Heterocycles

DOI: 10.1002/anie.201406464

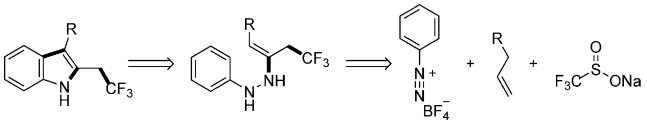
Cascade Multicomponent Synthesis of Indoles, Pyrazoles, and Pyridazinones by Functionalization of Alkenes**

*Kiran Matcha and Andrey P. Antonchick**

Abstract: *The development of multicomponent reactions for indole synthesis is demanding and has hardly been explored. The present study describes the development of a novel multicomponent, cascade approach for indole synthesis. Various substituted indole derivatives were obtained from simple reagents, such as unfunctionalized alkenes, diazonium salts, and sodium triflinate, by using an established straightforward and regioselective method. The method is based on the radical trifluoromethylation of alkenes as an entry into Fischer indole synthesis. Besides indole synthesis, the application of the multicomponent cascade reaction to the synthesis of pyrazoles and pyridazinones is described.*

The indole moiety is a privileged heterocyclic scaffold prevalent in a large number of natural products and pharmaceuticals.[1] The demand for simple and efficient syntheses of indoles has burgeoned since the development of the classical Fischer indole synthesis.[2] In this context, developments in Fischer indole synthesis have received widespread attention, in particular the transition-metal-catalyzed intramolecular cyclization of enamides to indoles.[3] A few conceptually different reactions have also been reported to access the sequence of the Fischer indole synthesis downstream.[4] The coupling of hydrazine and aniline derivatives to alkynes has become another important and well-explored alternative synthesis route.[5] However, the coupling of aniline derivatives with alkenes is mostly focused on the intramolecular version;[6] an intermolecular version has not yet been well-studied.[7] Moreover, multicomponent reactions for the synthesis of indoles have been seldom explored.[8] Developing a novel multicomponent reaction would be a valuable alternative to the synthesis of indoles. The remarkable properties of the fluorine group has resulted in the trifluoromethylation of alkenes recently becoming an important tool to incorporate fluorine into organic compounds.[9,10] However, the application of alkene trifluoromethylation in the synthesis of heterocycles has only been seldom explored and not reported for indoles to date.[10] Herein, we describe alkene trifluoromethylation as an entry point for a regioselective multicomponent cascade synthesis of indole derivatives by Fischer indole synthesis. Furthermore, the developed process was applied to the regioselective synthesis of other nitrogen-containing heterocycles such as pyrazole and dihydropyridazinone derivatives.

Our research group is actively involved in developing novel methods for the synthesis and functionalization of heterocyclic compounds.[11,12] Furthermore, our continued interest in radical-mediated C–H functionalizations[12] led to a novel radical-mediated route being envisioned for the synthesis of indoles. We assumed that adding a trifluoromethyl radical to an alkene and subsequent trapping with an arenediazonium salt could provide an intermediate for the Fischer indole synthesis in a one-pot reaction (Scheme 1). A



Scheme 1. Multicomponent indole synthesis.

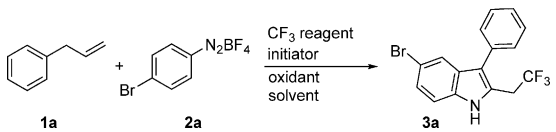
proof of concept was demonstrated by Heinrich et al. using aryl radicals.[4e] However, the reported approach was a two-step synthesis of indole and no substrate scope was explored.

To test our hypothesis, alkene **1a** was subjected to radical trifluoromethylation conditions by using a combination of CF_3SO_2Na, *t*BuOOH, and CuCl in the presence of arenediazonium salt **2a** (Table 1). To our delight, indole **3a** was isolated in 30% yield (entry 1). Moreover, product **3a** was isolated as a single regioisomer. It should be noted that arenediazonium salts are widely used as the source of aryl radicals after breaking C–N bonds and elimination of nitrogen,[13] although they have rarely been used as radical traps.[4e,14] Intrigued by the outcome of the anticipated reaction, we proceeded to optimize the reaction conditions (Table 1, and see the Supporting Information). The reaction was feasible in polar solvents, but failed in nonpolar solvents (entries 1–3). Acetonitrile turned out to be the best solvent, giving the desired product **3a** in 45% yield (entry 3). Further optimization revealed that various metal salts promote the reaction (entries 3–6), and among these salts, $AgNO_3$ afforded the best yield (entry 6). Although the metal-free initiator Bu_4NBr promoted the reaction, the yield was lower (entry 7). The initial choice of CF_3SO_2Na was found to be superior to many of the investigated trifluoromethylating reagents under the reaction conditions (entries 6, 8, and 9).

