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Visible-Light-Induced Hydrodifluoromethylation of Alkenes with a Bromodifluoromethylphosphonium Bromide

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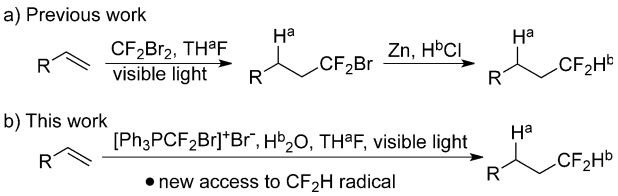
Abstract: *Bromodifluoromethylphosphonium bromide was solely used as the precursor of difluorocarbene. Herein, an unprecedented visible-light-induced hydrodifluoromethylation of alkenes with bromodifluoromethylphosphonium bromide using H_2O and THF as hydrogen sources for the synthesis of difluoromethylated alkanes is described. This difluoromethylation is characterized by mild reaction conditions, ready availability of reagents, and excellent functional-group tolerance.*

Hydroalkylation of alkenes is a fundamentally important transformation, as alkenes are among the most abundant carbon feedstocks in organic synthesis.[1] This reaction provides one of the most powerful methods for the formation of C–C bonds and has been widely used in the synthesis of high-value compounds.[2] Because of the importance of fluorine substitution onto small molecules for the pharmaceutical, agrochemical, and materials industries,[3] hydrofluoroalkylation of alkenes is of particular interest for the preparation of fluoroalkyl-substituted alkanes. Recently, hydrotrifluoromethylation[4] and hydroperfluoroalkylation[5] of alkenes have been well studied. The difluoromethyl group (CF_2H) is known to be isosteric and isopolar with the hydroxy (OH)[6] and thiol (SH)[7] units, and acts as a lipophilic hydrogen-bond donor.[8] Therefore, the hydroxyl, amino, and thio substituents of lead structures are routinely replaced by CF_2H group in drug discovery.[9] Accordingly, significant advances in the introduction of the CF_2H group into organic compounds,[10] including electrophilic,[11] nucleophilic,[12] and free-radical[13] difluoromethylation reactions, have been achieved. Among these reactions, the radical process is preferred for hydrodifluoromethylation of alkenes. Normally HCF_2SO_2Cl and its derivatives, difluoromethylsulfinate salts, are used as the CF_2H radical sources for radical difluoromethylation reactions.[13] However, these difluoromethylating reagents are prepared from gaseous HCF_2Cl through several steps.[13a,14] Therefore, a simple and practical access to the CF_2H radical sources is highly desired.

Recently, visible-light photoredox catalysis has been widely used in the preparation of fluorinated compounds.[15–17] Very recently, our group developed a visible-light-induced hydrobromodifluoromethylation of alkenes with CF_2Br_2 (Scheme 1 a).[17f] During this study, we found that the handling



Scheme 1. Visible-light-induced hydrodifluoromethylation of alkenes. THF = tetrahydrofuran.

process of the volatile CF_2Br_2 (bp. 24.5 °C) was cumbersome. Therefore, we wondered if it was possible to replace CF_2Br_2 with easily handled solid reagents, such as bromodifluoromethylphosphonium salts developed by Burton.[18] In continuation of our research interest in fluoroalkylation of alkenes,[4a,16g,17f,19] we herein disclose a visible-light-induced hydrodifluoromethylation of alkenes with bromodifluoromethylphosphonium bromide for the direct and efficient synthesis of the difluoromethylated alkanes, which are usually obtained by several steps (Scheme 1 b).[13d,17f,20] Importantly, this work represents an unprecedented and practical method of CF_2H radical generation from fluorinated phosphonium salts.

