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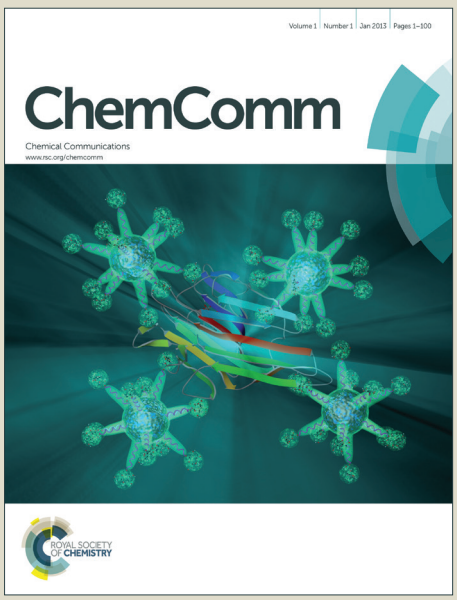

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ARTICLE TYPE

Flexible and Practical Synthesis of 3-Oxyindoles through Gold-Catalyzed Intermolecular Oxidation of *o*-Ethynylanilines

Chao Shu, Long Li, Xin-Yu Xiao, Yong-Fei Yu, Yi-Fan Ping, Jin-Mei Zhou and Long-Wu Ye*

Received (in XXX, XXX) Xth XXXXXXXXX 200X, Accepted Xth XXXXXXXXX 200X

DOI: 10.1039/b000000x

A novel gold-catalyzed intermolecular oxidation of *o*-ethynylanilines has been developed. A range of functionalized 3-oxyindoles are readily accessed by utilizing this strategy. Importantly, this gold-catalyzed oxidative process outcompetes the typical indole formation.

Functionalized 3-oxyindoles are privileged heterocyclic structural motifs because of their frequent occurrence in the structures of a great number of biologically active natural and non-natural products (Fig. 1).[1] In addition, they can also serve as valuable building blocks for the synthesis of complex molecules due to their latent reactivity and highly selective transformations they can undergo.[2] It is surprising, however, that only a few preparative methods have been reported.[3] Consequently, the development of novel methods for the synthesis of 3-oxyindoles is highly desirable, especially those with high efficiency, flexibility, and good modularity.

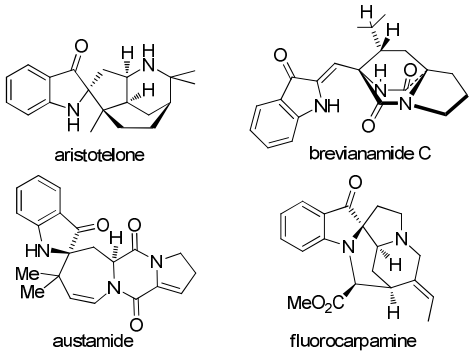
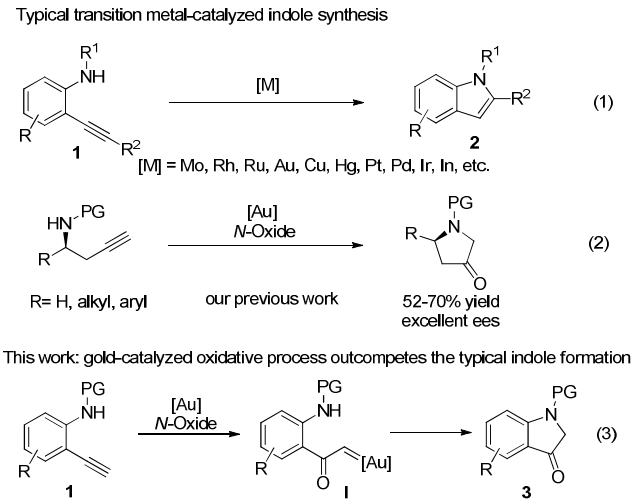


Fig. 1 Selected examples of naturally occurring 3-oxyindoles.

Over the past decade, transition metal-catalyzed intramolecular cyclization of *o*-alkynyl anilines has regained considerable attention, providing concise routes to prepare azaheterocycles, especially the indole compounds (eq. (1), Scheme 1).[4-6] Typically, for internal alkynes, cycloisomerization is initiated by coordination of transition metal to the alkyne to induce nucleophilic attack.[5] However, in the case of terminal alkynes, such a heterocyclization proceeds most likely through a metal vinylidene intermediate.[6] Substantial progress has also been made in the last few years on gold-catalyzed cyclization of *o*-alkynyl anilines to construct indoles.[7] In our recent study on gold–catalyzed cyclization reactions,[8] we have reported an oxidative cyclization of homopropargyl alcohols and homopropargyl amides to form the corresponding γ-lactones[8c] and γ-lactams[8b] respectively through gold catalysis. When the reaction scope was extended to aromatic substrate **1**, indole compound was formed in high efficiency and no trace of the desired 2-oxyindole product could be observed.[8b] Inspired by recent significant advances on gold-catalyzed intermolecular oxidation of alkynes via an α-carbonyl carbenoid route[9-10] and our recent work on this oxidative cyclization (eq. (2), Scheme 1),[8a] we seek to use *N*-oxides as the oxidants to investigate the oxidative cyclization,[11,8a] hoping to circumvent this typical indole formation (eq. (3), Scheme 1). Herein, we wish to report the realization of such a gold-catalyzed oxidative protocol and the development of a very practical solution to 3-oxyindoles synthesis, which outcompetes the occurrence of indole.