[*] Dr. K. Matcha, Dr. A. P. Antonchick
Abteilung Chemische Biologie
Max-Planck-Institut für Molekulare Physiologie
Otto-Hahn-Strasse 11, 44227 Dortmund (Germany)
E-mail: andrey.antonchick@mpi-dortmund.mpg.de
Dr. A. P. Antonchick
Fakultät Chemie und Chemische Biologie
Technische Universität Dortmund
Otto-Hahn-Strasse 6, 44221 Dortmund (Germany)

[**] We thank Prof. Dr. Herbert Waldmann for his generous support.
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201406464.

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



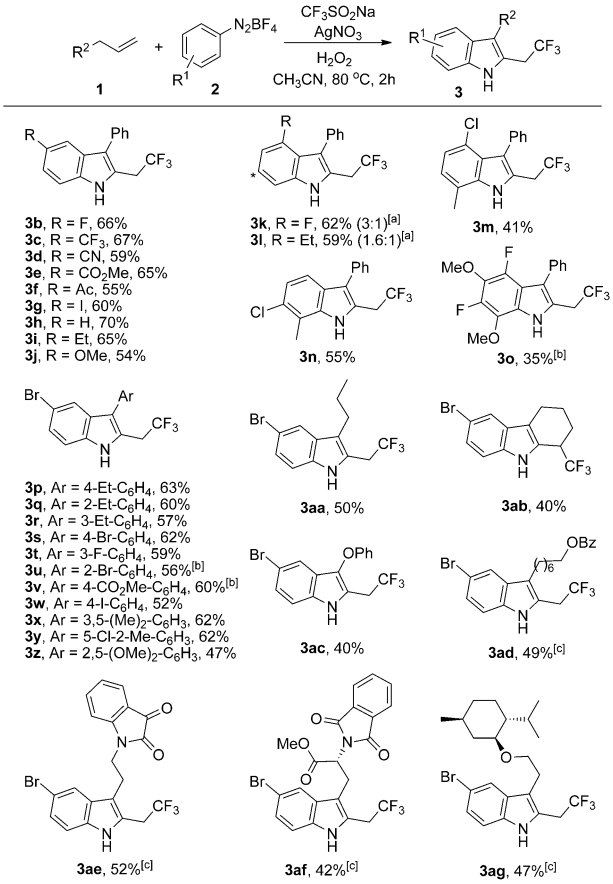
Entry	Solvent	Initiator (mol%)	CF_3 reagent (equiv)	Oxidant (equiv)	Yield [%][b]
1	DCE	CuCl (10)	CF_3SO_2Na (2)	*t*BuOOH (2)	30
2	MeOH	CuCl (10)	CF_3SO_2Na (2)	*t*BuOOH (2)	38
3	CH_3CN	CuCl (10)	CF_3SO_2Na (2)	*t*BuOOH (2)	45
4	CH_3CN	$Cu(OAc)_2$ (10)	CF_3SO_2Na (2)	*t*BuOOH (2)	58
5	CH_3CN	$[Fe(acac)_3]$ (10)	CF_3SO_2Na (2)	*t*BuOOH (2)	61
6	CH_3CN	$AgNO_3$ (10)	CF_3SO_2Na (2)	*t*BuOOH (2)	67
7	CH_3CN	Bu_4NBr (10)	CF_3SO_2Na (2)	*t*BuOOH (2)	55
8	CH_3CN	$AgNO_3$ (10)	CF_3TMS (2)	*t*BuOOH (2)	n.d.
9	CH_3CN	$AgNO_3$ (10)	Togni I (2)	*t*BuOOH (2)	n.d.
10	CH_3CN	$AgNO_3$ (10)	CF_3SO_2Na (2)	$PhI(OAc)_2$ (2)	n.d.
11	CH_3CN	$AgNO_3$ (10)	CF_3SO_2Na (2)	$K_2S_2O_8$ (2)	n.d.
12	CH_3CN	$AgNO_3$ (10)	CF_3SO_2Na (2)	H_2O_2 (2)	72
13	CH_3CN	$AgNO_3$ (20)	CF_3SO_2Na (2)	H_2O_2 (2)	72
14	CH_3CN	$AgNO_3$ (10)	CF_3SO_2Na (1.2)	H_2O_2 (1.2)	63
15	CH_3CN	$AgNO_3$ (10)	CF_3SO_2Na (2)	H_2O_2 (1.5)	71