Bromodifluoromethylphosphonium bromide was prepared from the reaction of PPh_3 and CF_2Br_2 in quantitative yield more than 40 years ago.[21] This reagent has been solely used as a precursor of difluorocarbene since then.[18,22] We considered that it might act as a bromodifluoromethylating reagent under visible-light irradiation. To test our idea, 4-phenyl-1-butene (**1a**) was chosen as the model substrate to react with bromodifluoromethylphosphonium bromide under visible-light irradiation in the presence of common photoredox catalysts (Scheme 2). We were excited to find that bromodifluoromethylphosphonium bromide could transfer the CF_2Br group to **1a** to give the bromodifluoromethylated products **2a** and **3a**. To the best of our knowledge, this is the first example of using fluoroalkylphosphonium salts as the fluoroalkylating reagents. We speculated that the CF_2Br radical was involved in this transformation. As shown in Scheme 2, a single electron transfer (SET) from the excited-state photoredox catalyst to bromodifluoromethylphosphonium bromide gives the CF_2Br radical, which then reacts with **1a** to afford **2a** and **3a**. Surprisingly, the difluormethylated

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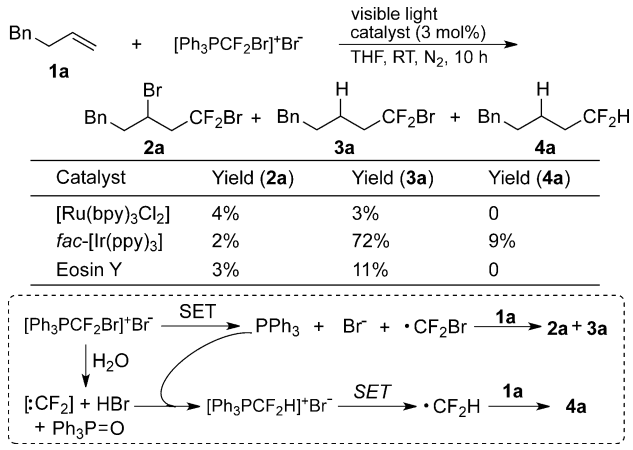


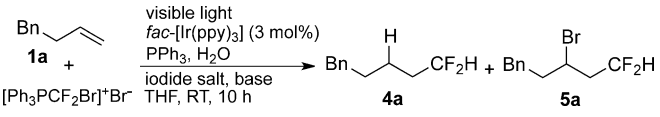
Catalyst	Yield (**2a**)	Yield (**3a**)	Yield (**4a**)
$[Ru(bpy)_3Cl_2]$	4%	3%	0
fac-$[Ir(ppy)_3]$	2%	72%	9%
Eosin Y	3%	11%	0

Scheme 2. Visible-light-induced bromodifluoromethylation of alkene **1a**. bpy = 4,4′-bipyridine, ppy = 2-phenylpyridine.

product **4a** was formed in 9% yield when *fac*-$[Ir(ppy)_3]$ was used as the photoredox catalyst. We surmized that **4a** was probably formed via the CF_2H radical (Scheme 2). First, bromodifluoromethylphosphonium bromide reacts with a trace amount of water in THF to give difluorocarbene, hydrogen bromide, and triphenylphosphine oxide.[23] Then, the reaction of difluorocarbene with hydrogen bromide and triphenylphosphane affords difluoromethylphosphonium bromide,[24] which subsequently undergoes a SET to give the active CF_2H radical. Finally the addition of CF_2H radical to **1a** yields **4a**.

Considering the importance of the difluormethylated compounds in drug discovery, we turned our attention to the difluoromethylation of alkenes with bromodifluoromethylphosphonium bromide. The proposed reaction mechanism clearly showed that both H_2O and PPh_3 were important for the formation of **4a** (Scheme 2). In fact, when H_2O and PPh_3 were added to the reaction mixture, neither **2a** nor **3a** was detected, and the difluormethylated compounds **4a** and **5a** were formed in 34% and 4% yields, respectively (Table 1, entry 1). To our delight, **4a** was selectively formed in moderate yields in the presence of iodide salts (entries 2–4). Among them, NaI gave the highest yield of 67%. Finally, the yield of **4a** was slightly improved (entries 5 and 6) when $KHCO_3$ and K_3PO_4 were added to the reaction mixture to neutralize the generated HBr (Scheme 2).

