ChemPubSoc Europe

DOI: 10.1002/chem.201405119

CHEMISTRY
A European Journal
Communication

Synthetic Methods

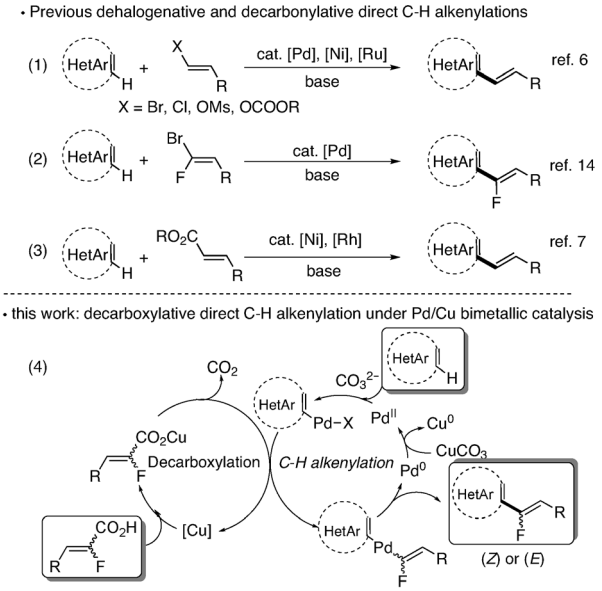
Pd- and Cu-Catalyzed Stereo- and Regiocontrolled Decarboxylative/C–H Fluoroalkenylation of Heteroarenes

Kevin Rousée, Cédric Schneider, Samuel Couve-Bonnaire,* Xavier Pannecoucke, Vincent Levacher, and Christophe Hoarau*[a]

Abstract: Pd/Cu-catalyzed decarboxylative/direct C–H alkenylations of heteroarenes with α-fluoroacrylic acid is reported. This method offers step-economical and stereocontrolled access to valuable heteroarylated monofluoroalkenes as both *Z* and *E* isomers, which are known to be useful in the synthesis of fluorinated biomolecules.

Transition metal-catalyzed C–C bond formation through direct C–H functionalization of heterocycles has proven to be an efficient modern alternative and complementary process to traditional cross-coupling methods.[1] Within the direct functionalization of ubiquitous C–H bonds, direct alkenylation,[2] an emerging tool for the construction of alkenylated (hetero)arenes, has recently received growing attention due to the significance of this motif in biologically active natural products, pharmaceuticals and organic materials.[3]

In recent years, current developments in the transition metal-catalyzed direct C–H alkenylation of heteroaromatics have been mainly focused on: (1) the Fujiwara-Moritani oxidative Heck-type coupling with simple alkenes,[4] (2) the hydroarylation of alkynes,[5] and (3) the direct C–H alkenylation with alkenyl halides or pseudohalides, more valuable coupling partners than alkenes or alkynes for controlling both the regio- and stereochemistry of this process.[6] Although prefunctionalized halo- or pseudohaloalkenes have been widely investigated [Scheme 1, Equations (1) and (2)], we turn our attention to the attractive acrylic acid derivatives due to their ready availability and easy access to both substituted *E* and *Z* isomers. Recently, the groups of Itami and Xu/Li have reported the first nickel and rhodium-catalyzed decarbonylative/C–H alkenylations of (hetero)arenes using acrylates as alkenylating reagent [Scheme 1, Equation (3)].[7] Herein, we report the first investigation of decarboxylative C–H alkenylation of heterocycles with acrylic acids [Scheme 1, Equation (4)], through a conventional catalytic cross-coupling process that combines the generation of an alkenylcopper intermediate as a transmetallating agent by copper-catalyzed extrusion of CO_2 with the catalytic C–H palladation of the heterocycle (Scheme 1).[8–11]



Scheme 1. Previous [(1)–(3)] and proposed [(4)] methodologies for direct C–H alkenylations of heterocycles using prefunctionalized alkenes.

α-Fluoroacrylic acid has been especially selected to address important challenges in catalytic decarboxylative cross-coupling chemistry, as well as in the attractive field of fluorinated biomolecules.[12] This choice originated indeed, from the following premises: 1) To establish a first proof of concept of direct C–H/C–CO_2H cross-coupling between heterocycles and acrylic acids, we anticipated that α-fluoroacrylic acids would be excellent candidates due to the electron-withdrawing effect of the fluorine atom that may facilitate the *ipso*-decarboxylative metallation process;[13] 2) Our recent successful use of *gem*-bromofluoroalkenes as efficient coupling partners in Pd-catalyzed direct C–H alkenylation of heteroarenes [Scheme 1, Equation (2)] demonstrating that fluoroalkenes are stable under such catalysis compared to their *gem*-dibromo-(dichloro)alkene counterparts leading to alkynylated products;[14] 3) importantly, the monofluoroalkenes[15] are highly valuable organic compounds, which have found many applications as, for example, materials,[16] drugs,[17] and peptidomimetics.[18] Herein, we report the first decarboxylative/C–H alkenylation of heterocycles with various (*E*)- and (*Z*)-α-fluoroacrylic acids offering an innovative step-economical, eco-friendly and

