Organic & Biomolecular Chemistry

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/obc

Organic & Biomolecular Chemistry

ARTICLE TYPE

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

Transition-metal-free Oxidative Carboazidation of Acrylamides via Cascade C-N and C-C Bond-Forming Reactions

Jun Qiu[a] and Ronghua Zhang*[a]

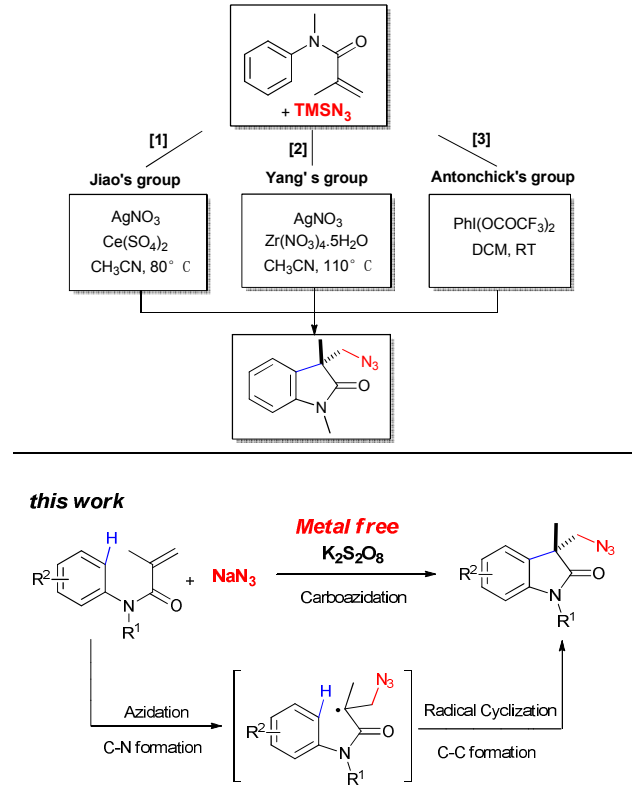
Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

A novel transition-metal-free oxidative carboazidation of acrylamides using inexpensive NaN_3 and $K_2S_2O_8$ was achieved, which not only provided an efficient method to prepare various N_3-substituted oxindoles, but also represented a novel strategy for C–N and C–C bond formation via a free-radical cascade process. This transformation exhibits excellent functional group tolerance, affording the desired oxindoles in good to excellent yields.

Organic azides are highly important and valuable compounds which have attracted much attention not only because of their widespread application as versatile intermediates and building blocks in organic synthesis but also because of their remarkable biological activity.[1] Moreover, azides have been found intensive application as reactive functionalities in materials science,[2] supramolecular chemistry,[3] medicinal chemistry[4] and biotechnology[5]. In the past decades, the application of a radical pathway for direct C-H azidation has been significantly realized.[6] Furthermore, the application of azidyl radicals to the C-H functionalization of unactivated alkenes, which provides a novel and concise pathway to the synthesis of alkyl azides, have been widely reported.[7]

On the other hand, oxindole frameworks represent an important structural motif that be demonstrated significant potential for use in a wide range of biological applications such as NMDA antagonist[8] and calcium channel blockers[9] as well as anti-angiogenic,[10] anti-cancer,[11] and analgesic effects.[12] Recently, difunctionalization of alkenes involving direct C-H functionalization of arenes has received increasing attention.[13] In particular, metal-catalyzed C-H functionalization/cyclization of unactivated alkenes provides some versatile strategies for the synthesis of various functionalized oxindoles.[14-18] For example, Fe-,[15] Ag-,[16] Cu-,[17] and Pd-[18] catalyzed oxidative tandem difunctionalization/cyclization reaction of N-arylacrylamides, including arylphosphorylation,[14a] alkylarylation,[14d,15a,19a-b] diarylation,[19c] arylcarbonylation,[19d] arylnitration,[19e-f] aryltrifluoromethylation[19g] and so on have independently developed. However, examples of metal-catalyzed azido-carbocyclization of arylacrylamides via a radical pathway to prepare azido oxindoles are quite rare. Jiao[16c] and Yang[16d] groups have independently reported a silver-catalyzed oxidative azido-carbocyclization of arylacrylamides to synthesize a variety of oxindoles using $TMSN_3$ as the N_3 source in the presence of heavy metal oxidants (Scheme 1, Eq.1 and Eq. 2).