[a] Reaction conditions, **1a** (0.2 mmol), **2a** (0.4 mmol), CF_3 reagent (equiv), oxidant (equiv), and initiator (mol%) in solvent (3 mL) at 80°C for 2 h. [b] Yield refers to isolated products after column chromatography. DCE = 1,2-dichloroethane, acac = acetylacetonoate.

Various oxidants were also screened to improve the yield (entries 10–12). The use of $PhI(OAc)_2$ and $K_2S_2O_8$ as the oxidant led to traces of the product. Nevertheless, the yield of product **3a** was improved to 72% by using H_2O_2 as the oxidant (entry 12). Increasing the $AgNO_3$ loading did not improve the yield, but lowering the amount led to lower yields (entries 12 and 13). Finally, lowering the amount of CF_3SO_2Na decreased the yield (entries 14 and 15).

The scope of the presented multicomponent reaction was explored with a variety of arenediazonium salts and alkenes under optimized reaction conditions (Scheme 2). Arenediazonium salts equipped with various functional groups at different positions on the arene were found to be well-tolerated in the reaction (**3b**–**3o**). In general, electron-withdrawing groups on the arenediazonium salts led to slightly better yields than electron-donating groups (**3b**–**3o**). Various functional groups at the *para*-position of the arenediazonium salts provided the corresponding indoles in good to moderate yields (**3b**–**3j**). *meta*-Substituted arenediazonium salts afforded mixtures of regioisomeric indoles in good yields (**3k**, **3l**). Moreover, the use of arenediazonium salts with substituents in the *ortho*-position led to the formation of the desired products in moderate to good yields (**3m**, **3n**). To our delight, the developed method allows the synthesis of hexasubstituted indole in acceptable yield (**3o**).

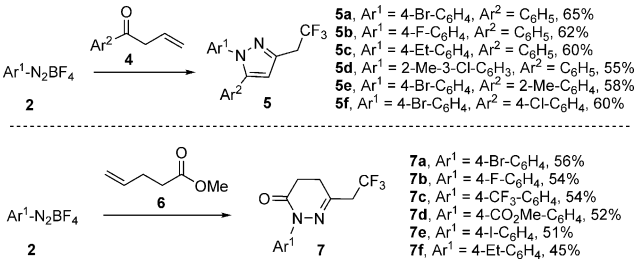
We then investigated the scope of the alkenes (Scheme 2). Initially, various substituted allylbenzenes were subjected to the reaction conditions (**3p**–**3z**). A number of allylbenzenes successfully provided the corresponding 3-arylindole derivatives in good yields. Allylbenzenes with electron-donating groups reacted faster than those with electron-withdrawing



Scheme 2. Scope of the indole synthesis. Reaction conditions: Alkene **1** (0.2 mmol), aryldiazonium salts **2** (0.4 mmol), CF_3SO_2Na (0.4 mmol), H_2O_2 (0.3 mmol), and $AgNO_3$ (0.02 mmol) in acetonitrile (3 mL) at 80°C for 2 h. [a] The structure of the major regioisomer is shown and the position of the substituent in the minor isomer is marked with a star. [b] Reaction time was 4 h. [c] *tert*-Butyl hydroperoxide (TBHP, 0.4 mmol) was used instead of H_2O_2.

groups (**3p**–**3z**). Various functional groups, including iodo groups and esters, are compatible with the reaction conditions. Disubstituted allylbenezenes also provided indoles in good to moderate yields (**3x**–**3z**). Furthermore, simple acyclic and cyclic alkenes such as 1-hexene and cyclohexene can be employed under the developed reaction conditions to form indoles smoothly (**3aa**, **3ab**). 3-Phenoxyindole was obtained from (allyloxy)benzene in moderate yield (**3ac**). Various indoles were readily obtained from complex alkenes (**3ad**–**3ag**). It is notable, that alkenes derived from amino acid derivatives successfully provided tryptophan derivatives in one step, thus illustrating the scope and compatibility of the presented multicomponent reaction (**3af**).