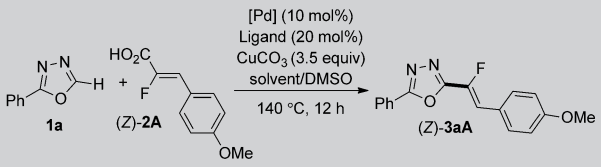
[a] *K. Rousée, Dr. C. Schneider, Dr. S. Couve-Bonnaire, Prof. X. Pannecoucke, Dr. V. Levacher, Prof. C. Hoarau*
Normandie Univ, COBRA, UMR 6014 et FR 3038; Univ Rouen; INSA Rouen; CNRS, IRCOF, 1 rue Tesnière 76821 Mont-Saint-Aignan Cedex (France)
E-mail: samuel.couve-bonnaire@insa-rouen.fr
christophe.hoarau@insa-rouen.fr

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201405119.

general stereocontrolled access to polysubstituted (*E*)- and (*Z*)-heteroaryl fluoroalkenes.

Inspired by recent Pd/Cu-catalyzed decarboxylative C–H arylations,[9] we started to explore the decarboxylative coupling of 1,3,4-oxadiazole **1a** with β-arylated α-fluoroacrylic acid **2A** prepared as pure *Z* isomer. Although any reaction occurred under the strictly Greaney's conditions (Table 1, entry 1),[9a] the use an

Table 1. Pd-catalyzed decarboxylative/C–H fluoroalkenylation under various reaction conditions.[a]

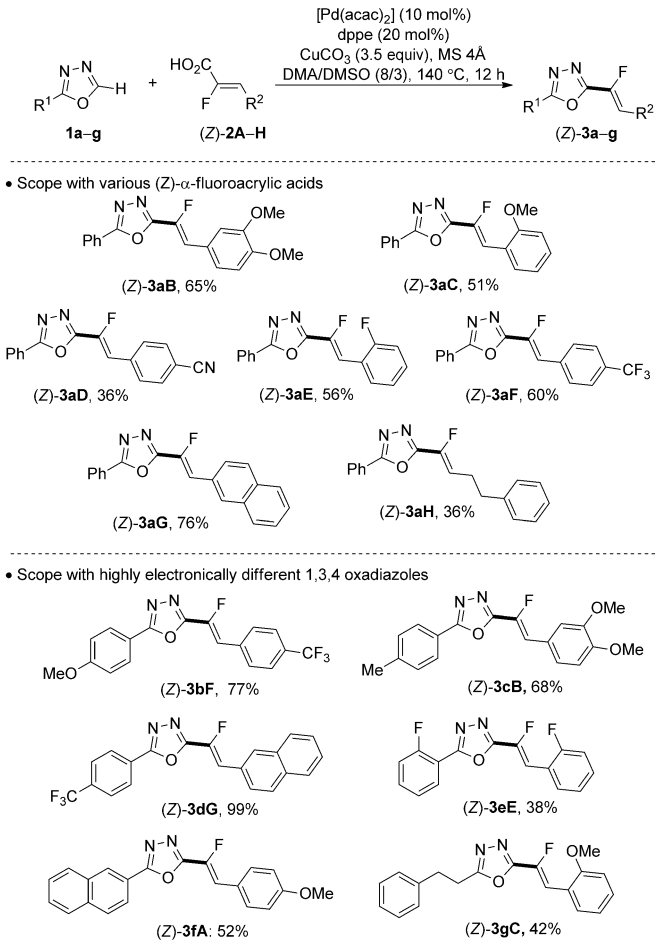


Entry	[Pd]	Ligand	**2A**/**1a** ratio	Solvent	Conc [M]	Yield [%][b]
1	$PdBr_2$	dcpe	1.5:1	1,4-dioxane	0.2	n.r.
2	$PdBr_2$	dcpe	1.5:1	DMA	0.2	42
3	$PdBr_2$	dppe	1.5:1	DMA	0.2	55
4	$[Pd(acac)_2]$	dppe	1.5:1	DMA	0.2	58
5	$[Pd(acac)_2]$	dppe	2:1	DMA	0.1	81, 65[c]

[a] Reaction conditions: [Pd] (10 mol%), ligand (20 mol%), **1a** (0.2 mmol), $CuCO_3$ (3.5 equiv), solvent/DMSO (8:3), MS 4 Å, 140 °C, 12 h. [b] Yield based on isolated product after flash chromatography. [c] Scale up on 1.0 mmol of **1a** under optimized conditions. dcpe = bis(cyclohexylphosphino)ethane, dppe = bis(diphenylphosphino)ethane, DMSO = dimethyl sulfoxide, DMA = dimethylacetamide.

