CHEMISTRY
A EUROPEAN JOURNAL

COMMUNICATION

DOI: 10.1002/chem.201201707

Trifluoromethylation of Allylsilanes under Copper Catalysis

Satoshi Mizuta,[a] Oscar Galicia-López,[a] Keary M. Engle,[a] Stefan Verhoog,[a] Katherine Wheelhouse,[b] Gerasimos Rassias,[b] and Véronique Gouverneur*[a]

Medicinal chemists commonly incorporate a trifluoromethyl group into druglike molecules to enhance binding selectivity, improve metabolic stability and increase lipophilicity.[1] To date, various methods are available for the introduction of the CF_3 group onto functionalized arenes and heteroarenes.[2] Numerous catalytic trifluoromethylation reactions of ketones or aldehydes have also been developed, leading to the formation of C_{sp^3}–CF_3 bonds, including elegant asymmetric variants.[3] The construction of C_{sp^3}–CF_3 stereogenicity from poorly activated substrates is less common. In this context, the direct selective installation of a CF_3 group on an allylic position remains a challenging synthetic problem.[4] Isolated examples of Pd-catalyzed trifluoromethylation of allylstannanes with CF_3I[5] and Cu-mediated nucleophilic trifluoromethylation of allyl bromide using the Ruppert–Prakash reagent (CF_3SiMe_3) are known,[6] giving linear allylic CF_3 products. Recently, Buchwald,[7] Wang,[8] and Liu[9] and their co-workers reported that terminal alkenes are amenable to allylic trifluoromethylation under copper catalysis, a reaction also affording linear allylic CF_3 products with very good control over *E*:*Z* geometry. Access to branched *acyclic* allylic CF_3 products has not been demonstrated, and only two branched *cyclic* products have been prepared through application of this C–H functionalization methodology.[7–9] To address this synthetic challenge, we reasoned that we could access allylic CF_3 products using alkenes temporarily activated with a regiodirecting silyl group. Since our first report in 2003, we have demonstrated that a diverse range of allylic fluorides are accessible upon electrophilic fluorination of allylsilanes under very mild conditions and have found that this reaction is broad in scope and tolerant of various functional groups.[10] The presence of the allylic trimethylsilyl group is essential to increase the nucleophilicity of the proximal alkene and to dictate the regiochemistry of the fluorination. Based on these principles and the availability of various electrophilic trifluoromethylating reagents[11] (e.g., hypervalent iodine reagents **I** and **II**,[12] and the sulfonium salts **III**[13] and **IV**[14]), we describe herein a copper-catalyzed trifluoromethylation reaction to prepare various branched allylic CF_3 products from allylsilanes (Figure 1).

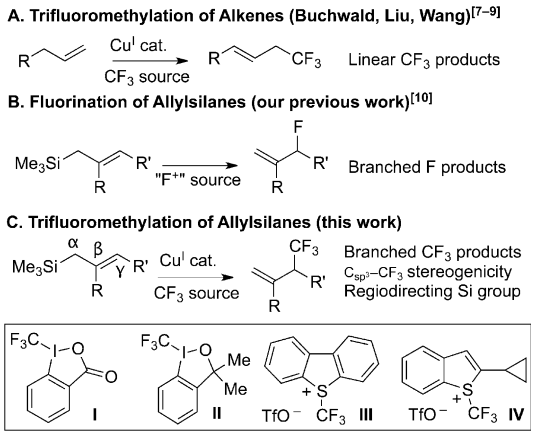


Figure 1. Trifluoromethylation of allylsilanes.

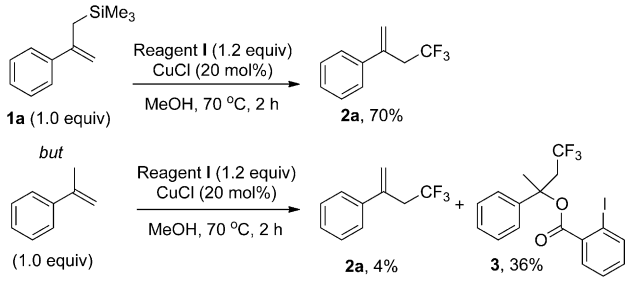
Preliminary experiments with the model substrate **1a** served to demonstrate that the trifluoromethylation of a silyl-activated alkene could be a valid route to access the allylic CF_3 product **2a**. The trifluoromethylation of trimethyl(2-phenylallyl)silane (**1a**) with Togni's reagent **I** was successfully performed in methanol at 70 °C in the presence of 20 mol % of CuCl. Compound **2a** was isolated in 70 % yield. In the absence of CuCl, no reaction took place. A control experiment with α-methylstyrene established that the trimethylsilyl (TMS) group is critical to induce allylic trifluoromethylation. When this structurally related non-silylated precursor was allowed to react under the same conditions as **1a**, adduct **3** was isolated in 36 % yield with only 4 % of the desired product **2a** (Scheme 1).