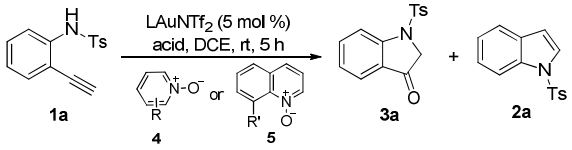


Scheme 1 Formation of 3-oxyindoles through gold-catalyzed intermolecular alkyne oxidation.

We used *o*-ethynylaniline **1a** as the model substrate for our initial study and some of the results are summarized in Table 1. The influence of different gold catalysts was first examined (Table 1, entries 1-7). Using 2-bromopyridine *N*-oxide as the oxidant and $Et_3PAuNTf_2$ as the gold catalyst, we were pleased to observe the desired 3-oxyindole **3a** formation albeit in a low yield (12%) other than indole **2a** (87%) (Table 1, entry 1). Further studies revealed that 3-oxyindole **3a** formation could become dominant when using the bulkier gold catalysts and $BrettPhosAuNTf_2$ gave the best results (Table 1, entry 7). To our

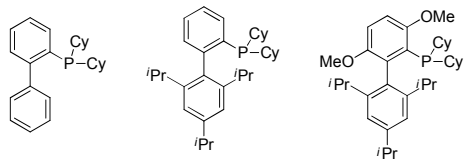
delight, it was found that the reaction yield could be substantially improved by varying the oxidants from the pyridine *N*-oxides to quinoline *N*-oxides. Strikingly, the use of 8-isopropylquinoline *N*-oxide **5b** as the oxidant completely suppressed the formation of indole **2a** and the desired 3-oxyindole **3a** could be furnished in 89% yield (Table 1, entry 11). However, the combination of **5b** with the $Et_3PAuNTf_2$ or $Ph_3PAuNTf_2$ still led to the formation of indole as the main product (Table 1, entries 12-13). This suggests that the use of the bulky BrettPhosAuNTf$_2$ is more crucial for the formation of 3-oxyindole. While the exact reason for this fine control of the reactivity remains unclear, we suspect that steric effects of the bulky gold catalysts might play an important role in preventing the cycloisomerization for the indole formation and stabilizing the gold carbenoids so as to favor the intermolecular alkyne oxidation. Further studies, including the theoretical calculations, are needed to elucidate it. Here, it should be

Table 1 Optimization of reaction conditions[a]



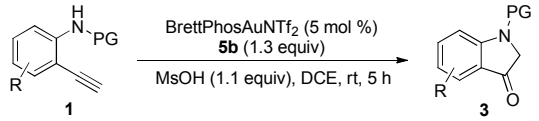
Entry	L	Oxidant (R)	Acid	Yield (%)[b] 3a	2a
1	Et_3P	**4a** (2-Br)	1.1 equiv MsOH	12	87
2	IPr	**4a** (2-Br)	1.1 equiv MsOH	32[c]	30
3	PPh_3	**4a** (2-Br)	1.1 equiv MsOH	11	88
4	$P(4\text{-}CF_3C_6H_4)_3$	**4a** (2-Br)	1.1 equiv MsOH	9	90
5	Cy-JohnPhos	**4a** (2-Br)	1.1 equiv MsOH	56	28
6	XPhos	**4a** (2-Br)	1.1 equiv MsOH	45	43
7	BrettPhos	**4a** (2-Br)	1.1 equiv MsOH	50[d]	10
8	BrettPhos	**4b** (3,5-Cl_2)	1.1 equiv MsOH	36[e]	10
9	BrettPhos	**4c** (2,6-Br_2)	1.1 equiv MsOH	32	45
10	BrettPhos	**5a** (R' = Me)	1.1 equiv MsOH	82	6
11	BrettPhos	**5b** (R' = ^{i}Pr)	1.1 equiv MsOH	89	<1
12	Et_3P	**5b** (R' = ^{i}Pr)	1.1 equiv MsOH	16	82
13	PPh_3	**5b** (R' = ^{i}Pr)	1.1 equiv MsOH	13	86
14[f]	BrettPhos	**5b** (R' = ^{i}Pr)	1.1 equiv MsOH	92[g]	<1
15[f]	BrettPhos	**5b** (R' = ^{i}Pr)	0.2 equiv MsOH	70[h]	<1

