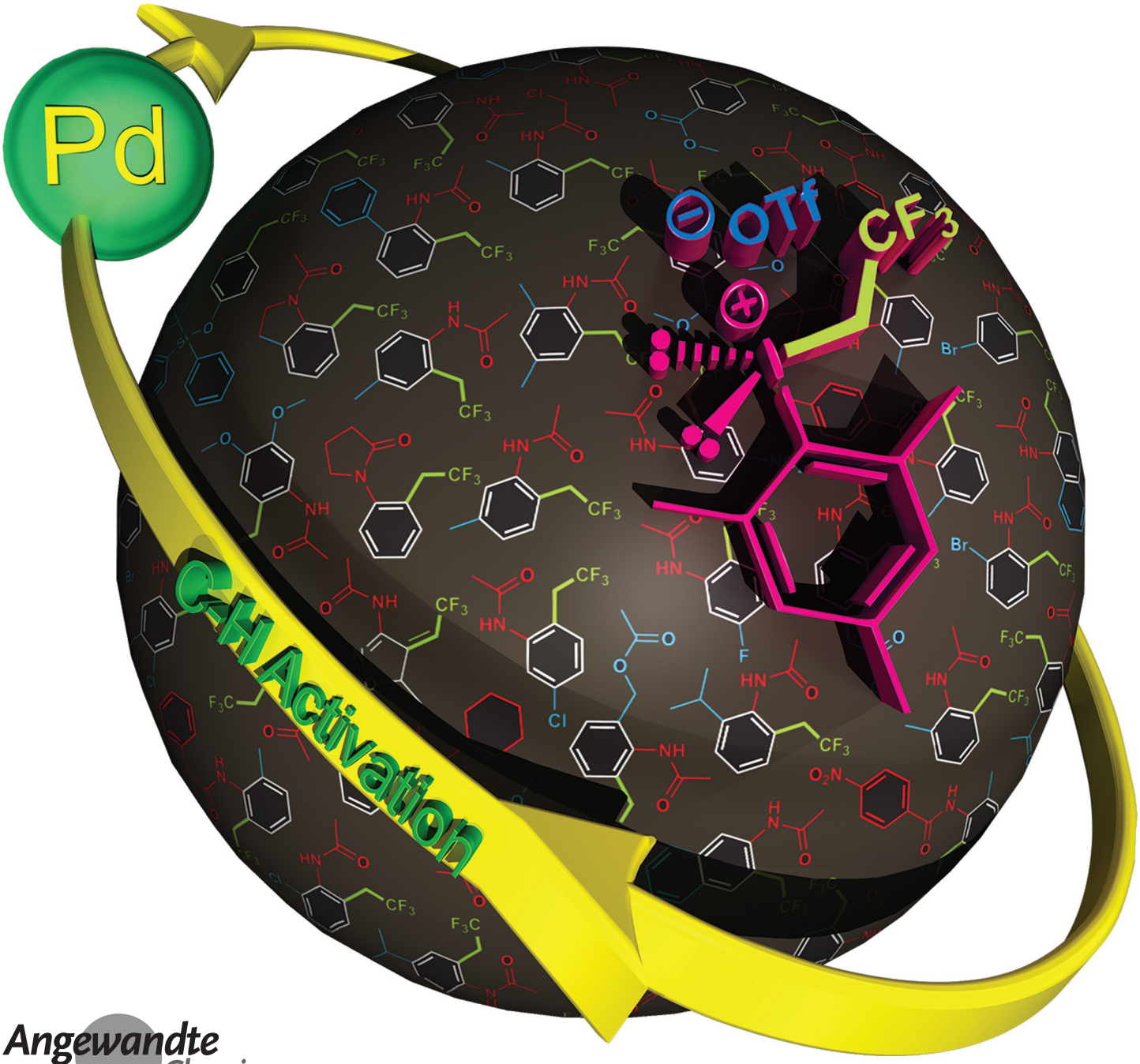
Trifluoroethylation

International Edition: DOI: 10.1002/anie.201510555
German Edition: DOI: 10.1002/ange.201510555

Mild and Efficient Palladium-Catalyzed Direct Trifluoroethylation of Aromatic Systems by C–H Activation

