

Trifluoromethylation

Copper-Catalyzed One-Pot Trifluoromethylation/Aryl Migration/Carbonyl Formation with Homopropargylic Alcohols**

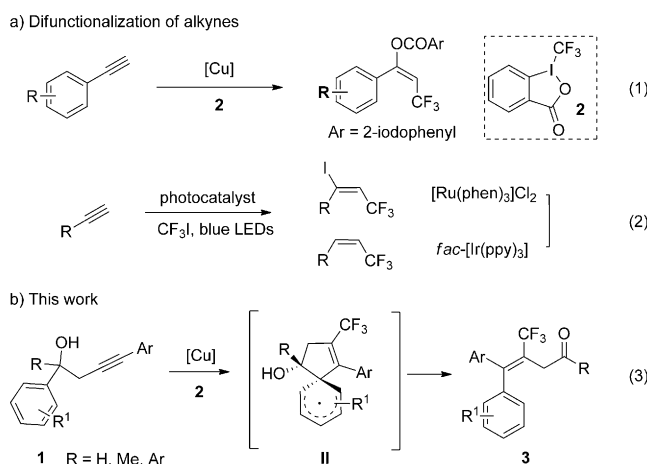
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Abstract: A novel copper-catalyzed one-pot functionalization of homopropargylic alcohols that involves trifluoromethylation, aryl migration, and formation of a carbonyl moiety has been developed. This reaction constitutes the first direct conversion of homopropargylic alcohols into CF₃-containing 3-butenal or 3-buten-1-one derivatives in a regioselective manner. Mechanistic studies indicate that the 1,4-aryl migration proceeds through a radical pathway.

Trifluoromethyl-containing compounds have gained much attention because of their unique electronegativity, metabolic stability, and lipophilicity, which improve the physical and biological properties of pharmaceuticals, agrochemicals, and materials.^[1] As a consequence, numerous versatile and efficient methods to incorporate the CF₃ group into target molecules have been reported.^[2,3] Transition-metal-catalyzed trifluoromethylation reactions have emerged as powerful synthetic methods and feature high regioselectivity, mild reaction conditions, and efficient conversion.^[4–7] Copper and palladium complexes were shown to be efficient in the construction of aryl–CF₃ bonds from aryl halides and aryl boronic acids.^[5] The formation of C(sp³)–CF₃ bonds has also been realized from allyl halides, allylsilanes, and even unactivated alkenes with copper as the catalyst.^[6] Furthermore, difunctionalizing trifluoromethylation reactions of alkenes have been developed to construct C(sp³)–CF₃ bonds with concomitant formation of carbon–nucleophile bonds.^[7]

Trifluoromethylated alkenes are commonly found in biologically active compounds and are featured in pharmaceuticals and agrochemicals.^[8] Commonly used strategies for the formation of vinyl–CF₃ bonds are based on transition-metal-mediated or -catalyzed trifluoromethylation reactions of vinylboronic acids,^[9] vinyl sulfonates,^[10] potassium vinyltrifluoroborates,^[11] α,β-unsaturated acids,^[12] or unactivated

alkenes^[13] and on the directing-group-assisted trifluoromethylation of alkenes.^[14] Furthermore, new synthetic methods for the difunctionalization of alkynes to construct olefinic



Scheme 1. Difunctionalization of alkynes to construct olefinic C(sp²)–CF₃ bonds.

Table 1: Optimization of the reaction conditions.^[a]

Entry	Catalyst	Solvent	Yield [%] ^[b]
1	[Cu(CH ₃ CN) ₄]PF ₆	CH ₂ Cl ₂	34
2	CuBr	CH ₂ Cl ₂	36
3	CuCN	CH ₂ Cl ₂	46
4	CuI	CH ₂ Cl ₂	51
5	CuOAc	CH ₂ Cl ₂	39
6	Cu(OTf) ₂	CH ₂ Cl ₂	38
7	FeCl ₂	CH ₂ Cl ₂	33
8	CuI	DMF	0
9	CuI	MeCN	0
10	CuI	toluene	0
11	CuI	CHCl ₃	62 (21 ^[f])
12 ^[c]	CuI	CHCl ₃	44
13 ^[d]	CuI	CHCl ₃	55
14 ^[e]	CuI	CHCl ₃	56
15	none	CH ₂ Cl ₂	0

[a] Reaction conditions: **1a** (0.2 mmol), Togni's reagent (**2**; 0.4 mmol), and the catalyst (0.04 mmol) in the specified solvent (1.5 mL) were stirred at 30 °C for 24 h under argon. [b] Yield of isolated product. [c] CuI (0.06 mmol). [d] CuI (0.02 mmol). [e] The reaction was performed at 50 °C. [f] The amount of recovered starting material is given in parentheses.