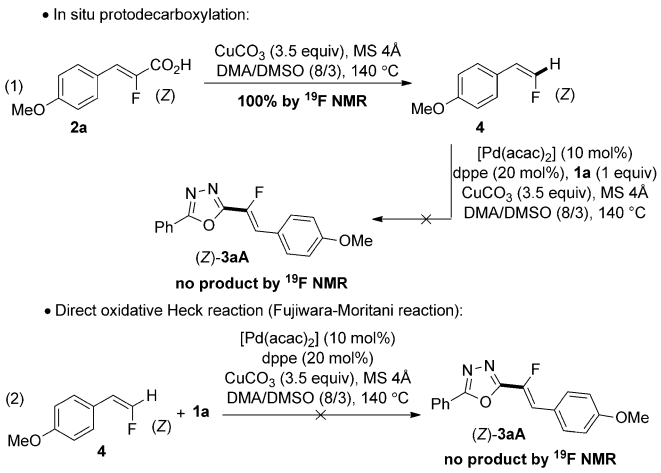
8:3 mixture of dimethylacetamide (DMA) and DMSO allowed us to obtain the desired product isolated in 42% yield (Table 1, entry 2) along with protodecarboxylative product **4** (Scheme 3) as side-product. Hopefully the hampering side process could be significantly and kinetically reduced by using 1,2-bis(diphenylphosphino)ethane (dppe) as ligand (Table 1, entry 3).[19] Common ligands of copper such as phenanthroline, BINAP and 2,2′-bipyridine did not have a beneficial effect on this competitive reaction and the decarboxylative coupling failed with monodentate phosphines.[19] We then performed the reaction with different palladium sources.[19] The best performance of the reaction was thus attained by using $Pd(acac)_2$ as a catalyst alongside increasing both the reaction dilution (0.2 M to 0.1 M)[20] and the amount of α-fluoroacrylic acid (1.5 to 2 equivalents; Table 1, entries 4 and 5). Under these optimized reaction conditions, the heteroarylated fluoroalkene **3aA** was produced in 81% isolated yield as pure *Z* isomer, demonstrating that the reaction proceeds with a complete retention of the stereochemistry. Interestingly, the optimized protocol was also easily scaled up from 0.2 to 1.0 mmol without a significant decrease in yields (Table 1, entry 5).

With these optimal reaction conditions in hand, we focused on the substrate scope of various 1,3,4-oxadiazoles **1a–g** with a broad panel of β-arylated α-fluoroacrylic acids **2A–G**. The electronic effect and the position of the substituents on the aromatic units of both coupling partners **1** and **2** invariably had no influence on the success of the reaction, since the α-fluorooxadiazolylalkenes **3a–f** were isolated in fair to quantitative yields (Scheme 2). In addition, the procedure was also successfully applied with the 5-alkylated 1,3,4-oxadiazole **1g** or the β-alkylated α-fluoroacrylic acid **2H** as coupling partners, indicating that the substituents of the azole and the α-fluoroacrylic acid have little influence on the performance of the reaction.



Scheme 2. Scope of decarboxylative/direct C–H monofluoroalkenylation of **1** with various (*Z*)-α-fluoroacrylic acids (*Z*)-**2**.

Notably, heteroarylated fluoroalkenes **3** were cleanly obtained without any other byproduct than the fluoroalkene **4** arising from the copper-catalyzed decarboxylative protonation side reaction. At this stage, we investigated the ability of the protodecarboxylative fluoroalkene product **4** to react with **1a** through a conventional Fujiwara–Moritani oxidative Heck-type coupling (Scheme 3).[21] To that purpose, the alkene **4** was generated from α-fluoroacrylic acid **2A**[22] and then either (a) allowed to react with **1a** [Scheme 3, Equation (1)] or (b) isolated beforehand and subsequently subjected to an oxidative Heck-type reaction [Scheme 3, Equation (2)]. Both scenarios failed, precluding a two-step mechanism initially involving a protodecarboxylation followed by a Fujiwara–Moritani oxidative Heck-type coupling. These control experiments strongly support the initial working hypothesis depicted in Scheme 1, namely that decarboxylative direct C–H alkenylation reaction would proceed through the expected conventional Pd/Cu bimetallic cat-



Scheme 3. Generation of α-fluoroalkene **4** by protodecarboxylation from **2a** and its evaluation in oxidative Heck-type alkenylation with **1a**.