Table 1: Optimization of reaction conditions of difluoromethylation.[a]



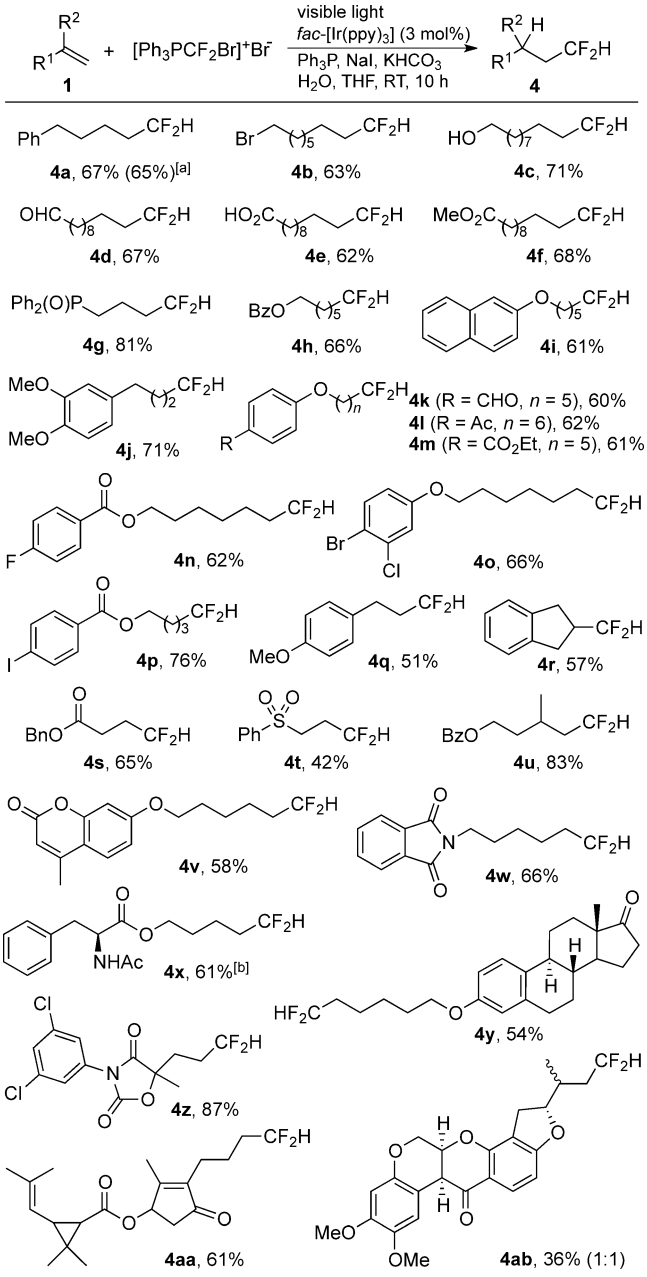
Entry	Iodide salt	Base	Yield [%][b]	
			4a	**5a**
1	–	–	34	4
2	nBu_4NI	–	51	0
3	KI	–	47	0
4	NaI	–	67	0
5	NaI	$KHCO_3$	72	0
6	NaI	K_3PO_4	70	0

[a] Reaction conditions: **1a** (0.1 mmol), bromodifluoromethylphosphonium bromide (0.5 mmol), *fac*-$[Ir(ppy)_3]$ (0.003 mmol), PPh_3 (0.5 mmol), H_2O (1.0 mmol), iodide salt (0.5 mmol), base (0.5 mmol), THF (2.0 mL), visible light, room temperature, under N_2, 10 h. [b] Yield determined by ^{19}F NMR spectroscopy using trifluoromethoxybenzene as an internal standard.