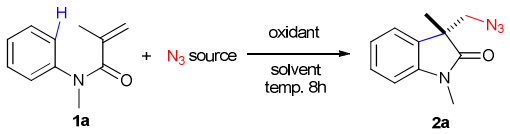


Scheme 1. Metal-free carboazidation of acrylamides

More recently, the transition-metal-free C–H functionalization reactions have attracted more attention due to the economical and environmental viewpoints.[20] It is worthy of note that the transition-metal-free C-H functionalization/cyclization of unactivated alkenes is still an extremely attractive yet challenging task.[19d, 19f, 21] In

particular, only a few transition-metal-free approaches on azidoarylation of N-arylacrylamide to form azido oxindoles have been reported. Antonchick and co-workers[21c] reported a metal-free oxidative azidoarylation of N-arylacrylamides using the $PhI(OCOCF_3)_2$ as the oxidant and $TMSN_3$ as the azide source (Scheme 1, Eq.3). Although several elegant studies on the azidoarylation of N-arylacrylamides have been achieved, it is still highly desirable to develop new strategies to prepare azido oxindoles that are highly efficient and utilizing cheap substrates and oxidants. Herein, we report a transition-metal-free radical cascade azidoarylation of arylacrylamide by using the very cheapest NaN_3 as the azide source and $K_2S_2O_8$ as the oxidant in aqueous solution, which allows for highly efficient access to oxindoles via cascade C–N and C–C bond formation (Scheme 1).

Table 1. Screening of reaction conditions.[a]



1a 2a

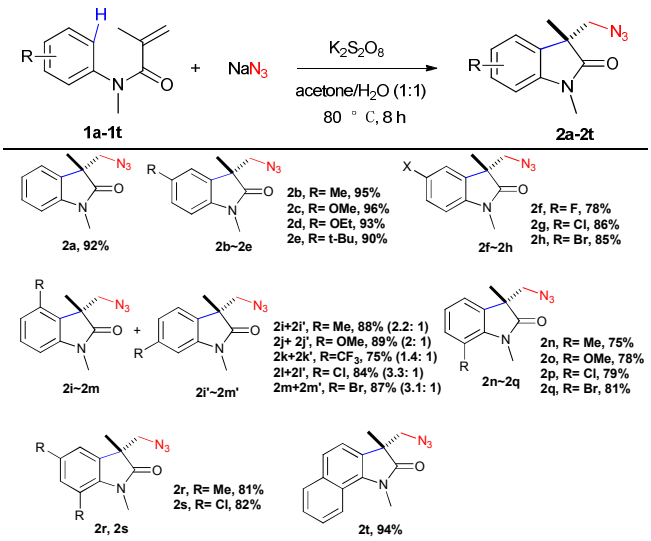
Entry	Oxidant	Slovent	Azide	T(°C)	Yield(%)[b]
1	$K_2S_2O_8$	H_2O	NaN_3	80	45
2	$K_2S_2O_8$	dioxane/H_2O (1:1)	NaN_3	80	n.d.
3	$K_2S_2O_8$	THF/H_2O (1:1)	NaN_3	80	n.d.
4	$K_2S_2O_8$	toluene/H_2O (1:1)	NaN_3	80	n.d.
5	$K_2S_2O_8$	DCE/H_2O (1:1)	NaN_3	80	40
6	$K_2S_2O_8$	DMF/H_2O (1:1)	NaN_3	80	81
7	$K_2S_2O_8$	CH_3CN/H_2O (1:1)	NaN_3	80	88
8	$K_2S_2O_8$	acetone/H_2O (1:1)	NaN_3	80	92
9	PIDA	acetone/H_2O (1:1)	NaN_3	80	22
10	TBHP	acetone/H_2O (1:1)	NaN_3	80	20
11	DDQ	acetone/H_2O (1:1)	NaN_3	80	n.d.
12	DTBP	acetone/H_2O (1:1)	NaN_3	80	n.d.
13	O_2[c]	acetone/H_2O (1:1)	NaN_3	80	n.d.
14	$K_2S_2O_8$	acetone/H_2O (1:1)	NaN_3	r.t.	n.d.
15	$K_2S_2O_8$	acetone/H_2O (1:1)	NaN_3	50	62
16	$K_2S_2O_8$	acetone/H_2O (1:1)	NaN_3	100	92
17	$K_2S_2O_8$	acetone/H_2O (1:1)	$TMSN_3$	80	53
18	$K_2S_2O_8$	acetone/H_2O (1:1)	$(PhO)_2PON_3$	80	n.d.

[a] Reaction conditions: 1a (0.25 mmol), oxidant (2 equiv) and azide (2 equiv) in solvent (2.5 mL) with stirring at different temperature for 8 h. [b] Yields of isolated product. [c] O_2 (1 atm.). r.t. = room temperature, n.d. = not detected, PIDA= phenyliodine diacetate, DDQ= 2,3-dichloro-5,6-dicyanobenzo-quinone, TBHP= tert-butyl hydrogen peroxide (anhydrous, about 5.5 m in decane), DTBP= di-tert-butyl peroxide.