With this result in hand, we next examined the trifluoromethylation of allylsilane (*Z*)-**1b**, a substrate that would potentially lead to the allylic product **2b** featuring C_{sp^3}–CF_3 stereogenicity. Our optimization study is presented in Table 1.[15] In the absence of catalyst, no reaction took place

[a] Dr. S. Mizuta, O. Galicia-López, K. M. Engle, S. Verhoog, Prof. V. Gouverneur
Chemistry Research Laboratory
University of Oxford
12, Mansfield Road, Oxford OX1 3TA (UK)
E-mail: veronique.gouverneur@chem.ox.ac.uk

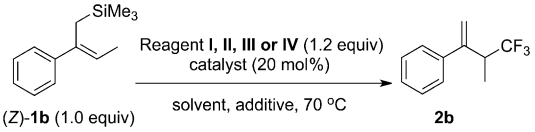
[b] Dr. K. Wheelhouse, Dr. G. Rassias
Medicines Discovery & Development
GlaxoSmithKline R&D
Gunnels Wood Road
Stevenage SG1 2NY (UK)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201201707.



Scheme 1. Evidence for TMS-driven allylic trifluoromethylation.

Table 1. Optimization study for the trifluoromethylation of **1b**.



Entry	Catalyst	Additive	Solvent/time	"CF_3"[a]	Yield [%][b]
1	–	–	MeOH/12 h	**I**	NR[c]
2	CuCl	–	MeOH/20 h	**I**	53
3	CuI	–	MeOH/20 h	**I**	50
4	$[Cu(OTf)]_2C_6H_6$[d]	–	MeOH/2 h	**I**	14
5	CuTc	–	MeOH/20 h	**I**	17
6	$[(MeCN)_4Cu]PF_6$	–	MeOH/17 h	**I**	23
7	$CuCl_2$	–	MeOH/20 h	**I**	12
8	CuCl	–	MeOH/20 h	**II**	29
9	CuCl	–	MeOH/20 h	**III**	–[e]
10	CuCl	–	MeOH/20 h	**IV**	–[e]
11	CuCl	–	DMF/20 h	**I**	34
12	CuCl	–	DMAc/ 20 h[f]	**I**	13
13	CuCl	–	*i*PrOH/20 h	**I**	17
14	CuCl	–	MeOH/2 h	**I**	53
15	$SnCl_4$	–	CH_2Cl_2/ 24 h[g]	**I**	44
16	$BF_3{\cdot}Et_2O$	–	CH_2Cl_2/ 24 h[g]	**I**	NR[c]
17	$Fe(OAc)_2$	–	MeOH/2 h	**I**	52
18	CuCl	Et_3N	MeOH/2 h	**I**	61
19	CuCl	iPr_2EtN	MeOH/2 h	**I**	75
20	$Fe(OAc)_2$	iPr_2EtN	MeOH/2 h	**I**	11

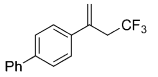
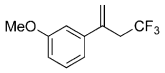
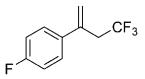
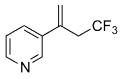
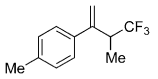
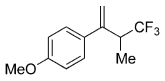
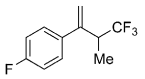
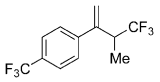
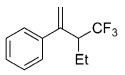
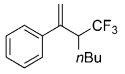
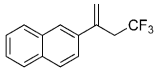
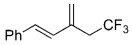
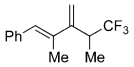
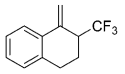
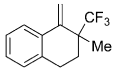
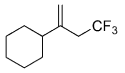
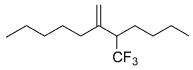
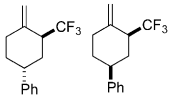
[a] The structures of reagents **I**, **II**, **III**, and **IV** are given in Figure 1. [b] Yield of isolated product. [c] No reaction, with recovery of **1b**. [d] Reaction performed with 2.0 equivalents of reagent **I**. [e] Decomposition. [f] DMAc = dimethylacetamide. [g] Reaction performed at room temperature.

