Organic LETTERS

Letter

pubs.acs.org/OrgLett

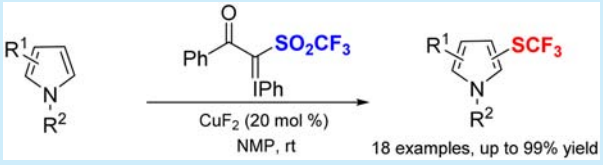
# Copper-Catalyzed Regioselective Trifluoromethylthiolation of Pyrroles by Trifluoromethanesulfonyl Hypervalent Iodonium Ylide

Zhongyan Huang, Yu-Dong Yang, Etsuko Tokunaga, and Norio Shibata*

Department of Nanopharmaceutical Sciences, Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya466-8555, Japan

Supporting Information

**ABSTRACT:** The copper-catalyzed trifluoromethylthiolation of pyrroles with a trifluoromethanesulfonyl hypervalent iodonium ylide under mild conditions has been achieved. A broad set of pyrroles could be transformed to the corresponding products in moderate to excellent yields. The reaction mechanism is hypothesized.




Much attention to synthetic fluorine chemistry has been paid as never before in recent years, even by chemists working in different areas, in particular, organometallics.[1] Enormous progress in fluorination and trifluoromethylation reactions in recent decades is a representative example.[2] The next topic that is expanding in this area is the development of the trifluoromethylthiolation reaction, due to the very unique character of the trifluoromethylthio (trifluoromethylsulfanyl, trifluoromethylsulfinyl, $SCF_3$) group. The electron-withdrawing effect of $SCF_3$ is similar to that of trifluoromethyl ($CF_3$), while the lipophilicity of $SCF_3$ ($\pi_R$ = 1.44) is the highest in the fluorinated functional groups.[1d] Since the $CF_3$ group has gained a prestigious position in pharmaceuticals, agrochemicals, and functional materials, the introduction of a $SCF_3$ group into drug candidates instead of the $CF_3$ group in target molecules is a highly potential strategy for creating new candidate drugs in research and development.[3] Early methods for the preparation of $SCF_3$ compounds can be divided into three categories: (1) halogen−fluorine exchange;[4] (2) trifluoromethylation of sulfur-containing compounds;[5] and (3) direct trifluoromethylthiolation of $SCF_3$-reagents. Obviously, direct trifluoromethylthiolation is ideal and practical since functionalization of the molecules can be performed at a late stage of a multistep synthesis. However, the reagents for trifluoromethylthiolation generally include liable trifluoromethylthiolate salts or toxic, gaseous reagents such as $ClSCF_3$ or $F_3CSSCF_3$.[6] Therefore, in recent years, much effort has focused on the development of shelf-stable reagents for this purpose. More recently, the transition-metal-catalyzed trifluoromethylthiolation of aryl halides, boronic acids, carboxylic acid, and benzylic C−H bonds has provided other options for trifluoromethylthiolation.[7] Currently, several shelf-stable reagents for electrophilic trifluoromethylthiolation have been developed (Figure 1).[2a,8] However, these reagents must be prepared in advance by trifluoromethylthiolation or related trifluoromethylation (Figure 1, **1**−**4**). In 2013, we disclosed a conceptually new reagent, a trifluoromethanesulfonyl hypervalent iodonium ylide **5**, for the trifluoromethylthiolation reaction of enamines, indoles, and *β*-keto esters. The reagent can be prepared easily from ubiquitous trifluoromethanesulfonyl ($SO_2CF_3$) compounds

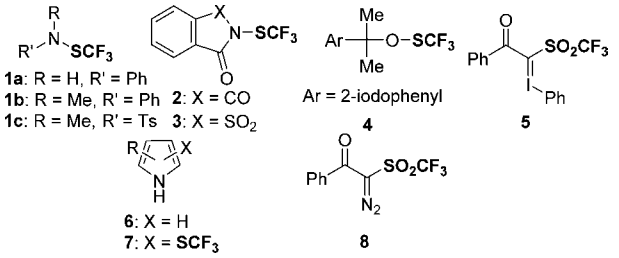



**Figure 1.** Structures of electrophilic trifluoromethylthiolation reagents and $SCF_3$ compounds.

but not from $SCF_3$ compounds, and electrophilic $SCF_3$ species are generated in situ during the reaction via thioperoxoate.[9] The reaction mechanism is fascinating and completely different from currently reported reagents. To show the clear proficiency of the reagent **5**, we report herein the trifluoromethylthiolation of pyrroles **6**, which remains a challenge. The modified reaction mechanism of **5** is disclosed based on the results using a diazotriflone **8** and TEMPO.

