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Stereospecific Synthesis of Tri- and Tetrasubstituted α-Fluoroacrylates by Mizoroki−Heck Reaction

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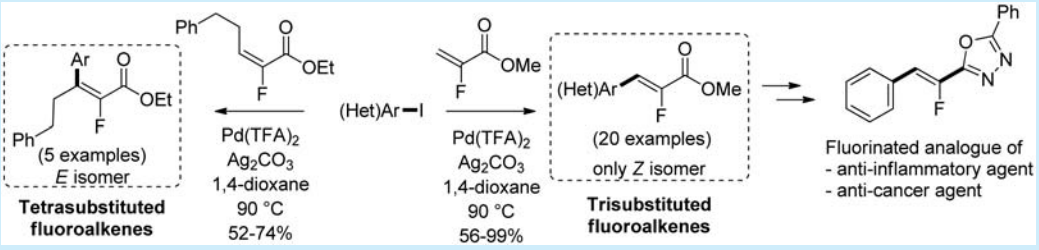
Supporting Information



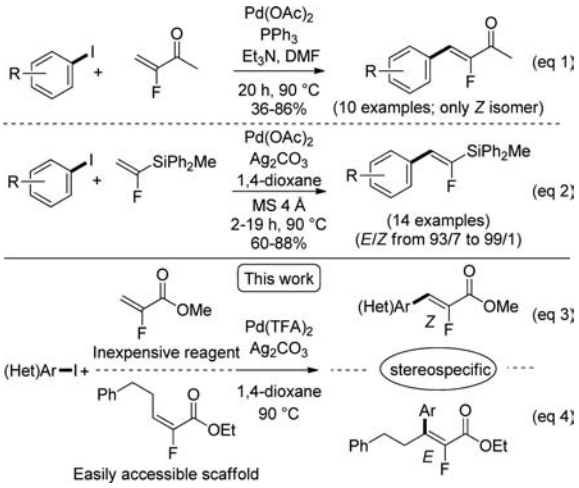
ABSTRACT: Ligand-free, efficient, palladium-catalyzed Mizoroki−Heck reaction between methyl α-fluoroacrylate and arene or hetarene iodides is reported for the first time. The reaction is stereospecific and provides fair to quantitative yields of fluoroalkenes. The Mizoroki−Heck reaction starting from more hindered and usually reluctant trisubstituted acrylate, to access tetrasubstituted fluoroalkenes, is also reported. Finally, the use of a three-step synthesis sequence, including Mizoroki−Heck reaction, allows the synthesis of fluorinated analogues of therapeutic agents with high yield.

Organofluorine chemistry is an area of tremendous expansion, and the market for organofluorine fine chemicals still keeps growing every year.[1] Fluorinated molecules have applications in almost all areas of science and clearly have a crucial impact on everyday life and on modern society. Among the fluoroorganic compounds, the fluoroacrylates have been proven to be versatile compounds that have found many applications in material sciences[2] and medicinal chemistry[3] and can also serve as relevant intermediates in the synthesis of peptidomimetics[4] and drugs.[5]

Common efficient strategies to synthesize α-fluoroacrylates rely almost exclusively on olefination reactions with carbonyl derivatives for which many different experimental procedures have been reported[6] (Wittig-type,[7] Horner−Wadworth−Emmons,[8] Peterson,[5a] Julia−Kocienski,[9] etc.). These reactions can lead to high *E*/*Z* selectivity[10] or very good yields of reaction[7] and more rarely to both excellent yield and selectivity.[8a,11] Moreover, numerous reactions suffer from limitations such as the need for a multistep preparation of the fluorinated reagents,[9,10b−d] the use of expensive reagents,[8] and/or the use of harsh experimental conditions (chromium salt,[11a] highly corrosive $TiCl_4$,[11b] etc.). As part of our ongoing project aimed at developing new catalytic access to fluoroalkene fine chemicals,[12] we turned our attention to an efficient alternative reaction accessing to fluoroacrylates based on the Mizoroki−Heck strategy, a powerful tool to synthesize alkenes.[13] Indeed, despite numerous reactions described with acrylates and derivatives, the Mizoroki−Heck reaction with α-fluoroacrylates has surprisingly been, to our knowledge, reported in a single example, without details about selectivity and yield of reaction, in a patent for the construction of bioactive heterocycles,[14] whereas this reaction could be a general new strategy to construct relevant fluoroalkene building blocks. As a matter of fact, complete methodological studies of the Mizoroki−Heck reaction with aryl halides have only been reported twice to produce monofluoroalkene derivatives (Scheme 1).[15]