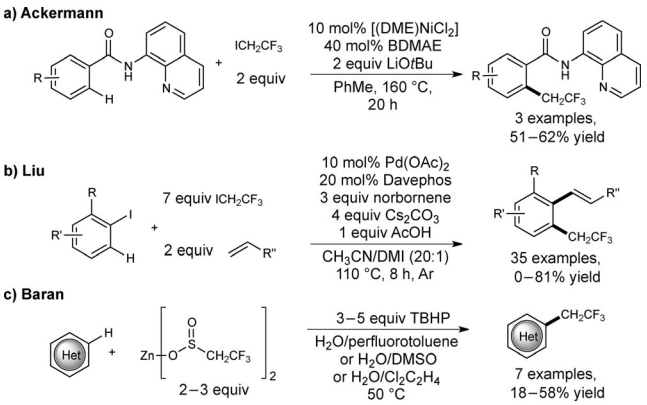
*Balázs L. Tóth[+], Szabolcs Kovács[+], Gergő Sályi, and Zoltán Novák**



Abstract: *The introduction of trifluoroalkyl groups into aromatic molecules is an important transformation in the field of organic and medicinal chemistry. However, the direct installation of fluoroalkyl groups onto aromatic molecules still represents a challenging and highly demanding synthetic task. Herein, a simple trifluoroethylation process that relies on the palladium-catalyzed C–H activation of aromatic compounds is described. With the utilization of a highly active trifluoroethyl(mesityl)iodonium salt, the developed catalytic method enables the first highly efficient and selective trifluoroethylation of aromatic compounds. The robust catalytic procedure provides the desired products in up to 95% yield at 25°C in 1.5 to 3 hours and tolerates a broad range of functional groups. The utilization of hypervalent reagents opens new synthetic possibilities for direct alkylations and fluoroalkylations in the field of transition-metal-catalyzed C–H activation.*

The potential of transition-metal-catalyzed C–H activation in organic chemistry has been extensively exploited over the last decade.[1] Both C–H activation of aromatic systems[1,2] and C(sp^3)–H functionalization[3] with the aid of directing groups have been evaluated, and several methods offer solutions for the construction of new carbon–carbon bonds. In contrast to the vast array of methods available for transition-metal-catalyzed arylation by C–H activation, the alkylation of aromatic molecules through C–H bond activation is less explored.[4] Fluorine-substituted alkyl groups are of particular importance for the pharmaceutical and agrochemical industries as well as for materials science, as the electronic properties and the lipophilicity, bioavailability, and metabolic stability of compounds can be fine-tuned by substitution with fluorine.[5] Therefore, the development of new synthetic methods for the installation of trifluoromethyl groups is an emerging area of synthetic organic chemistry. Despite the great number of trifluoromethylation methods already available,[6] the introduction of other alkyl groups bearing CF_3 groups has hardly been explored. The simplest alkyl homologue that contains a CF_3 moiety is the trifluoroethyl group. Considering its structural features, this group resembles OCF_3 and SCF_3 moieties, which are frequently used in medicinal chemistry.[7] Furthermore, trifluoroethyl groups connected to heteroatoms are present in several drugs, such as Flecainide (OCH_2CF_3), Polythiazide (SCH_2CF_3), or Quazepam (NCH_2CF_3). However, the synthesis and medical applications of trifluoroethyl-substituted aromatic compounds have not been studied in much detail.

The installation of trifluoroethyl groups at aromatic cores with concomitant formation of new carbon–carbon bonds can be achieved by various transition-metal-catalyzed coupling reactions.[8] Nickel- and palladium-catalyzed Suzuki-type reactions have enabled the trifluoroethylation of aromatic halides,[9] tosylates,[10] and diazo compounds.[11] In contrast, the direct introduction of trifluoroethyl groups by C–H bond functionalization or C–H activation is very rare. Only two synthetic methods for the direct installation of trifluoroethyl groups at aromatic cores by transition-metal-catalyzed C–H activation have been reported. Recently, Ackermann and co-workers described the first trifluoroethylation that proceeds by nickel-catalyzed C–H activation, utilizing 8-aminoquinoline as the directing group and ICH_2CF_3 as the alkylating agent (Scheme 1a).[12] Liu and co-workers described a Catellani-type palladium-catalyzed alkenylation/trifluoroethylation cascade reaction[13] and the synthesis of numerous olefinated trifluoroethyl arenes (Scheme 1b). Considering