An initial study was carried out using the N-methyl-N-phenylmethacrylamide **1a** and sodium azide as the model substrates, $K_2S_2O_8$ was used as the oxidant to examine suitable reaction conditions, and the results were summarized in Table 1. A number of solvents including H_2O, dioxane/H_2O, THF/H_2O, toluene/H_2O, DCE/H_2O, DMF/H_2O, CH_3CN/H_2O and acetone/H_2O were screened at 80°C for 8h (Table 1, entries 1-8). As we expected, treatment of **1a** with NaN_3 in the presence of 2 equiv. of $K_2S_2O_8$ in water at 80 °C for 8 h, afforded the desired oxindole **2a** in 45% isolated yield (Table 1, entry 1). We envisioned that this homogeneous phase system disfavored the reaction, and that two-phase system might be required to promote this reaction. The transformation did not proceed in such aqueous solutions as dioxane/H_2O, THF/H_2O and toluene/H_2O (Table 1, entries 2-4). It should be noted that good yields of the desired product **2a** were obtained using DMF/H_2O and CH_3CN/H_2O as the slovents (Table 1, entries 6-7). To our delight, further optimization showed that acetone/H_2O gave the best yield of 92% (Table 1, entry 8). To establish the reaction conditions that improve the reactivity, several oxidants such as $K_2S_2O_8$, DDQ, TBHP, PIDA, DTBP and O_2 were screened in acetone/H_2O (1:1) at 80°C for 8h (Table 1, entries 8-13). It was found that $K_2S_2O_8$ as the oxidant showed relative higher efficiency compared with other oxidants and thus was chosen as the oxidant for further optimization. Furthermore, the yields were remarkably diminished when $TMSN_3$ and $(PhO)_2PON_3$ were used as the azide sources instead of NaN_3 (Table 1, entries 17-18). Screening of the reaction temperature revealed that 80 °C was the best one (Table 1, entry 8). Therefore, we chose N-arylacrylamide together with sodium azide (2 equiv) and $K_2S_2O_8$ (2 equiv) in acetone/H_2O (1:1) at 80 °C for 8 h as our optimized reaction conditions.

With the optimized reaction conditions established, various substrates were subjected to the reaction and representative results were summarized in Table 2. To our delight, a variety of N-protected N-arylmethacrylamides, which have substituents at para and meta as well as ortho positions in the aniline, could be smoothly converted into the corresponding azide-substituted oxindoles in moderate to excellent yields (up to 96 %). For N-arylmethacrylamides bearing various electron- donating substituents (e.g., Me, OMe, OEt, *t*-Bu) in the ortho-position of the aromatic rings, the reactions were compatible with the process and could be successfully converted into the desired products in excellent yields (90-96%, table 2, **2b**–**2e**). It is noteworthy that the halo-substituted (F, Cl, Br) N-methyl-N-phenylmethacrylamides were also reacted well and afforded the corresponding halo-substituted azido oxindoles in good yields (78–86 %, table 2, **2f**– **2h**). Interestingly, the electronic effect of the substituents on aromatic ring was observed. For example, 90–96% yields were obtained when the substrates bearing an electron-donating group on the aromatic ring, while a little lower yields (78–86%) were provided that bearing electron-withdrawing groups (F, Cl, Br) on the para-position. Furthermore, the substrate bearing meta substituents on N-arylacrylamides underwent carboazidation smoothly and readily converted to a mixture of two regioisomers in

Table 2. Metal- free Carboazidation of Different Arylacrylamides.[a,b]

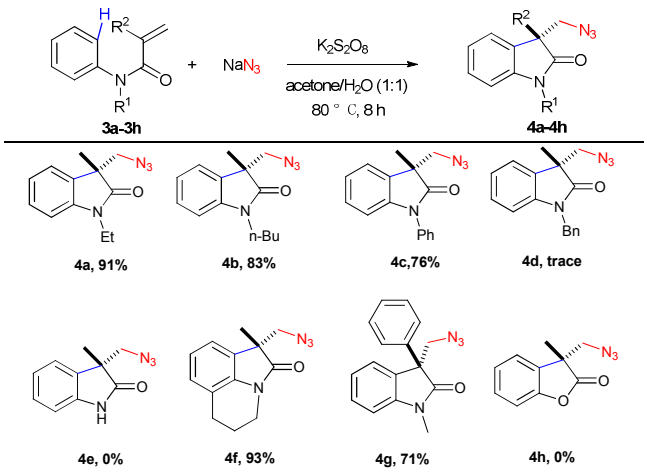


[a] All reactions were carried out in the presence of 0.5 mmol of **1a**–**1t**, NaN_3 (2.0 equiv.), $K_2S_2O_8$ (2.0 equiv.) in acetone/H_2O (1:1, 5 mL) at 80 °C for 8h. [b] Isolated yield.

moderate to good yields (75–89 %) with poor regioselectivity (Table 2, **2i–2m** and **2i'-2m'**). The N-arylacrylamides containing the ortho-position substituent groups exhibited a particularly distinct steric hindrance effect, and lower yields were observed as a result (Table 2, **2n**–**2q**). For example, when the methyl group on the aromatic ring of acrylamide was changed from para-, meta- to ortho-, the yields decreased from 95%, 88% to 65% (Table 2, **2b, 2i** and **2n**). In addition, 2,4-disubstituted N-arylacrylamides were also well tolerated in this carboazidation process, affording the azide oxindoles with good yields (Table 2, **2r** and **2s**). Gratifyingly, when the benzene ring was changed to naphthalene, the substrate also successfully provided the product of **2t** in 94% yield.