Pyrroles are an important class of nitrogen-containing heterocyclic compounds which are often encountered in natural products, biologically active molecules, and dyes for solar cells.[10] Thus, the development of synthetic methods that provide substituted pyrrole derivatives is of great importance.[11] Since the pyrroles are highly sensitive toward oxidation and polymerization, mild and neutral conditions should be required for the transformation. Initially trifluoromethylthiolation of pyrroles was examined by using toxic $ClSCF_3$, but the scope of substrates and yields were not satisfactory.[12] In 2012, Billard et al. attempted the trifluoromethylthiolation of pyrrole using the shelf-stable reagent, trifluoromethanesulfanylamide **1**, but failed, resulting in polymerization.[13] During the preparation of this manuscript, Shen et al. reported one example of trifluoromethylthiolation of 2,4-dimethyl-3-ethylpyrrole by *N*-trifluoromethylthiosaccharin (**3**) with $Me_3SiCl$ as an activator at 80 °C

**Received:** December 16, 2014
**Published:** February 16, 2015



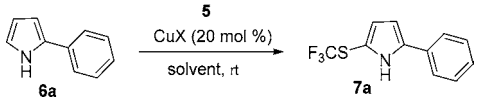


DOI: 10.1021/ol503616y
*Org. Lett.* 2015, 17, 1094−1097

for 12 h, although the method is not applied to other pyrrole derivatives.[8f]

We began our investigation with 2-phenyl pyrrole **6a** in the catalysis of CuCl in THF, which is the best condition for the trifluoromethylthiolation of enamines[9] (Table 1, entry 1).

**Table 1. Optimization of Reaction Conditions for Lewis Acid Catalyzed Trifluoromethylthiolation of 2-Phenyl Pyrrole (6a) with Reagent 5**[a]



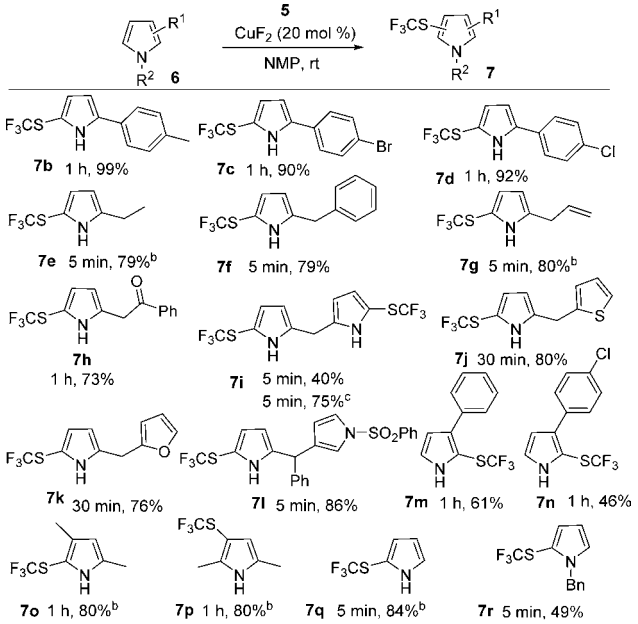

| entry | CuX | solvent | yield (%)[b] |
|---|---|---|---|
| 1 | CuCl | THF | 2 |
| 2 | CuBr | THF | 2 |
| 3 | CuI | THF | 3 |
| 4 | $CuCl_2$ | THF | 7 |
| 5 | $CuF_2$ | THF | 73 |
| 6 | $CuF_2$ | dioxane | 15 |
| 7 | $CuF_2$ | $CH_2Cl_2$ | n.d. |
| 8 | $CuF_2$ | toluene | n.d. |
| 9 | $CuF_2$ | acetone | 16 |
| 10 | $CuF_2$ | HFIP | n.d. |
| 11 | $CuF_2$ | DMF | 71 |
| 12 | $CuF_2$ | NMP | 94 |
| 13[c] | $CuF_2$ | NMP | 91 |
| 14[d] | $CuF_2$ | NMP | 93 |
| 15[e] | $CuF_2$ | NMP | 83 |
| 16 | – | NMP | n.d. |