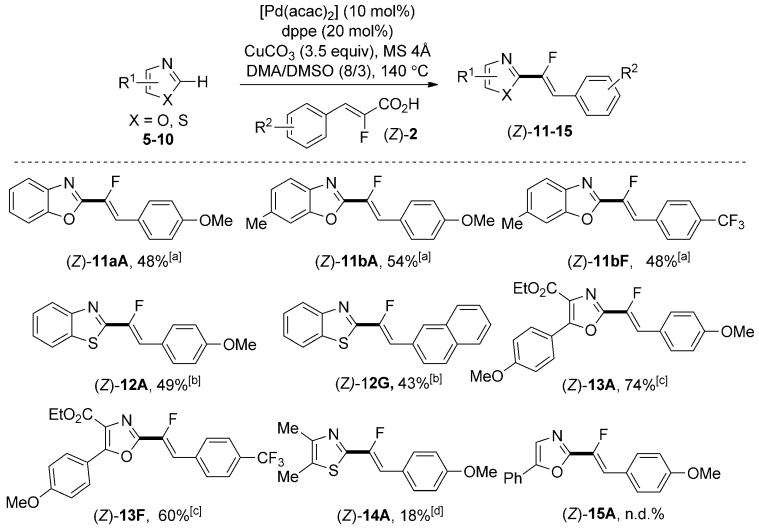
acid (*Z*)-**2A** with somewhat more difficulty leading to the expected (*Z*)-monofluoroathiazolylalkene (*Z*)-**14A** (isolated in 18% yield) with $Pd(TFA)_2$ catalyst whereas no reaction occurred with 5-phenyloxazole. Moreover, the use of harder bases such as Cs_2CO_3 or *t*BuOLi,[19] extensively used in direct C–H coupling of less acidic 1,3-diazoles,[2,23] are not tolerated heightening the protodecarboxylation side-reaction of α-fluoroacrylic acids.

As a final part of the study, we turned our attention to the formation of the monofluoro(hetero)arylalkene as *E* isomers from an enriched mixture of (*E*)-α-fluoroacrylic acids (Scheme 5). Despite the inherent difficulty of the steric hindrance, we found that the optimized procedure for decarboxylative direct C–H alkenylation of 1,3,4-oxadiazoles with (*Z*)-α-fluoroacrylic acids (Scheme 2) remained highly effective with (*E*)-α-fluoroacrylic acids.

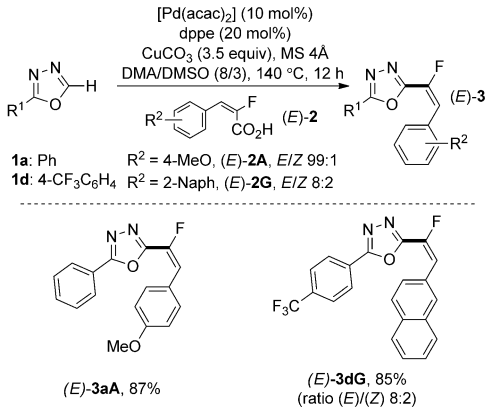
In conclusion, we have demonstrated that α-fluoroacrylic acids could be used as coupling partners in Pd/Cu-catalyzed decarboxylative direct C–H alkenylation with a wide range of

alysis, which is also in accordance with the observation that the reaction occurs with complete retention of stereochemistry at the double bond.

To extend the scope of the methodology, we examined the selective decarboxylative direct C–H fluoroalkenylation of various 1,3-diazoles that are less acidic than the oxazodiazole series (Scheme 4). Benzoxazoles were first selected due to their high acidity in the 1,3-diazoles series. Although low yields were obtained under the above optimized conditions, switching the DMA/DMSO mixed solvent to pure DMSO afforded the expected C-2 monofluoroalkenylated benzoxazoles (*Z*)-**11aA**, (*Z*)-**11bA** and (*Z*)-**11bF** in fair yields, regardless of the highly electronically-different α-fluoroacrylic acids **2A** and **2F** used. Concerning the oxazole series, the activated 4-carboxyoxazole displayed a good reactivity with the two highly electronically-different α-fluoroacrylic acids **2A** and **2F** under the optimized reaction conditions. However, the optimal result was obtained with 1,2-bis(dicyclohexylphosphino)-ethane (dcpe) as a ligand in line with previous observations in this heterocycle series by Greaney and co-workers.[9a] The optimized procedure remained effective for the direct C–H fluoroalkenylation of benzothiazole to produce (*Z*)-**12A** and (*Z*)-**12G** in 49% and 43% yields with CuBr as an additive, which is often used to promote the palladium catalysis cycle (Scheme 1).[23] In that case, the formation of benzothiazolylcopper as intermediate is thus suggested to generate the σ-arylpalladium complex through transmetallation with $Pd(acac)_2$. The less acidic 4,5-dimethylthiazole reacted with α-fluoroacrylic



Scheme 4. Scope of decarboxylative/direct C–H monofluoroalkenylation of various heterocycles (**5**–**10**) with various (*Z*)-α-fluoroacrylic acids (*Z*)-**2**. [a] DMSO (0.1 M). [b] CuBr (10 mol%) was added. [c] dcpe instead of dppe. [d] $Pd(TFA)_2$ (10 mol%), 1,4-dioxane/DMSO.