Encouraged by the above results, we further investigated the reactions between the N-proctected-N-phenylmethacrylamides and sodium azide under the standard reaction conditions. To our delight, an investigation into different N-protection groups revealed that the electron-donating protecting groups such as ethyl, n-Butyl and phenyl were appropriate for the reactions and furnished the corresponding oxindoles in very good yields (Table 3, **4a, 4b** and **4c**). Much to our surprise, substrates bearing benzyl and protecting group was tolerated but only a trace amount of the desired oxindole was isolated (Table 3, **4d**). Unfortunately, replacement of the methyl substituent with a hydrogen atom or tosyl did not work at all and not furnish corresponding products (Table 3, **4e**). To our best knowledge, Tetrahydroisoquinoline structural motifs are commonly founed in many biologically active compounds. Acrylamides prepared from these amines provided the corresponding tricyclic oxindole derivatives in excellent yield under the developed reaction conditions (Table 3, **4f**). In addition, the substitutent on the alkene moiety was changed from methyl to phenyl, the yield decreased to 71% (Table 3, **4g**). However, when the frameworks of the substrates were changed by

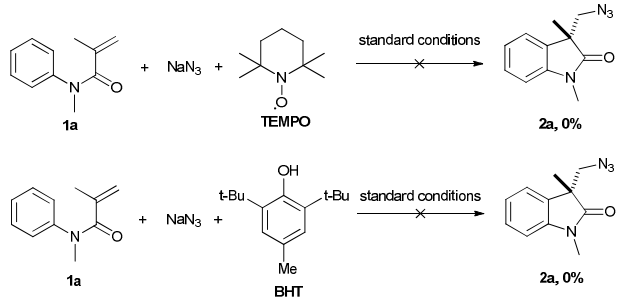
Table 3. Metal- free Carboazidation of Different Arylacrylamides.[a,b]



[a] All reactions were carried out in the presence of 0.5 mmol of **3a**–**3h**, NaN_3 (2.0 equiv.), $K_2S_2O_8$ (2.0 equiv.) in acetone/H_2O (1:1, 5 mL) at 80 °C for 8h. [b] Isolated yield.

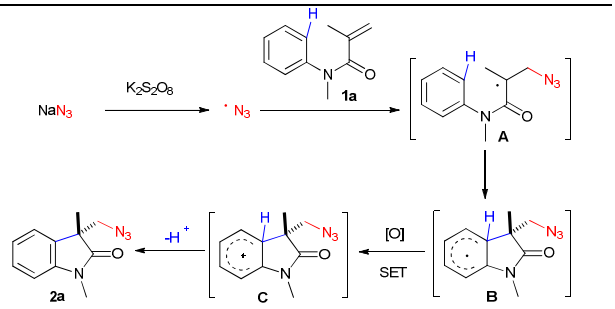
replacing the heteroatoms from N to O, no desired product was observed (Table 2, **4h**).

In order to gain more insight into the reaction mechanism, several control experiments were performed. As illustrated in Scheme 2. First, we used the well-known radical-trapping reagents 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and 2,6-ditertbutyl-4-methylphenol (BHT) as the radical scavengers. Chemical trapping was carried out using **1a** with NaN_3 and $K_2S_2O_8$ in the presence of 1.0 equiv radical scavenger under standardized reaction conditions, and only a trace of desired products were obtained with 87% and 76% of **1a** recovered. This observation was consistent with the hypothesis that the reaction likely involved free-radical intermediates and proceeded via a single-electron-transfer (SET) process triggered by a free radical.



Scheme 2. Investigation of the possible key intermediates.

Although the mechanism is not completely clear yet, a plausible mechanism for our methodology is hypothesized on the basis of literature[6-7, 13-21] and the above mechanistic studies (Scheme 3). Initially, potassium peroxydisulphate may decompose to the sulfate radical anion upon heating. Then, NaN_3 reacts with the sulfate radical anion to form the azidyl radical. Subsequently, the addition of the azidyl radical to the activated alkene **1a** results in the formation of the radical intermediate **A**, followed by intramolecular carbocyclization to generate the corresponding radical intermediate **B**. Further intermediate **B** undergoes one-electron oxidation reaction with



Scheme 3. Plausible Mechanism for Carboazidation of Arylacrylamides

sulfate radical anion to release the intermediate **C** via a single electron transfer (SET) process. Finally, hydrogen abstraction of cationic intermediate **C** by $K_2S_2O_8$ leads to the final oxindole **2a**.

In conclusion, we have demonstrated a novel transition-metal-free oxidative azido-carbocyclization of activated alkenes for the synthesis of azido oxindoles using the $K_2S_2O_8$ as oxidant. Radical addition and C-H functionalization processes are involved in this transformation with the cascade-type formation of C-N and C-C bonds. This methodology provides an economical and efficient way for the construction of azido-containing oxindoles, which avoids pre-functional azides and expensive transition metals and oxidants. Further applications of this new transformation to other substrates and the synthesis of more valuable compounds are underway in our group.

We are grateful to the Natural Science Foundation of China (no. 20972113/B020502) for support.