Scheme 1. Existing methods for trifluoroethylation by C–H functionalization. BDMAE = bis(2-dimethylaminoethyl)ether.

the reaction conditions of these transformations, a simpler functionalization method was developed by Baran and co-workers for the fluoroalkylation of selected nitrogen heterocycles, which was based on a zinc sulfinate as the active reagent (Scheme 1c).[14] Although these state-of-the-art trifluoroethylation methods have demonstrated the possibility of directly introducing trifluoroethyl groups into aromatic systems, the narrow substrate scope, the forcing reaction conditions, the formation of complex reaction mixtures, and occasional selectivity problems still suggest the need for further method development to efficiently introduce fluoroalkyl groups into aromatic cores by C–H activation.

We anticipated that the application of electrophilic fluoroalkylation reagents[15,16] in combination with transition-metal-catalyzed C–H activation would be useful owing to their high reactivity. The utilization of a highly active trifluoroethylation agent could solve this challenging synthetic problem and open new synthetic possibilities for the direct trifluoroethylation and other alkylation reactions of aromatic systems.

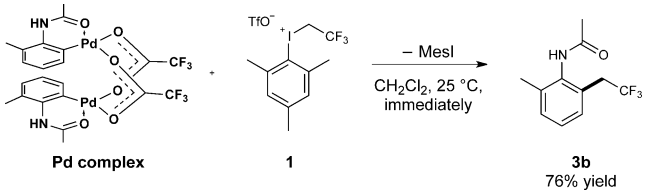
Anilides are perfect substrates for this study owing to the efficient directing ability of the amide moiety in C–H activation, and their straightforward and versatile transformability. We envisioned that dimeric organopalladium com-

[*] B. L. Tóth,[+] Dr. Sz. Kovács,[+] G. Sályi, Dr. Z. Novák
MTA-ELTE "Lendület" Catalysis and Organic Synthesis Research Group, Institute of Chemistry
Eötvös University, Faculty of Science
Pázmány Péter stny. 1/A, H-1117 Budapest (Hungary)
E-mail: novakz@elte.hu
Homepage: http://zng.elte.hu/
[+] These authors contributed equally to this work.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201510555.

plexes of anilides could react with a hypervalent iodonium salt, benefitting from synergistic effects between the neighboring palladium atoms.

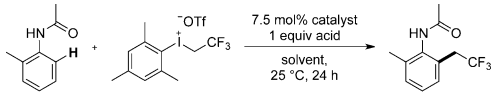
The feasibility of this concept was confirmed by the stoichiometric reaction of mesityl(trifluoroethyl)iodonium triflate and the trifluoroacetate-bridged dimeric complex of 2-methylacetanilide and palladium (Scheme 2). To our delight, the desired product was formed rapidly in CH_2Cl_2 at 25 °C and isolated in 76% yield.



Scheme 2. Proof-of-concept studies: Trifluoroethylation in the presence of the shown palladacycle dimer with mesityl(trifluoroethyl)iodonium triflate in CH_2Cl_2 at 25 °C.

Next, we studied the feasibility of the trifluoroethylation of acetanilide **2b** with mesityl(trifluoroethyl)iodonium triflate under catalytic conditions. Thorough optimization studies in terms of catalyst and catalyst loading, temperature, solvent, and acidic additives revealed suitable conditions for this coupling (Table 1). In particular, $Pd(OAc)_2$ (7.5 mol%) was used as the catalyst in dichloromethane, which is a frequently used reaction medium for C–H activation with hypervalent iodonium salts. To our delight, the reaction provided the desired product (**3b**) with 40% conversion. To improve the efficiency of the coupling, we added Brønsted acids to the reaction mixture. Whereas the reaction proceeded with only 20% conversion in the presence of acetic acid (entry 2), the addition of 1 equiv of trifluoroacetic acid (TFA) led to full conversion (100%, entry 3). Amongst various palladium catalysts, $PdCl_2$ was completely inactive, whereas the use of either $Pd(TFA)_2$ or $Pd_2(dba)_3$ led to high conversion within 24 hours (entries 4–6). We also tested several solvents (entries 7–11), but only 1,2-dichloroethane proved to be a suitable medium for the coupling (100% conversion, entry 11) aside from dichloromethane.