[a]Reaction conditions: pyrrole **6a** (0.1 mmol), reagent **5** (0.2 mmol), CuX (20 mol %), solvent (0.75 mL), stirred at rt for 1 h. [b]Yields were determined by $^{19}F$ NMR spectroscopy with trifluoromethylbenzene as the internal standard. [c]30 mol % of $CuF_2$ was used. [d]10 mol % of $CuF_2$ was used. [e]5 mol % of $CuF_2$ was used.

However, disappointingly, only 2% of the desired product **7a** was obtained. After screening several Lewis acids, we found that a catalytic amount of $CuF_2$ was very effective for this transformation and 73% of **7a** was afforded, while other metal salts gave low yields (entries 2–5; for more details, see Table S2 in the Supporting Information (SI)). These results potentially indicate the critical influence of acidity of Lewis acids in trifluoromethylthiolation. Amide solvents were found to be suitable (entries 6–12) following solvent optimization. The cyclic amide NMP was more efficient than the acyclic amide DMF, and **7a** was obtained in 94% yield (entries 11 and 12). When 0–30 mol % of catalyst was screened, 20 mol % of $CuF_2$ in NMP was observed to be the best conditions (entries 12–16).

With these optimized conditions in hand, we surveyed the substrate scope (Scheme 1). The 2-aryl pyrroles **6b–d** were smoothly converted to trifluoromethylthiolated products **7b–d** in excellent yields independent of the electronic character of the aryl moieties. The halogens (Br, Cl) in **6** were tolerated during the transformation (**7c** and **d**). Aliphatic substituted pyrrole **6e** was also transformed under the same conditions to provide **7e** in 79% yield. It should be mentioned that the pyrroles **6f–h** having active methylene moieties such as benzyl, allyl, and benzoyl substituents were trifluoromethylthiolated in high yields without any polymerization or complexation. 2,2′-Dipyrromethane (**6i**), a precursor to porphyrins, afforded bis-trifluoromethylthiolated product **7i** in 40% yield, and a

**Scheme 1. Trifluoromethylthiolation of Pyrroles 6 with 5**[a]




[a]Reaction conditions: pyrrole **6** (0.2 mmol), reagent **5** (0.4 mmol), $CuF_2$ (20 mol %), NMP (1.5 mL), stirred at rt. [b]Yields were determined by $^{19}F$ NMR spectroscopy with trifluoromethylbenzene as the internal standard. [c]4.0 equiv of reagent **5** were used.

satisfactory yield (75%) of **7i** with 4 equiv of **5**. Selective trifluoromethylthiolation of pyrrole rings was achieved in the presence of thienyl and furanyl groups to provide **7j** and **7k**, in 80% and 76% yield, respectively. Even for the reaction of a substrate that contained two different electronic characteristic pyrroles, regio- and chemoselective trifluoromethylthiolation occurred on the 2-position of the electron-rich part of pyrrole to afford **7l** in 86% yield. Indeed, *tert*-butyl 1*H*-pyrrole-1-carboxylate (*N*-Boc pyrrole) did not react with **5** under the same conditions. Despite the steric hindrance, 3-aryl pyrroles **6m** and **n** were identified to solely afford 3-aryl-2-$SCF_3$ products **7m** and **n** in moderate yields (62% and 41%, respectively). Disubstituted 2,4- and 2,5-dimethyl pyrroles (**6o** and **6p**) were converted into 2-$SCF_3$ and 3-$SCF_3$ products **7o** and **7p** in high yields. Interestingly, unsubstituted pyrrole (**6q**) also gave the corresponding 2-$SCF_3$ product **7q** under standard conditions in high yield without any polymerization. *N*-Benzyl pyrrole (**6r**) was converted into 2-$SCF_3$ product **7r** in a moderate yield of 49%, presumably due to the steric hindrance.