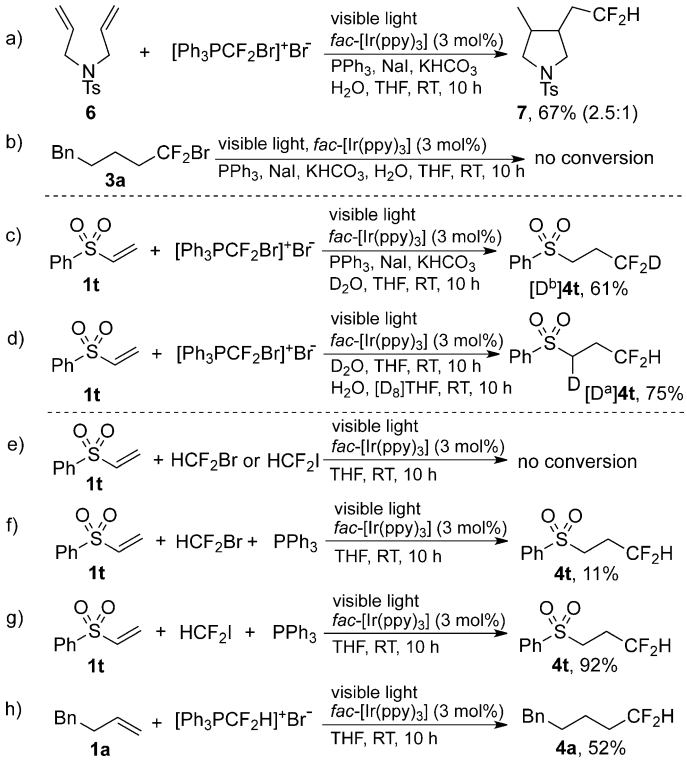
With the established optimal reaction conditions in hand (Table 1, entry 5), we next engaged in expanding the substrate scope of the visible-light-induced hydrodifluoromethylation of alkenes. A variety of terminal alkenes (**1**) were transformed into the corresponding products **4** in moderate to good yields (Scheme 3). Various functional groups including hydroxy, ether, aldehyde, carboxylic acid, ester, bromide, and phosphine oxide were well tolerated (**1b–m**). Styrenes (**1q** and **1r**), the α,β-unsaturated ester **1s**, and the α,β-unsaturated sulfone **1t** reacted effectively to afford the corresponding products in moderate yields. Moreover, the geminally disubstituted alkene **1u** exhibited good reactivity in this transformation. However, the reaction of internal alkenes gave the desired products in very low yields. It was noteworthy that this reaction allowed the direct hydrodifluoromethylation of complex starting materials such as derivatives of 4-methylumbelliferone (**1v**), phthalimide (**1w**), L-phenylalanine (**1x**), and estrone (**1y**). To further extend the application of this protocol, several biologically active compounds including one fungicide (Vinclozolin; **1z**) and two insecticides (Allethrin; **1aa** and Rotenone; **1ab**) were tested. Gratifyingly, these compounds were transformed into the hydrodifluoromethylated products **4z–ab** in moderate yields. To demonstrate the practicality of this reaction, the hydrodifluoromethylation of **1a** on a 10.0 mmol scale proceeded smoothly to give **4a** in 65% yield (1.20 g).

A series of experiments were performed to gain insight into the reaction mechanism. Firstly, the reaction of the diene **6** provided the cyclized product **7** in moderate yield with a moderate d.r. value (Scheme 4a). This result revealed that this transformation proceeded through a radical process. When **3a** was subjected to the standard reaction conditions, no reaction was observed (Scheme 4b), thus showing that **4** was not formed from the intermediate **3**. Then, the reaction of **1s** was performed with D_2O and $[D_8]$THF respectively (Schemes 4c and 4d). The exclusive formation of the deuterated products $[D^b]$**4t** and $[D^a]$**4t** unambiguously confirmed that H_2O serves as the hydrogen source of difluoromethyl group and one of the hydrogen atoms of THF is transferred to the alkene. No reaction happened when **1t** was treated with either bromodifluoromethane or iododifluoromethane (Scheme 4e), whereas the reaction of **1t** and either bromodifluoromethane or iododifluoromethane in the presence of PPh_3 afforded **4t** in low to excellent yields (Schemes 4f and g). Furthermore, the hydrodifluoromethylation of **1a** with difluoromethylphosphonium bromide[18] gave **4a** in 52% yield (Scheme 4h). These results demonstrate that the active intermediate was difluoromethylphosphonium salt.

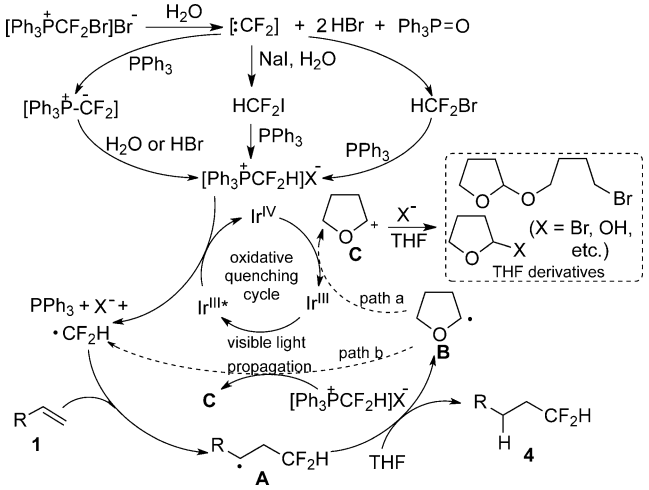
On basis of these experiments, a plausible reaction mechanism was shown in Scheme 5. The reaction of bromodifluoromethylphosphonium bromide with H_2O gives difluorocarbene,[23] which is then converted into HCF_2I and HCF_2Br. Both of these two compounds react with PPh_3 to