Table 1: Optimization studies.[a]



Entry	Catalyst	Solvent	Acid	Conv. [%][b]
1	$Pd(OAc)_2$	CH_2Cl_2	–	40
2	$Pd(OAc)_2$	CH_2Cl_2	AcOH	20
3	**$Pd(OAc)_2$**	**CH_2Cl_2**	**TFA**	**100**[c]
4	$PdCl_2$	CH_2Cl_2	TFA	0
5	$Pd(TFA)_2$	CH_2Cl_2	TFA	91
6	$Pd_2(dba)_3$	CH_2Cl_2	TFA	97
7	$Pd(OAc)_2$	DMSO	TFA	0
8	$Pd(OAc)_2$	EtOAc	TFA	23
9	$Pd(OAc)_2$	Et_2O	TFA	50
10	$Pd(OAc)_2$	toluene	TFA	96
11	**$Pd(OAc)_2$**	**1,2-DCE**	**TFA**	**100**

[a] Reaction conditions: **2b** (0.05 mmol, 1 equiv), **1** (1.2 equiv), $Pd(OAc)_2$ (7.5 mol%), acid (1 equiv), solvent (0.5 mL), 25 °C, 24 hours. [b] Conversions determined by GC analysis. [c] For conversions achieved with lower Pd catalyst loadings, see the Supporting Information. dba = dibenzylideneacetone, 1,2-DCE = 1,2-dichloroethane, TFA = trifluoroacetic acid.

The progress of the trifluoroethylation of 2-methylacetanilide under the optimized reaction conditions was monitored by in situ IR analysis, in particular by monitoring the characteristic peak of the product at 1638 cm^{-1}. We observed the straightforward formation of the desired trifluoroethylated coupling product after the addition of TFA, and the reaction was complete in three hours. (Figure 1).[17]

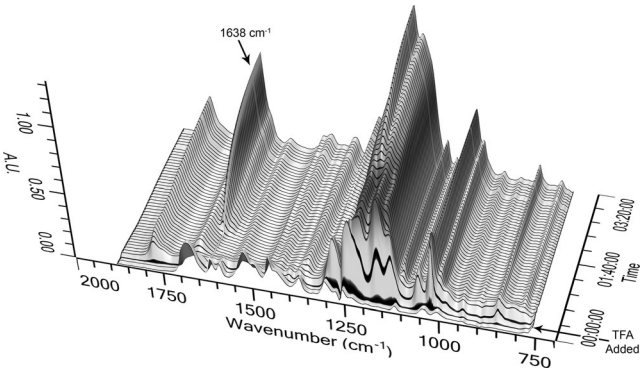
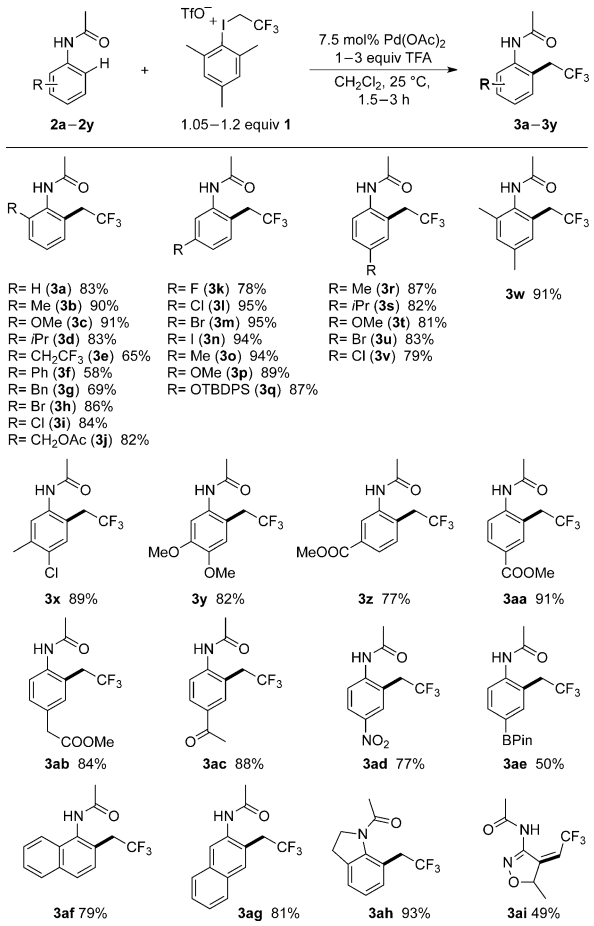