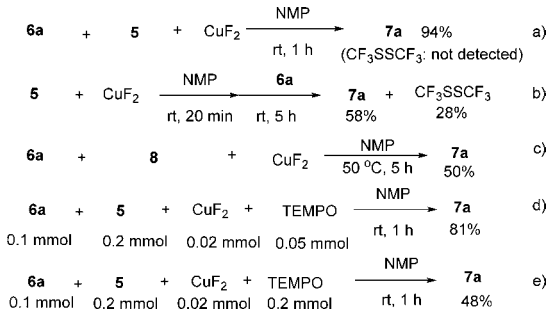
The reaction was monitored by the $^{19}F$ NMR spectrum (282 MHz, $CDCl_3$) of a mixture of **5** and $CuF_2$ in NMP, in the absence of pyrroles, using trifluorobenzene as an internal standard (Figure S1; see SI). The reagent **5** (−78.2 ppm) promptly disappeared within 5 min at rt, and a substantial amount of $CF_3SSCF_3$ (−46 ppm) appeared with other small signals at −35.9, −56.4, −76.6 ppm. The amount of $CF_3SSCF_3$ slightly increased over 60 min, while other small signals gradually disappeared. We then added pyrrole **6a** into the $CF_3SSCF_3$ mixture, and the resulting mixture was additionally stirred. After 10 h of stirring, the $CF_3SSCF_3$ still existed and product **7a** was not detected. These results strongly indicate that $CF_3SSCF_3$ is not a reactive species but other friable signals, at −35.9, −56.4, and −76.6 ppm, might be related to real reactive species for trifluoromethylthiolation.



DOI: 10.1021/ol503616y
*Org. Lett.* 2015, 17, 1094–1097

It should be noted that the success of the trifluoromethylthiolation of **6** is highly dependent on the reaction procedure. For a successful transformation, the reagent **5** should be added into the mixture of substrates **6a** and $CuF_2$ in NMP providing **7a** in 94% yield (Scheme 2a; also see entry 12 in Table 1). On

**Scheme 2. Reactions of 6a and Reagent 5 or 8 under Different Conditions To Elucidate Reaction Mechanism**

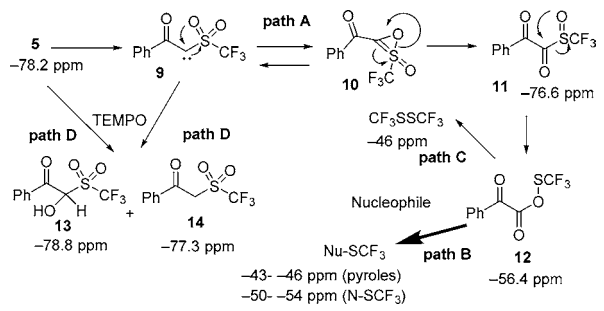



the other hand, **6a** was added into the mixture of **5** and $CuF_2$ in NMP after 20 min of stirring, and the formation of **7a** was significantly decreased to 58% accompanied by disulfide $CF_3SSCF_3$ (−46 ppm) in 28% yield (Scheme 2b). We next attempted the reaction of **6a** using 2-diazo-1-phenyl-2-(trifluoromethylsulfonyl)ethanone (**8**)[14] instead of **5** to ascertain the potential generation of carbines. With our expectation, the desired **7a** was isolated in 50% yield after 5 h of stirring at 50 °C, although the reagent was less effective than **5** under the same reaction conditions (Scheme 2c). The effect of a radical scavenger, 2,2,6,6-tetramethylpiperidinyl-1-oxyl (TEMPO), was also examined. The trifluoromethylthiolation of **6a** to **7a** was partially inhibited dependent on the amount of TEMPO (Scheme 2d and e); 48% of **7a** was obtained even in the presence of 2 equiv of TEMPO. These results strongly indicate that two independent pathways would exist together involving an electrophilic trifluoromethylthiolation and a radical reaction process.

We further monitored the reaction of **5** with TEMPO, and $CuF_2$ in NMP in the absence of pyrroles, by the $^{19}F$ NMR spectrum (282 MHz, $CDCl_3$, Figure S2; see SI). Within 10 min, reagent **5** disappeared and substantial amounts of side products were detected at −78.8 and −77.3 ppm, which were provided for a representative $SO_2CF_3$.[15] The GCMS experiments of the mixture implied them to be triflones **14** (MW 252 observed) and **13** (MW 268 observed), although **13** was not ascertained by isolation due to decomposition. The addition of pyrrole **6a** after 2 h of stirring did not change the $^{19}F$ NMR spectra, which suggests the reactive species for trifluoromethylthiolation is not generated at this point.