Patrick et al.[15a] reported in 2008 the synthesis of 3-fluorobenzalacetone derivatives starting from 3-fluoro-3-buten-

Scheme 1. Mizoroki−Heck Reaction between Aryl Iodides and Fluorinated Alkenes



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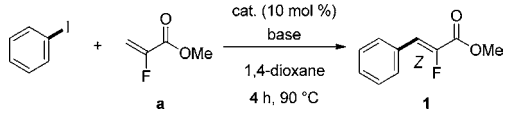
2-one as fluorinated reagent requiring its presynthesis through the formation of chlorofluorocarbene from the ozone depleter Freon-21 (Scheme 1, eq 1). In 2011, Hirotaki and Hanamoto reported the synthesis of β-aryl-(1-fluorovinyl)methyldiphenylsilane from expensive (1-fluorovinyl)methyldiphenylsilane (around \$34/mmol) as fluorinated reagent (Scheme 1, eq 2).[15b] Recently, synthesis of fluoroalkene derivatives ((*Z*)-β-fluoro-β-(trifluoromethyl)styrene) was reported by Liu, Lu, and co-workers through a palladium-catalyzed oxidative Heck reaction.[16] Herein, we report the first stereoselective, efficient synthesis of fluoroacrylate derivatives by a ligand-free Mizoroki–Heck reaction starting from methyl α-fluoroacrylate, a cheap commercially available fluorinated reagent (around \$1/mmol) (Scheme 1, eq 3). We have also succeeded acceding to tetrasubstituted fluorinated alkenes using scarce and reluctant trisubstituted alkenes as coupling partner in the Mizoroki–Heck reaction (Scheme 1, eq 4).

We started the optimization process by carrying out the reaction between α-fluoroacrylate **a** and phenyl iodide (Table 1).

Table 1. Optimization of the Fluoroalkenylation Reaction



entry	Ph-I (equiv)	a (equiv)	cat.	base (equiv)	volume vial (mL)	yield[a] (%)
1	2	1	$Pd(OAc)_2$	Ag_2CO_3 (3)	10	14
2	2	1	**$Pd(TFA)_2$**	Ag_2CO_3 (3)	10	50
3	2	1	$Pd(TFA)_2$	Ag_2CO_3 (3)	**2**	73
4	**1**	**1.5**	$Pd(TFA)_2$	Ag_2CO_3 (3)	2	**99**
5	1	1.5	-	Ag_2CO_3 (3)	2	0
6[b]	1	1.5	$Pd(TFA)_2$	Ag_2CO_3 (3)	2	86
7	1	1.5	$Pd(TFA)_2$	Ag_2CO_3 (**2**)	2	**99**
8	1	1.5	$Pd(TFA)_2$	Ag_2CO_3 (**1**)	2	92
9[c]	1	1.5	$Pd(TFA)_2$	Ag_2CO_3 (2)	2	98

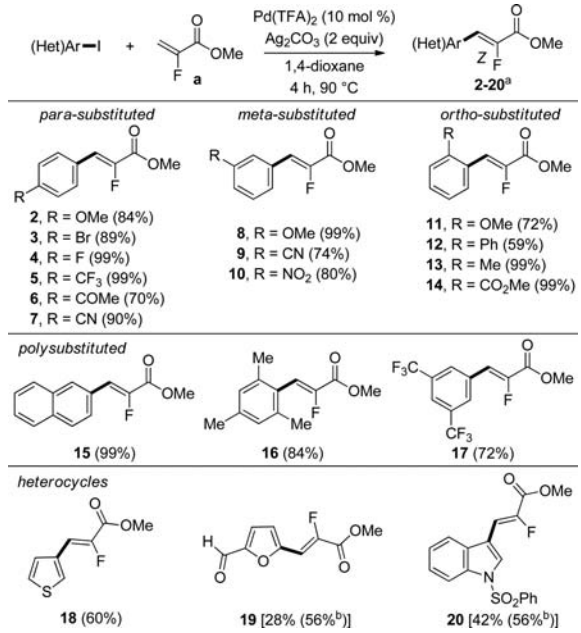
[a]Yield based on isolated product after flash chromatography. [b]5 mol % of $Pd(TFA)_2$. [c]Reaction performed at 60 °C.