(Table 1, entry 1). Various $Cu^{I/II}$ salts led to product formation with Togni's reagent **I** but were not equally efficient (Table 1, entries 2–7). The reaction of allylsilane **1b** with CuCl in methanol gave the branched product **2b** in 53% yield after 20 h (Table 1, entry 2). 2-Phenylbutene resulting from protodesilylation was observed in the crude reaction mixture but this side product could be separated by careful purification with silica gel column chromatography. CuI was a competent catalyst (Table 1, entry 3) but $[Cu(OTf)]_2C_6H_6$, CuTc (copper(I)-thiophene-2-carboxylate), $[(CH_3CN)_4Cu]PF_6^-$ and $CuCl_2$ gave **2b** in significantly lower yields (Table 1, entries 4–7). Fluoride-induced protodesilylation was predominant with $[(CH_3CN)_4Cu]PF_6^-$. We next examined the effect of the CF_3 source. Under CuCl catalysis, 3,3-dimethyl-1-(trifluoromethyl)-1,2-benzodioxole, reagent **II** (also developed by Togni), was less efficient than **I**, and both sulfonium salts **III** (Umemoto's reagent) and **IV** (Shibata's reagent) led to decomposition of the starting material (Table 1, entries 8–10). For the copper-catalyzed reactions using reagent **I**, methanol was identified as the best solvent (Table 1, entries 11–13). Further optimization revealed that the reaction was not progressing significantly after 2 h, likely due to the thermal decomposition of Togni's reagent **I** over extended period of time (Table 1, entry 14).[16] Shorter reaction time favored trifluoromethylation over competitive protodesilylation.

A series of Lewis acids were tested as alternative catalysts for this reaction.[17] Trifluoromethylation of **1b** took place in the presence of 20 mol% of $SnCl_4$ in dichloromethane furnishing **2b** in 44% yield, while no reaction took place with $BF_3{\cdot}Et_2O$ (Table 1, entries 15 and 16). Pleasingly, the inexpensive and green catalyst $Fe(OAc)_2$ led to **2b** in similar yield to that obtained with CuCl (52%, Table 1, entry 17). With the aim of suppressing protodesilylation, the reaction was carried out in the presence of a base. Significant improvement was observed when the copper-catalyzed reaction was performed in the presence of iPr_2NEt or Et_3N (Table 1, entries 18 and 19). Since the presence of iPr_2NEt led to a complex reaction mixture under Fe^{II} catalysis (Table 1, entry 20), we performed subsequent reactions in methanol using 20 mol% CuCl, and 1.2 equivalents of Togni's reagent **I** at 70°C with or without iPr_2EtN depending, in part, on the sensitivity of the substrate to protodesilylation (Table 2).

Several trends emerge upon examining the impact of *para*-aryl substitution for allylsilanes **1c**, **1e**, and **1g–j** on the efficiency of the reaction. Electron-releasing groups typically led to higher chemical yields than electron-withdrawing groups. This reactivity profile held for **1c–e** (Table 2, entries 1–3) and the branched products **2g–2l** featuring C_{sp^3}–CF_3 stereogenicity (Table 2, entries 5–10 and 17). The generation of branched allyl CF_3 products bearing substitution on the γ-position required the use of an excess of Togni's reagent **I** (2 equiv) and iPr_2EtN (2 equiv) to maximize the yields (Table 2, entries 5–10 and 17). The reaction tolerates the presence of a pyridine ring (42% yield for **2f**, Table 2, entry 4), and pleasingly, the 2-naphtyl and 2-styryl substituted products **2l** and **2m** were isolated with yields above 80% (Table 2, entries 11 and 12). A significant drop in yield was observed for the more substituted allyl CF_3 product **2o** (Table 2, entry 13). For this substrate, the addition of base did not prove to be beneficial. The branched cyclic trifluoromethylated product **2p** was isolated in 50% yield (Table 2, entry 14) but the reaction did not proceed with the cyclic allylsilane **1q**, which is disubstituted at the γ-position (Table 2, entry 15). Allylic quaternary C_{sp^3}–CF_3 stereogenicity therefore does not appear to be within the scope of this method. Secondary and primary alkyl groups are tolerated on the β-position with yields around 40% (Table 2, entries 16 and