Scheme 5. Decarboxylative direct C–H monofluoroalkenylation of 1,3,4-oxadiazoles **1a,d** with (*E*)-α-fluoroacrylic acids (*E*)-**2A,G**.

heteroarenes. This innovative methodology is functional-group tolerant, step-economical and proceeds in moderate to good yields. It also proposes an innovative stereo- and regiocontrolled access to (*Z*)- and (*E*)-α-heteroaryl monofluoroalkenes, versatile molecules for further fast and step-economical preparation of fluorinated biomolecules. This work extends the boundaries of the current highly attractive field of catalytic C–H functionalization of molecules since it involves for the first time the acrylic acid series as coupling partners in direct C–H alkenylation.

Acknowledgements

This work has been partially supported by INSA Rouen, Rouen University, CNRS EFRD, Labex SynOrg (ANR-11-LABX-0029).

Keywords: alkenylation · C–H activation · decarboxylation · fluoroalkenes · heterocycles · palladium

[1] For recent reviews see: a) I. V. Seregin, V. Gevorgyan, *Chem. Soc. Rev.* **2007**, *36*, 1173; b) K. Fagnou, *Top. Curr. Chem.* **2009**, *292*, 35; c) I. A. I. Mkhalid, J. H. Barnard, T. B. Marder, J. M. Murphy, J. F. Hartwig, *Chem. Rev.* **2010**, *110*, 890; d) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624; e) C. L. Sun, B.-J. Li, Z.-J. Shi, *Chem. Commun.* **2010**, *46*, 677; f) O. Daugulis, *Top. Curr. Chem.* **2009**, *292*, 57; g) M. Wasa, K. M. Engle, J.-Q. Yu, *Isr. J. Chem.* **2010**, *50*, 605; h) L. Ackermann, H. K. Potukuchi, *Org. Biomol. Chem.* **2010**, *8*, 4503; i) K. Hirano, M. Miura, *Synlett* **2011**, 294; j) P. Herrmann, T. Bach, *Chem. Soc. Rev.* **2011**, *40*, 2022; k) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315; l) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215; m) W. Shi, C. Liu, A. Lei, *Chem. Soc. Rev.* **2011**, *40*, 2761; n) K. M. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res.* **2012**, *45*, 788.

[2] For recent reviews of C–H alkenylation : a) S. Messaoudi, J.-D. Brion, M. Alami, *Eur. J. Org. Chem.* **2010**, *34*, 6495; b) R. Rossi, F. Bellina, M. Lessi, *Synthesis* **2010**, 4131; c) J. Le Bras, J. Muzart, *Chem. Rev.* **2011**, *111*, 1170; d) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780; e) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068; f) S. I. Kozhushkov, L. Ackermann, *Chem. Sci.* **2013**, *4*, 886.

[3] a) P. A. Searle, T. F. Molinski, *J. Am. Chem. Soc.* **1995**, *117*, 8126; b) M. Nett, Ö. Erol, S. Kehraus, M. Kock, A. Krick, E. Eguereva, E. Neu, G. M. König, *Angew. Chem. Int. Ed.* **2006**, *45*, 3863; *Angew. Chem.* **2006**, *118*, 3947; c) M. Velusamy, Y.-C. Hsu, J. T. Lin, C.-W. Chang, C.-P. Hsu, *Chem. Asian J.* **2010**, *5*, 87; d) G. Zhang, F.-I. Wu, X. Jiang, P. Sun, C.-H. Cheng, *Synth. Met.* **2010**, *160*, 1906.