The experimental conditions described by Hirotaki and Hanamoto proved to be unsuccessful with a poor 14% yield of reaction (Table 1, entry 1). Among the palladium(II) or -(0) catalysts tested,[17] only the more electrophilic palladium(II)-trifluoroacetate allowed us to prepare **1** with 50% yield (Table 1, entry 2). After a screening of bases, only Ag_2CO_3 proved to be efficient for the reaction to proceed.[17] Taking into account the volatility of the fluorinated reagent **a**, we reduced the size of the reaction's vial, decreasing the gaseous space above the reaction liquid media, allowing us to increase the isolated yield to 73% (Table 1, entry 3). Then, to ensure sufficient quantity of the fluorinated reagent **a** in the media, we changed the number of equivalents of Ph-I/**a** from 2/1 to 1/1.5 resulting in a quantitative yield of **1** (Table 1, entry 4). As expected, the reaction did not proceed in the absence of catalyst (Table 1, entry 5). Decreasing the catalyst loading to 5 mol % allowed to obtain the product **1** in very good 86% yields (Table 1, entry 6). Pleasingly, a quantitative yield was also obtained using 2 equiv of Ag_2CO_3 (Table 1, entry 7), with 1 equiv leading to an interesting 92% yield of **1** (Table 1, entry 8). Finally decreasing the reaction temperature to 60 °C allowed us to obtain an excellent 98% yield of **1** (Table 1, entry 9). It has to be noted that it was not necessary to use dry vials, operate under inert atmosphere, or use molecular sieves[15b] which simplified the process. During all experiments, the methyl 3-phenyl-2-fluoroacrylate **1** was only produced as exclusive *Z*-isomer, no trace of *E*-isomer being observed in ^{19}F NMR of the crude mixture. Typically, a 32–37 Hz coupling constant value between the vinylic proton and the fluorine atom was obtained indicating the corresponding *Z*-configuration.

We also applied our optimized procedure to other phenyl halides (Ph-Br, Ph-Cl) and pseudohalide (Ph-OTf) without success.[17] Finally, using the catalytic system $Pd(TFA)_2$ (10 mol %)/PPh_3 (20 mol %) overnight led to the production of compound **1** in 35% yield from bromobenzene.[17]

We then applied our optimized procedure to substituted aryl and heteroaryl iodides (Scheme 2). For *para*-substituted aryl

Scheme 2. Scope of the Reaction with Substituted Aryl and Hetaryl Iodides



[a]Yield based on isolated product after flash chromatography. [b]Reaction performed overnight (12 h).

iodides, whatever the electronic effect of the substituted moiety, the reaction was efficient giving a range from 70% to quantitative yields. Dihalogenated aryl derivatives revealed to be suitable substrates giving the fluorinated acrylates **3** and **4** in high yields. Interestingly, in the presence of 4-bromophenyl iodide, the reaction was chemoselective furnishing **3** in 89% yields with a reactive C–Br bound for further catalytic reactions. Compounds **6** and **7** bearing a ketone and a nitrile moeties, respectively, which could be easily postfunctionnalized, have also been synthesized in high yields.

Then, *meta*-substituted aryl iodides were studied furnishing good to excellent yields in methyl 3-aryl-2-fluoroacrylates whatever the substitution: methoxy (**8**), cyano (**9**), or nitro (**10**). Finally, *ortho*-substituted aryl iodides were engaged in the reaction with success. For example, valuable methyl 2-carboxylate phenyl iodide reacted to furnish 3-aryl-2-fluoroacrylate **14** in quantitative yield. The reaction proved to be highly efficient and tolerant toward various functional groups. Nevertheless, it has to be noted than the presence of labile hydrogen, i.e., iodophenol, iodoaniline, or iodobenzoic acid, was prohibited. No reaction occurred with those starting materials. Polysubstituted aryl