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$C(sp^2)-CF_3$ bonds have recently been explored.^[15] In 2012, the groups of Szabo^[15a] and Sodeoka^[15b] independently studied the oxy-trifluoromethylation of alkynes for the construction of $C(sp^2)-CF_3$ bonds [Scheme 1, Eq. (1)]. Very recently, Cho and co-workers successfully performed the iodo-trifluoromethylation and hydro-trifluoromethylation of alkynes using CF_3I as the trifluoromethylating reagent, and two different products could be isolated depending on the choice of visible-light photoredox catalyst, base, and solvent [Scheme 1, Eq. (2)].^[15c] These trifluoromethylation reactions of alkynes, however, are mainly limited to additions to terminal alkynes. There are few reports on constructing olefinic $C(sp^2)-CF_3$ bonds through the addition of trifluoromethyl radicals to internal alkynes,^[16] in spite of the fact that carbon–carbon triple bonds can easily be converted into multisubstituted alkenes by addition reactions. Therefore, an efficient method for the catalytic trifluoromethylation of alkynyl carbon atoms is highly desired. Herein, we report an unprecedented and highly regioselective route to CF_3 -containing tetrasubstituted 3-butenal and 3-buten-1-one derivatives under copper catalysis, which combines alkyne trifluoromethylation, 1,4-aryl migration, and formation of a carbonyl moiety in a one-pot reaction. Importantly, this reaction involves an intramolecular 1,4-aryl migration,^[17] which proceeds via a 5-*ipso* cyclization intermediate [II; Scheme 1, Eq. (3)].^[18]

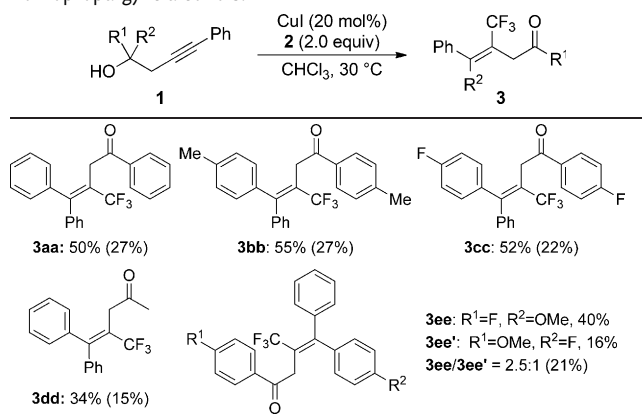
Our investigation commenced with the reaction of 1,4-diphenylbut-3-yn-1-ol (**1a**) with Togni's reagent (**2**) and $[Cu(CH_3CN)_4]PF_6$ (20 mol %) in CH_2Cl_2 at 30 °C under argon atmosphere. The unexpected trifluoromethylated 3-butenal **3a** was formed in 34% yield (Table 1, entry 1). The structure of **3a** was determined by X-ray crystallographic analysis (see the Supporting Information).^[19] Encouraged by this result, we then screened different copper salts, including $CuBr$, $CuCN$, $Cu(OTf)_2$, $CuOAc$, and CuI , for this trifluoromethylation/aryl migration reaction (entries 2–6), and found that CuI was slightly more effective, increasing the yield to 51%. $FeCl_2$ showed poor catalytic activity towards this transformation (entry 7). Next, a solvent screen

revealed that the reaction was highly solvent-dependent: The highest yields were obtained for reactions conducted in $CHCl_3$, whereas no desired product was detected in DMF, MeCN, and toluene (entries 8–11). Changing the catalyst loading^[20] or increasing the reaction temperature did not improve the yield further (entries 12–14). Other attempts to promote this transformation proved to be ineffective (see the Supporting Information). A control experiment revealed that the copper catalyst was essential for the reaction (entry 15). Consequently, the reaction proceeded efficiently in the presence of CuI (20 mol %) in $CHCl_3$ at 30 °C.