Based on these new results and the facts of ESI-MASS spectral detection of the intermediates **10**, **11**, and **12** in the previous paper,[9] we propose a modified reaction mechanism (Scheme 3). First, carbene **9** should be generated via a copper carbenoid or copper catalysis. Next, oxathiirene **10** (which is in equilibrium with carbine **9** via path A) would rearrange to give sulfoxide **11**, and subsequent intramolecular nucleophilic collapse would then form the true reactive species, thioperoxoate **12**. The transfer trifluoromethylthiolation from **12** to the nucleophile (Nu) via an electrophilic path A would yield the desired products Nu-$SCF_3$. In the absence of a nucleophile, the thioperoxoate **12** is collapsed into $CF_3SSCF_3$ via radical path C, although path A is more rapid than path B. The friable signals

**Scheme 3. Modified Proposed Reaction Mechanism for Trifluoromethylthiolation by Reagent 5**




at −56.4 and −76.6 ppm could be assigned to be **12** and **11** by comparison of the reported data of the R-S(O)$CF_3$ and R-O-$SCF_3$ compounds,[15] although further detailed studies are required. Alternatively, when TEMPO is added, via a radical or single electron transfer path D, the hydroxylated triflones **13** and reduction product **14** are formed. In the presence of TEMPO, paths A and D are almost equally competitive; thus, the electrophilic trifluoromethylthiolation via path B is not fully inhibited by the addition of TEMPO (Scheme 2e).

The $^{19}F$ NMR chemical shift prediction based on the computations with several methods (HF, EDF2, B3LYP) could also support the proposed reaction mechanism indicated in Scheme 2 (Table S1; see SI). With the comparisons of calculations and observations of isolated compounds **14** and $CF_3SSCF_3$, the chemical shifts generated by computations using B3LYP 6-31G** would be the closest to those observed. Hence, the observed chemical shifts, −76.6, −56.4, and −78.8 ppm, were assigned to **11**, **12**, and **13**.

In summary, we have developed a copper-catalyzed trifluoromethylthiolation of pyrroles with trifluoromethanesulfonyl hypervalent iodonium ylide **5**. A broad scope of pyrroles were transformed into the corresponding products in good to excellent yields. The reaction conditions are rather mild with high reaction yields achieved. In particular, the general method for the trifluoromethylthiolation of pyrroles was achieved for the first time by reagent **5**. Reagent **5** exhibited a very unique reaction mechanism for the electrophilic trifluoromethylthiolation. The diazo-triflone **8** also underwent trifluoromethylthiolation. The transformation exhibited unexpected efficiency when copper fluoride was used. The effects of the catalyst and solvent are now being investigated in our laboratory.

## ■ ASSOCIATED CONTENT

### Supporting Information

Figures S1, S2, Table S1, experimental procedures, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION

### Corresponding Author

*E-mail: nozshiba@nitech.ac.jp.

### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

This research was financially supported in part by the Platform for Drug Discovery, Informatics, and Structural Life Science from MEXT Japan, the Advanced Catalytic Transformation



DOI: 10.1021/ol503616y
*Org. Lett.* 2015, 17, 1094−1097

(ACT-C) from the Japan Science and Technology (JST) Agency, and Scientific Research (B) (25288045), Exploratory Research (25670055) from JSPS, and Kobayashi International Scholarship Foundation.

## REFERENCES

(1) (a) Kirsch, P. *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*; Wiley-VCH: Weinheim, Germany, 2004. (b) Hiyama, T. *Organofluorine Compounds: Chemistry and Properties*; Springer: Berlin, 2000. (c) Uneyama, K. *Organofluorine Chemistry*; Blackwell: Oxford, U.K., 2006. (d) Banks, R. E.; Smart, B. E.; Tatlow, J. C. *Organofluorine Chemistry: Principles and Commercial Applications*; Plenum Press: New York, 1994. (e) O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308. (f) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. *Chem. Rev.* **2014**, *114*, 2432.