After investigating the scope of the developed transformation for the synthesis of indoles, we turned our attention to the synthesis of different heterocyclic scaffolds by introducing perturbation into the developed cascade reaction (Scheme 3). To our delight, the use of aryl allyl ketones (**4**) instead of simple alkenes (**1**) under the optimized reaction conditions conveniently provided 1,5-diarylpyrazoles in a one-pot multicomponent cascade process (**5a**–**5f**). The presence of trifluoromethylated 1,5-diarylpyrazoles in various pharmaceuticals and agrochemicals further raised our interest

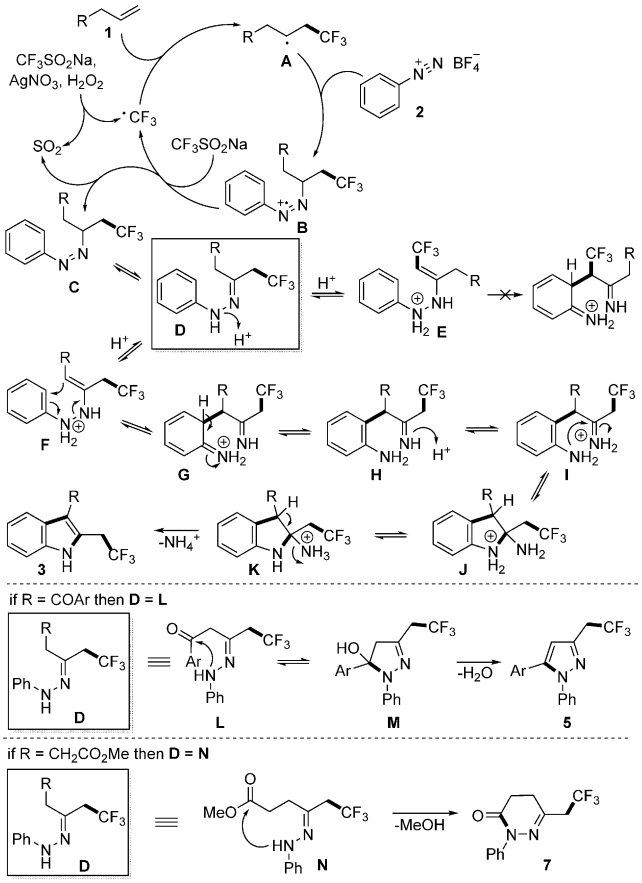


Scheme 3. Scope of the 1,5-diarylpyrazole and dihydropyridazinone synthesis. Reaction conditions: Alkene **4** or **6** (0.2 mmol), aryldiazonium salts **2** (0.4 mmol), CF_3SO_2Na (0.4 mmol), H_2O_2 (0.3 mmol), and $AgNO_3$ (0.02 mmol) in acetonitrile (3 mL) at 80 °C for 2 h.

in their synthesis.[15] A similar synthesis of pyrazoles by functionalization of alkenes was previously reported by using aryl radicals produced from arenediazonium salts.[16] The scope of the reaction studied with respect to the aryldiazonium salts and aryl allyl ketones was found to be general, tolerating various substituents at different positions of the arenes (**5a**–**5f**).

Furthermore, the application of methyl 4-pentenoate (**6**) instead of simple alkenes (**1**) under the same reaction conditions allowed access to novel heterocyclic scaffolds such as dihydropyridazinones (**7a**–**7f**). The scope of the dihydropyridazinone synthesis was also investigated. A wide range of *para*-substituted arenediazonium salts provided the corresponding products (**7a**–**7f**). Nevertheless, diarylpyrazoles (**5**) and dihydropyridazinones (**7**) were formed quickly and regioselectively. The developed method is not sensitive to humidity and oxygen in air. The possibility of the divergent and selective syntheses of various important heterocyclic scaffolds under simple conditions amplifies the importance of the developed multicomponent process.