Table 2: Copper-catalyzed trifluoromethylation and aryl migration of secondary homopropargylic alcohols.^[a,b]

[a] Reaction conditions: CuI (0.04 mmol, 20 mol %), **1** (0.2 mmol, 1.0 equiv), Togni's reagent (**2**; 0.2 mmol, 2.0 equiv), $CHCl_3$ (1.5 mL), 30 °C, 24 h, argon atmosphere. [b] Yields of isolated products, the amount of recovered starting material is given in parentheses.

Table 3: Copper-catalyzed trifluoromethylation/aryl migration of tertiary homopropargylic alcohols.^[a,b]



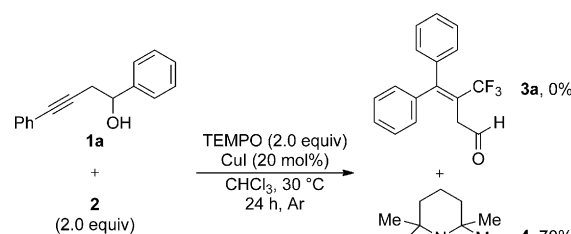
[a] Reaction conditions: CuI (0.04 mmol, 20 mol%), **1** (0.2 mmol, 1.0 equiv), Togni's reagent (**2**; 0.2 mmol, 2.0 equiv), CHCl₃ (1.5 mL), 30 °C, 24 h, argon atmosphere. [b] Yields of isolated products, the amount of recovered starting material is given in parentheses.

With the optimized reaction conditions established, we next set out to evaluate the scope of the trifluoromethylation/aryl migration reaction with various secondary homopropargylic alcohols **1b–1w**. The results are summarized in Table 2. The effects of the substitution pattern of the aryl ring that is attached to the triple bond were not obvious. Alcohols with both electron-rich (**1b–1d**) and electron-poor (**1e–1g**) aryl substituents were found to undergo migration, affording the corresponding products **3b–3g** in moderate yields. Even ester and trifluoromethyl groups were tolerated under the reaction conditions (**1h, 1i**). It is noteworthy that a substrate with 5-methylthiophene attached to the triple bond (**1j**) successfully provided the desired product in 43 % yield. Then, a number of alcohols derived from substituted benzaldehydes were tested. Substrates **1k–1o**, which bear electron-donating substituents in the *ortho*, *meta*, or *para* position of the aryl group, were efficiently transformed into the β -trifluoromethyl-substituted 3-butenals **3k–3o** in moderate yields. With a fluorine substituent in the *para* position, the desired product **3p** was formed in 58 % yield. However, for substrates with chloro, bromo, or CF₃ groups in the *para* position (**1q–1s**), not only the expected products **3q–3s** were obtained, but also isomers with a six-membered ring (**4q–4s**), which were isolated in 9 %, 13 %, and 32 % yield, respectively. A hydroxy group was also tolerated under the reaction conditions, and **3t** was isolated in moderate yield.^[19] Substrates with two or three identical substituents on the aryl ring provided the products (**3u, 3v**) in moderate to good yields. Even a 5-methylfuran derivative could undergo the migration to give **3w** in 31 % yield.

Next, various tertiary homopropargylic alcohols were investigated (Table 3). Symmetric α,α -diaryl homopropargylic alcohols with electron-deficient or electron-rich aryl groups (**1aa–1cc**) afforded the desired β -vinyl β -trifluoromethyl ketone derivatives in moderate yields. The reaction of unsymmetric substrate **1dd** was highly chemoselective, with only the product of phenyl migration being observed. How-

ever, when **1ee** was chosen as the substrate to investigate the selectivity of the aryl migration, the two isomeric products **3ee** and **3ee'** could be isolated in a ratio of 2.5:1.

To gain insight into the reaction mechanism, we performed a control experiment. First, the reaction was completely inhibited when 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), a radical scavenger, was added to the system under the standard reaction conditions (Scheme 2); instead, the TEMPO–CF₃ adduct (**4**) was formed in 70 % yield, as estimated by ¹⁹F NMR spectroscopy. Furthermore, we tried to capture some radical intermediates by electron spin resonance (ESR) with the 2-methyl-2-nitrosopropane dimer (MNP) as the radical trap (Figure 1). An ESR spectrum of a typical reaction mixture with MNP displayed a signal with six peaks, which confirmed the presence of a CF₃ radical (trace b).^[21] These results indicate that the reaction was initiated by the CF₃ radical. When MNP was added to the reaction mixture at a later stage, a different signal was observed, which might be the radical intermediate **A** (trace c; see also Scheme 3) caught by the MNP, which is in line with the species detected by HRMS–ESI (for details see the Supporting Information).