(2) For selected reviews, see: (a) Boiko, V. N. *Beilstein J. Org. Chem.* **2010**, *6*, 880. (b) Landelle, G.; Panossian, A.; Pazenok, S.; Vors, J.-P.; Leroux, F. R. *Beilstein J. Org. Chem.* **2013**, *9*, 2476. (c) Thili, A.; Billard, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 6818. (d) Liang, T.; Neumann, C. N.; Ritter, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 8214. (e) Toulgoat, F.; Alazet, S.; Billard, T. *Eur. J. Org. Chem.* **2014**, 2415. (f) Zhu, W.; Wang, J.; Wang, S.; Gu, Z.; Acena, J. L.; Izawa, K.; Liu, H.; Soloshonok, V. A. *J. Fluorine Chem.* **2014**, *167*, 37. (g) Xu, X.-H.; Matsuzaki, K.; Shibata, N. *Chem. Rev.* **2015**, *115*, 731.

(3) (a) Ferry, A.; Billard, T.; Langlois, B. R.; Bacqué, E. *Angew. Chem., Int. Ed.* **2009**, *48*, 8551. (b) Chen, C.; Chu, L.; Qing, F.-L. *J. Am. Chem. Soc.* **2012**, *134*, 12454. (c) Chen, C.; Xie, Y.; Chu, L.; Wang, R.-W.; Zhang, X.; Qing, F.-L. *Angew. Chem., Int. Ed.* **2012**, *51*, 10. (d) Alazet, S.; Zimmer, L.; Billard, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 10814. (e) Alazet, S.; Ollivier, K.; Billard, T. *Beilstein J. Org. Chem.* **2013**, *9*, 2354. (f) Deng, Q.-H.; Rettenmeier, C.; Wadepohl, H.; Gade, L. H. *Chem.—Eur. J.* **2014**, *20*, 93. (g) Vinogradova, E. V.; Müller, P.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2014**, *53*, 3125. (h) Zhu, S.-Q.; Xu, X.-H.; Qing, F.-L. *Eur. J. Org. Chem.* **2014**, 4453.

(4) (a) Scherer, O. *Angew. Chem.* **1939**, *52*, 457. (b) Nodiff, E. A.; Lipschutz, S.; Craig, P. N.; Gordon, M. *J. Org. Chem.* **1960**, *25*, 60. (c) Kremsner, J. M.; Rack, M.; Pilger, C.; Kappe, C. O. *Tetrahedron Lett.* **2009**, *50*, 3665.

(5) (a) Wakselman, C.; Tordeux, M. J. *Chem. Soc. Commun.* **1984**, 793. (b) Soloshonok, V.; Kukhar, V.; Pustovit, Y.; Nazaretian, V. *Synlett* **1992**, 657. (c) Kieltsch, I.; Eisenberger, P.; Togni, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 754. (d) Capone, S.; Kieltsch, I.; Flögel, O.; Lelais, G.; Togni, A.; Seebach, D. *Helv. Chim. Acta* **2008**, *91*, 2035. (e) Ausín, C.; Kauffman, J. S.; Duff, R. J.; Shivaprasad, S.; Beaucage, S. L. *Tetrahedron* **2010**, *66*, 68. (f) Yasui, H.; Yamamoto, T.; Tokunaga, E.; Shibata, N. *J. Fluorine Chem.* **2011**, *132*, 186.

(6) (a) Man, E. H.; Coffman, D. D.; Muetterties, E. L. *J. Am. Chem. Soc.* **1959**, *81*, 3575. (b) Andreades, S.; Harris, J. F.; Sheppard, W. A. *J. Org. Chem.* **1964**, *29*, 898. (c) Hanack, M.; Kühnle, A. *Tetrahedron Lett.* **1981**, *22*, 3047. (d) Kolasa, A. *J. Fluorine Chem.* **1987**, *36*, 29. (e) Popov, V. I.; Haas, A.; Lieb, M. *J. Fluorine Chem.* **1990**, *47*, 131. (f) Adams, D. J.; Clark, J. H. *J. Org. Chem.* **2000**, *65*, 1456. (g) Adams, D. J.; Goddard, A.; Clark, J. H.; Macquarrie, D. J. *Chem. Commun.* **2000**, 987.