Scheme 3. Substrate scope of hydrodifluoromethylation of alkenes. Yields are those of the isolated products. Reaction conditions: **1** (0.5 mmol), bromodifluoromethylphosphonium bromide (2.5 mmol), *fac*-[Ir(ppy)$_3$] (0.015 mmol), PPh_3 (2.5 mmol), H_2O (5.0 mmol), NaI (2.5 mmol), $KHCO_3$ (2.5 mmol), THF (10.0 mL), visible light, room temperature, under N_2, 10 h. [a] **1a** (10.0 mmol). [b] The starting material **1w** is an N-Boc protected phenylalanine derivative. The substrate **1w** was treated under the standard reaction conditions with subsequent protection with acetyl group gave product **4w**.



Scheme 4. Mechanistic investigations. Ts = 4-toluenesulfonyl.



Scheme 5. Proposed reaction mechanism.

give the corresponding difluoromethylphosphonium salts. Alternatively, difluorocarbene might be captured by PPh_3 to give difluoromethylene ylide,[24] which was then treated with either H_2O or HBr to produce difluoromethylphosphonium salts. The irradiation of visible-light excited *fac*-[Ir^{III}(ppy)$_3$] to *fac*-[Ir^{III}(ppy)$_3$]*. Then, a SET from *fac*-[Ir^{III}(ppy)$_3$]* to the difluoromethylphosphonium salts generates the CF_2H radical, which subsequently adds to the alkene **1** for the formation of the radical intermediate **A**. Finally, **A** abstracts a hydrogen from THF to give the hydrodifluoromethylated product **4** and radical intermediate **B**. The intermediate **B** may be oxidized by either *fac*-[Ir^{IV}(ppy)$_3$] (path a, oxidative quenching cycle) or difluoromethylphosphonium salts[25] (path b, propagation) to give the cation intermediate **C**,[26] which is then converted into the THF derivatives (for details see the Supporting Information).

In conclusion, we have developed the a new application of bromodifluoromethylphosphonium bromide as a difluoro-

methylation agent. The visible-light-induced reaction of alkenes with bromodifluoromethylphosphonium bromide in the presence of PPh_3, H_2O, and THF provided efficient access to the hydrodifluoromethylated alkanes. The in situ generated difluoromethylphosphonium salt and CF_2H radical are involved in this transformation.

Keywords: alkenes · fluorine · photoredox catalysis · radicals · synthetic methods