Scheme 2. Control experiment for mechanistic insights. Yields determined by ¹⁹F NMR spectroscopy.

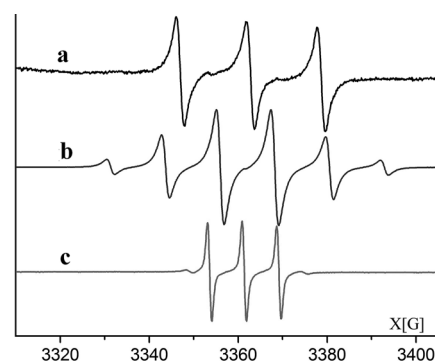
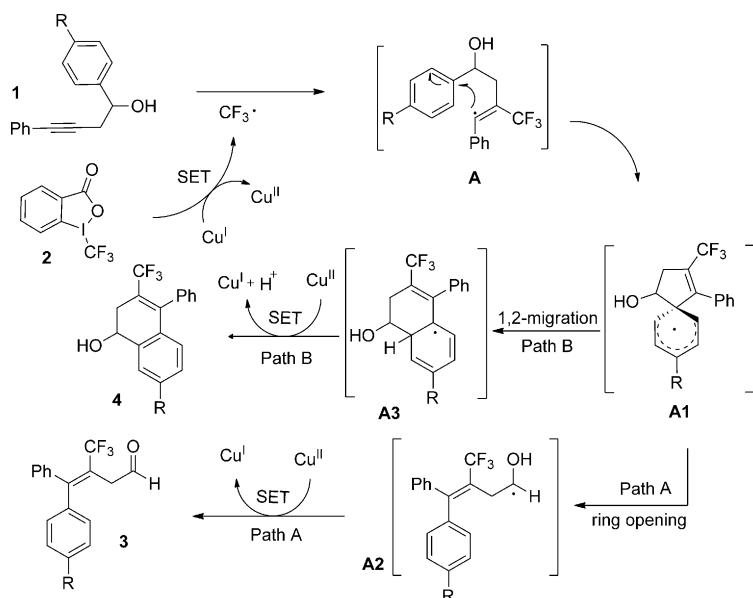


Figure 1. ESR studies. a) ESR spectrum of a solution of 2-methyl-2-nitrosopropane (MNP; $5 \times 10^{-2} \text{ mol L}^{-1}$) in CHCl₃ stirred for 1 h. b) ESR spectrum of a solution of **1a** ($5 \times 10^{-2} \text{ mol L}^{-1}$, 0.2 mmol), Togni's reagent **2** (0.1 mol L^{-1} , 0.4 mmol), MNP (0.1 mol L^{-1} , 0.4 mmol), and CuI ($1 \times 10^{-2} \text{ mol L}^{-1}$, 0.04 mmol) in CHCl₃ (4 mL) stirred for 1 h. c) A solution of **1a** ($5 \times 10^{-2} \text{ mol L}^{-1}$, 0.2 mmol), Togni's reagent **2** ($5 \times 10^{-2} \text{ mol L}^{-1}$, 0.2 mmol), and CuI ($1 \times 10^{-2} \text{ mol L}^{-1}$, 0.04 mmol) in CHCl₃ (4 mL) was stirred for 8 h, then a solution of MNP (0.2 mmol) was added; the spectrum was recorded 30 min later.



Scheme 3. Proposed mechanism.

To gain further understanding of the reaction mechanism, we conducted computational studies using **1a** as a model compound.^[22] The calculation indicated that 1,4-aryl migration can proceed through a radical pathway. Single-electron transfer (SET) between radical intermediate **A** and the Cu^{II} species, which would lead to a cationic transition state during the migration, was found to be unfavorable (for details, see the Supporting Information).

