C–H Functionalization

DOI: 10.1002/anie.201303550

Metal-Free Radical Azidoarylation of Alkenes: Rapid Access to Oxindoles by Cascade C–N and C–C Bond-Forming Reactions**

*Kiran Matcha, Rishikesh Narayan, and Andrey P. Antonchick**

The importance of nitrogen-containing compounds has inspired chemists to continue developing mild and efficient C–N bond-forming transformations.[1] The amination of alkenes represents the state-of-the art in organic synthesis.[2] Azides offer substantial benefits for the synthesis of nitrogen-containing compounds and have been recognized as versatile intermediates. Organic azides possess unique properties orthogonal to those of many functional groups, demonstrate unique reactivity, and are stable under physiological conditions.[3] The established methods of alkyl azide synthesis are based on the transformation of functionalized alkanes using multistep procedures. Direct azidation methods for the synthesis of alkyl azides from alkenes are much less developed. The groups led by Carreira and Renaud developed broadly applicable radical hydroazidation and carboazidation of unactivated alkenes using organic azides as radical traps for carbon-centered radicals.[4] The application of azidyl radicals in the functionalization of alkenes represents a straightforward approach to alkyl azides. Nevertheless, these processes are limited to selective hydrogen abstraction by cleavage of $C(sp^3)$–H bonds by azidyl radicals generally leading to generation of carbon-centered radicals and other nitrogen-centered radicals.[5] Several methods of azidyl radical addition to alkenes followed by formation of carbon–heteroatom bonds have been reported.[6] Straightforward methods for alkyl azide synthesis by the addition of the azidyl radical to alkenes followed by formation of C–C bonds have never been reported and are in high demand. Here we describe the development of the unprecedented functionalization of alkenes by the addition of azidyl radicals followed by trapping with arenes (azidoarylation) under metal-free reaction conditions at ambient temperature.

2-Oxindoles are a large class of natural products with unique biological activity and represent one of the privileged scaffolds for library design and drug discovery.[7] Among the methods available for their synthesis,[8] the recently reported radical-mediated cyclizations of *N*-arylacrylamides have received special attention. These methods are based on a cascade sequence consisting of C–C (or C–P) followed by C–C bond-forming reactions catalyzed by transition metals at typically high temperature.[9] Very recently, a metal-free radical acetoarylation of *N*-arylacrylamides was reported.[10] Therefore, we realized that choosing *N*-arylacrylamides as a platform to investigate the unprecedented azidoarylation of alkenes would result in a cascade of C–N and C–C bond-forming reactions. The presented method is a complimentary metal-free approach to the synthesis of 2-oxindoles. Moreover, in contrast to other oxindole syntheses, the resulting products, substituted 2-oxindoles with an appended azide group, can be used to create further molecular complexity around the privileged scaffold of 2-oxindoles or can be applied for bioorthogonal transformation under physiological conditions.[11]

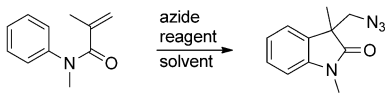
Recently, our group has employed azidyl radicals as intermediates in the cross-dehydrogenative coupling of heterocycles with aldehydes and unactivated alkanes.[12] The azidyl radicals were generated by oxidation of azides in the presence of hypervalent iodine(III) reagents at ambient temperature.[13,14] Intrigued by these results, we hypothesized that these azidyl radicals could be used for the azidoarylation of alkenes as well. We decided to take advantage of the mild reaction conditions for generation of azidyl radicals to achieve the desired products of azidoarylation. Indeed, the desired azidoarylation product **2a** was obtained in 45% yield from the reaction of **1a** with NaN_3 in presence of $PhI(OCOCF_3)_2$ (Table 1, entry 1). Replacing NaN_3 with $TMSN_3$ further improved the yield to 70% (Table 1, entry 2). Not surprisingly, attempted base-promoted conjugate addition of azide to olefin **1a** did not result in formation of product **2a** (Table 1, entries 3 and 4).[15] The differences in yield observed for **2a** after reducing the amount of oxidant from 2 equiv to 1 equiv (Table 1, entries 2 and 5) led us to investigate the optimal reaction conditions. Experiments with varying amounts of oxidant suggested that 1.2 equiv is required to achieve complete conversion of **1a** to **2a** with higher yield (Table 1, entries 5–8). Although few solvents did not promote the desired transformation (Table 1, entries 9 and 10), DCM was found to be superior with 91% yield for **2a** (Table 1, entries 11–14). Significant amounts of unreacted **1a** were observed when the amounts of $PhI(OCOCF_3)_2$ and $TMSN_3$ were decreased further (see the Supporting Information for details). Among the hypervalent iodine reagents screened, $C_6F_5I(OCOCF_3)_2$ performed well although the yields were lower than with $PhI(OCOCF_3)_2$ (Table 1, entry 15). Less reactive $PhI(OAc)_2$ did not lead to full conversion (Table 1, entry 16). No reaction was observed with $(PhO)_2PON_3$, while NaN_3 was less effective than $TMSN_3$ (Table 1, entries 17 and 18). Finally, an open-flask experiment performed on a large scale with 1 gram of **1a** provided **2a** in 90% yield within a short time under ambient conditions (Table 1, entry 19).

