Organic LETTERS

Letter

pubs.acs.org/OrgLett

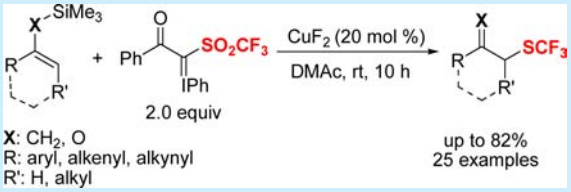
Trifluoromethylthiolation of Allylsilanes and Silyl Enol Ethers with Trifluoromethanesulfonyl Hypervalent Iodonium Ylide under Copper Catalysis

Sadayuki Arimori, Masahiro Takada, and Norio Shibata*

Department of Frontier Materials, Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466-8555, Japan

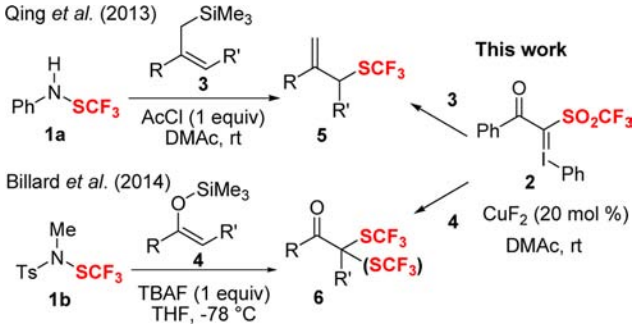
Supporting Information

ABSTRACT: Electrophilic trifluoromethylthiolation of allylsilanes and silyl enol ethers with trifluoromethanesulfonyl hypervalent iodonium ylide has been conducted. In the presence of a catalytic amount of CuF_2, the reaction proceeded in modest to high yields under mild conditions.



Organofluorine compounds now constitute a major family of pharmaceuticals and agrochemicals that have attracted considerable interest over several years in these markets.[1] Among them, trifluoromethylthio (SCF_3) compounds are currently appealing and have been given special attention[2] due to their impressive lipophilicity, which plays an important role in transport across cell walls. Moreover, enhanced lipophilicity of molecules is also beneficial in material science due to the improvement of physical property.[3] Thus, the development of efficient methods for the synthesis of SCF_3 compounds is of great importance.[4] Shelf-stable electrophilic trifluoromethylthiolation reagents such as SCF_3-phthalimide,[5] SCF_3-anilines[6] (**1**), SCF_3-ether,[7] and SCF_3-saccharine[8] have been developed for this purpose. In 2013, we also disclosed a new type of reagent, trifluoromethanesulfonyl hypervalent iodonium ylide **2**, for the same purpose.[9] Our reagent **2** has a fundamentally novel structure with a trifluoromethyl sulfonyl (SO_2CF_3) moiety, instead of an essential SCF_3 unit in regular reagents. Besides, the SO_2CF_3 group directly connects to the carbon atom in **2**, while regular SCF_3 reagents have a connection between the heteroatom and the SCF_3 group. Hence the reaction mechanism of **2** for electrophilic trifluoromethylthiolation is rather complex and unique, although the utility of **2** is still limited to the trifluoromethylthiolation of enamines, indoles, and β-keto esters. As part of our continuing interest in the potential use of **2**, which stems from its structural and mechanistic uniqueness, we expand herein the further scope and utility of **2** for the trifluoromethylthiolation of allylsilanes **3** and silyl enol ethers **4**. Although the trifluoromethylthiolation of **3** and **4** has been reported by others, a different reagent (**1a** or **1b**) using different conditions is likely to be required, depending on the substrates, **3**[10] or **4**.[11] Moreover, the trifluoromethylthiolation of **4** tends to give a mixture of mono- and bis-SCF_3 products. Reagent **2** is advantageous in that a wide variety of cyclic and linear allylsilanes **3** and silyl enol ethers **4** are nicely transformed into corresponding SCF_3-products **5** and **6** in good to high yields under the same conditions of copper catalysis (Scheme 1). No bis-SCF_3 product was observed for the trifluoromethylthiolation of silyl enol ethers **4**.

Scheme 1. Electrophilic Trifluoromethylthiolation of Allylsilanes and Silyl Enol Ethers by 1a,b and 2



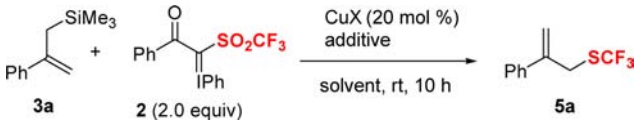
Trimethyl(2-phenylallyl)silane (**3a**) was selected as a model substrate for the optimization of reaction conditions (Table 1). We first attempted the trifluoromethylthiolation of **3a** with **2** under the best conditions reported for enamines (20 mol % CuCl in 1,4-dioxane at room temperature), but no reaction proceeded (run 1). The combination of catalyst and solvent was found to be very important after careful screening (runs 2−11), and desired SCF_3 product **5a** was obtained in 80% yield with CuF_2 in NMP or DMAc (runs 5 and 7). Neither catalyst additives nor a higher reaction temperature under the best conditions (run 7) improved the yield of **5a** (runs 12−16).