A mechanism for the multicomponent indole synthesis is depicted in Scheme 4. Initially, an electrophilic trifluoromethyl radical produced by a combination of CF_3SO_2Na, $AgNO_3$, and H_2O_2 was added at the terminal position of the alkene to give radical intermediate **A** (Scheme 4). Intermediate **A** was readily trapped by the arenediazonium salt **2** to produce cation radical **B**. Intermediate **B** was further reduced to intermediate **C**. Although it is proposed that **B** was reduced to **C** by CF_3SO_2Na, the possible role of $AgNO_3$ or H_2O_2 could not be ruled out. The reduction of intermediates similar to **B** to an azo compound (**C**) was previously shown under oxidative and reductive reaction conditions.[4e,13c] Moreover, the yield of product **3a** was reduced to 38% in the control experiment without H_2O_2. Intermediate **C** then undergoes a [1,3]-hydride shift to give a phenylhydrazone (**D**), which is the first intermediate in the classical Fischer indole synthesis. Intermediate **D** then isomerizes to ene-hydrazines **E** and **F**. Nevertheless, only intermediate **F** undergoes the [3,3] sigmatropic rearrangement which defines the regioselectivity of the developed synthesis. The presence of the trifluoromethyl group in ene-hydrazine **E** suppressed the [3,3] sigmatropic rearrangement. A rearrangement of **F** via intermediate **G** produces imine **H**. Nucleophilic attack of the amino group on the imine in **I** followed by elimination of ammonia from intermediate **K** provides indole **3** (Scheme 4). In contrast to



Scheme 4. Mechanism for the multicomponent formation of indoles (**3**), pyrazoles (**5**), and dihydropyridazinones (**7**).

the indole formation, the sigmatropic rearrangement (**F** to **G**) was interrupted by the nucleophilic attack of the amino group on the ketone in intermediate **L** that gave intermediate **M**, which was followed by elimination of water to afford pyrazole **5**. A similar interruption of the indole synthesis in intermediate **N** facilitated the formation of dihydropyridazinone **7**.

In conclusion, we developed a multicomponent route for the synthesis of indoles. In the developed method, alkene trifluromethylation was elegantly demonstrated to provide entry into Fischer indole synthesis. Further novel aspects of the developed process include intermolecular reactions combining alkenes and arenediazonium salts to give indoles as well as efficient application of arenediazonium salts as radical traps. The developed process represents multiple functionalizations of C–H bonds in alkenes and provides access to the divergent and selective syntheses of trifluoromethylated heterocycles under similar reaction conditions. The desired products are formed under mild reaction conditions in a short time. A comprehensive scope of the developed process and the tolerance of a variety of functional groups were successfully demonstrated. Moreover, we believe that the presented method creates the basis for further developments in the synthesis of heterocycles from alkenes in the presence of various radical sources.

Received: June 22, 2014
Published online: October 6, 2014

Keywords: arenediazonium salt · indole · multicomponent reaction · radicals · trifluoromethylation

[1] a) G. W. Gribble, *Heterocyclic Scaffolds II: Reactions and Applications of Indoles*, Springer, Berlin, **2010**; b) R. J. Sundberg, *Indoles*, Academic, New York, **1996**; c) N. Kaushik, N. Kaushik, P. Attri, N. Kumar, C. Kim, A. Verma, E. Choi, *Molecules* **2013**, *18*, 6620 – 6662; d) M. Baumann, I. R. Baxendale, S. V. Ley, N. Nikbin, *Beilstein J. Org. Chem.* **2011**, *7*, 442 – 495; e) A. J. Kochanowska-Karamyan, M. T. Hamann, *Chem. Rev.* **2010**, *110*, 4489 – 4497; f) M. Somei, F. Yamada, *Nat. Prod. Rep.* **2005**, *22*, 73 – 103.

[2] a) M. Inman, C. J. Moody, *Chem. Sci.* **2013**, *4*, 29 – 41; b) M. Platon, R. Amardeil, L. Djakovitch, J.-C. Hierso, *Chem. Soc. Rev.* **2012**, *41*, 3929 – 3968; c) D. F. Taber, P. K. Tirunahari, *Tetrahedron* **2011**, *67*, 7195 – 7210; d) S. Cacchi, G. Fabrizi, A. Goggiamani, *Org. Biomol. Chem.* **2011**, *9*, 641 – 652; e) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2011**, *111*, 215 – 283; f) R. Vicente, *Org. Biomol. Chem.* **2011**, *9*, 6469 – 6480; g) J. Barluenga, F. Rodríguez, F. J. Fañanás, *Chem. Asian J.* **2009**, *4*, 1036 – 1048; h) G. R. Humphrey, J. T. Kuethe, *Chem. Rev.* **2006**, *106*, 2875 – 2911.