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

[**] We thank Prof. Dr. H. Waldmann for generous support.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201303550.

Table 1: Optimization of reaction conditions.[a]



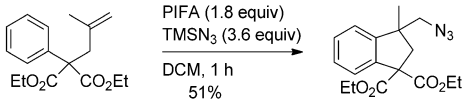
1a **2a**

Entry	Solv.	Reagent (equiv]	Azide (equiv]	*t* [h]	Yield [%][b]
1	DCE	$PhI(OCOCF_3)_2$ (2.0)	NaN_3 (2)	2	45
2	DCE	$PhI(OCOCF_3)_2$ (2.0)	$TMSN_3$ (2)	1	70
3[c]	DCE	DBU (1.0)	$TMSN_3$ (5)	12	n.d.
4[c]	DCE	Et_3N (1.0)	$TMSN_3$ (5)	12	n.d.
5	DCE	$PhI(OCOCF_3)_2$ (1)	$TMSN_3$ (2)	1	65
6	DCE	$PhI(OCOCF_3)_2$ (1.1)	$TMSN_3$ (2)	1	80
7	DCE	$PhI(OCOCF_3)_2$ (1.2)	$TMSN_3$ (2)	1	83
8	DCE	$PhI(OCOCF_3)_2$ (1.3)	$TMSN_3$ (2)	1	79
9	Et_2O	$PhI(OCOCF_3)_2$ (1.2)	$TMSN_3$ (2)	12	n.d.
10	MeOH	$PhI(OCOCF_3)_2$ (1.2)	$TMSN_3$ (2)	12	n.d.
11	EtOAc	$PhI(OCOCF_3)_2$ (1.2)	$TMSN_3$ (2)	1	63
12	CH_3CN	$PhI(OCOCF_3)_2$ (1.2)	$TMSN_3$ (2)	1	72
13	PhH	$PhI(OCOCF_3)_2$ (1.2)	$TMSN_3$ (2)	1	65
14	DCM	$PhI(OCOCF_3)_2$ (1.2)	$TMSN_3$ (2)	1	91
15	DCM	$C_6F_5I(OCOCF_3)_2$ (1.2)	$TMSN_3$ (2)	1	82
16	DCM	$PhI(OAc)_2$ (1.2)	$TMSN_3$ (2)	12	n.d.
17	DCM	$PhI(OCOCF_3)_2$ (1.2)	NaN_3 (2)	12	n.d.
18	DCM	$PhI(OCOCF_3)_2$ (1.2)	$(PhO)_2PON_3$ (2)	12	n.d.
19[d]	DCM	$PhI(OCOCF_3)_2$ (1.2)	$TMSN_3$ (2)	1	90

[a] Conditions: **1a** (0.2 mmol), reagent (equiv), azide (equiv) in solvent (1.5 mL). [b] Yields of isolated product after chromatography on silica gel. [c] Acetic acid (5 equiv) was also used. [d] Reaction performed with 1 gram of **1a**. n.d. = not determined, TMS = trimethylsilyl, DBU = 1,8-diazabicycloundec-7-ene, DCE = 1,2-dichloroethane, DCM = dichloromethane.

