c) C.-M. Hu, J. Chen, *J. Chem. Soc. Chem. Commun.* **1993**, 72.

[7] For use of XCF_2R^1 as a nucleophile, see: a) K. Fujikawa, Y. Fujioka, A. Kobayashi, H. Amii, *Org. Lett.* **2011**, *13*, 5560; b) C. Guo, R.-W. Wang, F.-L. Qing, *J. Fluorine Chem.* **2012**, *143*, 135; c) S. Ge, W. Chaladaj, J. F. Hartwig, *J. Am. Chem. Soc.* **2014**, *136*, 4149.

[8] For use of XCF_2R^1 as an electrophile, see: a) Z. Feng, Q.-Q. Min, Y.-L. Xiao, B. Zhang, X. Zhang, *Angew. Chem. Int. Ed.* **2014**, *53*, 1669; *Angew. Chem.* **2014**, *126*, 1695; b) Q.-Q. Min, Z. Yin, Z. Feng, W.-H. Guo, X. Zhang, *J. Am. Chem. Soc.* **2014**, *136*, 1230; c) Y.-L. Xiao, W.-H. Guo, G.-Z. He, Q. Pan, X. Zhang, *Angew. Chem. Int. Ed.* **2014**, *53*, 9909; *Angew. Chem.* **2014**, *126*, 10067.

[9] a) X. Jiang, S. Sakthivel, K. Kulbitski, G. Nisnevich, M. Gandelman, *J. Am. Chem. Soc.* **2014**, *136*, 9548; b) X. Jiang, M. Gandelman, *J. Am. Chem. Soc.* **2015**, *137*, 2542.

[10] For pioneering studies on Pd/Ni-catalyzed cross-coupling of akyl halides with aryl borons, see: Pd: a) T. Ishiyama, S. Abe, N. Miyaura, A. Suzuki, *Chem. Lett.* **1992**, *21*, 691; b) J. H. Kirchhoff, M. R. Netherton, I. D. Hills, G. C. Fu, *J. Am. Chem. Soc.* **2002**, *124*, 13662; Ni: c) J. Zhou, G. C. Fu, *J. Am. Chem. Soc.* **2004**, *126*, 1340.

[11] a) T.-Y. Luh, M.-K. Leung, K.-T. Wong, *Chem. Rev.* **2000**, *100*, 3187; b) M. R. Netherton, G. C. Fu, *Adv. Synth. Catal.* **2004**, *346*, 1525.

[12] It has been demonstrated that the defluorination reaction could occur when 1-bromo-1,1-difluoroalkanes are employed as coupling partners in the presence of palladium. S. Peng, F.-L. Qing, Y.-Q. Li, C.-M. Hu, *J. Org. Chem.* **2000**, *65*, 694.

[13] The use of DMSO as a solvent led to the β-hydride elimination product **5a**.

[14] M. A. Oberli, S. L. Buchwald, *Org. Lett.* **2012**, *14*, 4606.

[15] M. Tobisu, H. Kinuta, Y. Kita, E. Remond, N. Chatani, *J. Am. Chem. Soc.* **2012**, *134*, 115.

[16] N. A. McGrath, M. Brichacek, J. T. Njardarson, *J. Chem. Educ.* **2010**, *87*, 1348.

[17] A. Singh, U. Anandhi, M. A. Cinellu, P. R. Sharp, *Dalton Trans.* **2008**, 2314.

[18] a) A. Wilsily, F. Tramutola, N. A. Owston, G. C. Fu, *J. Am. Chem. Soc.* **2012**, *134*, 5794; b) S. L. Zultanski, G. C. Fu, *J. Am. Chem. Soc.* **2013**, *135*, 624; c) G. D. Jones, J. L. Martin, C. McFarland, O. R. Allen, R. E. Hall, A. D. Haley, R. J. Brandon, T. Konovalova, P. J. Desrochers, P. Pulay, D. A. Vicic, *J. Am. Chem. Soc.* **2006**, *128*, 13175; d) O. Gutierrez, J. C. Tellis, D. N. Primer, G. A. Molander, M. C. Kozlowski, *J. Am. Chem. Soc.* **2015**, *137*, 4896.

[19] J. Cornella, E. Gomez-Bengoa, R. Martin, *J. Am. Chem. Soc.* **2013**, *135*, 1997.

[20] An alternative pathway through the carbometalation of the in situ generated *gem*-difluorinated alkene **5** with a [Ni] species and subsequent reduction of an in situ generated Ni^{II} complex was ruled out. As no product **3a** was observed when **5a** was treated with arylboronic acid **2a** under standard reaction conditions. For details see the Supporting Information.

Received: February 6, 2016
Published online: April 6, 2016