Figure 1. Monitoring of the catalytic trifluoroethylation by in situ IR analysis. The trifluoroethylation of 2-methylacetanilide was performed with **1** and $Pd(OAc)_2$ (7.5 mol%) in CH_2Cl_2 at 25 °C.

With the optimized conditions in hand, the substrate scope was investigated with various acetanilides (Scheme 3). When simple acetanilide was reacted with the mesityl(trifluoroethyl)iodonium salt, the transformation afforded the desired *ortho*-trifluoroethylated product (**3a**) in 83% yield in 1.5 hours. Substituents in *ortho* position to the directing group generally have deleterious effects on C–H activation. However, we found that this transformation tolerates the presence of *ortho* substituents very well. Anilides bearing methyl, methoxy, isopropyl, trifluoroethyl, phenyl, and benzyl groups in the *ortho* position were trifluoroethylated with high efficiency (**3b**–**3g**, 58–91% yield). The presence of halogens (Br, Cl) and protected alcohols was also well tolerated, as exemplified by the formation of **3h**–**3j** in 82–86% yield.

Furthermore, anilides with a fluoro, chloro, bromo, or even an iodo substituent in the *meta* position were trifluoroethylated in excellent yields (**3k**–**3n**, 78–95%). Electron-donating groups, such as methyl, methoxy, and silyl-protected hydroxy moieties, in *meta* position were also tolerated, and the desired products were afforded in excellent yields (**3o**–**3q**). Finally, *para*-substituted anilides were examined. Methyl-, isopropyl-, methoxy-, and halogen-substituted anilides provided the expected products **3r**–**3v** in 79–87% yield under the optimized reaction conditions. Furthermore, the coupling of disubstituted acetanilides afforded the trifluoroethylated compounds (**3w**–**3y**) in similarly good yields (82–91%).

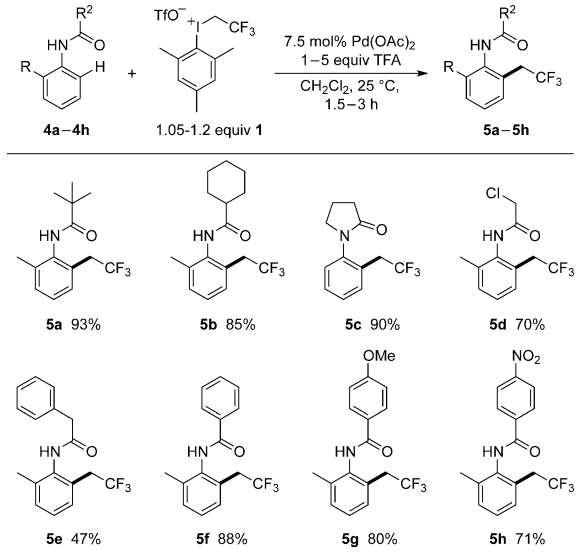


Scheme 3. Palladium-catalyzed trifluoroethylation of anilides. Reaction conditions: **2a–2y** (1 mmol), **1** (1.05–1.2 equiv), $Pd(OAc)_2$ (7.5 mol%), TFA (1–3 equiv), CH_2Cl_2 (1 mL), 25 °C.

Importantly, this novel method is not limited to substrates bearing electron-donating groups or halogens. Whereas the presence of electron-withdrawing groups generally has deleterious effects on C–H activation and electrophilic substitution, this mild trifluoroethylation procedure enables the direct transformation of such challenging substrates. The efficiency and broad scope of the reaction was well illustrated by acetanilides with electron-withdrawing ester, acetyl, and nitro groups in *meta* or *para* position. In all cases, the desired trifluoroethylated products (**3z–3ad**) were formed with high levels of efficiency (77–91%). As a unique substrate for further cross-couplings, 3-pinacolboratoacetanilide (**2ae**) was also successfully trifluoroethylated in 50% yield, demonstrating the robustness of the method and its compatibility with functionality associated with cross-couplings and other metal-catalyzed processes. To further expand the substrate scope, we tested the suitability of bicyclic aromatic systems and heterocyclic rings. With 1-acetamidonaphthalene, the trifluoroethyl group was introduced in the 2-position, whereas 2-acetamidonaphthalene was selectively trifluoroethylated in the 3-position; the desired products **3af** and **3ag** were obtained in 79% and 81% yield, respectively.