[3] For a review, see a) Z. Shi, F. Glorius, *Angew. Chem. Int. Ed.* **2012**, *51*, 9220 – 9222; *Angew. Chem.* **2012**, *124*, 9354 – 9356; for selected articles, see b) Y. Wei, I. Deb, N. Yoshikai, *J. Am. Chem. Soc.* **2012**, *134*, 9098 – 9101; c) Z.-H. Guan, Z.-Y. Yan, Z.-H. Ren, X.-Y. Liu, Y.-M. Liang, *Chem. Commun.* **2010**, *46*, 2823 – 2825; d) Y. Tan, J. F. Hartwig, *J. Am. Chem. Soc.* **2010**, *132*, 3676 – 3677; e) R. Bernini, G. Fabrizi, A. Sferrazza, S. Cacchi, *Angew. Chem. Int. Ed.* **2009**, *48*, 8078 – 8081; *Angew. Chem.* **2009**, *121*, 8222 – 8225; f) W. Yu, Y. Du, K. Zhao, *Org. Lett.* **2009**, *11*, 2417 – 2420; g) S. Würtz, S. Rakshit, J. J. Neumann, T. Drçge, F. Glorius, *Angew. Chem. Int. Ed.* **2008**, *47*, 7230 – 7233; *Angew. Chem.* **2008**, *120*, 7340 – 7343; h) Y. Du, R. Liu, G. Linn, K. Zhao, *Org. Lett.* **2006**, *8*, 5919 – 5922.

[4] a) F. Zhan, G. Liang, *Angew. Chem. Int. Ed.* **2013**, *52*, 1266 – 1269; *Angew. Chem.* **2013**, *125*, 1304 – 1307; b) A. Porcheddu, M. G. Mura, L. De Luca, M. Pizzetti, M. Taddei, *Org. Lett.* **2012**, *14*, 6112 – 6115; c) M. Inman, C. J. Moody, *Chem. Commun.* **2011**, *47*, 788 – 790; d) M. Inman, A. Carbone, C. J. Moody, *J. Org. Chem.* **2012**, *77*, 1217 – 1232; e) B. A. Haag, Z.-G. Zhang, J.-S. Li, P. Knochel, *Angew. Chem. Int. Ed.* **2010**, *49*, 9513 – 9516; *Angew. Chem.* **2010**, *122*, 9703 – 9706; f) M. R. Heinrich, O. Blank, A. Wetzel, *J. Org. Chem.* **2007**, *72*, 476 – 484; g) S. Wagaw, B. H. Yang, S. L. Buchwald, *J. Am. Chem. Soc.* **1998**, *120*, 6621 – 6622.

[5] For reviews, see a) G. Abbiati, F. Marinelli, E. Rossi, A. Arcadi, *Isr. J. Chem.* **2013**, *53*, 856 – 868; b) K. Krüger née Alex, A. Tillack, M. Beller, *Adv. Synth. Catal.* **2008**, *350*, 2153 – 2167; For recent works see c) S. Cai, K. Yang, D. Z. Wang, *Org. Lett.* **2014**, *16*, 2606 – 2609; d) G. Zhang, H. Yu, G. Qin, H. Huang, *Chem. Commun.* **2014**, *50*, 4331 – 4334; e) C. Wang, H. Sun, Y. Fang, Y. Huang, *Angew. Chem. Int. Ed.* **2013**, *52*, 5795 – 5798; *Angew. Chem.* **2013**, *125*, 5907 – 5910; f) D. Zhao, Z. Shi, F. Glorius, *Angew. Chem. Int. Ed.* **2013**, *52*, 12426 – 12429; *Angew. Chem.* **2013**, *125*, 12652 – 12656; g) A. Gogoi, S. Guin, S. K. Rout, B. K. Patel, *Org. Lett.* **2013**, *15*, 1802 – 1805; h) C. Wang, Y. Huang, *Org. Lett.* **2013**, *15*, 5294 – 5297; i) W. Song, L. Ackermann, *Chem. Commun.* **2013**, *49*, 6638 – 6640; j) B. Liu, C. Song, C. Sun, S. Zhou, J. Zhu, *J. Am. Chem. Soc.* **2013**, *135*, 16625 – 16631; k) B. Yao, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2012**, *51*, 12311 – 12315; *Angew. Chem.* **2012**, *124*, 12477 – 12481; l) L. Ackermann, A. V. Lygin, *Org. Lett.* **2012**, *14*, 764 – 767.