[4] a) E. Capito, J. M. Brown, A. Ricci, *Chem. Commun.* **2005**, 1854; b) N. P. Grimster, C. Gauntlett, C. R. A. Godfrey, M. J. Gaunt, *Angew. Chem. Int. Ed.* **2005**, *44*, 3125; *Angew. Chem.* **2005**, *117*, 3185; c) E. M. Beck, N. P. Grimster, R. Hatley, M. J. Gaunt, *J. Am. Chem. Soc.* **2006**, *128*, 2528; d) S. H. Cho, S. J. Hwang, S. Chang, *J. Am. Chem. Soc.* **2008**, *130*, 9254; e) A. García-Rubia, R. G. Arrayµs, J. C. Carretero, *Angew. Chem. Int. Ed.* **2009**, *48*, 6511; *Angew. Chem.* **2009**, *121*, 6633; f) J. Wu, X. Cui, L. Chen, G. Jiang, Y. Wu, *J. Am. Chem. Soc.* **2009**, *131*, 13888; g) A. García-Rubia, B. Urones, R. G. Arrayás, J. C. Carretero, *Chem. Eur. J.* **2010**, *16*, 9676; h) M. Miyasaka, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2010**, *75*, 5421; i) T. Ueyama, S. Mochida, T. Fukutani, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2011**, *13*, 706; j) Z. Li, L. Ma, C. Tang, J. Xu, X. Wu, H. Yao, *Tetrahedron Lett.* **2011**, *52*, 5643; k) M. Ye, G.-L. Gao, J.-Q. Yu, *J. Am. Chem. Soc.* **2011**, *133*, 6964; l) S. Cui, L. Wojtas, J. C. Antilla, *Org. Lett.* **2011**, *13*, 5040; m) Y. Huang, F. Song, Z. Wang, P. Xi, N. Wu, Z. Wang, J. Lan, J. You, *Chem. Commun.* **2012**, *48*, 2864.

[5] For selected examples in C–H addition of heteroarenes to alkynes, see: a) W. Lu, C. Jia, T. Kitamura, Y. Fujiwara, *Org. Lett.* **2000**, *2*, 2927; b) Y. Nakao, K. S. Kanyiva, S. Oda, T. Hiyama, *J. Am. Chem. Soc.* **2006**, *128*, 8146; c) Y. Nakao, K. S. Kanyiva, T. Hiyama, *J. Am. Chem. Soc.* **2008**, *130*, 2448; d) Y. Nakao, N. Kashihara, K. S. Kanyiva, T. Hiyama, *J. Am. Chem. Soc.* **2008**, *130*, 16170; e) Y. Kuninobu, K. Kikuchi, Y. Tokunaga, K. Takai, *Tetrahedron* **2008**, *64*, 5974; f) C.-C. Tsai, W.-C. Shih, C.-H. Fang, C.-Y. Li, T.-G. Ong, G. P. A. Yap, *J. Am. Chem. Soc.* **2010**, *132*, 11887; g) D. J. Schipper, M. Hutchinson, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 6910; h) R. Gao, C. S. Yi, *J. Org. Chem.* **2010**, *75*, 3144; i) L. L. Suarez, M. F. Greaney, *Chem. Commun.* **2011**, *47*, 7992; j) S. R. Kandukuri, J. A. Schiffner, M. Oestreich, *Angew. Chem. Int. Ed.* **2012**, *51*, 1265; *Angew. Chem.* **2012**, *124*, 1291; k) Z. Ding, N. Yoshikai, *Angew. Chem. Int. Ed.* **2012**, *51*, 4698 – 4701; *Angew. Chem.* **2012**, *124*, 4776; l) J.-R. Huang, Q.-R. Zhang, C.-H. Qu, X.-H. Sun, L. Dong, Y.-C. Chen, *Org. Lett.* **2013**, *15*, 1878.

[6] For selected examples in C–H/C-X alkenylation of heteroarenes, see a) J. Koubachi, S. El Kazzouli, S. Berteina-Raboin, A. Mouaddib, G. Guillaumet, *Synthesis* **2008**, 2537; b) F. Besselièvre, S. Piguel, F. Mahuteau-Betzer, D. Grierson, *Org. Lett.* **2008**, *10*, 4029; c) A. L. Gottumukkala, F. Derridj, S. Djebbar, H. Doucet, *Tetrahedron Lett.* **2008**, *49*, 2926; d) F. Besselièvre, S. Piguel, F. Mahuteau-Betzer, D. S. Grierson, *Org. Lett.* **2008**, *10*, 4029; e) C. Verrier, C. Hoarau, F. Marsais, *Org. Biomol. Chem.* **2009**, *7*, 647; f) J. J. Mousseau, J. A. Bull, A. B. Charrette, *Angew. Chem. Int. Ed.* **2010**, *49*, 1115 – 1118; *Angew. Chem.* **2010**, *122*, 1133; g) S. Sahnoun, S. Messaoudi, J. D. Brion, M. Alami, *Eur. J. Org. Chem.* **2010**, 6097; h) M. Špulák, R. Lubojacký, P. Šenel, J. KuneŠ, M. Pour, *J. Org. Chem.* **2010**, *75*, 241; i) R. Vabre, F. Chevot, M. Legraverend, S. Piguel, *J. Org. Chem.* **2011**, *76*, 9542; j) F. Mahuteau-Betzer, S. Piguel, *Tetrahedron Lett.* **2013**, *54*, 3188.