Notes and references

[a] *Department of Chemistry, Tongji University, Shanghai 200092, P. R. China, and Key Laboratory of Yangtze River Water Environment,Ministry of Education, Siping Road 1239, Shanghai, 200092, P. R. China.. E-mail: rhzhang@tongji.edu.cn*

† Electronic Supplementary Information (ESI) available: Experiment procedure and NMR data. See DOI: 10.1039/b000000x

1 *(a)* T. M. V. D. Pinho e Melo, In Organic Azides: Syntheses and Applications, Bräse, S., Banert, K., Eds. Wiley-VCH: Weinheim, 2010, **53**. *(b)* S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem. Int. Ed.* 2005, **44**, 5188. *(c)* S. Bräse, K. Banert, In Organic Azides Wiley-VCH: Weinheim, 2010. (d) N. Jung, S. Bräse, *Angew. Chem. Int. Ed.* 2012, **51**, 12169. *(e)* D. M. Huryn, M. Okabe, *Chem. Rev.* 1992, **92**, 1745. *(f)* M. Minozzi, D. Nanni, Spagnolo, P. *Chem.-Eur. J.* 2009, **15**, 7830. *(g)* G. Lapointe, A. Kapat, K. Weidner, P. Renaud, *Pure. Appl. Chem.* 2012, **84**, 1633. *(h)* S. Chiba, *Synlett* 2012, 23, 21. *(i)* E. F. V. Scriven, K. Turnbull, *Chem. Rev.* 1988, **88**, 297. *(j)* T. G. Driver, *Org. Biomol. Chem.* 2010, **8**, 3831. *(k)* B. Zhang, A. Studer, *Org. Lett.* 2014, **16**, 1790.

2 *(a)* P. Wu, A. K. Feldman, K. Nugent, C. J. A. Hawker, A. Scheel, B. Voit, J. Pyun, J. M. J. Fréchet, K. B. Sharpless, V. V. Fokin, *Angew. Chem., Int. Ed.* 2004, **43**, 3928. *(b)* D. I. Rozkiewicz, D. Jańczewski, W. Verboon, B. J. Ravoo, D. N. Reinhoudt, *Angew. Chem., Int. Ed.* 2006, **45**, 5292. *(c)* H. Nandivada, X. Jiang, J. Lahann, *Adv. Mater.* 2007, **19**, 2197. (d) W. H. Binder, R. Macromol. Sachsenhofer, *Rapid Commun.*2007, **28**, 15. *(e)* J. F. Lutz, *Angew. Chem. Int. Ed.* 2007, **46**, 1018. *(f)* P. Wu, M. Malkoch, J. N. Hunt, R. Vestberg, E. Kaltgrad, M. G. Finn, V. V. Fokin, K. B. Sharpless, C. J. Hawker, *Chem. Commun.*2005, 5775.

3 *(a)* Ryu, E.H. Zhao, Y. *Org. Lett.* 2005, **7**, 1035. *(b)* J. D. Megiatto, D. I. Schuster, *J. Am. Chem. Soc.* 2008, **130**, 12872.

4 *(a)* A. D. Moorhouse, A. M. Santos, M. Gunaratnam, M. Moore, S. Neidle, J. E.Moses, *J. Am. Chem. Soc.* 2006, **128**, 15972. *(b)* D. Hein, C. X. M. Liu, D. Wang, *Pharm. Res.* 2008, **25**, 2216. *(d)* A. D. Moorhouse, J. E. Moses, *ChemBioChem.* 2008, **3**, 715.

5 *(a)* Q. Wang, T. R. Chan, R. Hilgraf, V. V. Fokin, K. B. Sharpless, M. G. Finn, *J. Am. Chem. Soc.* 2003, **125**, 3192. *(b)* A. E. Speers, B. F. Cravatt, *Chem. Biol.* 2004, **11**, 535. *(c)* G. A. Burley, J. Gierlich, M. R. Mofid, H. Nir, S. Tal, Y. Eichen, T. Carell, *J. Am. Chem. Soc.* 2006, **128**, 1398. *(d)* R. Breinbauer, M. Kohn, *ChemBioChem.* 2003, **4**, 1147. *(e)* R. Manetsch, A. Krasiñski, Z. Radiæ, J. Raushel, P. Taylor, K. B. Sharpless, H. C. Kolb, *J. Am. Chem. Soc.* 2004, **126**, 12809. *(f)* C. Park, H. Kim, S. Kim, C. Kim, *J. Am. Chem. Soc.* 2009 , **131**, 16614.