(7) (a) Teverovskiy, G.; Surry, D. S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2011**, *50*, 7312. (b) Zhang, C.-P.; Vivic, D. A. *J. Am. Chem. Soc.* **2012**, *134*, 183. (c) Weng, Z.; He, W.; Chen, C.; Lee, R.; Tan, D.; Lai, Z.; Kong, D.; Yuan, Y.; Huang, K.-W. *Angew. Chem., Int. Ed.* **2013**, *52*, 1548. (d) Rueping, M.; Tolstoluzhsky, N.; Nikolaienko, P. *Chem.—Eur. J.* **2013**, *19*, 14043. (e) Pluta, R.; Nikolaienko, P.; Rueping, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 1650. (f) Xu, C.; Shen, Q. *Org. Lett.* **2014**, *16*, 2046. (g) Kang, K.; Xu, C.; Shen, Q. *Org. Chem. Front.* **2014**, *1*, 294. (h) Hu, F.; Shao, X.; Zhu, D.; Lu, L.; Shen, Q. *Angew. Chem., Int. Ed.* **2014**, *53*, 6105.

(8) For selected examples, see: (a) Baert, F.; Colomb, J.; Billard, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 10382. (b) Alazet, S.; Zimmer, L.; Billard, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 10814. (c) Shao, X.; Wang, X.; Yang, T.; Lu, L.; Shen, Q. *Angew. Chem., Int. Ed.* **2013**, *52*, 3457. (d) Wang, X.; Yang, T.; Cheng, X.; Shen, Q. *Angew. Chem., Int. Ed.* **2013**, *52*, 12860. (e) Bootwicha, T.; Liu, X.; Pluta, R.; Atodiresei, I.; Rueping, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 12856. (f) Xu, C.; Ma, B.; Shen, Q. *Angew. Chem., Int. Ed.* **2014**, *53*, 9316. (g) Alazet, S.; Zimmer, L.; Billard, T. *Chem.—Eur. J.* **2014**, *20*, 8589.

(9) Yang, Y.-D.; Azuma, A.; Tokunaga, E.; Yamasaki, M.; Shiro, M.; Shibata, N. *J. Am. Chem. Soc.* **2013**, *135*, 8782.

(10) (a) d'Ischia, M.; Napolitano, A.; Pezzella, A. In *Comprehensive Heterocyclic Chemistry III: Pyrroles and Their Benzo Derivatives: Applications*, Vol. 3; Katritzky, A. R., Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Elsevier: Amsterdam, 2008; pp 353−388. (b) Young, I. S.; Thornton, P. D.; Thompson, A. *Nat. Prod. Rep.* **2010**, *27*, 1801.

(11) Selected examples to synthesize pyrroles: (a) Xin, X.; Wang, D.; Li, X.; Wan, B. *Angew. Chem., Int. Ed.* **2012**, *51*, 1693. (b) Michlik, S.; Kempe, R. *Nat. Chem.* **2013**, *5*, 140. (c) Komatsubara, M.; Umeki, T.; Fukuda, T.; Iwao, M. *J. Org. Chem.* **2014**, *79*, 529. (d) Estévez, V.; Villacampa, M.; Menéndez, J. C. *Chem. Soc. Rev.* **2014**, *43*, 4633.

(12) (a) Haas, A.; Niemann, U. *Chem. Ber.* **1977**, *110*, 67. (b) Dorn, S.; Eggenbeg, P.; Gerstenberger, M. R. C.; Haas, A.; Niemann, U.; Zobrist, P. *Helv. Chim. Acta* **1979**, *62*, 1442. (c) Gerstenberger, M. R. C.; Haas, A.; Liebig, F. *J. Fluorine Chem.* **1982**, *19*, 461. (d) Bélanger, P. C.; Atkinson, J. G.; Rooney, C. S.; Britcher, S. F.; Remy, D. C. *J. Org. Chem.* **1983**, *48*, 3234.

(13) Ferry, A.; Billard, T.; Bacqué, E.; Langlois, B. R. *J. Fluorine Chem.* **2012**, *134*, 160.

(14) Pang, W.; Zhu, S.; Xing, C.; Luo, N.; Jiang, H.; Zhu, S. *J. Fluorine Chem.* **2008**, *129*, 343.

(15) Dolbier, W. R. *Guide to Fluorine NMR for Organic Chemists*; John Wiley & Sons: Hoboken, New Jersey, USA, 2009.



DOI: 10.1021/ol503616y
*Org. Lett.* 2015, 17, 1094−1097