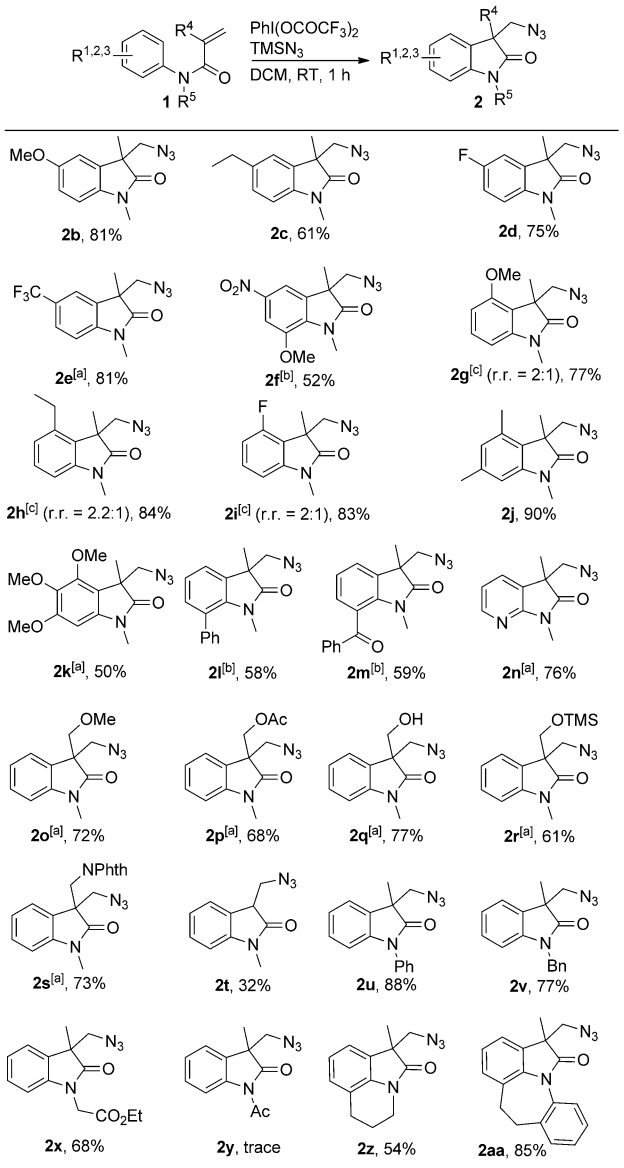
To explore the scope of this radical azidoarylation of alkenes, various *N*-arylacrylamides were subjected to the optimized reaction conditions. First we tested the reactivity of *N*-arylacrylamides equipped with different *N*-arenes (Scheme 1). In general, very smooth azidoarylation occurred for *N*-arylacrylamides having substituents at *para* and *meta* as well as *ortho* positions in the aniline. High yields were consistently obtained for *para*-substituted *N*-arylacrylamides containing either electron-donating and electron-withdrawing substituents (Scheme 1, compounds **2b–e**). A similar trend was also noticed with *meta* monosubstituted *N*-arylacrylamides although the unavoidable formation of regioisomers was observed (Scheme 1, compounds **2g–i**). Polysubstituted derivatives provided corresponding oxindoles in good to excellent yields (Scheme 1, compounds **2j** and **2k**). *N*-arylacrylamide substrates with substituents at the *ortho* position provided the corresponding oxindoles in moderate yields (Scheme 1, compounds **2l** and **2m**). Notably, the developed method allows the formation of aza-2-oxindole derivatives in good yield (Scheme 1, compound **2n**). The synthesis of aza-2-oxindole derivatives by the radical carboarylation of alkenes has never been reported before.[9] After investigating the arene scope, we moved on to explore the effect of substituents on nitrogen and at the α-position of the acrylamide. Various protected α-hydroxymethyl derivatives provided the corresponding products in good yields (Scheme 1, compounds **2o–r**). In particular, the substrate with the unprotected hydroxymethyl group survived under these oxidative conditions to provide the desired oxindole in good yield (Scheme 1, compound **2q**). Additionally, compound **2r** was obtained by simply quenching the reaction of **2q** with Et_3N. An imide-containing alkene also underwent smooth ring closure to oxindole (Scheme 1, compound **2s**). Gratifyingly, unsubstituted acrylate provided oxindole in acceptable yield (Scheme 1, compound **2t**), even though the application of this substrate in similar transformations was reported to be unsuccessful.[9] Poor yield was obtained for a substrate with a phenyl group at the α-position of acrylamide. Substrates bearing phenyl, benzyl and methyl ester protecting groups furnished the corresponding oxindoles in very good yields (Scheme 1, compounds **2u–x**). Notably, when the benzyl-protected derivative was used, only selective formation of oxindole **2v** was observed. Protecting groups like tosyl and acetyl groups were tolerated but the desired oxindoles were isolated in very poor yields. Tetrahydroisoquinoline and dibenzazepine structural motifs are commonly encountered in many biologically active compounds. Acrylamides prepared from these amines provided the corresponding tricyclic (Scheme 1, compound **2z**) and tetracyclic oxindole derivatives (Scheme 1, compound **2aa**) under the developed reaction conditions.