The trifluoroethylation was also effective in the case of *N*-acetylindoline, which was regioselectively trifluoroethylated in 93% yield (**3ah**). Furthermore, acetamidoisoxazole **2ai** also proved to be an excellent example for the C–H activation of heterocyclic systems, and trifluoroethylated **3ai** was formed in 49% yield. Interestingly, this substrate underwent double-bond isomerization, leading to the isoxazole structure with an *exo* double bond.

We next focused on the *ortho* C–H trifluoroethylation of anilides with directing groups other than the simple acetyl moiety; pivalamide and cyclohexylamide groups were also found to be feasible. The corresponding products **5a** and **5b** were thus obtained in excellent yields (Scheme 4).



Scheme 4. Palladium-catalyzed trifluoroethylation of aromatic amides. Reaction conditions: **4a–4h** (1 mmol), **1** (1.05–1.2 equiv), $Pd(OAc)_2$ (7.5 mol%), TFA (1–5 equiv), CH_2Cl_2 (1 mL), 25 °C.

Utilization of an anilide substrate with a cyclic pyrrolidinone scaffold afforded the desired monosubstituted product in 90% yield (**5c**). The amides that had been prepared from *ortho*-toluidine and 2-chloroacetyl and 2-phenylacetyl chloride were trifluoroethylated in 70% and 47% yield, respectively (**5d**, **5e**). We also examined the applicability of various benzamide directing groups with electron-donating or -withdrawing groups. Only the aniline core was trifluoroethylated in *ortho* position under the optimized reaction conditions, and the corresponding products (**5f–5h**) were isolated in good yields.

In conclusion, we have developed a novel method for the direct palladium-catalyzed trifluoroethylation of aromatic compounds by C–H activation. The utilization of a mesityl-(trifluoroethyl)iodonium salt in stoichiometric amount enables the highly efficient and selective trifluoroethylation of anilides at room temperature within a short period of time. The application of hypervalent reagents opens new possibilities in the field of organic synthesis, in particular when considering the difficulties commonly associated with the direct fluoroalkylation of aromatic systems.

Experimental Section

A 4 mL screw-cap vial was charged with $Pd(OAc)_2$ (0.075 mmol, 7.5 mol%, 16.8 mg), the amide derivative (1 mmol), and mesi-

tyl(2,2,2-trifluoroethyl)iodonium trifluoromethanesulfonate (1.05–1.2 equiv), and then equipped with a stir bar. CH_2Cl_2 (1 mL) was added as the solvent. TFA (1–5 equiv) was instantly added dropwise, and the mixture was stirred at room temperature for 1.5–3 h. After the appropriate time, the mixture was diluted with EtOAc (25 mL) and extracted with concentrated $NaHCO_3$ solution (2×10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$ and evaporated onto Celite with a rotary evaporator. The crude product was purified by column chromatography (hexane/EtOAc).

Acknowledgements

This work was supported by a "Lendület" Research Scholarship of the Hungarian Academy of Sciences (LP2012-48/2012). We thank Professor Brian M. Stoltz (Caltech) for proofreading this manuscript.

Keywords: anilides · C–H activation · iodonium salts · palladium · trifluoroethylation

How to cite: *Angew. Chem. Int. Ed.* **2016**, *55*, 1988–1992
Angew. Chem. **2016**, *128*, 2028–2032

[1] For reviews on C–H activation, see: a) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147–1169; b) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315–1345; c) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780–1824; d) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem. Int. Ed.* **2012**, *51*, 10236–10254; *Angew. Chem.* **2012**, *124*, 10382–10401; e) C. Zheng, S.-L. You, *RSC Adv.* **2014**, *4*, 6173–6214; f) Z. Chen, B. Wang, J. Zhang, W. Yu, Z. Liu, Y. Zhang, *Org. Chem. Front.* **2015**, *2*, 1107–1295.