6 *(a)* W. Song, S. I. Kozhushkov, L. Ackermann, *Angew. Chem.* 2013, **125**, 6706.; *Angew. Chem. Int. Ed.* 2013, **52**, 6576. *(b)* C. Tang, N. Jiao, *J. Am. Chem. Soc.* 2012, **134**, 18924. *(c)* D. Lu-briks, I. Sokolovs, E. Suna, *J. Am. Chem. Soc.* 2012, **134**, 15436. *(d)* H. Tohma, M. Egi, M. Ohtsubo, H. Watanabe, S. Takiza-wa, Y. Kita, *Chem. Commun.* 1998, 173. *(e)* C. Viuf, M. Bols, Angew. Chem.2001, 113, 643. *Angew. Chem. Int. Ed.* 2001, **40**, 623. *(f)* A. P. Krasutsky, C. J. Kuehl, V. V. Zhdankin, *Synlett* 1995, 1081. *(g)* Y. Kita, H. Tohma, M. Inagaki, K. Hatanaka, T. Yakura, *Tetrahedron Lett.* 1991, **32**, 4321. *(h)* V. V. Zhdankin, A. P. Krasutsky, C. J. Kuehl, A. J. Simonsen, J. K. Woodward, B. Mis-mash, J. T. Bolz, *J. Am. Chem. Soc.* 1996, **118**, 5192. *(i)* P. V. Chouthaiwale, G. Suryavanshi, A. Sudalai,*Tetrahedron Lett.* 2008, **49**, 6401. *(j)* P. Magnus, J. Lacour, W. Weber, *J. Am. Chem. Soc.* 1993, **115** , 9347. *(k)* M. V. Vita, J. Waser, *Org. Lett.* 2013, **15**, 3246. *(l)* Q. H. Deng, T. Bleith, H. Wadepohl, L. H. Gade, *J. Am. Chem. Soc.* 2013, **135**, 5356.

7 *(a)* R. Chung, E. Yu, C. D. Incarvito, D. J. Austin, *Org. Lett.* 2004, **6**, 3881. *(b)* G. Bencivenni, T. Lanza, M. Minozzi, D. Nanni, P. Spagnolo, G. Zanardi, *Org. Biomol. Chem.* 2010, **8**, 3444. *(c)* A. Hassner, L. A. Levy, *J. Am. Chem. Soc.* 1965, **87**, 4203. *(d)* P. Magnus, J. Lacour, P. A. Evans, M. B. Roe, C. Hulme, *J. Am. Chem. Soc.* 1996, **118**, 3406. *(e)* W. S. Trahanovsky, M. D. Rob-bins, *J. Am. Chem. Soc.* 1971, **93**, 5256. *(f)* W. E. Fristad, T. A. Brandvold, J. R. Peterson, S. R. Thompson, *J. Org. Chem.* 1985, **50**, 3647. *(g)* M. Tiecco, L. Testaferri, C. Santi, C. Tomassini, F. Marini, L. Bagnoli, A. Temperini, *Angew. Chem.* 2003, **115**, 3239. *Angew. Chem. Int. Ed.* 2003, **42**, 3131. *(h)* A. Kapat, A. Kçnig, F. Montermini, P. Renaud, *J. Am. Chem. Soc.* 2011, **133**, 13890. *(i)* P. Renaud, C. Ollivier, P. Panchaud, *Angew. Chem.* 2002, **114**, 3610. *Angew. Chem. Int. Ed.*2002, **41**, 3460. *(j)* B. B. Snider, H. Lin, *Synth. Commun.* 1998, **28**, 1913.

8 T. H. Kang, Y. Murakami, K. Matsumoto, H. Takayama, M. Kitajima, N. Aimi, H. Watanabe, *Eur. J. Pharmacol.* 2002, **455**, 27.

9 *(a)* A. M. Swensen, J. Herrington, R. M. Bugianesi, G. Dai, R. J. Haedo, K. S. Ratliff, M. M. Smith, V. A. Warren, S. P. Arneric, C. Eduljee, D. Parker, T. P. Snutch, S. B. Hoyt, C. London, J. L. Duffy, G. J. Kaczorowski, O. B. McManus, *Mol. Pharmacol.* 2012, **81**, 488.

10 J. L. Whatmore, E. Swann, P. Barraja, J. J. Newsome, M. Bunderson, H. D. Beall, J. E. Tooke, C. J. Moody, *Angiogenesis* 2002, **5**, 45.

11 S. Peddibhotla, *Curr. Bioactive Compd.* 2009, **5**, 20.

12 C. Abbadie, O. B. McManus, S. Y. Sun, R. M. Bugianesi, G. Dai, R. J. Haedo, J. B. Herrington, G. J. Kaczorowski, M. M. Smith, A. M. Swensen, V. A. Warren, B. Williams, S. P. Arneric, C. Eduljee, T. P. Snutch, E. W. Tringham, N. Jochnowitz, A. Liang, D. Euan MacIntyre, E. McGowan, S. Mistry, V. V. White, S. B. Hoyt, C. London, K. A. Lyons, P. B. Bunting, S. Volksdorf, J. L.Duffy, *J. Pharmacol. Exp. Ther.* 2010, **334**, 545.