With these optimized conditions in hand (Table 1, run 7), we examined diverse allylsilanes **3b−o** to explore the substrate scope of trifluoromethylthiolation (Scheme 2). It was found that the reaction of linear 2-aryl-substituted allylsilanes **3b−i** proceeded smoothly, and corresponding SCF_3 compounds **5b−**

Received: January 7, 2015
Published: February 17, 2015

DOI: 10.1021/acs.orglett.5b00057
Org. Lett. 2015, 17, 1063−1065

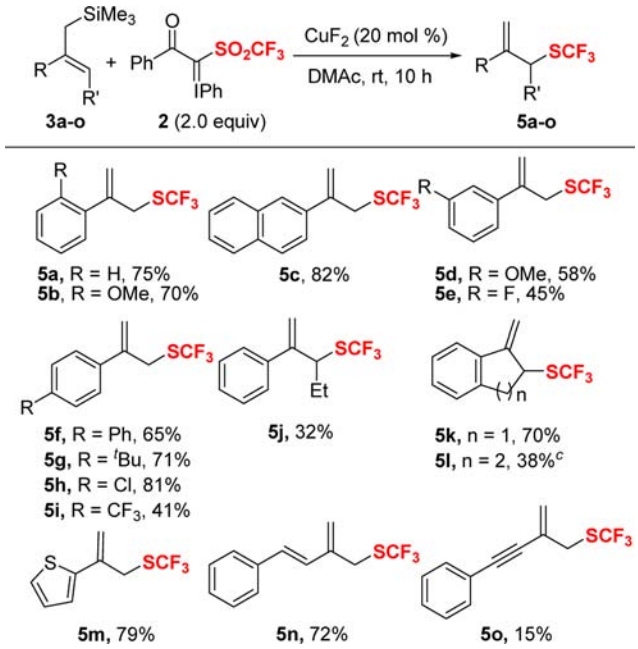
Table 1. Optimization of Cu-Catalyzed Trifluoromethylthiolation[a]



run	CuX	additive (mol %)	solvent	yield[b] (%)
1	CuCl		dioxane	0
2	CuF_2		dioxane	0
3	CuF_2		THF	23
4	CuF_2		DMF	34
5	CuF_2		NMP	80
6[c]	CuF_2		NMP	52
7	CuF_2		DMAc	80
8	CuF_2		CH_2Cl_2	5
9	CuF_2		MeCN	0
10	CuCl		DMAc	2
11	CuOAc		DMAc	62
12	CuF_2	$PhNMe_2$ (20)	DMAc	50
13	CuF_2	2,4,6-collidine (20)	DMAc	65
14	CuF_2	CsF (10)	DMAc	74
15	CuF_2	TBAF (10)	DMAc	68
16[d]	CuF_2		DMAc	61

[a]Reaction conditions: **3a** (0.25 mmol), **2** (0.50 mmol), CuX (20 mol %), solvent (1.25 mL), rt, 10 h, under N_2 atmosphere. [b]^{19}F-NMR yields with PhF as an internal standard. [c]Compound **2** (0.25 mmol) was used. [d]The reaction was carried out at 50 °C. TBAF = tetrabutylammonium fluoride. NMP = *N*-methyl-2-pyrrolidone. DMAc = *N*,*N*-dimethylacetamide

Scheme 2. Scope of Cu-Catalyzed Trifluoromethylthiolation of Allylsilanes 3[a,b]

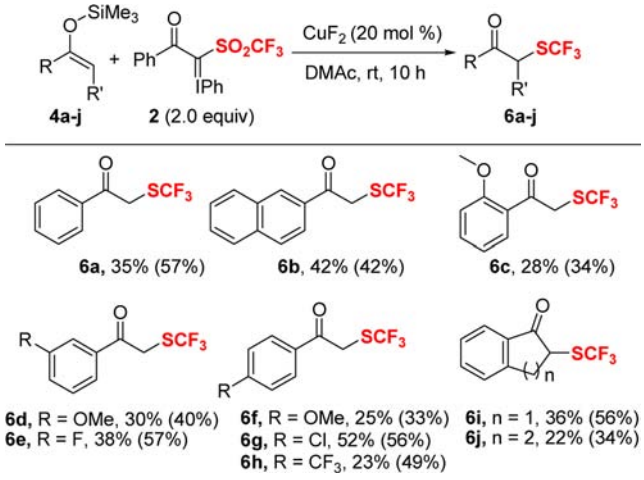


[a]Reaction conditions: **3** (0.25 mmol), **2** (0.50 mmol), CuF_2 (20 mol %), DMAc (1.25 mL), rt, 10 h, under N_2 atmosphere. [b]Isolated yields. [c]NMP was used as a solvent.