Furthermore, we applied our method in the synthesis of a dihydroindene derivative, which we obtained in moderate yield from a precursor containing a nonconjugated alkene and a less nucleophilic aromatic part [Eq. (1)].



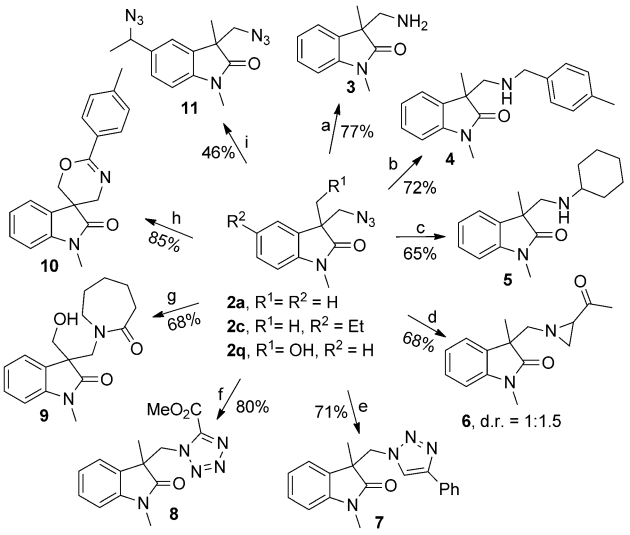
(1)

Organic azides react with a variety of functional groups due to their dipolar nature and their ability to generate reactive intermediates. The past few years have witnessed extensive applications of azides in organic synthesis, chemical biology, and material science. The transformation of organic azides has become an important means of incorporating nitrogen functionalities in organic compounds and for creating molecular complexity. On the other hand, the 2-oxindole scaffold is a common motif for many biologically active natural products and pharmaceuticals. 2-Oxindoles with an appended azide obtained by the presented methodology can be used to create a focused compound library. Therefore, we embarked upon exploring the diverse postsynthetic transformations of the azide moiety (Scheme 2). The Staudinger reaction of **2a** with PPh_3 furnished primary amine **3**. The aza-Wittig reaction of **2a** with *para*-tolualdehyde and cyclohexanone in the presence of PPh_3 provided imines that were reduced with $NaBH_4$ to give benzylamine **4** and cyclohexylamine **5,** respectively, in one pot (Scheme 2). Compound **2a** was also used in a Brønsted acid promoted olefin aziridation



Scheme 1. General reaction scheme; scope of the azidoarylation. Reaction conditions: **1** (0.2 mmol), $PhI(OCOCF_3)_2$ (0.24 mmol) ,and $TMSN_3$ (0.48 mmol) in DCM (1.5 mL) at room temperature for 1 h. Yields are given for isolated products after column chromatography. [a] Using $PhI(OCOCF_3)_2$ (0.28 mmol), $TMSN_3$ (0.56 mmol). [b] Using $PhI(OCOCF_3)_2$ (0.36 mmol), $TMSN_3$ (0.72 mmol). [c] Structure of major regioisomer is shown. r.r. = regioisomer ratio.

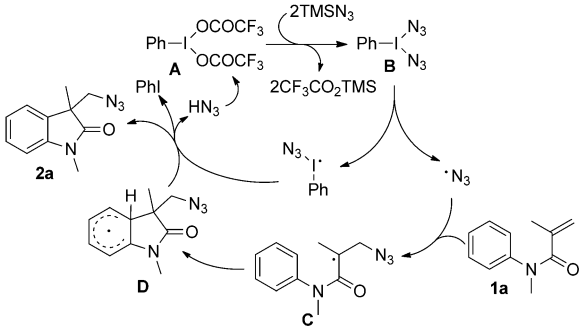
to obtain aziridine **6**. Moreover, Cu-catalyzed click reaction conditions were employed to obtain triazole **7** in good yield from **2a** and phenyl acetylene. A thermal [3+2] dipolar cycloaddition between methylcyanoformate and azide **2a** resulted in tetrazole **8** (Scheme 2). Finally, the hydroxyl-group-assisted Schmidt reaction of **2q** with cyclohexanone and *para*-tolualdehyde provided cyclic amide **9** and an oxazoline **10**, respectively, in good yields. These representative transformations clearly demonstrate the potential molecular complexity that can be created starting from the azide-appended oxindoles (Scheme 2). Notably, **2c** can be further transformed to diazide **11** by metal-free benzylic C–H bond