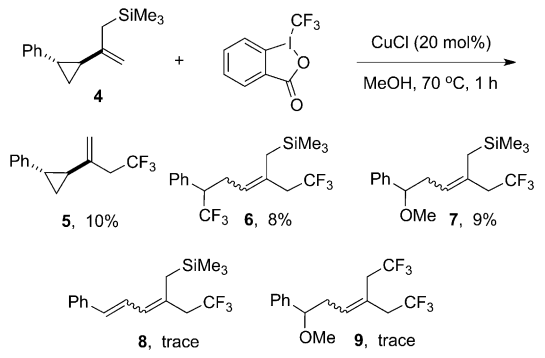
Table 2. Copper-catalyzed trifluoromethylation of **1c–t**.[a,b]

Entry	Allylsilane	Product		Yield [%][c,d]
1	**1c**		**2c**	74
2	**1d**		**2d**	70
3[e]	**1e**		**2e**	59
4	**1f**		**2f**	42
5[f]	**1g**		**2g**	40
6[f]	**1h**		**2h**	40
7[f]	**1i**		**2i**	17
8[f]	**1j**		**2j**	6
9[f]	**1k**		**2k**	42 (86)
10[f]	**1l**		**2l**	48 (96)
11	**1m**		**2m**	83
12	**1n**		**2n**	84
13[g]	**1o**		**2o**	38 (57)
14	**1p**		**2p**	50 (68)
15[h]	**1q**		**2q**	trace
16	**1r**		**2r**	42
17[f]	**1s**		**2s**	40 (58)
18[i]	**1t**		**2t**	44 *anti*/*syn* = 4.6:1[j]

[a] Reaction conditions: allylsilane (1 equiv), CuCl (20 mol%), CF_3 reagent **I** (1.2 equiv) in MeOH at 70 °C for 2 h on a 0.25–0.5 mmol scale. [b] **1g–1l**, **1o**, and **1s** were used as mixture of *Z*/*E* isomers (Z major). [c] Yield of isolated product. [d] Numbers in parentheses refer to yields based on recovery of allylsilane. [e] 1.4 equivalents of reagent **I**. [f] 2.0 equivalents of the CF_3 reagent **I** and 2.0 equivalents of iPr_2EtN. [g] Reaction time 12 h. [h] Reaction time 24 h. [i] Reaction time 3 h. [j] The d.r. was determined by ^{19}F NMR analysis of the crude product.

17). We also explored the trifluoromethylation of allylsilane **1t** possessing a stereogenic center proximal to the site of trifluoromethylation.[18] The reaction proceeded in 44% yield in favor of the *anti* diastereomer **2t** (d.r. = 4.6:1). In previous work, we have shown that a structurally related allylsilane subjected to electrophilic fluorination led to an advanced intermediate of an 1α-fluoro vitamin D_3 analogue with a similar sense and level of diastereocontrol (d.r. = 3:1 in favor of the *anti* isomer).[19] Further experimentation revealed that allylsilanes lacking an alkyl or aryl group at the β-position are unreactive.[15] The stabilization offered by the β-substituent is therefore essential for the trifluoromethylation to proceed.