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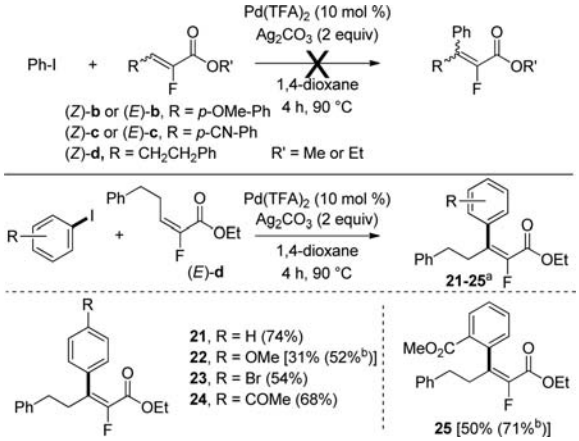
iodides were also suitable substrates, and results were independent of the position as well as of the nature of the substituents borne by the aromatic ring (compounds **15**−**17**). It is noteworthy that the reaction was successfully applied to various heterocyclic iodides. Indeed, 3-iodothiophene gave the corresponding acrylate **18** in a good 60% yield. Valuables 5-carboxaldehyde-2-iodofuran and *N*-protected 3-iodoindole required longer reaction time (12 h) in order to obtain relevant 3-heteroaryl-2-fluoroacrylates **19** and **20** in fair 56% yields. Unfortunately, the reaction failed with 2- and 4-iodopyridines or iodopyrazine. All of the reactions were stereospecific toward the formation of the *Z*-isomer.

Next, we examined the Mizoroki−Heck reaction starting with trisubstituted 2-fluoroacrylates as substrates. Nevertheless, we have to take into account the well-known poor reactivity of disubstituted alkenes for which few examples have been reported so far.[19] In this case, we used trisubstituted olefins for which, to our knowledge, no example of Mizoroki−Heck reaction has been published so far regarding the synthesis of tetrasubstituted olefins. Indeed, only a few works in oxidative Heck reaction leading to tetrasubstituted alkenes have been recently reported in nonfluorinated series.[20] The reaction carried out with (*Z*)- or (*E*)-trisubstituted 3-aryl-2-fluoroacrylates bearing an electron-donating (**b**) or electron-withdrawing group (**c**) in Mizoroki−Heck reaction did not furnish tetrasubstituted fluoroacrylate probably due to steric hindrance (Scheme 3).

Scheme 3. Mizoroki−Heck Reaction with Trisubstituted α-Fluoroacrylates

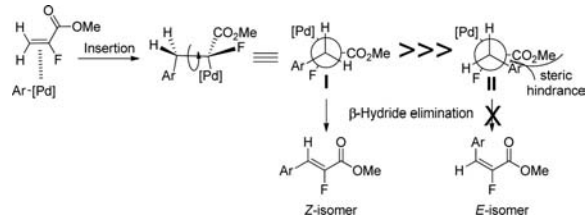


[a]Yield based on isolated product after flash chromatography. [b]Reaction performed overnight (12 h) with a ratio of 2/1 equiv of Ar−I/(*E*)-**d**.

Therefore, we postulated that introducing a less constrained substituent such as an alkyl group should resolve this problem, and so we synthesized and tested the ethyl (*Z*)- and (*E*)-2-fluoro-5-phenylpent-2-enoate **d**. The compound (*Z*)-**d** was unreactive, whereas pleasingly, compound (*E*)-**d** reacted to furnish fair to good yields in the corresponding tetrasubstituted alkenes as (*E*)-isomers. Five tetrasubstituted α-fluoroacrylates **21**−**25** have been synthesized (Scheme 3). To obtain moderate 52% yield of **22** and good 71% yield of **25**, it was necessary to use 2 equiv of aryl iodides with a reaction carried out overnight. These interesting results proved that the Mizoroki−Heck reaction can be used toward the synthesis of tetrasubstituted fluoroalkenes.

At this stage, it is still rather unclear if the mechanism of the reaction is going through a common Pd(II)/Pd(0) catalytic cycle[13a,b] or Pd(II)/Pd(IV) system as proposed by different authors.[18] As far as the stereospecificity is concerned, we can, as assumed in previous reports,[15] postulate that the intermediate **I** is highly favored compared to intermediate **II** because of steric hindrance (Scheme 4). Indeed, the crucial β-hydride elimination