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[1] *The Chemistry of Double Bonded Functional Groups* (Ed.: S. Patai), Wiley, Chichester, **1997**.
[2] For selected reviews, see: a) B. B. Snider, *Chem. Rev.* **1996**, *96*, 339; b) A. R. Chianese, S. J. Lee, M. R. Gagné, *Angew. Chem. Int. Ed.* **2007**, *46*, 4042; *Angew. Chem.* **2007**, *119*, 4118; c) F. Dénès, A. Pérez-Luna, F. Chemla, *Chem. Rev.* **2010**, *110*, 2366.
[3] For selected reviews, see: a) K. Müller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881; b) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320; c) W. K. Hagmann, *J. Med. Chem.* **2008**, *51*, 4359; d) N. A. Meanwell, *J. Med. Chem.* **2011**, *54*, 2529.
[4] a) X. Wu, L. Chu, F.-L. Qing, *Angew. Chem. Int. Ed.* **2013**, *52*, 2198; *Angew. Chem.* **2013**, *125*, 2254; b) H. Egami, R. Shimizu, S. Kawamura, M. Sodeoka, *Angew. Chem. Int. Ed.* **2013**, *52*, 4000; *Angew. Chem.* **2013**, *125*, 4092; c) D. J. Wilger, N. J. Gesmundo, D. A. Nicewicz, *Chem. Sci.* **2013**, *4*, 3160; d) S. Mizuta, S. Verhoog, K. M. Engle, T. Khotavivattana, M. O. Duill, K. Wheelhouse, G. Rassias, M. Médebielle, V. Gouverneur, *J. Am. Chem. Soc.* **2013**, *135*, 2505; e) P. Yu, J.-S. Lin, L. Li, S.-C. Zheng, Y.-P. Xiong, L.-J. Zhao, B. Tan, X.-Y. Liu, *Angew. Chem. Int. Ed.* **2014**, *53*, 11890; *Angew. Chem.* **2014**, *126*, 12084.
[5] a) S. Barata-Vallejo, A. Postigo, *J. Org. Chem.* **2010**, *75*, 6141; b) S. Sumino, A. Fusano, I. Ryu, *Org. Lett.* **2013**, *15*, 2826; c) C. Yu, N. Iqbal, S. Park, E. J. Cho, *Chem. Commun.* **2014**, *50*, 12884; d) P. Dudziński, A. V. Matsnev, J. S. Thrasher, G. Haufe, *Org. Lett.* **2015**, *17*, 1078.
[6] a) J. A. Erickson, J. I. McLoughlin, *J. Org. Chem.* **1995**, *60*, 1626; b) Y. Xu, L. Qian, A. V. Pontsler, T. M. McIntyre, G. D. Prestwich, *Tetrahedron* **2004**, *60*, 43; c) M. A. Chowdhury, K. R. A. Abdellatif, Y. Dong, D. Das, M. R. Suresh, E. E. Knaus, *J. Med. Chem.* **2009**, *52*, 1525.
[7] F. Narjes, K. F. Koehler, U. Koch, B. Gerlach, S. Colarusso, C. Steinkühler, M. Brunetti, S. Altamura, R. De Francesco, V. G. Matassa, *Bioorg. Med. Chem. Lett.* **2002**, *12*, 701.
[8] a) G. K. S. Prakash, M. Mandal, S. Schweizer, N. A. Petasis, G. A. Olah, *J. Org. Chem.* **2002**, *67*, 3718; b) Y. Li, J. Hu, *Angew. Chem. Int. Ed.* **2005**, *44*, 5882; *Angew. Chem.* **2005**, *117*, 6032; c) G. K. S. Prakash, C. Weber, S. Chacko, G. A. Olah, *Org. Lett.* **2007**, *9*, 1863.
[9] a) W. F. Goure, K. L. Leschinsky, S. J. Wratten, J. P. Chupp, *J. Agric. Food Chem.* **1991**, *39*, 981; b) S. Kaneko, T. Yamazaki, T. Kitazume, *J. Org. Chem.* **1993**, *58*, 2302.
[10] a) J. Hu, W. Zhang, F. Wang, *Chem. Commun.* **2009**, 7465; b) Y. Lu, C. Liu, Q.-Y. Chen, *Curr. Org. Chem.* **2015**, *19*, 1638.
[11] a) T. Iida, R. Hashimoto, K. Aikawa, S. Ito, K. Mikami, *Angew. Chem. Int. Ed.* **2012**, *51*, 9535; *Angew. Chem.* **2012**, *124*, 9673; b) P. S. Fier, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2013**, *52*, 2092; *Angew. Chem.* **2013**, *125*, 2146; c) L. Li, F. Wang, C. Ni, J. Hu, *Angew. Chem. Int. Ed.* **2013**, *52*, 12390; *Angew. Chem.* **2013**, *125*, 12616; d) C. S. Thomoson, W. R. Dolbier, Jr., *J. Org. Chem.* **2013**, *78*, 8904; e) V. V. Levin, A. A. Zemtsov, M. I. Struchkova, A. D. Dilman, *Org. Lett.* **2013**, *15*, 917; f) G. Liu, X. Wang, X. Xu, X. Lu, E. Tokunaga, S. Tsuzuki, N. Shibata, *Org. Lett.* **2013**, *15*, 1044; g) B. Pégot, C. Urban, A. Bourne, T. N. Le, S. Bouvet, J. Marrot, P. Diter, E. Magnier, *Eur. J. Org. Chem.* **2015**, 3069.