Based on the above experiments and density functional theory (DFT) studies, a possible reaction mechanism for the trifluoromethylation and aromatization of alkynes was proposed (Scheme 3). The CF₃ radical, generated from Togni's reagent (**2**) and Cu^I, undergoes radical addition to alkyne **1** to afford radical **A**. A 5-*ipso* cyclization occurs on the benzene ring, leading to radical **A1**,^[17] which then undergoes intramolecular 1,4-aryl migration to form a new C(sp³)-centered radical intermediate **A2**.^[18] Finally, oxidation of radical **A2** with Cu^{II} gives the desired product **3** and releases the copper(I) catalyst (Path A). The radical intermediate **A1** can undergo 1,2-migration to afford the radical intermediate **A3** (Path B),^[17a] which would give the side products **4** through a SET process.

In conclusion, we have developed an unprecedented one-pot reaction of homopropargylic alcohols that involves copper-catalyzed trifluoromethylation, 1,4-aryl migration, and formation of a carbonyl group. A series of 3-butenal and 3-buten-1-one derivatives containing a C=C–CF₃ subunit have been obtained in moderate to good yields under mild conditions. The control experiment and ESR studies indicate that the reaction is initiated by the addition of the CF₃ radical to the alkyne. 1,4-Aryl migration can proceed through 5-*ipso* cyclization, which leads to the high regioselectivity.

Experimental Section

General procedure for the trifluoromethylation/aryl migration of homopropargylic alcohol **1**: In a glass tube, Togni's reagent **2** (126.0 mg, 0.4 mmol) and CuI (7.6 mg, 0.04 mmol) were successively added to a solution of **1** (0.2 mmol) in CHCl₃ (1.5 mL). The reactor was flushed with argon and sealed. The reaction mixture was stirring at 30°C for 24 h; then, the reaction mixture was partitioned between CH₂Cl₂ and a saturated aqueous NaHCO₃ solution (15 mL each). The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂ (2 × 15 mL). The combined organic extracts were washed with saturated aqueous NaHCO₃ solution, dried over Na₂SO₄, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate) to afford **3**.

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- [1] a) P. Kirsch, *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*, Wiley-VCH, Weinheim, **2004**; b) M. Shimizu, T. Hiyama, *Angew. Chem.* **2005**, *117*, 218; *Angew. Chem. Int. Ed.* **2005**, *44*, 214; c) M. Schlosser, *Angew. Chem.* **2006**, *118*, 5558; *Angew. Chem. Int. Ed.* **2006**, *45*, 5432; d) K. Müller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881; e) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320; f) W. K. Hagmann, *J. Med. Chem.* **2008**, *51*, 4359; g) I. Ojima, *Fluorine in Medicinal Chemistry and Chemical Biology*, Wiley-Blackwell, Chichester, **2009**, p. 3; h) S. K. Ritter, *Chem. Eng. News* **2012**, *90*, 10.
- [2] For recent reviews on trifluoromethylation reactions, see: a) J. Ma, D. Cahard, *J. Fluorine Chem.* **2007**, *128*, 975; b) Y. Zheng, J.-A. Ma, *Adv. Synth. Catal.* **2010**, *352*, 2745; c) T. Furuya, A. S. Kamlet, T. Ritter, *Nature* **2011**, *473*, 470; d) A. D. Dilman, V. V. Levin, *Eur. J. Org. Chem.* **2011**, 831; e) O. A. Tomashenko, V. V. Grushin, *Chem. Rev.* **2011**, *111*, 4475; f) T. Besset, C. Schneider, D. Cahard, *Angew. Chem.* **2012**, *124*, 5134; *Angew. Chem. Int. Ed.* **2012**, *51*, 5048; g) X.-F. Wu, H. Neumann, M. Beller, *Chem. Asian J.* **2012**, *7*, 1744; h) A. Studer, *Angew. Chem.* **2012**, *124*, 9082; *Angew. Chem. Int. Ed.* **2012**, *51*, 8950; i) Y. Ye, M. S. Sanford, *Synlett* **2012**, 2005; j) G. K. S. Prakash, P. V. Jog, P. T. D. Batamack, G. A. Olah, *Science* **2012**, *338*, 1324.
- [3] For recent examples, see: a) D. A. Nagib, M. E. Scott, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2009**, *131*, 10875; b) B. Morandi, E. M. Carreira, *Angew. Chem.* **2010**, *122*, 950; *Angew. Chem. Int. Ed.* **2010**, *49*, 938; c) A. E. Allen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2010**, *132*, 4986; d) P. V. Pham, D. A. Nagib, D. W. C. MacMillan, *Angew. Chem.* **2011**, *123*, 6243; *Angew. Chem. Int. Ed.* **2011**, *50*, 6119; e) D. A. Nagib, D. W. C. MacMillan, *Nature* **2011**, *480*, 224; f) B. Morandi, B. Mariampillai, E. M. Carreira, *Angew. Chem.* **2011**, *123*, 1133; *Angew. Chem. Int. Ed.* **2011**, *50*, 1101; g) Y. Fujiwara, J. A. Dixon, F. O'Hara, E. D. Funder, D. D. Dixon, R. A. Rodríguez, R. D. Baxter, H. Herlé, N. Sach, M. R. Collins, Y. Ishihara, P. S. Baran, *Nature* **2012**, *492*, 95.
- [4] a) V. V. Grushin, W. J. Marshall, *J. Am. Chem. Soc.* **2006**, *128*, 12644; b) G. G. Dubinina, H. Furutachi, D. A. Vicić, *J. Am. Chem. Soc.* **2008**, *130*, 8600; c) N. D. Ball, J. W. Kampf, M. S. Sanford, *J. Am. Chem. Soc.* **2010**, *132*, 2878; d) Y. Ye, N. D. Ball, J. W. Kampf, M. S. Sanford, *J. Am. Chem. Soc.* **2010**, *132*, 14682; e) X. Wang, L. Truesdale, J.-Q. Yu, *J. Am. Chem. Soc.* **2010**, *132*,