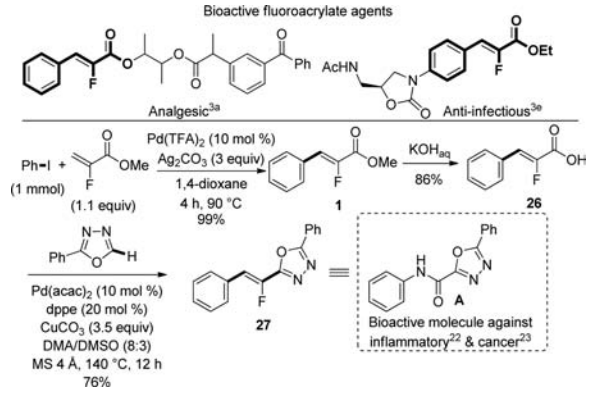
Scheme 4. Geometry Required for the β-H Elimination



requires the Pd−Cα and Cβ−H bonds to be aligned in a *syn* coplanar arrangement[13a,b] and the exclusive formation of trisubstituted alkene *Z*-isomer showed that the sterically demanding ester group, compared to fluorine atom, is pushed away in *trans* relationship with the aryl moiety. Nevertheless, this model did not allow explaining why the trisubstituted fluoroalkene (*E*)-**d** is reactive and not the isomer (*Z*)-**d**. So, a complete survey of the mechanism needs to be undertaken and will be reported in due course.

Finally, the 2-fluoroacrylate derivatives are very relevant compounds which can be used, for example, as therapeutic agents as depicted in Scheme 5.[3a,e] Moreover, taking into account

Scheme 5. Fluoroacrylate-Containing Biomolecules and Synthesis of Fluorinated Analogue of Therapeutic Agents



the electronic and steric similarities of the fluoroalkene moiety with the amide function,[1b,21] our reaction should be used in structure−activity relationship studies and/or to produce fluorinated analogues of biomolecules. In this context, we demonstrated the usefulness of the Mizoroki−Heck reaction by synthesizing a fluorinated analogue of the potent biomolecule **A** against inflammation[22] or various types of cancer.[23] This product could be obtained through a three-step sequence synthesis: (a) a quantitative Mizoroki−Heck reaction, (b) a saponification, and (c) an efficient Pd/Cu-catalyzed decarboxylative/C−H fluoroalkenylation with phenyloxadiazole as partner.[12b] The fluoroanalogue **27** of potent therapeutic agent **A** was thus obtained in 65% overall yield (Scheme 5).

To resume, we have developed an efficient alternative for the production of α-fluoroacrylates commonly synthesized by olefination reactions. Herein we have developed the first ligand-free palladium catalyzed Mizoroki−Heck reaction with

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methyl α-fluoroacrylate as fluorine and alkene sources. The reaction proved to be highly tolerant in regard to numerous organic functionalities, was stereospecific, and importantly, gave good to quantitative yields in fluoroalkenes. Whereas the trisubstituted alkenes did not usually participate in the carbopalladation reaction (reluctant substrates), this reaction have been successfully extended to the use of trisubstituted (*E*)-3-alkyl-2-fluoroacrylate as substrate allowing the formation in fair to good yields of the corresponding tetrasubstituted fluoroacrylates. These results constituted the first example of the Mizoroki−Heck reaction for the synthesis of tetrasubstituted alkenes. Finally, we used this methodology to produce a fluorinated analogue of a therapeutic agent against inflammation and various types of cancer.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b03571.

Experimental procedures, optimization tables, characterization data, and NMR spectra of new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Kirsch, P. *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*; Wiley-VCH: Weinheim, 2013. (b) Uneyama, K. *Organofluorine Chemistry*; Blackwell: Oxford, 2006. (c) O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308. (d) Bégué, J.-P.; Bonnet-Delpon, D. *Bioorganic and Medicinal Chemistry of Fluorine*; John Wiley & Sons, Inc.: Hoboken, NJ, 2008. (e) *Fluorine in Medicinal Chemistry and Chemical Biology*; Ojima, I., Ed.; Wiley-Blackwell: Chichester, UK, 2009.

(2) (a) *Handbook of Fluoropolymer Science and Technology*; Smith, D. W., Iacono, S. T., Iyer, S. S., Eds; John Wiley & Sons, Inc.: Hoboken, NJ, 2014. (b) Cracowski, J.-M.; Montembault, V.; Bosc, D.; Ameduri, B.; Odobel, F.; Fontaine, L. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 1403.