[2] For examples of *meta*-selective C–H activation, see: a) R. J. Phipps, M. J. Gaunt, *Science* **2009**, *323*, 1593–1597; b) H. A. Duong, R. E. Gilligan, M. L. Cooke, R. J. Phipps, M. J. Gaunt, *Angew. Chem. Int. Ed.* **2011**, *50*, 463–466; *Angew. Chem.* **2011**, *123*, 483–486; c) D. Leow, G. Li, T.-S. Mei, J.-Q. Yu, *Nature* **2012**, *486*, 518–522; d) N. Hofmann, L. Ackermann, *J. Am. Chem. Soc.* **2013**, *135*, 5877–5884; e) J. Luo, S. Preciado, I. Larrosa, *J. Am. Chem. Soc.* **2014**, *136*, 4109–4112; f) Y.-J. Liu, H. Xu, W.-J. Kong, M. Shang, H.-X. Dai, J.-Q. Yu, *Nature* **2014**, *515*, 389–393; g) J. Yang, *Org. Biomol. Chem.* **2015**, *13*, 1930–1941; h) Z. Dong, J. Wang, G. Dong, *J. Am. Chem. Soc.* **2015**, *137*, 5887–5890; i) M. Bera, A. Maji, S. K. Sahoo, D. Maiti, *Angew. Chem. Int. Ed.* **2015**, *54*, 8515–8519; *Angew. Chem.* **2015**, *127*, 8635–8639; j) C. J. Teskey, A. Y. W. Lui, M. F. Greaney, *Angew. Chem. Int. Ed.* **2015**, *54*, 11677–11680; *Angew. Chem.* **2015**, *127*, 11843–11846; k) J. Li, S. Warratz, D. Zell, S. De Sarkar, E. E. Ishikawa, L. Ackermann, *J. Am. Chem. Soc.* **2015**, *137*, 13894–13901; l) J. Li, S. De Sarkar, L. Ackermann, *Top. Organomet. Chem.* **2015**, *55*, 217–257.

[3] a) H. Li, B.-J. Lia, Z.-J. Shi, *Catal. Sci. Technol.* **2011**, *1*, 191–206; b) O. Baudoin, *Chem. Soc. Rev.* **2011**, *40*, 4902–4911; c) B.-J. Lia, Z.-J. Shi, *Chem. Soc. Rev.* **2012**, *41*, 5588–5598; d) G. Rouquet, N. Chatani, *Angew. Chem. Int. Ed.* **2013**, *52*, 11726–11743; *Angew. Chem.* **2013**, *125*, 11942–11959.

[4] a) S.-Y. Zhang, G. He, W. A. Nack, Y. Zhao, Q. Li, G. Chen, *J. Am. Chem. Soc.* **2013**, *135*, 2124–2127; b) H. Schönherr, T. Cernak, *Angew. Chem. Int. Ed.* **2013**, *52*, 12256–12267; *Angew. Chem.* **2013**, *125*, 12480–12492; c) P. S. Thuy-Boun, G. Villa, D. Dang, P. Richardson, S. Su, J.-Q. Yu, *J. Am. Chem. Soc.* **2013**, *135*, 17508–17513; d) H. Wang, S. Yu, Z. Qi, X. Li, *Org. Lett.* **2015**, *17*, 2812–2815; e) P.-X. Shen, X.-C. Wang, P. Wang, R.-Y. Zhu, J.-Q. Yu, *J. Am. Chem. Soc.* **2015**, *137*, 11574–11577.

[5] a) K. Müller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881–1886; b) D. O'Hagan, *Chem. Soc. Rev.* **2008**, *37*, 308–319; c) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320–330; d) J. Wang, M. Sánchez-Roselló, J. L. Aceña, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok, H. Liu, *Chem. Rev.* **2014**, *114*, 2432–2506.