[7] a) L. Meng, Y. Kamada, K. Muto, J. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed.* **2013**, *52*, 10048; *Angew. Chem.* **2013**, *125*, 10232; b) L. Zhang; R. Qiu, X. Xue, Y. Pan, C. Xu, D. Wang, X. Wang, L. Xu, H. Li, *Chem. Commun.* **2014**, *50*, 12385; R. Qiu, X. Xue, Y. Pan, C. Xu, D. Wang, X. Wang, L. Xu, H. Li, *Chem. Commun.* **2014**, *50*, 12385.

[8] Reviews on the decarboxylative coupling reactions: a) L. J. Gooβen, G. J. Deng, L. M. Levy, *Science* **2006**, *313*, 662; b) O. Baudoin, *Angew. Chem. Int. Ed.* **2007**, *46*, 1373; *Angew. Chem.* **2007**, *119*, 1395; c) S. M. Bonesi, M. Fagnoni, A. Albini, *Angew. Chem. Int. Ed.* **2008**, *47*, 10022; *Angew. Chem.* **2008**, *120*, 10172; d) L. J. Gooβen, N. Rodriguez, K. Gooβen, *Angew. Chem. Int. Ed.* **2008**, *47*, 3100; *Angew. Chem.* **2008**, *120*, 3144; e) L. J. Gooβen, F. Collet, K. Gooβen, *Isr. J. Chem.* **2010**, *50*, 617; f) S. M. Bonesi, M. Fagnoni, *Chem. Eur. J.* **2010**, *16*, 13572; g) R. Shang, L. Liu, *Sci. China Chem.* **2011**, *54*, 1670; h) N. Rodríguez, L. J. Gooβen, *Chem. Soc. Rev.* **2011**, *40*, 5030; i) J. Cornella, I. Larrosa, *Synthesis* **2012**, *44*, 653; j) L. J. Gooβen, K. Gooβen in *Topics in Organometallic Chemistry, Vol. 44: Inventing Reactions* (Ed.: L. J. Gooβen), Springer, Berlin, **2013**, Chapter 6.

[9] The only decarboxylative/C–H (hetero)arylation of azole to have been reported: a) F. Zhang, M. F. Greaney, *Angew. Chem. Int. Ed.* **2010**, *49*, 2768; *Angew. Chem.* **2010**, *122*, 2828; b) K. Xie, Z. Yang, X. Zhou, X. Li, S. Wang, Z. Tan, X. An, C.-C. Guo, *Org. Lett.* **2010**, *12*, 1564.

[10] Only traditional decarboxylative cross-couplings with cinnamic acid have been repported: a) L. J. Gooβen, N. Rodriguez, B. Melzer, C. Linder, G. J. Deng, L. M. Levy, *J. Am. Chem. Soc.* **2007**, *129*, 4824; b) Z. Wang, Q. Ding, X. He, J. Wu, *Org. Biomol. Chem.* **2009**, *7*, 863; c) M. Yamashita, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2010**, *12*, 592; d) M. Yamashita, K. Hirano, T. Satoh, M. Miura, *Adv. Synth. Catal.* **2011**, *353*, 631; e) G. Cahiez, A. Moyeux, M. Poizat, *Chem. Commun.* **2014**, *50*, 8982.

[11] Decarboxylative alkenylation of sp3 C–H bonds via a radical process: a) Z. Cui, X. Shang, X.-F. Shao, Z.-Q. Liu, *Chem. Sci.* **2012**, *3*, 2853; b) H. Yang, P. Sun, Y. Zhu, H. Yan, L. Lu, X. Qu, T. Li, J. Mao, *Chem. Commun.* **2012**, *48*, 7847.

[12] a) T. Hiyama in *Organofluorine Compounds: Chemistry and Applications* (Ed. H. Yamamoto), Springer-Verlag, Berlin, **2000**; b) Approximately 30 – 40% of agrochemicals and 20 – 25% of pharmaceuticals on the market are estimated to contain fluorine: A. M. Thayer, *Chem. Eng. News* **2006**, *84*, 15; Reviews: c) J.-P. Bégué, D. Bonnet-Delphon, *J. Fluorine Chem.* **2006**, *127*, 992; d) K. L. Kirk, *J. Fluorine Chem.* **2006**, *127*, 1013; e) K. Muller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881; f) W. K. Hagmann, *J. Med. Chem.* **2008**, *51*, 4359; g) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320; h) J. Wang, M. Sánchez-Roselló, J.-L. Aceña, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok, H. Liu, *Chem. Rev.* **2014**, *114*, 2432.