(3) (a) Honda, H.; Sato, S.; Isomae, K.; Ookawa, J.; Kuwamura, T. (SS Pharmaceutical Co.) DE3407806, 1984. (b) Jaeger, E. P.; Jurs, P. C.; Stouch, T. R. E. *Eur. J. Med. Chem.* **1993**, *28*, 275. (c) Hibi, S.; Kikuchi, K.; Yoshimura, H.; Nagai, M.; Tagami, K.; Abe, S.; Hishinuma, I.; Nagakawa, J.; Miyamoto, N. (Eisai Co., Ltd.), WO9613478, 1996. (d) Kaneko, T.; Clark, R.; Ohi, N.; Ozaki, F.; Kawahara, T.; Kamada, A.; Okano, K.; Yokohama, H.; Muramoto, K.; Arai, T.; Ohkuro, M.; Takenaka, O.; Sonoda, J. (Eisai Co., Ltd.) WO9806720, 1998. (e) Wiedeman, P. E.; Djuric, S. W.; Pilushchev, M.; Sciotti, R. J.; Madar, D. J.; Kopecka, H. US20020115669(A1), 2002. (f) Sun, J.; Yang, Y.; Huang, Y. (Chengdu Inst Biology CAS), CN103254053(A), 2013.

(4) (a) Pierry, C.; Couve-Bonnaire, S.; Guilhaudis, L.; Neveu, C.; Marotte, A.; Lefranc, B.; Cahard, D.; Ségalas-Milazzo, I.; Leprince, J.; Pannecoucke, X. *ChemBioChem* **2013**, *14*, 1620. (b) Dutheuil, G.; Pierry, C.; Villiers, E.; Couve-Bonnaire, S.; Pannecoucke, X. *New J. Chem.* **2013**, *37*, 1320.

(5) (a) Welch, J. T.; Lin, J. *Tetrahedron* **1996**, *52*, 291. (b) Van der Veken, P.; Senten, K.; Kertesz, I.; De Meester, I.; Lambeir, A.-M.; Maes, M.-B.; Scharpé, S.; Haemers, L. A.; Augustyns, K. *J. Med. Chem.* **2005**, *48*, 1768. (c) Chang, W.; Mosley, R. T.; Bansal, S.; Keilman, M.; Lam, A. M.; Furman, P. A.; Otto, M. J.; Sofia, M. J. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 2938.

(6) For general reviews about fluoroalkenes dealing with α-fluoroacrylates, see: (a) Landelle, G.; Bergeron, M.; Turcotte-Savard, M. O.; Paquin, J.-F. *Chem. Soc. Rev.* **2011**, *40*, 2867. (b) Yanai, H.; Taguchi, T. *Eur. J. Org. Chem.* **2011**, *2011*, 5939.

(7) Zoute, L.; Dutheuil, G.; Quirion, J.-C.; Jubault, P.; Pannecoucke, X. *Synthesis* **2006**, *2006*, 3409.

(8) (a) Moghadam, G. E.; Penne, J. S. *Bull. Soc. Chim. Fr.* **1985**, 448. (b) Sano, S.; Kuroda, Y.; Saito, K.; Ose, Y.; Nagao, Y. *Tetrahedron* **2006**, *62*, 11881.

(9) Larnaud, F.; Pfund, E.; Linclau, B.; Lequeux, T. *Tetrahedron* **2014**, *70*, 5632 and references cited therein.

(10) (a) Lemonnier, G.; Zoute, L.; Dupas, G.; Quirion, J.-C.; Jubault, P. *J. Org. Chem.* **2009**, *74*, 4124. (b) Satoh, T.; Itoh, N.; Onda, K.-I.; Kitoh, Y.; Yamakawa, K. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2800. (c) Yoshimatsu, M.; Murase, Y.; Itoh, A.; Tanabe, G.; Muraoka, O. *Chem. Lett.* **2005**, *34*, 998. (d) Qian, J.; Yi, W.; Lv, M.; Cai, C. *Synlett* **2014**, *26*, 127.

(11) (a) Barma, D. K.; Kundu, A.; Zhang, H.; Mioskowski, C.; Falck, J. R. *J. Am. Chem. Soc.* **2003**, *125*, 3218. (b) Augustine, J. K.; Bombrun, A.; Venkatachaliah, S.; Jothi, A. *Org. Biomol. Chem.* **2013**, *11*, 8065.