Scheme 2. Range of reactions on the azide unit. Reaction conditions: a) PPh_3, THF/H_2O (1:1), RT, 12 h; b) PPh_3, 4-TolCHO, RT, 12 h then $NaBH_4$, MeOH, RT, 1 h; c) PPh_3, cyclohexanone, RT, 12 h then $NaBH_4$, MeOH, RT, 1 h; d) $CH_2CHCOMe$, CF_3SO_3H, CH_3CN, 0 °C–RT, 4 h; e) $CuSO_4{\cdot}5H_2O$ (3 mol %), sodium ascorbate (8 mol %), PhCCH, $tBuOH/H_2O$ (2:1), RT, 12 h; f) $CNCO_2Me$, $PhCH_3$, 110 °C, 24 h; g) cyclohexanone, $BF_3{\cdot}OEt_2$, DCM, 0 °C–RT, 12 h; h) 4-TolCHO, $BF_3{\cdot}OEt_2$, DCM, 0 °C–RT, 4 h; [i] $PhI(OCOCF_3)_2$,$TMSN_3$, DCM, RT, 1 h.

functionalization under conditions similar to those used for the azidoarylation. Moreover, the presented methodology could be a complimentary tool to access a useful library of diverse oxindole compounds that are difficult to prepare by other approaches.

A plausible mechanism for our methodology is depicted in Scheme 3. A double ligand exchange between $PhI(OCOCF_3)_2$ (**A**) and $TMSN_3$ would provide intermediate **B**. Intermediate



Scheme 3. Proposed mechanism for the azidoarylation of alkenes leading to oxindoles.

B undergoes thermal homolytic cleavage, thanks to the weak I–N bond, to generate an azide radical. The azide radical attacks alkene **1a** to give radical **C**, which is trapped by the arene to give intermediate **D**. Rearomatization of **D** provides oxindole **2a**.

In conclusion, we have developed an unprecedented and efficient azidoarylation of alkenes under mild and metal-free reaction conditions leading to biologically interesting 2-

oxindoles. A notable feature of the developed process is cascade-type formation of C–N and C–C bonds initiated by the addition of azidyl radical. This process represents a novel strategy for the synthesis of nitrogen-containing compounds.

Received: April 25, 2013
Published online: June 20, 2013

Keywords: azidation · hypervalent compounds · metal-free reactions · oxindoles · radicals

[1] a) R. Hili, A. K. Yudin, *Nat. Chem. Biol.* **2006**, *2*, 284 – 287; b) M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 17272 – 17277; c) F. Fache, E. Schulz, M. L. Tommasino, M. Lemaire, *Chem. Rev.* **2000**, *100*, 2159 – 2232.

[2] For reviews see: a) R. I. McDonald, G. Liu, S. S. Stahl, *Chem. Rev.* **2011**, *111*, 2981 – 3019; b) J. W. W. Chang, T. M. U. Ton, P. W. H. Chan, *Chem. Rec.* **2011**, *11*, 331 – 357; c) F. Cardona, A. Goti, *Nat. Chem.* **2009**, *1*, 269 – 275; d) R. M. de Figueiredo, *Angew. Chem.* **2009**, *121*, 1212 – 1215; *Angew. Chem. Int. Ed.* **2009**, *48*, 1190 – 1193; For recent works see: e) J. A. Souto, C. Martinez, I. Velilla, K. Muniz, *Angew. Chem.* **2013**, *125*, 1363 – 1367; *Angew. Chem. Int. Ed.* **2013**, *52*, 1324 – 1328; f) H. Zhang, W. Pu, T. Xiong, Y. Li, X. Zhou, K. Sun, Q. Liu, Q. Zhang, *Angew. Chem.* **2013**, *125*, 2589 – 2593; *Angew. Chem. Int. Ed.* **2013**, *52*, 2529 – 2533; g) W. Kong, P. Feige, T. de Haro, C. Nevado, *Angew. Chem.* **2013**, *125*, 2529 – 2533; *Angew. Chem. Int. Ed.* **2013**, *52*, 2469 – 2473; h) P. Chávez, J. Kirsch, C. H. Hövelmann, J. Streuff, M. Martínez-Belmonte, E. C. Escudero-Adán, E. Martin, K. Muniz, *Chem. Sci.* **2012**, *3*, 2375 – 2382; i) U. Farid, T. Wirth, *Angew. Chem.* **2012**, *124*, 3518 – 3522; *Angew. Chem. Int. Ed.* **2012**, *51*, 3462 – 3465; j) A. Yoshimura, K. R. Middleton, C. Zhu, V. N. Nemykin, V. V. Zhdankin, *Angew. Chem.* **2012**, *124*, 8183 – 8186; *Angew. Chem. Int. Ed.* **2012**, *51*, 8059 – 8062; k) C. Röben, J. A. Souto, Y. Gonzalez, A. Lishchynskyi, K. Muniz, *Angew. Chem.* **2011**, *123*, 9650 – 9654; *Angew. Chem. Int. Ed.* **2011**, *50*, 9478 – 9482.