[6] a) L. Fra, A. Millán, J. A. Souto, K. Muñiz, *Angew. Chem. Int. Ed.* **2014**, *53*, 7349 – 7353; *Angew. Chem.* **2014**, *126*, 7477 – 7481; b) B. Zhang, A. Studer, *Org. Lett.* **2014**, *16*, 1216 – 1219; c) T. W. Liwosz, S. R. Chemler, *Chem. Eur. J.* **2013**, *19*, 12771 – 12777; d) S. Maity, N. Zheng, *Angew. Chem. Int. Ed.* **2012**, *51*, 9562 – 9566; *Angew. Chem.* **2012**, *124*, 9700 – 9704; e) K. Sun, S. Liu, P. M. Bec, T. G. Driver, *Angew. Chem. Int. Ed.* **2011**, *50*, 1702 – 1706; *Angew. Chem.* **2011**, *123*, 1740 – 1744; f) D. Tsvelikhovsky, S. L. Buchwald, *J. Am. Chem. Soc.* **2010**, *132*, 14048 – 14051; g) M. Shen, B. E. Leslie, T. G. Driver, *Angew. Chem. Int. Ed.* **2008**, *47*, 5056 – 5059; *Angew. Chem.* **2008**, *120*, 5134 – 5137; h) C. M. Coleman, D. F. O'Shea, *J. Am. Chem. Soc.* **2003**, *125*, 4054 – 4055.

[7] a) A. Cajaraville, S. López, J. A. Varela, C. Saá, *Org. Lett.* **2013**, *15*, 4576 – 4579; b) J. Barluenga, M. A. Fernández, F. Aznar, C. Valdés, *Chem. Eur. J.* **2005**, *11*, 2276 – 2283; c) A. M. Schmidt, P. Eilbracht, *J. Org. Chem.* **2005**, *70*, 5528 – 5535; d) P. Köhling, A. M. Schmidt, P. Eilbracht, *Org. Lett.* **2003**, *5*, 3213 – 3216; e) A. M. Schmidt, P. Eilbracht, *Org. Biomol. Chem.* **2005**, *3*, 2333 – 2343.

[8] For a review, see a) M. Shiri, *Chem. Rev.* **2012**, *112*, 3508 – 3549; For recent works see b) W. Hao, W. Geng, W.-X. Zhang, Z. Xi, *Chem. Eur. J.* **2014**, *20*, 2605 – 2612; c) J. M. Knapp, J. S. Zhu, D. J. Tantillo, M. J. Kurth, *Angew. Chem. Int. Ed.* **2012**, *51*, 10588 – 10591; *Angew. Chem.* **2012**, *124*, 10740 – 10743; d) L. E. Kaïm, L. Grimaud, *Synlett* **2010**, 2296 – 2298; e) O. Leogane, H. Lebel, *Angew. Chem. Int. Ed.* **2008**, *47*, 350 – 352; *Angew. Chem.* **2008**, *120*, 356 – 358; f) J. Barluenga, A. Jiménez-Aquino, C. Valdés, F. Aznar, *Angew. Chem. Int. Ed.* **2007**, *46*, 1529 – 1532; *Angew. Chem.* **2007**, *119*, 1551 – 1554.

[9] For reviews, see a) E. Merino, C. Nevado, *Chem. Soc. Rev.* **2014**, *43*, 6598 – 6608; b) J. Xu, X. Liu, Y. Fu, *Tetrahedron Lett.* **2014**, *55*, 585 – 594.