- 3648; f) N. D. Ball, J. B. Gary, Y. Ye, M. S. Sanford, *J. Am. Chem. Soc.* **2011**, *133*, 7577; g) C.-P. Zhang, Z.-L. Wang, Q.-Y. Chen, C.-T. Zhang, Y.-C. Gu, J.-C. Xiao, *Angew. Chem.* **2011**, *123*, 1936; *Angew. Chem. Int. Ed.* **2011**, *50*, 1896; h) O. A. Tomashenko, E. C. Escudero-Adán, M. M. Belmonte, V. V. Grushin, *Angew. Chem.* **2011**, *123*, 7797; *Angew. Chem. Int. Ed.* **2011**, *50*, 7655; i) I. Popov, S. Lindeman, O. Daugulis, *J. Am. Chem. Soc.* **2011**, *133*, 9286; j) N. D. Litvinas, P. S. Fier, J. F. Hartwig, *Angew. Chem.* **2012**, *124*, 551; *Angew. Chem. Int. Ed.* **2012**, *51*, 536; k) T. Liu, X. Shao, Y. Wu, Q. Shen, *Angew. Chem.* **2012**, *124*, 555; *Angew. Chem. Int. Ed.* **2012**, *51*, 540; l) L. Chu, F.-L. Qing, *J. Am. Chem. Soc.* **2012**, *134*, 1298; m) Y. Zhao, J. Hu, *Angew. Chem.* **2012**, *124*, 1057; *Angew. Chem. Int. Ed.* **2012**, *51*, 1033; n) X.-G. Zhang, H.-X. Dai, M. Wasa, J.-Q. Yu, *J. Am. Chem. Soc.* **2012**, *134*, 11948; o) Y. Li, L. P. Wu, H. Neumann, M. Beller, *Chem. Commun.* **2013**, *49*, 2628.
- [5] a) M. Oishi, H. Kondo, H. Amii, *Chem. Commun.* **2009**, 1909; b) E. J. Cho, T. D. Senecal, T. Kinzel, Y. Zhang, D. A. Watson, S. L. Buchwald, *Science* **2010**, *328*, 1679; c) H. Morimoto, T. Tsubogo, N. D. Litvinas, J. F. Hartwig, *Angew. Chem.* **2011**, *123*, 3877; *Angew. Chem. Int. Ed.* **2011**, *50*, 3793; d) X. Mu, S. Chen, X. Zhen, G. Liu, *Chem. Eur. J.* **2011**, *17*, 6039; e) Y. Ye, M. S. Sanford, *J. Am. Chem. Soc.* **2012**, *134*, 9034; f) M. Presset, D. Oehrich, F. Rombouts, G. A. Molander, *J. Org. Chem.* **2013**, *78*, 12837.
- [6] For recent examples of copper-catalyzed C(sp³)-CF₃ bond-forming reactions, see: a) A. T. Parsons, S. L. Buchwald, *Angew. Chem.* **2011**, *123*, 9286; *Angew. Chem. Int. Ed.* **2011**, *50*, 9120; b) 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; c) X. Wang, Y. Ye, S. Zhang, J. Feng, Y. Xu, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* **2011**, *133*, 16410; d) L. Chu, F.-L. Qing, *Org. Lett.* **2012**, *14*, 2106; e) Y. Miyake, S.-I. Ota, Y. Nishibayashi, *Chem. Eur. J.* **2012**, *18*, 13255; f) R. Shimizu, H. Egami, Y. Hamashima, M. Sodeoka, *Angew. Chem.* **2012**, *124*, 4655; *Angew. Chem. Int. Ed.* **2012**, *51*, 4577; g) S. Mizuta, O. Galicia-López, K. M. Engle, S. Verhoog, K. Wheelhouse, G. Rassias, V. Gouverneur, *Chem. Eur. J.* **2012**, *18*, 8583.