[3] Reviews: a) S. Bräse, K. Banert, *Organic Azides*, Wiley-VCH, Weinheim, **2010**; b) S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem.* **2005**, *117*, 5320 – 5374; *Angew. Chem. Int. Ed.* **2005**, *44*, 5188 – 5240.

[4] For reviews on hydroazidation and carboazidation see: a) G. Lapointe, A. Kapat, K. Weidner, P. Renaud, *Pure Appl. Chem.* **2012**, *84*, 1633 – 1641; b) M. Minozzi, D. Nanni, P. Spagnolo, *Chem. Eur. J.* **2009**, *15*, 7830 – 7840; for recent examples on hydroazidation see c) E. K. Leggans, T. J. Barker, K. K. Duncan, D. L. Boger, *Org. Lett.* **2012**, *14*, 1428 – 1431; d) A. Kapat, A. König, F. Montermini, P. Renaud, *J. Am. Chem. Soc.* **2011**, *133*, 13890 – 13893; e) J. Waser, B. Gaspar, H. Nambu, E. M. Carreira, *J. Am. Chem. Soc.* **2006**, *128*, 11693 – 11712; f) J. Waser, H. Nambu, E. M. Carreira, *J. Am. Chem. Soc.* **2005**, *127*, 8294 – 8295; for recent examples on carboazidation see g) G. Lapointe, K. Schenk, P. Renaud, *Chem. Eur. J.* **2011**, *17*, 3207 – 3212; h) K. Weidner, A. Giroult, P. Panchaud, P. Renaud, *J. Am. Chem. Soc.* **2010**, *132*, 17511 – 17515.

[5] For C–H abstraction by nitrogen-centered radicals see: a) S. Z. Zard, *Chem. Soc. Rev.* **2008**, *37*, 1603 – 1618; b) L. Stell in *Radical in Organic Synthesis, Vol. 2* (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, **2001**, pp. 407 – 424.

[6] For diazidation see: a) R. Chung, E. Yu, C. D. Incarvito, D. J. Austin, *Org. Lett.* **2004**, *6*, 3881 – 3884; b) B. B. Snider, H. Lin, *Synth. Commun.* **1998**, *28*, 1913 – 1922; c) P. Magnus, J. Lacour, P. A. Evans, M. B. Roe, C. Hulme, *J. Am. Chem. Soc.* **1996**, *118*, 3406 – 3418; d) W. E. Fristad, T. A. Brandvold, J. R. Peterson, S. R. Thompson, *J. Org. Chem.* **1985**, *50*, 3647 – 3649; for haloazidation see e) P. V. Chouthaiwale, P. U. Karabal, G. Suryavanshi, A. Sudalai, *Synthesis* **2010**, 3879 – 3882; f) A. Hassner, L. A. Levy, *J. Am. Chem. Soc.* **1965**, *87*, 4203 – 4204; for selenoazidations see: g) M. Tiecco, L. Testaferri, C. Santi, C. Tomassini, F. Marini, L. Bagnoli, A. Temperini, *Angew. Chem.* **2003**, *115*, 3239 – 3241; *Angew. Chem. Int. Ed.* **2003**, *42*, 3131 – 3133; h) W. S. Trahanovsky, M. D. Robbins, *J. Am. Chem. Soc.* **1971**, *93*, 5256 – 5258.