[13] a) K. Chuchev, J. J. Belbruno, *Theochem* **2007**, *807*, 1; b) L. J. Gooβen, W. R. Thiel, N. Rodriguez, C. Linder, B. Melzer, *Adv. Synth. Catal.* **2007**, *349*, 2241; c) L. J. Gooβen, C. Linder, N. Rodriguez, P. P. Lange, A. Fromm, *Chem. Commun.* **2009**, *46*, 7173; d) J. Shi, X.-Y. Huang, J.-P. Wang, R. Li, *J. Phys. Chem. A* **2010**, *114*, 6263; e) S.-L. Zhang, Y. Fu, R. Shang, Q.-X. Guo,

L. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 638; f) L. J. Gooβen, N. Rodriguez, C. Linder, P. P. Lange, A. Fromm, *ChemCatChem* **2010**, *2*, 430; g) J. S. Dickstein, J. M. Curto, O. Gutierrez, C. A. Mulrooney, M. C. Kozlowski, *J. Org. Chem.* **2013**, *78*, 4744.

[14] C. Schneider, D. Massi, S. Couve-Bonnaire, X. Pannecoucke, C. Hoarau, *Angew. Chem. Int. Ed.* **2013**, *52*, 3246; *Angew. Chem.* **2013**, *125*, 3328.

[15] a) G. Landelle, N. Bergeron, M.-O. Turcotte-Savard, J.-F. Paquin, *Chem. Soc. Rev.* **2011**, *40*, 2867; b) H. Yanai, T. Taguchi, *Eur. J. Org. Chem.* **2011**, 5939; c) S. Hara, *Top Curr. Chem.* **2012**, *327*, 59.

[16] a) F. Babudri, G. M. Farinola, F. Naso, R. Ragni, *Chem. Commun.* **2007**, 1003; b) F. Babudri, A. Cardone, G. M. Farinola, C. Martinelli, R. Mendichi, F. Naso, M. Striccoli, *Eur. J. Org. Chem.* **2008**, 1977.

[17] Monofluoralkenes as a) antitumoral: S. Osada, S. Sano, M. Ueyama, Y. Chuman, H. Kodama, K. Sakaguchi, *Bioorg. Med. Chem.* **2010**, *18*, 605; b) antimicrobial: Y. Asahina, K. Iwase, F. Iinuma, M. Hosaka, T. ishizaki, *J. Med. Chem.* **2005**, *48*, 3194; c) anti-HIV: S. Oishi, H. Kamitani, Y. Kodera, K. Watanabe, K. Kobayashi, T. Narumi, K. Tomita, H. Ohno, T. Naito, E. Kodama, M. Matsuoka, N. Fujii, *Org. Biomol. Chem.* **2009**, *7*, 2872; d) anti-diabetic: S. D. Edmondson, L. Wei, J. Xu, J. Shang, S. Xu, J. Pang, A. Chaudhary, D. C. Dean, H. He, B. Leiting, K. A. Lyons, R. A. Patel, S. B. Patel, G. Scapin, J. K. Wu, M. G. Beconi, N. A. Thornberry, A. E. Weber, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2409.

[18] a) K. Uneyama, *Organofluorine Chemistry*, Blackwell, Oxford, **2006**; b) S. Couve-Bonnaire, D. Cahard, X. Pannecoucke, *Org. Biomol. Chem.* **2007**, *5*, 1151 and references therein; c) C. Pierry, S. Couve-Bonnaire, L. Guilhaudis, C. Neveu, A. Marotte, B. Lefranc, D. Cahard, I. Segalas-Milazzo, J. Leprince, X. Pannecoucke, *ChemBioChem* **2013**, *14*, 1620.

[19] See the Supporting Information for all details.

[20] F. Klotter, A. Studer, *Angew. Chem. Int. Ed.* **2014**, *53*, 2473.

[21] a) A. Myers, D. Tanaka, M. R. Mannion, *J. Am. Chem. Soc.* **2002**, *124*, 11250; b) N. Sharma, A. Sharma, A. Shard, R. Kumar, ##. Saima, A. K. Sinha, *Chem. Eur. J.* **2011**, *17*, 10350.

[22] First example of protodecarboxylation of (*E*)-α-fluoroacrylic acids: E. Elkik, C. Francesch, *Bull. Chem. Soc. Fr.* **1968**, 1371.

[23] a) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174; b) R. Bellina, R. Rossi, *Tetrahedron* **2009**, *65*, 10269; c) J. Roger, A. L. Gottumukkala, H. Doucet, *ChemCatChem* **2010**, *2*, 20; d) K. Hirano, M. Miura, *Synlett* **2011**, 294; e) C. Verrier, P. Lassalas, L. Théveau, G. Quéguiner, F. Trécourt, F. Marsais, C. Hoarau, *Beilstein J. Org. Chem.* **2011**, *7*, 1584.

Received: September 3, 2014
Published online on October 9, 2014