- [7] a) Y. Li, A. Studer, *Angew. Chem.* **2012**, *124*, 8345; *Angew. Chem. Int. Ed.* **2012**, *51*, 8221; b) X. Mu, T. Wu, H.-Y. Wang, Y.-L. Guo, G. Liu, *J. Am. Chem. Soc.* **2012**, *134*, 878; c) Y. Yasu, T. Koike, M. Akita, *Angew. Chem.* **2012**, *124*, 9705; *Angew. Chem. Int. Ed.* **2012**, *51*, 9567; d) R. Zhu, S. L. Buchwald, *J. Am. Chem. Soc.* **2012**, *134*, 12462; e) D.-F. Lu, C.-L. Zhu, H. Xu, *Chem. Sci.* **2013**, *4*, 2478; f) Y.-T. He, L.-H. Li, Y.-F. Yang, Y.-Q. Wang, J.-Y. Luo, X.-Y. Liu, Y.-M. Liang, *Chem. Commun.* **2013**, *49*, 5687; g) H. Egami, R. Shimizu, S. Kawamura, M. Sodeoka, *Angew. Chem.* **2013**, *125*, 4092; *Angew. Chem. Int. Ed.* **2013**, *52*, 4000; h) H. Egami, S. Kawamura, A. Miyazaki, M. Sodeoka, *Angew. Chem.* **2013**, *125*, 7995; *Angew. Chem. Int. Ed.* **2013**, *52*, 7841; i) H. Egami, R. Shimizu, Y. Usui, M. Sodeoka, *Chem. Commun.* **2013**, *49*, 7346; j) N. O. Ilchenko, P. G. Janson, K. J. Szabó, *J. Org. Chem.* **2013**, *78*, 11087; k) R. Zhu, S. L. Buchwald, *Angew. Chem.* **2013**, *125*, 12887; *Angew. Chem. Int. Ed.* **2013**, *52*, 12655; l) P. Gao, X.-B. Yan, T. Tao, F. Yang, T. He, X.-R. Song, X.-Y. Liu, Y.-M. Liang, *Chem. Eur. J.* **2013**, *19*, 14420; m) L. Li, M. Deng, S.-C. Zheng, Y.-P. Xiong, B. Tan, X.-Y. Liu, *Org. Lett.* **2014**, *16*, 504; n) F. Wang, X.-X. Qi, Z.-L. Liang, P.-H. Chen, G.-S. Liu, *Angew. Chem.* **2014**, *126*, 1912; *Angew. Chem. Int. Ed.* **2014**, *53*, 1881.
- [8] a) J. Borvendeg, I. Hermann, O. Csuka, *Acta Physiol. Hung.* **1996**, *84*, 405; b) V. Erdelyi-Tóth, F. Gyergyay, I. Számel, E. Pap, J. Královanszky, E. Bojti, M. Csörgo, S. Drabant, I. Klebovich, *Anti-Cancer Drugs* **1997**, *8*, 603; c) E. L. Amweg, D. P. Weston, N. M. Ureda, *Environ. Toxicol. Chem.* **2005**, *24*, 966.
- [9] a) L. Chu, F.-L. Qing, *Org. Lett.* **2010**, *12*, 5060; b) T. Liu, Q. Shen, *Org. Lett.* **2011**, *13*, 2342.
- [10] a) E. J. Cho, S. L. Buchwald, *Org. Lett.* **2011**, *13*, 6552.
- [11] a) A. T. Parsons, T. D. Senecal, S. L. Buchwald, *Angew. Chem.* **2012**, *124*, 3001; *Angew. Chem. Int. Ed.* **2012**, *51*, 2947.
- [12] a) Z.-B. He, T. Luo, M.-Y. Hu, Y.-J. Cao, J.-B. Hu, *Angew. Chem.* **2012**, *124*, 4010; *Angew. Chem. Int. Ed.* **2012**, *51*, 3944.
- [13] a) N. Iqbal, S. Choi, E. Kim, E. J. Cho, *J. Org. Chem.* **2012**, *77*, 11383.
- [14] a) C. Feng, T.-P. Loh, *Chem. Sci.* **2012**, *3*, 3458; b) C. Feng, T.-P. Loh, *Angew. Chem.* **2013**, *125*, 12640; *Angew. Chem. Int. Ed.* **2013**, *52*, 12414.