[7] For reviews on oxindoles see: a) J. E. M. N. Klein, R. J. K. Taylor, *Eur. J. Org. Chem.* **2011**, 6821 – 6841; b) A. Millemaggi, R. J. K. Taylor, *Eur. J. Org. Chem.* **2010**, 4527 – 4547; c) F. Zhou, Y.-L. Liu, J. Zhou, *Adv. Synth. Catal.* **2010**, *352*, 1381 – 1407; d) B. M. Trost, M. K. Brennan, *Synthesis* **2009**, 3003 – 3025; e) C. V. Galliford, K. A. Scheidt, *Angew. Chem.* **2007**, *119*, 8902 – 8912; *Angew. Chem. Int. Ed.* **2007**, *46*, 8748 – 8758; f) C. Marti, E. M. Carreira, *Eur. J. Org. Chem.* **2003**, 2209 – 2219.

[8] Synthesis of oxindoles from aniline derivatives: for transition-metal-mediated syntheses see: a) C. Tsukano, M. Okuno, Y. Takemoto, *Angew. Chem.* **2012**, *124*, 2817 – 2820; b) C. Dey, E. P. Kundig, *Chem. Commun.* **2012**, *48*, 3064 – 3066; c) T. Wu, X. Mu, G. Liu, *Angew. Chem.* **2011**, *123*, 12786 – 12789; *Angew. Chem. Int. Ed.* **2011**, *50*, 12578 – 12581; d) X. Mu, T. Wu, H.-y. Wang, Y.-l. Guo, G. Liu, *J. Am. Chem. Soc.* **2012**, *134*, 878 – 881; e) L. Liu, N. Ishida, S. Ashida, M. Murakami, *Org. Lett.* **2011**, *13*, 1666 – 1669; f) S. Ueda, T. Okada, H. Nagasawa, *Chem. Commun.* **2010**, *46*, 2462 – 2464; g) G. An, W. Zhou, G. Zhang, H. Sun, J. Han, Y. Pan, *Org. Lett.* **2010**, *12*, 4482 – 4485; h) S. Jaegli, J. Dufour, H.-l. Wei, T. Piou, X.-H. Duan, J.-P. Vors, L. Neuville, J. Zhu, *Org. Lett.* **2010**, *12*, 4498 – 4450; i) Y.-X. Jia, E. P. Kündig, *Angew. Chem.* **2009**, *121*, 1664 – 1667; *Angew. Chem. Int. Ed.* **2009**, *48*, 1636 – 1639; j) A. Perry, R. J. K. Taylor, *Chem. Commun.* **2009**, 3249 – 3251; k) L. Ackermann, R. n. Vicente, N. Hofmann, *Org. Lett.* **2009**, *11*, 4274 – 4276; l) Y.-X. Jia, J. M. Hillgren, E. L. Watson, S. P. Marsden, E. P. Kundig, *Chem. Commun.* **2008**, 4040 – 4042; m) A. Pinto, Y. Jia, L. Neuville, J. Zhu, *Chem. Eur. J.* **2007**, *13*, 961 – 967; n) E. J. Hennessy, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 12084 – 12085; for non-transition-metal-mediated syntheses see: o) C. Dey, D. Katayev, K. E. O. Ylijoki, E. P. Kundig, *Chem. Commun.* **2012**, *48*, 10957 – 10959; p) A. Beyer, J. Buendia, C. Bolm, *Org. Lett.* **2012**, *14*, 3948 – 3951; q) S. Ghosh, S. De, B. N. Kakde, S. Bhunia, A. Adhikary, A. Bisai, *Org. Lett.* **2012**, *14*, 5864 – 5867; for metal-free syntheses see: r) D. C. Fabry, M. Stodulski, S. Hoerner, T. Gulder, *Chem. Eur. J.* **2012**, *18*, 10834 – 10838; s) J. Wang, Y. Yuan, R. Xiong, D. Zhang-Negrerie, Y. Du, K. Zhao, *Org. Lett.* **2012**, *14*, 2210 – 2213; t) H.-L. Wei, T. Piou, J. Dufour, L. Neuville, J. Zhu, *Org. Lett.* **2011**, *13*, 2244 – 2247.

[9] Metal-mediated radical synthesis of oxindoles from aniline derivatives: a) W.-T. Wei, M.-B. Zhou, J.-H. Fan, W. Liu, R.-J. Song, Y. Liu, M. Hu, P. Xie, J.-H. Li, *Angew. Chem.* **2013**, *125*, 3726 – 3729; *Angew. Chem. Int. Ed.* **2013**, *52*, 3638 – 3641; b) Y.-M. Li, M. Sun, H.-L. Wang, Q.-P. Tian, S.-D. Yang, *Angew. Chem.* **2013**, *125*, 4064 – 4068; *Angew. Chem. Int. Ed.* **2013**, *52*, 3972 – 3976.