[12] a) G. K. S. Prakash, S. K. Ganesh, J.-P. Jones, A. Kulkarni, K. Masood, J. K. Swabeck, G. A. Olah, *Angew. Chem. Int. Ed.* **2012**, *51*, 12090; *Angew. Chem.* **2012**, *124*, 12256; b) P. S. Fier, J. F. Hartwig, *J. Am. Chem. Soc.* **2012**, *134*, 5524; c) X. Shen, W. Zhang, C. Ni, Y. Gu, J. Hu, *J. Am. Chem. Soc.* **2012**, *134*, 16999; d) X.-L. Jiang, Z.-H. Chen, X.-H. Xu, F.-L. Qing, *Org. Chem. Front.* **2014**, *1*, 774; e) C. Matheis, K. Jouvin, L. J. Goossen, *Org. Lett.* **2014**, *16*, 5984; f) V. V. Levin, A. L. Trifonov, A. A. Zemtsov, M. I. Struchkova, D. E. Arkhipov, A. D. Dilman, *Org. Lett.* **2014**, *16*, 6256.
[13] a) Y. Fujiwara, J. A. Dixon, R. A. Rodriguez, R. D. Baxter, D. D. Dixon, M. R. Collins, D. G. Blackmond, P. S. Baran, *J. Am. Chem. Soc.* **2012**, *134*, 1494; b) Z. Li, Z. Cui, Z.-Q. Liu, *Org. Lett.* **2013**, *15*, 406; c) X.-J. Tang, C. S. Thomoson, W. R. Dolbier, Jr., *Org. Lett.* **2014**, *16*, 4594; d) X.-J. Tang, W. R. Dolbier, Jr., *Angew. Chem. Int. Ed.* **2015**, *54*, 4246; *Angew. Chem.* **2015**, *127*, 4320; e) C. S. Thomoson, X.-J. Tang, W. R. Dolbier, Jr., *J. Org. Chem.* **2015**, *80*, 1264; f) Z. He, P. Tan, C. Ni, J. Hu, *Org. Lett.* **2015**, *17*, 1838; g) Z. Zhang, X. Tang, C. S. Thomoson, W. R. Dolbier, Jr., *Org. Lett.* **2015**, *17*, 3528.
[14] S.-J. Laurent, WO 2004/002951A2, **2004**.
[15] a) K. Zeitler, *Angew. Chem. Int. Ed.* **2009**, *48*, 9785; *Angew. Chem.* **2009**, *121*, 9969; b) T. P. Yoon, M. A. Ischay, J. Du, *Nat. Chem.* **2010**, *2*, 527; c) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102; d) J. Xuan, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 6828; *Angew. Chem.* **2012**, *124*, 6934; e) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322; f) D. A. Nicewicz, T. M. Nguyen, *ACS Catal.* **2014**, *4*, 355.
[16] a) J. D. Nguyen, J. W. Tucker, M. D. Konieczynska, C. R. J. Stephenson, *J. Am. Chem. Soc.* **2011**, *133*, 4160; b) D. A. Nagib, D. W. C. MacMillan, *Nature* **2011**, *480*, 224; c) Y. Yasu, T. Koike, M. Akita, *Angew. Chem. Int. Ed.* **2012**, *51*, 9567; *Angew. Chem.* **2012**, *124*, 9705; d) Y. Ye, M. S. Sanford, *J. Am. Chem. Soc.* **2012**, *134*, 9034; e) P. Xu, J. Xie, Q. Xue, C. Pan, Y. Cheng, C. Zhu, *Chem. Eur. J.* **2013**, *19*, 14039; f) N. Iqbal, J. Jung, S. Park, E. J. Cho, *Angew. Chem. Int. Ed.* **2014**, *53*, 539; *Angew. Chem.* **2014**, *126*, 549; g) Q.-Y. Lin, X.-H. Xu, F.-L. Qing, *J. Org. Chem.* **2014**, *79*, 10434; h) D. Cantillo, O. de Frutos, J. A. Rincón, C. Mateos, C. O. Kappe, *Org. Lett.* **2014**, *16*, 896; i) A. Carboni, G. Dagousset, E. Magnier, G. Masson, *Org. Lett.* **2014**, *16*, 1240; j) S. H. Oh, Y. R. Malpani, N. Ha, Y.-S. Jung, S. B. Han, *Org. Lett.* **2014**, *16*, 1310; k) J. W. Beatty, J. J. Douglas, K. P. Cole, C. R. J. Stephenson, *Nat. Commun.* **2015**, *6*, 7919; l) R. Tomita, T. Koike, M. Akita, *Angew. Chem. Int. Ed.* **2015**, *54*, 12923; *Angew. Chem.* **2015**, *127*, 13115.
[17] a) Q.-Y. Lin, L. Chu, F.-L. Qing, *Chin. J. Chem.* **2013**, *31*, 885; b) J. Jung, E. Kim, Y. You, E. J. Cho, *Adv. Synth. Catal.* **2014**, *356*, 2741; c) M. Rueda-Becerril, O. Mahé, M. Drouin, M. B. Majewski, J. G. West, M. O. Wolf, G. M. Sammis, J.-F. Paquin, *J. Am. Chem. Soc.* **2014**, *136*, 2637; d) Y.-M. Su, Y. Hou, F. Yin, Y.-M. Xu, Y. Li, X. Zheng, X.-S. Wang, *Org. Lett.* **2014**, *16*, 2958; e) L. Wang, X.-J. Wei, W.-L. Jia, J.-J. Zhong, L.-Z. Wu, Q. Liu, *Org. Lett.* **2014**, *16*, 5842; f) Q.-Y. Lin, X.-H. Xu, F.-L. Qing, *Org. Biomol. Chem.* **2015**, *13*, 8740; g) A. Singh, J. J. Kubik, J. D. Weaver, *Chem. Sci.* **2015**, *6*, 7206.
[18] D. J. Burton, *J. Fluorine Chem.* **1983**, *23*, 339.
[19] a) L. Chu, F.-L. Qing, *Org. Lett.* **2012**, *14*, 2106; b) X. Jiang, F.-L. Qing, *Angew. Chem. Int. Ed.* **2013**, *52*, 14177; *Angew. Chem.* **2013**, *125*, 14427; c) K. Zhang, J.-B. Liu, F.-L. Qing, *Chem. Commun.* **2014**, *50*, 14157; d) W. Yu, X.-H. Xu, F.-L. Qing, *Adv. Synth. Catal.* **2015**, *357*, 2039; e) B. Yang, X.-H. Xu, F.-L. Qing, *Org. Lett.* **2015**, *17*, 1906.