- [15] a) P. G. Janson, I. Ghoneim, N. O. Ilchenko, K. J. Szabó, *Org. Lett.* **2012**, *14*, 2882; b) H. Egami, R. Shimizu, S. Kawamura, M. Sodeoka, *Tetrahedron Lett.* **2012**, *53*, 5503; c) N. Iqbal, J. Jung, S. Park, E. J. Cho, *Angew. Chem.* **2014**, *126*, 549; *Angew. Chem. Int. Ed.* **2014**, *53*, 539; d) G.-C. Ge, X.-J. Huang, C.-H. Ding, S.-L. Wan, L.-X. Dai, X.-L. Hou, *Chem. Commun.* **2014**, *50*, 3048.
- [16] For the addition of trifluoromethyl radicals to internal alkynes, see: a) T. Kitazume, N. Ishikawa, *J. Am. Chem. Soc.* **1985**, *107*, 5186; b) Y. Takeyama, Y. Ichinose, K. Oshima, K. Utimoto, *Tetrahedron Lett.* **1989**, *30*, 3159; c) Y.-P. Xiong, M.-Y. Wu, X.-Y. Zhang, C.-L. Ma, L. Huang, L.-J. Zhao, B. Tan, X.-Y. Liu, *Org. Lett.* **2014**, *16*, 1000.
- [17] For a review on radical aryl migration reactions, see: a) A. Studer, M. Bossart, *Tetrahedron* **2001**, *57*, 9649; for radical 1,4-aryl migration reactions, see: b) A. Gheorghe, B. Quiclet-Sire, X. Vila, S. Z. Zard, *Org. Lett.* **2005**, *7*, 1653; c) J. Sandoval-Lira, J. M. Hernández-Pérez, F. Sartillo-Piscil, *Tetrahedron Lett.* **2012**, *53*, 6689; d) W. Thaharn, D. Soorukram, C. Kuhakarn, P. Tuchinda, V. Reutrakul, M. Pohmakotr, *Angew. Chem.* **2014**, *126*, 2244; *Angew. Chem. Int. Ed.* **2014**, *53*, 2212.
- [18] For aryl migration reactions that involve trifluoromethylation, see: a) X.-W. Liu, F. Xiong, X.-P. Huang, L. Xu, P.-F. Li, X.-X. Wu, *Angew. Chem.* **2013**, *125*, 7100; *Angew. Chem. Int. Ed.* **2013**, *52*, 6962; b) Z.-M. Chen, W. Bai, S.-H. Wang, B.-M. Yang, Y.-Q. Tu, F.-M. Zhang, *Angew. Chem.* **2013**, *125*, 9963; *Angew. Chem. Int. Ed.* **2013**, *52*, 9781; c) W. Kong, M. Casimiro, E. Merino, C. Nevado, *J. Am. Chem. Soc.* **2013**, *135*, 14480; d) W. Kong, M. Casimiro, N. Fuentes, E. Merino, C. Nevado, *Angew. Chem.* **2013**, *125*, 13324; *Angew. Chem. Int. Ed.* **2013**, *52*, 13086; e) H. Egami, R. Shimizu, Y. Usui, M. Sodeoka, *Chem. Commun.* **2013**, *49*, 7346.
- [19] CCDC 996521 (**3a**) and 984301 (**3t**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif (see the Supporting Information).
- [20] A higher catalyst loading led to product decomposition.
- [21] C.-X. Zhao, Y.-Y. Peng, Y.-L. Qu, *Chem. J. Chin. Univ.* **1992**, *13*, 1448.
- [22] See the Supporting Information for details of the theoretical study.