[6] a) K. L. Kirk, *Org. Process Res. Dev.* **2008**, *12*, 305–321; b) O. A. Tomashenko, V. V. Grushin, *Chem. Rev.* **2011**, *111*, 4475–4521; c) S. Barata-Vallejo, A. Postigo, *Coord. Chem. Rev.* **2013**, *257*, 3051–3069; d) E. Merino, C. Nevado, *Chem. Soc. Rev.* **2014**, *43*, 6598–6608; e) B. Lantaño, M. R. Torviso, S. M. Bonesi, S. Barata-Vallejo, A. Postigo, *Coord. Chem. Rev.* **2015**, *285*, 76–108; f) X. Liu, C. Xu, M. Wang, Q. Liu, *Chem. Rev.* **2015**, *115*, 683–730; g) X. Yang, T. Wu, R. J. Phipps, F. D. Toste, *Chem. Rev.* **2015**, *115*, 826–870; h) C. Alonso, E. M. de Marigorta, G. Rubiales, F. Palacios, *Chem. Rev.* **2015**, *115*, 1847–1935.

[7] G. Landelle, A. Panossian, F. R. Leroux, *Curr. Top. Med. Chem.* **2014**, *14*, 941–951.

[8] J.-B. Han, J.-H. Hao, C.-P. Zhang, H.-L. Qin, *Curr. Org. Chem.* **2015**, *19*, 1554–1565.

[9] a) Y. Zhao, J. Hu, *Angew. Chem. Int. Ed.* **2012**, *51*, 1033–1036; *Angew. Chem.* **2012**, *124*, 1057–1060; b) A. Liang, X. Li, D. Liu, J. Li, D. Zou, Y. Wu, Y. Wu, *Chem. Commun.* **2012**, *48*, 8273–8275; c) X. Zhang, C. Yang, *Adv. Synth. Catal.* **2015**, *357*, 2721–2727.

[10] F. Leng, Y. Wang, H. Li, J. Li, D. Zou, Y. Wu, Y. Wu, *Chem. Commun.* **2013**, *49*, 10697–10699.

[11] G. Wu, Y. Deng, C. Wu, X. Wang, Y. Zhang, J. Wang, *Eur. J. Org. Chem.* **2014**, 4477–4481.

[12] W. Song, S. Lackner, L. Ackermann, *Angew. Chem. Int. Ed.* **2014**, *53*, 2477–2480; *Angew. Chem.* **2014**, *126*, 2510–2513.

[13] H. Zhang, P. Chen, G. Liu, *Angew. Chem. Int. Ed.* **2014**, *53*, 10174–10178; *Angew. Chem.* **2014**, *126*, 10338–10342.

[14] Y. Fujiwara, J. A. Dixon, F. O'Hara, E. D. Funder, D. D. Dixon, R. A. Rodriguez, R. D. Baxter, B. Herlé, N. Sach, M. R. Collins, Y. Ishihara, P. S. Baran, *Nature* **2012**, *492*, 95–99.

[15] For electrophilic trifluoromethylations, see: a) C. Zhang, *Org. Biomol. Chem.* **2014**, *12*, 6580–6589; b) S. Barata-Vallejo, B. Lantaño, A. Postigo, *Chem. Eur. J.* **2014**, *20*, 16806–16829; c) J. Charpentier, N. Früh, A. Togni, *Chem. Rev.* **2015**, *115*, 650–682.

[16] For other electrophilic fluoroalkylations with iodonium salts, see: a) T. Umemoto, Y. Gotoh, *J. Fluorine Chem.* **1985**, *28*, 235–239; b) T. Umemoto, Y. Gotoh, *J. Fluorine Chem.* **1986**, *31*, 231–236; c) T. Umemoto, Y. Gotoh, *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3823–3825; d) T. Umemoto, Y. Gotoh, *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2008–2010; e) C. Lu, D. VanDerveer, D. D. DesMarteau, *Org. Lett.* **2008**, *10*, 5565–5568; f) M. S. Yusubov, A. V. Maskaev, V. V. Zhdankin, *ARKIVOC* **2008**, *i*, 370–409; g) G. L. Tolnai, A. Székely, Z. Makó, T. Gáti, J. Daru, T. Bihari, A. Stirling, Z. Novák, *Chem. Commun.* **2015**, *51*, 4488–4491.

[17] For details see the Supporting Information.

Received: November 13, 2015
Revised: December 9, 2015
Published online: January 14, 2016