Mechanistically, the superior reactivity of the *para*-substituted 2-aryl allylsilanes featuring electron-releasing groups could be attributed to the intermediacy of a benzylic carbocation following C–CF_3 bond formation (**E** or **C**, see Scheme 4); however, a similar reactivity pattern would also be expected if the reaction proceeded via an electrophilic CF_3 radical species. Silicon has the ability to stabilize efficiently β-carbocations (29–30 kcal mol^{-1})[20] through $\sigma_{Si-C} \rightarrow p$ hyperconjugation and to a lesser degree β-carboradicals (2.6–4.5 kcal mol^{-1}).[21] A pathway involving radical species is consistent with our findings and is certainly possible under copper-catalysis.[22] To gain further insight into the reaction mechanism, 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) was allowed to react with one equivalent of allylsilane (*Z*)-**1b** and 1.2 equivalents of the hypervalent iodine(III) reagent **I** in the presence of 20 mol% CuCl. Under these conditions, we recovered the starting material **1b** along with trace amounts of **2b** and of the TEMPO–CF_3 adduct (diagnostic signal at $\delta = -55$ ppm in the ^{19}F NMR spectrum).[15] These experimental results provide supportive evidence that a CF_3 radical may be involved as a reactive species in the reaction mechanism. To investigate this further, we next subjected the cyclopropane radical clock **4** to our standard reaction conditions (Scheme 2). This transformation led to a complex but tractable mixture of products. The trifluoromethylated cyclopropane **5** was isolated in 10% yield along with the ring-opened (bis)trifluoromethylated product **6** (8%), and the methoxy adduct **7** (9%). Trace amounts of the diene **8** and the (bis)trifluoromethylated methoxy adduct **9** could also be detected. The presence of the trifluoromethylated cyclopropane **5** and the ring-



Scheme 2. Trifluoromethylation of the cyclopropane radical clock **3**.

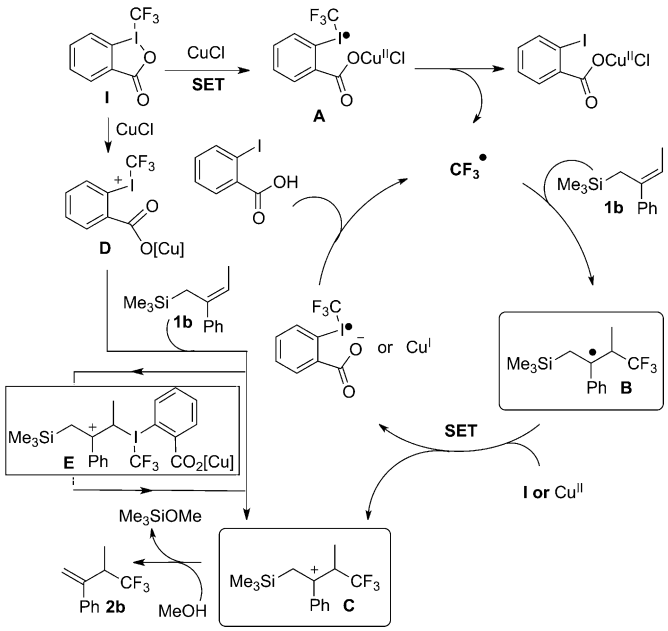
opened adduct **7** trapped with methanol indicates that a silyl-stabilized β-carbocation is a plausible intermediate undergoing either rapid desilylation or ring opening followed by intermolecular capture with the solvent. The formation of product **6** is however consistent with a radical pathway involving CF_3 radical addition followed by ring opening leading to a trifluoromethylated benzylic radical species possibly sequestered by a second CF_3 radical.

To investigate the fate of the silyl group, we carried out the trifluoromethylation using cyclic allylsilane **10**. This is a conformationally restricted substrate that does not possess the requisite coplanarity of the involved orbitals for σ–p hyperconjugative vertical stabilization. Interestingly, the reaction took place under CuCl catalysis with the formation of the allylic CF_3 product **11**, which clearly indicates that the silyl group is trapped with methanol (Scheme 3).[23]

10 **11**, 46%

Scheme 3. Trifluoromethylation of the cyclic allylsilane **10**.

Taken together, this collection of data leads us to propose the reaction pathways detailed in Scheme 4.



Scheme 4. Suggested mechanism.

In a first mechanistic scenario, Cu^I catalytically activates the Togni reagent **I** via single-electron transfer (SET), a process leading to the CF_3-containing radical species **A**.[9,22] Decomposition of intermediate **A** releases the electrophilic CF_3 radical. This radical reacts with the allylsilane **1b** resulting in the trifluoromethylated benzylic radical intermediate **B** further stabilized by the proximal silyl group. Oxidation of **B** with either Cu^{II} or **I** gives intermediate **C**, a carbocationic species that is more stabilized by the β-silyl group than **B**. Subsequent desilylation with methanol[23] gives the desired allylic CF_3 product **2b**. A mechanism with the Cu^I catalyst acting as a Lewis acid could also be operative. Upon activation of **I** leading to cationic active species **D**, electrophilic trifluoromethylation of allylsilane can take place affording intermediate **C** either directly or via reductive elimination from the λ^3-iodane species **E**.[24] Both the cationic and the radical mechanisms could operate in parallel, progressing at different rates.