i were obtained in modest to high yields (41−82%). The electron-donating groups (OMe, ^{t}Bu), electron-withdrawing groups (Cl, CF_3, F) on the aryl group, and sterically demanding aryl groups (biphenyl, naphthyl) could be applied in the same reaction conditions. Allylsilane **3j** with a branched structure was also converted into CF_3S product **5j**, although the yield was only 32%. Cyclic allylsilanes **3k** and **3l** gave the desired products **5k** and **5l** in 70% and 38% yield, respectively. Allylsilanes having 2-thiophenyl **3m**, alkenyl **3n**, and alkynyl **3o** groups could be applied in the same reaction conditions providing CF_3S products **5m−o** in good yields. The stereochemistry of **3n** was retained in **5n** during the reaction.

The trifluoromethylthiolation of silyl enol ethers **4** with **2** was examined next. Under the same reaction conditions (Table 1, run 7), silyl enol ethers **4** were nicely trifluoromethylthiolated furnishing **6** in moderate to good yields (Scheme 3). The

Scheme 3. Scope of Cu-Catalyzed Trifluoromethylthiolation of Silyl Enol Ethers 4[a,b]



[a]Reaction conditions: **4** (0.25 mmol), **2** (0.50 mmol), CuF_2 (20 mol %), DMAc (1.25 mL), rt, 10 h, under N_2 atmosphere. [b]Isolated yields. The values in parentheses are ^{19}F-NMR yields with PhF as an internal standard.

naphthyl group, as well as electron-donating (OMe) and electron-withdrawing (Cl, CF_3, F) groups on the aromatic ring of **4** did not affect the reaction much and proceeded well to give **6** in modest to good yields. Additionally, cyclic silyl enol ethers **4i,j** were also compatible in this system. It should be noted that mono-trifluoromethylthiolated products **6** were selectively obtained in all cases, although a reported method[11] predominantly gave bis-trifluoromethylthiolated products.

In conclusion, we have developed copper-catalyzed trifluoromethylthiolation reactions of various allylsilanes **3** and silyl enol ethers **4** with **2** under mild conditions. The protocol of this reaction is concise compared to previously reported procedures[10,11] and tolerates diverse substrates. The present results expand the scope and utility of reagent **2**, and further application of **2** is now under investigation.

■ ASSOCIATED CONTENT

Supporting Information

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.

DOI: 10.1021/acs.orglett.5b00057
Org. Lett. 2015, 17, 1063−1065

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 (ACT-C) from the Japan Science and Technology (JST) Agency, and Kobayashi International Foundation.