13 *(a)* X. Mu, T. Wu, H. Wang, Y. Guo, G. Liu, *J. Am. Chem. Soc.* 2012 , **134**, 878. *(b)* J. Tsuji, Palladium Reagents and Catalysts, Wiley, New York, 2004. *(c)* K. Muñiz, *Angew. Chem. Int. Ed.,* 2009, **48**, 9412. *(d)* H. Du, B. Zhao, Y. Shi, *J. Am. Chem. Soc.,* 2007, **129**, 762. *(e)* H. Du, W. Yuan, B. Zhao, Y. Shi, *J. Am. Chem. Soc.,* 2007, **129**, 11688. *(f)* A. Minatti, K. Muñiz, *Chem. Soc. Rev.,* 2007, **36**, 1142. *(g)* L.V. Desai, M. S. Sanford, *Angew. Chem. Int. Ed.,* 2007, **46**, 5737. *(h)* C. H. Hövelmann, J. Streuff, L. Brelot, K. Muñiz, *Chem. Commun.,* 2008, 2334. *(i)* G. Liu, S. S. Stahl, *J. Am. Chem. Soc.,* 2006, **128**, 7179. *(j)* E. J. Alexanian, C. Lee, E. J. Sorensen, *J. Am. Chem. Soc.,* 2005, **127**, 7690. *(k)* Y. Li, D. Song, V. M. Dong, *J. Am. Chem. Soc.,* 2008, **130**, 2962. *(l)* Y. Zhang, M. S. Sigman, *J. Am. Chem. Soc.,*

2007, **129**, 3076. *(m)* M. J. Schultz, M. S. Sigman, *J. Am. Chem. Soc.,* 2006, **128**, 1460. *(n)* F. E. Michael, B. M. Cochran, *J. Am. Chem. Soc.*, 2006, **128**, 4246

14 *(a)* Y. M. Li, Sun, M. H. L. Wang, Q. P. Tian, S. D. Yang, *Angew. Chem. Int. Ed.* 2013, **52**, 3972. *(b)* J. Xie, P. Xu, H. Li, Q. Xue, H. Jin, Y. Cheng, C. Zhu, *Chem. Commun*.2013, **49**, 5672. *(c)* J. E. M. N. Klein, R. J. K. Taylor, *Eur. J. Org. Chem.* 2011, **34**, 6821. *(d)* M. Zhou, C. Wang, R. Song, Y. Liu, W. Wei, J. Li, *Chem. Commun.* 2013 , **49** , 10817.

15 *(a)* W. T. Wei, Zhou, B. M. J. H. Fan, W. Liu, R. J. Song, Y. Liu, M. Hu, P. Xie, J. H. Li, *Angew. Chem. Int. Ed.* 2013, **52**, 3638. *(b)* X. Xu, Y. Tang, X. Li, G. Hong, M. Fang, X. Du. *J. Org. Chem.* 2014, **79**, 446. *(c)* F. Jia, K. Liu, H. Xi, S. Lu, Z. Li. *Tetrahedron Letters* 2013, **54**, 6337. *(d)* T. Shen, Y. Yuan, S. Song, N. Jiao. *Chem. Commun.,* 2014, **50**, 4115.

16 *(a)* H. Wang, L. Guo, X. Duan *Chem. Commun.,* 2013, **49**, 10370. *b)* F. Yin, X. Wang, *Org. Lett.* 2014, 16, 1128. *(c)* Y. Yuan, T. Shen, K. Wang, N. Jiao. *Chem. Asian J.* 2013, **8**, 2932. *(d)* Y. Li, M. Sun, H. Wang, Q. Tian, S. Yang. *Angew. Chem. Int. Ed.* 2013, **52**, 3972. *(e)* H. Wang, L. Guo, X. Duan. *Adv. Synth. Catal.* 2013, **355**, 2222. *(f)* X. H. Wei, Y. M. Li, A. X. Zhou, T. T. Yang, S. D. Yang, *Org. Lett.* 2013, **15**, 4158.

17 *(a)* S. L. Zhou, L. N. Guo, H. Wang, X. H. Duan. *Chem. Eur. J.* 2013, **19**, 12970. *(b)* H. Egami, R. Shimizu, M. Sodeoka, *Journal of Fluorine Chemistry* 2013, 152, 51. *(c)* F. Yang, P. Klumphu, Y. M. Liang, B. H. Lipshutz. *Chem. Commun.,* 2014, **50**, 936. *(d)* B. Zhou, W. Hou, Y. Yang, H. Feng, Y. Li. *Org. Lett.*, 2014, **16**, 1322. *(e)* S. L. Zhou, L. N. Guo, S. Wang, X. H. Duan. *Chem. Commun.*, 2014, **50**, 3589. *(f)* Z. Li, Y. Zhang, L. Zhang, Z. Q. Liu. *Org. Lett.*, 2014, **16**, 382.

18 *(a)* S. Jaegli, J. Dufour, H. L. Wei, T. Piou, X. H. Duan, J. P. Vors, L. Neuville, J. Zhu, *Org. Lett.* 2010, **12**, 4498. *(b)* T. Wu, X. Mu, G. Liu, *Angew. Chem. Int. Ed.* 2011, **50**, 12578. *(c)* S. Jaegli, J. Dufour, H. Wei, T. Piou, X. Duan, J. Vors, L. Neuville, J. Zhu, *Org. Lett.*2010, **12**, 4498. *(d)* S. Jaegli, W. Erb, P. Retailleau, J. Vors, L. Neuville, J. Zhu, *Chem. Eur. J.* 2010, **16**, 5863. *(e)* T. Wu, X. Mu, G. Liu, *Angew. Chem.*2011, **123**, 12786. *Angew. Chem. Int. Ed.* 2011, **50**, 12578. *(f)* X. Mu, T. Wu, H. Wang, Y. Guo, G. Liu, *J. Am. Chem. Soc.* 2012, **134**, 878. *(g)* G. Broggini, V. Barbera, E. M. Beccalli, E. Borsini, S. Galli, G. Lanza, G. Zecchi, *Adv. Synth. Catal.* 2012, **354**, 159. *(h)* G. An, W. Zhou, G. Zhang, H. Sun, J. Han, Y. Pan, *Org. Lett.* 2010, **12**, 4482. *(i)* A. Pinto, Y. Jia, L. Neuville, J. Zhu,*Chem. Eur. J.* 2007, **1**3, 961. *(j)* X. Han, X. Lu, *Org. Lett.* 2009, **11**, 2381.