In summary, we have developed an allylic trifluoromethylation of allylsilanes,[25] a method allowing access to various branched cyclic and acyclic allylic CF_3 products including compounds featuring C_{sp^3}–CF_3 stereogenicity. A preliminary analysis suggests that the mechanism is complex and involves multiple reaction pathways featuring radical and/or cationic intermediates. Current efforts focus on further examining the mechanistic details of this reaction to expand its scope and efficiency.

Experimental Section

Representative protocol for trifluoromethylation of allylsilanes: A 5 mL vial containing a magnetic stir bar was charged with allylsilane **1a** (47.6 mg, 0.25 mmol) and CuCl (5.0 mg, 20 mol%). Then MeOH (0.5 mL) and Togni's trifluoromethylating reagent **I** (0.3 mmol) were added under argon, and the reaction mixture was stirred for 2 h at 70 °C. Saturated aqueous $NaHCO_3$ was then added at room temperature. After extraction with diethyl ether, the combined organic phases were washed with distilled water and brine, then dried over $MgSO_4$, and concentrated in vacuo. After silica-gel column chromatography, **2a** (32.6 mg, 70% yield) was obtained as a colorless oil.

Acknowledgements

The authors thank the European Union (grant PIIF-GA-2010–274903 to S. M.), the CONACyT Mexico Program (grant 205456 to O. G. L.), the Skaggs-Oxford Scholarship Program and NSF GRFP (predoctoral fellowships to K. M.E.), the EPSRC, and GSK (industrial studentship to S. V.) for generous funding. We are most grateful to Prof. N. Shibata for providing a sample of reagent **IV** and Dr T. Yamamoto for early experiments.

Keywords: allylsilanes · copper · homogeneous catalysis · radicals · trifluoromethylation

[1] a) K. Müller, C. Fäh, F. Diederich, *Science* **2007**, *317*, 1881–1886; b) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320–330.

[2] For examples of (hetero)aryl–CF_3 bond formation: a) X.-S. Wang, L. Truesdale, J.-Q. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 3648–3649; b) R. Shimizu, H. Egami, T. Nagi, J. Chae, Y. Hamashima, M. Sodeoka, *Tetrahedron Lett.* **2010**, *51*, 5947–5949; c) M. S. Wiehn, E. V. Vinogradova, A. Togni, *J. Fluorine Chem.* **2010**, *131*, 951–957; d) X. Mu, S. Chen, X. Zhen, G. Liu, *Chem. Eur. J.* **2011**, *17*, 6039–6042;

e) D. A. Nagib, D. W. C. MacMillan, *Nature* **2011**, *480*, 224–228; f) L. Chu, F.-L. Qing, *J. Am. Chem. Soc.* **2012**, *134*, 1298–1304; g) L. Chu, F.-L. Qing, *J. Am. Chem. Soc.* **2010**, *132*, 7262–7263; h) K. Zhang, X.-L. Qiu, Y. Huang, F.-L. Qing, *Eur. J. Org. Chem.* **2012**, 58–61; i) Y. Ji, T. Brueckl, R. D. Baxter, Y. Fujiwara, I. B. Seiple, S. Su, D. G. Blackmond, P. S. Baran, *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 14411–14415.

[3] For recent contributions, see: a) D. A. Nagib, M. E. Scott, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2009**, *131*, 10875–10877; b) S. Noritake, N. Shibata, Y. Nomura, Y. Huang, A. Matsnev, S. Nakamura, T. Toru, D. Cahard, *Org. Biomol. Chem.* **2009**, *7*, 3599–3604; c) A. E. Allen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2010**, *132*, 4986–4987; d) V. Matoušek, A. Togni, V. Bizet, D. Cahard, *Org. Lett.* **2011**, *13*, 5762–5765.