[10] Metal-free radical synthesis of oxindoles from aniline derivatives: M.-B. Zhou, R.-J. Song, X.-H. Ouyang, Y. Liu, W.-T. Wei, G.-B. Deng, J.-H. Li, *Chem. Sci.* **2013**, *4*, 2690 – 2694.

[11] Reviews on bioorthogonal chemistry: a) E. M. Sletten, C. R. Bertozzi, *Acc. Chem. Res.* **2011**, *44*, 666 – 676; b) E. M. Sletten, C. R. Bertozzi, *Angew. Chem.* **2009**, *121*, 7108 – 7133; *Angew. Chem. Int. Ed.* **2009**, *48*, 6974 – 6998; c) R. K. V. Lim, Q. Lin, *Chem. Commun.* **2010**, *46*, 1589 – 1600.

[12] a) K. Matcha, A. P. Antonchick, *Angew. Chem.* **2013**, *125*, 2136 – 2140; *Angew. Chem. Int. Ed.* **2013**, *52*, 2082 – 2086; b) A. P. Antonchick, L. Burgmann, *Angew. Chem.* **2013**, *125*, 3349 – 3353; *Angew. Chem. Int. Ed.* **2013**, *52*, 3267 – 3271.

[13] For recent results from our group using I^{III} reagents: a) R. Samanta, J. Lategahn, A. P. Antonchick, *Chem. Commun.* **2012**, *48*, 3194 – 3196; b) R. Samanta, K. Kulikov, C. Strohmann, A. P. Antonchick, *Synthesis* **2012**, *44*, 2325 – 2332; c) R. Samanta, J. O. Bauer, C. Strohmann, A. P. Antonchick, *Org. Lett.* **2012**, *14*, 5518 – 5521; d) R. Samanta, A. P. Antonchick, *Synlett* **2012**, 809 – 813; e) A. P. Antonchick, R. Samanta, K. Kulikov, J. Lategahn, *Angew. Chem.* **2011**, *123*, 8764 – 8767; *Angew. Chem. Int. Ed.* **2011**, *50*, 8605 – 8608.

[14] For reviews on the chemistry of I^{III} compounds see: a) M. S. Yusubov, V. V. Zhdankin, *Curr. Org. Synth.* **2012**, *9*, 247 – 272; b) L. F. Silva, Jr., B. Olofsson, *Nat. Prod. Rep.* **2011**, *28*, 1722 – 1754; c) E. A. Merritt, B. Olofsson, *Synthesis* **2011**, 517 – 538; d) J. P. Brand, D. F. Gonzalez, S. Nicolai, J. Waser, *Chem. Commun.* **2011**, *47*, 102 – 115; e) V. V. Zhdankin, *ARKIVOC* **2009**, 1 – 62; f) M. Uyanik, K. Ishihara, *Chem. Commun.* **2009**, 2086 – 2099; g) T. Dohi, M. Ito, N. Yamaoka, K. Morimoto, H. Fujioka, Y. Kita, *Tetrahedron* **2009**, *65*, 10797 – 10815; h) V. V. Zhdankin, P. J. Stang, *Chem. Rev.* **2008**, *108*, 5299 – 5358; i) S. Quideau, L. Pouysegu, D. Deffieux, *Synlett* **2008**, 467 – 495.

[15] For reports on conjugate addition of azides see: a) T. Angelini, D. Lanari, R. Maggi, F. Pizzo, G. Sartori, L. Vaccaro, *Adv. Synth. Catal.* **2012**, *354*, 908 – 916; b) T. Angelini, S. Bonollo, D. Lanari, F. Pizzo, L. Vaccaro, *Org. Lett.* **2012**, *14*, 4610 – 4613; c) I. Adamo, F. Benedetti, F. Berti, P. Campaner, *Org. Lett.* **2006**, *8*, 51 – 54; d) L.-W. Xu, C.-G. Xia, J.-W. Li, S.-L. Zhou, *Synlett* **2003**, *2003*, 2246 – 2248; e) T. E. Horstmann, D. J. Guerin, S. J. Miller, *Angew. Chem.* **2000**, *112*, 3781 – 3784; *Angew. Chem. Int. Ed.* **2000**, *39*, 3635 – 3638; f) J. K. Myers, E. N. Jacobsen, *J. Am. Chem. Soc.* **1999**, *121*, 8959 – 8960; g) D. J. Guerin, T. E. Horstmann, S. J. Miller, *Org. Lett.* **1999**, *1*, 1107 – 1109.