(12) (a) Schneider, C.; Masi, D.; Couve-Bonnaire, S.; Pannecoucke, X.; Hoarau, C. *Angew. Chem., Int. Ed.* **2013**, *52*, 3246. (b) Rousée, K.; Schneider, C.; Couve-Bonnaire, S.; Pannecoucke, X.; Levacher, V.; Hoarau, C. *Chem. - Eur. J.* **2014**, *20*, 15000. (c) Rousée, K.; Schneider, C.; Bouillon, J.-P.; Levacher, V.; Hoarau, C.; Couve-Bonnaire, S.; Pannecoucke, X. *Org. Biomol. Chem.* **2016**, *14*, 353.

(13) (a) Bräse, S.; de Meijere, A. In *Metal-Catalyzed Cross-Coupling Reactions and More*, 1st ed.; de Meijere, A., Bräse, S., Oestreich, M., Eds.; Wiley-VCH: Weinheim, 2014; Vol. 2, pp 533−663. (b) *The Mizoroki−Heck Reaction*; Oestreich, M., Ed.; John Wiley & Sons, Ltd: Chichester, UK, 2009. (c) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.

(14) Taracido, I. C.; Harrington, E. M.; Hersperger, R.; Lattmann, R.; Miltz, W.; Weigand, K. (Novartis Institutes for Biomedical Research) US20090291942(A1), 2009.

(15) (a) Patrick, T. B.; Agboka, T. Y.; Gorrell, K. *J. Fluorine Chem.* **2008**, *129*, 983. (b) Hirotaki, K.; Hanamoto, T. *J. Org. Chem.* **2011**, *76*, 8564.

(16) Li, Y.; Tu, D.-H.; Gu, Y.-J.; Wang, B.; Wang, Y.-Y.; Liu, Z.-T.; Liu, Z.-W.; Lu, J. *Eur. J. Org. Chem.* **2015**, *2015*, 4340.

(17) See the Supporting Information for more details.

(18) (a) Ohff, M.; Ohff, A.; Van der Boom, M. E.; Milstein, D. *J. Am. Chem. Soc.* **1997**, *119*, 11687. (b) Shaw, B. L. *New J. Chem.* **1998**, *22*, 77. (c) Sundermann, A.; Uzan, O.; Martin, J. M. L. *Chem. - Eur. J.* **2001**, *7*, 1703. (d) Yao, Q.; Kinney, E. P.; Yang, Z. *J. Org. Chem.* **2003**, *68*, 7528.

(19) (a) Moreno-Mañas, M.; Perez, M.; Pleixats, R. *Tetrahedron Lett.* **1996**, *37*, 7449. (b) Gürtler, C.; Buchwald, S. L. *Chem. - Eur. J.* **1999**, *5*, 3107. (c) Calo, V.; Nacci, A.; Monopoli, A.; Laera, S.; Cioffi, N. *J. Org. Chem.* **2003**, *68*, 2929. (d) Calo, V.; Nacci, A.; Monopoli, A.; Cotugno, P. *Angew. Chem., Int. Ed.* **2009**, *48*, 6101. (e) Gottumukkala, A. L.; de Vries, J. G.; Minnaard, A. J. *Chem. - Eur. J.* **2011**, *17*, 3091. (f) Xu, D.; Lu, C.; Chen, W. *Tetrahedron* **2012**, *68*, 1466.

(20) (a) Lee, H. S.; Kim, K. H.; Kim, S. H.; Kim, J. N. *Adv. Synth. Catal.* **2012**, *354*, 2419. (b) He, Z.; Kirchberg, S.; Frohlich, R.; Studer, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 3699. (c) He, Z.; Wibbeling, B.; Studer, A. *Adv. Synth. Catal.* **2013**, *355*, 3639. (d) Gigant, N.; Quintin, F.; Bäckvall, J. E. *J. Org. Chem.* **2015**, *80*, 2796.

(21) Couve-Bonnaire, S.; Cahard, D.; Pannecoucke, X. *Org. Biomol. Chem.* **2007**, *5*, 1151 and references therein.

(22) Singh, A. K.; Parthsarthy, R.; Lohani, M. *J. Chem. Pharm. Res.* **2012**, *4*, 779.

(23) Chinnaiyan, A. M.; Lnu, S.; Cao, Q. (The Regents of the University of Michigan) WO2011103016(A2), 2011.

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