[4] For selected syntheses of allylic CF_3 compounds with C_{sp^3}–CF_3 stereogenicity, see: a) T. Davies, R. N. Haszeldine, A. E. Tipping, *J. Chem. Soc. Perkin Trans. 1* **1980**, 927–932; b) Y. Takeyama, Y. Ichinose, K. Oshima, K. Utimoto, *Tetrahedron Lett.* **1989**, *30*, 3159–3162; c) N. Nguyen, B. E. Harris, K. B. Clark, W. J. Leigh, *Can. J. Chem.* **1990**, *68*, 1961–1966; d) W. J. Leigh, K. Zheng, N. Nguyen, N. H. Werstiuk, J. Ma, *J. Am. Chem. Soc.* **1991**, *113*, 4993–4999; e) T. Konno, T. Takehana, M. Mishima, T. Ishihara, *J. Org. Chem.* **2006**, *71*, 3545–3550; f) X. Gao, Y. J. Zhang, M. J. Krische, *Angew. Chem.* **2011**, *123*, 4259–4261; *Angew. Chem. Int. Ed.* **2011**, *50*, 4173–4175.

[5] a) T. Kitazume, N. Ishikawa, *J. Am. Chem. Soc.* **1985**, *107*, 5186–5191; b) J.-X. Duan, Q.-Y. Chen, *J. Chem. Soc. Perkin Trans. 1* **1994**, 725–730.

[6] a) Y. Kobayashi, K. Yamamoto, I. Kumadaki, *Tetrahedron Lett.* **1979**, *20*, 4071–4072; b) J. Kim, J. M. Shreeve, *Org. Biomol. Chem.* **2004**, *2*, 2728–2734.

[7] A. T. Parsons, S. L. Buchwald, *Angew. Chem.* **2011**, *123*, 9286–9289; *Angew. Chem. Int. Ed.* **2011**, *50*, 9120–9123.

[8] J. Xu, Y. Fu, D.-F. Luo, Y.-Y. Jiang, B. Xiao, Z.-J. Liu, T.-J. Gong, L. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 15300–15303.

[9] X. Wang, Y. Ye, S. Zhang, J. Feng, Y. Xu, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* **2011**, *133*, 16410–16413.

[10] a) B. Greedy, J.-M. Paris, T. Vidal, V. Gouverneur, *Angew. Chem.* **2003**, *115*, 3413–3416; *Angew. Chem. Int. Ed.* **2003**, *42*, 3291–3294; b) M. C. Pacheco, V. Gouverneur, *Org. Lett.* **2005**, *7*, 1267–1270; c) M. Tredwell, K. Tenza, M. C. Pacheco, V. Gouverneur, *Org. Lett.* **2005**, *7*, 4495–4497; d) M. Tredwell, V. Gouverneur, *Org. Biomol. Chem.* **2006**, *4*, 26–32; e) S. Thibaudeau, R. Fuller, V. Gouverneur, *Org. Biomol. Chem.* **2004**, *2*, 1110–1112; f) Y.-h. Lam, C. Bobbio, I. R. Cooper, V. Gouverneur, *Angew. Chem.* **2007**, *119*, 5198–5202; *Angew. Chem. Int. Ed.* **2007**, *46*, 5106–5110.

[11] For reviews, see: a) N. Shibata, A. Matsnev, D. Cahard, *Beilstein J. Org. Chem.* **2010**, *6*, No. 65; b) Y. Macé, E. Magnier, *Eur. J. Org. Chem.* **2012**, 2479–2494.

[12] a) P. Eisenberger, S. Gischig, A. Togni, *Chem. Eur. J.* **2006**, *12*, 2579–2586; b) I. Kieltsch, P. Eisenberger, A. Togni, *Angew. Chem.* **2007**, *119*, 768–771; *Angew. Chem. Int. Ed.* **2007**, *46*, 754–757; c) P. Eisenberger, I. Kieltsch, N. Armanino, A. Togni, *Chem. Commun.* **2008**, 1575–1577; d) K. Niedermann, N. Früh, E. Vinogradova, M. S. Wiehn, A. Togni, *Angew. Chem.* **2011**, *123*, 1091–1095; *Angew. Chem. Int. Ed.* **2011**, *50*, 1059–1063; e) E. Mejía, A. Togni, *ACS Catal.* **2012**, *2*, 521–527.