[10] For recent studies, see a) J.-S. Lin, Y.-P. Xiong, C.-L. Ma, L.-J. Zhao, B. Tan, X.-Y. Liu, *Chem. Eur. J.* **2014**, *20*, 1332 – 1340; b) W. Kong, M. Casimiro, N. Fuentes, E. Merino, C. Nevado, *Angew. Chem. Int. Ed.* **2013**, *52*, 13086 – 13090; *Angew. Chem.* **2013**, *125*, 13324 – 13328; c) W. Kong, M. Casimiro, E. b. Merino, C. Nevado, *J. Am. Chem. Soc.* **2013**, *135*, 14480 – 14483; d) H. Egami, R. Shimizu, S. Kawamura, M. Sodeoka, *Angew. Chem. Int. Ed.* **2013**, *52*, 4000 – 4003; *Angew. Chem.* **2013**, *125*, 4092 – 4095; e) P. Xu, J. Xie, Q. Xue, C. Pan, Y. Cheng, C. Zhu, *Chem. Eur. J.* **2013**, *19*, 14039 – 14042; f) L. Li, M. Deng, S.-C. Zheng, Y.-P. Xiong, B. Tan, X.-Y. Liu, *Org. Lett.* **2014**, *16*, 504 – 507; g) 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 – 14424; h) R. Zhu, S. L. Buchwald, *J. Am. Chem. Soc.* **2012**, *134*, 12462 – 12465.

[11] a) S. Manna, K. Matcha, A. P. Antonchick, *Angew. Chem. Int. Ed.* **2014**, *53*, 8163 – 8166; *Angew. Chem.* **2014**, *126*, 8302 – 8305; b) S. Manna, A. P. Antonchick, *Angew. Chem. Int. Ed.* **2014**, *53*, 7324 – 7327; *Angew. Chem.* **2014**, *126*, 7452 – 7455; c) A. P. Antonchick, R. Samanta, K. Kulikov, J. Lategahn, *Angew. Chem. Int. Ed.* **2011**, *50*, 8605 – 8608; *Angew. Chem.* **2011**, *123*, 8764 – 8767; d) R. Samanta, A. P. Antonchick, *Angew. Chem. Int. Ed.* **2011**, *50*, 5217 – 5220; *Angew. Chem.* **2011**, *123*, 5323 – 5326.

[12] For a review from our research group, see a) R. Samanta, K. Matcha, A. P. Antonchick, *Eur. J. Org. Chem.* **2013**, 5769 – 5804; for recent studies, see b) R. Narayan, A. P. Antonchick, *Chem. Eur. J.* **2014**, *20*, 4568 – 4572; c) K. Matcha, R. Narayan, A. P. Antonchick, *Angew. Chem. Int. Ed.* **2013**, *52*, 7985 – 7989; *Angew. Chem.* **2013**, *125*, 8143 – 8147; d) A. P. Antonchick, L. Burgmann, *Angew. Chem. Int. Ed.* **2013**, *52*, 3267 – 3271; *Angew. Chem.* **2013**, *125*, 3349 – 3353; e) K. Matcha, A. P. Antonchick, *Angew. Chem. Int. Ed.* **2013**, *52*, 2082 – 2086; *Angew. Chem.* **2013**, *125*, 2136 – 2140.

[13] For reviews on aryl radicals from aryldiazonium salts, see a) D. P. Hari, B. König, *Angew. Chem. Int. Ed.* **2013**, *52*, 4734 – 4743; *Angew. Chem.* **2013**, *125*, 4832 – 4842; b) G. Pratsch, M. R. Heinrich, *Top. Curr. Chem.* **2011**, *320*, 33 – 60; c) M. R. Heinrich, *Chem. Eur. J.* **2009**, *15*, 820 – 833.

[14] For a review, see a) B. Höfling, M. R. Heinrich, *Synthesis* **2011**, 173 – 189; for recent works see b) P. Markus, M. R. Heinrich, *Synthesis* **2011**, 1515 – 1525; c) O. Blank, N. Raschke, M. R. Heinrich, *Tetrahedron Lett.* **2010**, *51*, 1758 – 1760; d) O. Blank, A. Wetzel, D. Ullrich, M. R. Heinrich, *Eur. J. Org. Chem.* **2008**, 3179 – 3189; e) M. R. Heinrich, O. Blank, A. Wetzel, *Synlett* **2006**, 3352 – 3354; f) O. Blank, M. R. Heinrich, *Eur. J. Org. Chem.* **2006**, 4331 – 4334.

[15] For reviews, see a) R. P. Fernández, P. Goya, J. Elguero, *ARKIVOC* **2014**, 233 – 293; b) S. Fustero, M. Sánchez-Roselló, P. Barrio, A. Simón-Fuentes, *Chem. Rev.* **2011**, *111*, 6984 – 7034.

[16] A. Citterio, M. Ramperti, E. Vismara, *J. Heterocycl. Chem.* **1981**, *18*, 763 – 766.