19 *(a)* Y. Meng, L. Guo, H. Wang, X. Duan, *Chem. Commun.*2013, **49**, 7540. *(b)* Z. Zhou, H. Hua, J. Luo, Z. Chen, P. Zhou, X. Liu, Y. Liang, *Tetrahedron* 2013, **69**, 10030. *(c)* W. Fu, F. Xu, Y. Fu, M. Zhu, J. Yu, C. Xu, D. J. Zou, *Org. Chem.* 2013, **78**, 12202. *(d)* M. Zhou, R. Song, X. Ouyang, Y. Liu, W. Wei, G. Deng, J. Li, *Chem. Sci.* 2013, **4**, 2690. *(e)* T. Shen, Y. Yuan, N. Jiao, *Chem. Commun.* 2014, **50**, 554. *(f)* Y. Li, X. Wei, X. Li, S. Yang, *Chem. Commun.* 2013, **49**, 11701. *(g)* P. Xu, J. Xie, Q. Xue, C. Pan, Y. Cheng, C. Zhu, *Chem. Eur. J.*2013, **19**, 14039.

20 *(a)* W. Tu, L. Liu, P. E. Floreancig, *Angew. Chem. Int. Ed.* 2008, **47**, 4184. *(b)* C. L. Sun, H. Li, D. G. Yu, M. Yu, X. Zhou, X. Y. Lu, K. Huang, S. F. Zheng, B. J. Li, Z. J. Shi, *Nat. Chem.,* 2010, **2**, 1044. *(c)* W. Liu, H. Cao, H. Zhang, H. Zhang, K. H. Chung, C. He, H. Wang, F. Y. Kwong, A. Lei, *J. Am. Chem. Soc.,* 2010, **132**, 16737. *(d)* H. J. Kim, J. Kim, S. H. Cho, S. Chang, *J. Am. Chem. Soc.,* 2011, **133**, 16382. *(e)* T. Froehr, C. P. Sindlinger, U. Kloeckner, P. Finkbeiner, B. J. Nachtsheim, *Org. Lett.,* 2011, **13**, 3754. *(f)* T. Truong, O. Daugulis, *J. Am. Chem. Soc.,* 2011, **133**, 4243. *(g)* S. Ghosh, S. De, B. N. Kakde, S. Bhunia, A. Adhikary, A. Bisai, *Org. Lett.,* 2012, **14**, 5864. *(h)* W. Liu, F. Tian, X. Wang, H. Yu, Y. Bi, *Chem. Commun.,* 2013, **49**, 2983. *(i)* B. Li, X. Qin, J. You, X. Cong, J. Lan, *Org. Biomol. Chem.,* 2013, **11**, 1290.

21 *(a)* T. Wu, H. Zhang, G. Liu, *Tetrahedron* 2012, 68, 5229. *(b)* X. Li, X. Xu, P. Hu, X. Xiao, C. Zhou, *J. Org. Chem.* 2013, **78**, 7343. *(c)* K. Matcha, R. Narayan, A. P. Antonchick, *Angew. Chem. Int. Ed.* 2013, **52**, 7985. *(d)* H. Wang, L. N. Guo, X. H. Duan, *Org. Lett.,* 2013, **15**, 5254. *(e)* L. Li, M. Deng, S. Zheng, Y. Xiong, B. Tan, X. Y. Liu. *Org. Lett.,* 2014, **16**, 504. *(f)* H. L. Wei, T. Piou, J. Dufour, L. Neuville, J. Zhu. *Org. Lett.,* 2011, **13**, 2244. *(g)* M. Stodulski, A. Goetzinger, S. V. K, T, Gulder. *Chem. Commun.,* 2014, **50**, 3435. *(h)* D. C. Fabry, M. Stodulski, S. Hoerner, T. Gulder. *Chem. Eur. J.* 2012, **18**, 10834. *(i)* T. Shen, Y. Yuan, N. Jiao. *Chem. Commun.,* 2014, **50**, 554. *(j)* K. Matcha, R. Narayan, A. P. Antonchick. *Angew. Chem. Int. Ed.* 2013, **52**, 7985. *(k)* Z. Z. Zhou, H. L. Hua, J. Y. Luo, Z. S. Chen, P. X. Zhou, X. Y. Liu, Y. M. Liang. *Tetrahedron* 2013, **69**, 100.