■ REFERENCES

(1) (a) Leroux, F.; Jeschke, P.; Schlosser, M. *Chem. Rev.* **2005**, *105*, 827. (b) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; Pozo, C. d.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. *Chem. Rev.* **2014**, *114*, 2432. (c) Zhu, W.; Wang, J.; Wang, S.; Gu, Z.; Aceña, J. L.; Izawa, K.; Liu, H.; Soloshonok, V. A. *J. Fluorine Chem.* **2014**, *167*, 37.
(2) (a) Leo, A.; Hansch, C.; Elkins, D. *Chem. Rev.* **1971**, *71*, 525. (b) Hansch, C.; Leo, A.; Unger, S. H.; Kim, K. H.; Nikaitani, D.; Lien, E. J. *J. Med. Chem.* **1973**, *16*, 1207. (c) Clavel, J.-L.; Langlois, B.; Nantermet, R.; Tordeux, M.; Wakselman, C. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3371.
(3) Le, T.; Epa, V. C.; Burden, F. R.; Winkler, D. A. *Chem. Rev.* **2012**, *112*, 2889.
(4) (a) Tlili, A.; Billard, T. A. *Angew. Chem., Int. Ed.* **2013**, *52*, 6818. (b) Xu, X.-H.; Matsuzaki, K.; Shibata, N. *Chem. Rev.* **2015**, *115*, 731. (c) Yang, X.; Wu, T.; Phipps, R. J.; Toste, F. D. *Chem. Rev.* **2015**, *115*, 826. (d) Ferry, A.; Billard, T.; Langlois, B. R.; Bacqué, E. *Angew. Chem., Int. Ed.* **2009**, *48*, 8551. (e) Baert, F.; Colomb, J.; Billard, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 10382. (f) Pluta, R.; Nikolaienko, P.; Rueping, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 1650. (g) Hu, F.; Shao, X.; Zhu, D.; Lu, L.; Shen, Q. *Angew. Chem., Int. Ed.* **2014**, *53*, 6105. (h) Shao, X.; Liu, T.; Lu, L.; Shen, Q. *Org. Lett.* **2014**, *16*, 4783. (i) Yang, Y.; Lu, L.; Shen, Q. *Chem. Commun.* **2014**, DOI: 10.1039/c4cc08655d. (j) Kang, K.; Xu, C.; Shen, Q. *Org. Chem. Front.* **2014**, *1*, 294. (k) Zhai, L.; Li, Y.; Yin, J.; Jin, K.; Zhang, R.; Fu, X.; Duan, C. *Tetrahedron* **2013**, *69*, 10262. (l) Weng, Z.; He, W.; Chen, C.; Lee, R.; Tan, D.; Lai, Z.; Kong, D.; Yuan, Y.; Huang, K.-W. *Angew. Chem., Int. Ed.* **2013**, *53*, 1548. (m) Chan, C.; Xie, Y.; Chu, L.; Wang, R.-W.; Zhang, X.; Qing, F.-L. *Angew. Chem., Int. Ed.* **2012**, *51*, 2492. (n) Rong, M.; Li, D.; Huang, R.; Huang, Y.; Hau, X.; Weng, Z. *Eur. J. Org. Chem.* **2014**, 5010. (o) Huang, Y.; He, X.; Li, H.; Weng, Z. *Eur. J. Org. Chem.* **2014**, 7324. (p) Zhu, S.-Q.; Xu, X.-H.; Qing, F.-L. *Eur. J. Org. Chem.* **2014**, 4453. (q) Liu, J.-B.; Xu, X.-H.; Chen, Z.-H.; Qing, F.-L. *Angew. Chem., Int. Ed.* **2015**, *54*, 897. (r) Adams, D. J.; Goddard, A.; Clark, J. H.; Macquarri, D. J. *Chem. Commun.* **2000**, 987. (s) Xu, J.; Mu, X.; Chen, P.; Ye, J.; Liu, G. *Org. Lett.* **2014**, *16*, 3942. (t) Zhang, C.-P.; Vicic, D. A. *J. Am. Chem. Soc.* **2012**, *134*, 183. (u) Chen, C.; Chu, L.; Qing, F.-L. *J. Am. Chem. Soc.* **2012**, *134*, 12454. (v) Tran, L.; Popov, I.; Draugulis, O. *J. Am. Chem. Soc.* **2012**, *134*, 18232. (w) Li, S.-G.; Zard, S.-Z. *Org. Lett.* **2013**, *15*, 5898. (x) Huang, Y.; He, X.; Lin, X.; Rong, M.; Weng, Z. *Org. Lett.* **2014**, *16*, 3284. (y) Chen, C.; Xu, X.-H.; Yang, B.; Qing, F.-L. *Org. Lett.* **2014**, *16*, 3372. (z) Xu, C.; Shen, Q. *Org. Lett.* **2014**, *16*, 2046. (aa) Dai, X.; Cahard, D. *Synlett* **2015**, *26*, 40.
(5) Munavalli, S.; Rohrbaugh, D. K.; Rossman, D. I.; Berg, F. J.; Wagner, G. W.; Durst, H. D. *Synth. Commun.* **2000**, *30*, 2847.
(6) Ferry, A.; Billard, T.; Langlois, B.; Bacqué, E. *J. Org. Chem.* **2008**, *73*, 9362.
(7) Shao, X.; Wang, X.; Yang, T.; Lu, L.; Shen, Q. *Angew. Chem., Int. Ed.* **2013**, *52*, 3457.
(8) Xu, C.; Ma, B.; Shen, Q. *Angew. Chem., Int. Ed.* **2014**, *53*, 9316.
(9) Yang, Y.-D.; Azuma, A.; Tokunaga, E.; Yamasaki, M.; Shiro, M.; Shibata, N. *J. Am. Chem. Soc.* **2013**, *135*, 8782.
(10) Liu, J.; Chu, L.; Qing, F.-L. *Org. Lett.* **2013**, *15*, 894.
(11) Alazet, S.; Zimmer, L.; Billard, T. *Chem.—Eur. J.* **2014**, *20*, 8589.

DOI: 10.1021/acs.orglett.5b00057
Org. Lett. 2015, 17, 1063−1065