[13] a) T. Umemoto, S. Ishihara, *Tetrahedron Lett.* **1990**, *31*, 3579–3582; b) T. Umemoto, S. Ishihara, *J. Am. Chem. Soc.* **1993**, *115*, 2156–2164; c) T. Umemoto, K. Adachi, *J. Org. Chem.* **1994**, *59*, 5692–5699.

[14] A. Matsnev, S. Noritake, Y. Nomura, E. Tokunaga, S. Nakamura, N. Shibata, *Angew. Chem.* **2010**, *122*, 582–586; *Angew. Chem. Int. Ed.* **2010**, *49*, 572–576.

[15] For details, see the Electronic Supporting Information.

[16] For evidence of thermal decomposition of Togni's reagent, see reference [12b] and S. Fantasia, J. M. Welch, A. Togni, *J. Org. Chem.* **2010**, *75*, 1779–1782.

[17] For Lewis acid activation of Togni's reagent, see reference [3c] and R. Koller, K. Stanek, D. Stolz, R. Aardoom, K. Niedermann, A. Togni, *Angew. Chem.* **2009**, *121*, 4396–4400; *Angew. Chem. Int. Ed.* **2009**, *48*, 4332–4336.

[18] 3-Phenyl-1-trimethylsilylmethylcyclohexene does not react.

[19] G. Giuffredi, C. Bobbio, V. Gouverneur, *J. Org. Chem.* **2006**, *71*, 5361–5364.

[20] a) M. Sugawara, J.-i. Yoshida, *J. Org. Chem.* **2000**, *65*, 3135–3142; b) J. B. Lambert, *Tetrahedron* **1990**, *46*, 2677–2689; c) J. B. Lambert, Y. Zhao, R. W. Emblidge, L. A. Salvador, X. Liu, J.-H. So, E. C. Chelius, *Acc. Chem. Res.* **1999**, *32*, 183–190.

[21] a) T. Kawamura, J. K. Kochi, *J. Am. Chem. Soc.* **1972**, *94*, 648–650; b) D. Griller, K. U. Ingold, *J. Am. Chem. Soc.* **1974**, *96*, 6715–6720; c) R. A. Jackson, K. U. Ingold, D. Griller, A. S. Nazran, *J. Am. Chem. Soc.* **1985**, *107*, 208–211; d) N. Auner, R. Walsh, J. Westrup, *J. Chem. Soc. Chem. Commun.* **1986**, 207–208.

[22] For a review on Cu-catalyzed reactions via SET: C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3464–3484.

[23] Trapping with Cl^- is possible followed by substitution with methanol.

[24] For a similar reductive elimination, see reference [17].

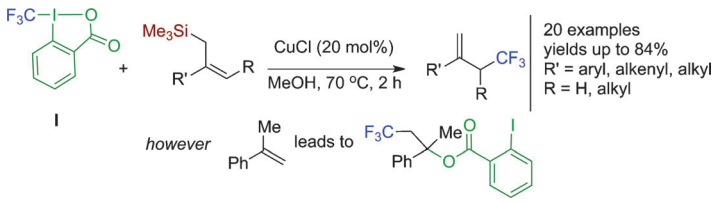
[25] Very recently, Sodeoka has reported a similar reaction: R. Shimizu, H. Egami, Y. Hamashima, M. Sodeoka, *Angew. Chem.* **2012**, *124*, 4655–4658; *Angew. Chem. Int. Ed.* **2012**, *51*, 4577–4580.

Received: April 5, 2012
Published online: ■■ ▮▮, 0000

Homogeneous Catalysis

*S. Mizuta, O. Galicia-López, K. M. Engle, S. Verhoog, K. Wheelhouse, G. Rassias, V. Gouverneur** ..... ▮▮▮▮–▮▮▮▮

Trifluoromethylation of Allylsilanes under Copper Catalysis



Branched allylic CF_3 products are accessible by copper-catalyzed trifluoromethylation of allylsilanes with the Togni reagent **I**. The silyl group is critical to control the outcome of this reaction because in its absence, a product of addition between the alkene and the Togni reagent is formed preferentially. The reaction is inhibited with 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and is likely to operate via multiple reaction pathways.