[20] a) G. K. S. Prakash, J. Hu, Y. Wang, G. A. Olah, *Org. Lett.* **2004**, *6*, 4315; b) C. Ni, J. Hu, *Tetrahedron Lett.* **2005**, *46*, 8273; c) Y. Li, J. Liu, L. Zhang, L. Zhu, J. Hu, *J. Org. Chem.* **2007**, *72*, 5824.
[21] D. J. Burton, D. G. Naae, *J. Am. Chem. Soc.* **1973**, *95*, 8467.
[22] a) P. A. Krasutsky, M. Jones, Jr., *J. Org. Chem.* **1980**, *45*, 2425; b) G.-H. Shiue, U. Misslitz, X.-T. Ding, M. Jones, Jr., A. de Meijere, *Tetrahedron Lett.* **1985**, *26*, 5399; c) J. Weber, L. Xu, U. H. Brinker, *Tetrahedron Lett.* **1992**, *33*, 4537; d) R. M. Flynn, D. J. Burton, D. M. Wiemers, *J. Fluorine Chem.* **2008**, *129*, 583.
[23] R. M. Flynn, R. G. Manning, R. M. Kessler, D. J. Burton, S. W. Hansen, *J. Fluorine Chem.* **1981**, *18*, 525.
[24] D. J. Burton, Z.-Y. Yang, W. Qiu, *Chem. Rev.* **1996**, *96*, 1641.
[25] $E_{red} = -1.22$ V vs. SCE for difluoromethylphosphonium bromide; for details see the Supporting Information.
[26] C.-J. Wallentin, J. D. Nguyen, P. Finkbeiner, C. R. J. Stephenson, *J. Am. Chem. Soc.* **2012**, *134*, 8875.

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