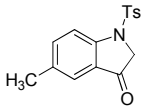
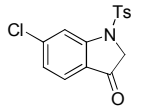
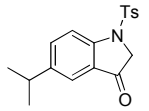
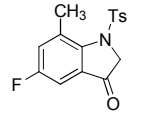
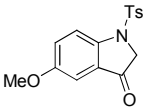
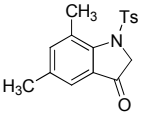
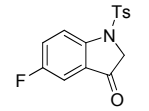
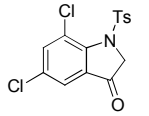
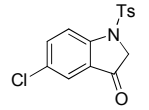
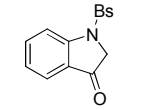
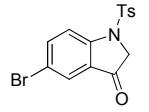
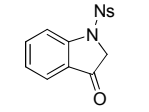
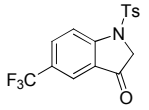
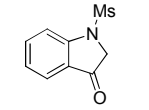
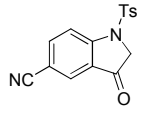
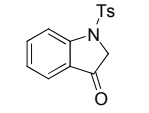
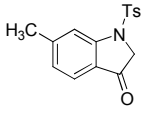
[a] Reaction conditions: [**1a**] = 0.05 M, oxidant (2.0 equiv); DCE: 1, 2-dichloroethane. [b] Estimated by ^{1}H NMR using diethyl phthalate as internal reference. [c] 25% of **1a** remained unreacted. [d] 30% of **1a** remained unreacted. [e] 40% of **1a** remained unreacted. [f] 1.3 equiv of **5b** was used. [g] Yield of isolated **3a** was 91%. [h] 25% of **1a** remained unreacted.



mentioned that the treatment of indole **2a** with BrettPhosAuNTf$_2$ (5 mol %), **5b** (2.0 equiv) and MsOH (1.1 equiv) in DCE could not afford the 3-oxyindole **3a** and only **2a** was recovered. indicating that **3a** should be formed directly from the *o*-ethynylaniline substate **1a** but not indole **2a**. In addtion, lowering the amount of *N*-oxide gave a slightly improved yield (Table 1, entry 14). However, only 75% conversion was observed in 5 h when the amount of MsOH was reduced to 0.2 equiv (Table 1, entry 15). Notably, without a gold catalyst, the reaction failed to give even a trace of 3-oxyindole **3a** under the acidic reaction conditions, and $PtCl_2$ and $AgNTf_2$ could not catalyze this reaction.

Table 2 Reaction scope for the formation of indolin-3-ones[a]

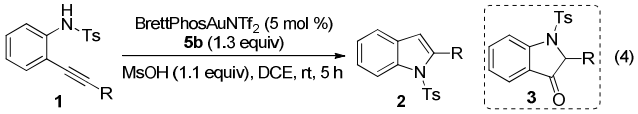


Entry	Product	3	Yield	Entry	Product	3	Yield
1		**3b**	87%	10[b]		**3k**	90%
2		**3c**	84%	11[b]		**3l**	79%
3		**3d**	85%	12[d]		**3m**	74%
4[b]		**3e**	92%	13[d]		**3n**	88%
5[b]		**3f**	93%	14		**3o**	85%
6[b]		**3g**	91%	15		**3p**	88%
7[b]		**3h**	81%	16		**3q**	90%
8[b,c]		**3i**	65%	17[e]		**3a**	87%
9		**3j**	93%				

[a] Reactions run in vials; [**1**] = 0.05 M; isolated yields are reported. [b] 0.2 equiv of MsOH was used, 8 h. [c] Indole **2i** was formed in 34% yield. [d] No MsOH was used, 10 h. [e] 10 mmol scale, 2.5 mol % gold catalyst was used, 8 h.

With this significantly improved protocol in hand, we then examined the scope of this gold-catalyzed oxidative cyclization reaction. Various *o*-ethynylaniline derivatives **1** were suitable substrates for this cyclization to furnish the corresponding 3-oxyindoles **3** with mostly good to excellent yields. Except for the substrate **1i**, which also afforded indole **2i** in 34% yield (Table 2, entry 8), only 3-oxyindole formation was observed in all cases. Notably, for the substrates bearing an electron-withdrawing group, the reaction resulted in the formation of a complex product mixture under the optimal conditions. However, we were delighted to find that the reduced amounts of MsOH could give a much improved yield (Table 2, entries 4-8 and entries 10-11). In the case of disubstituted substrates **1m-1n**, without using any acid is preferred (Table 2, entries 12-13). In addition, *o*-ethynylanilines containing a Bs (4-bromobenzenesulfonyl), a Ns (2-nitrobenzenesulfonyl) or a Ms group also reacted to give the corresponding **3o-3q** in excellent yields (Table 2, entries 14-16). To test the practicality of the current catalytic system, the reaction was carried out in a 10 mmol scale in the presence of 2.5 mol % gold catalyst and the desired 3-oxyindole **3a** was afforded in 87% yield, highlighting the value of this new catalysis (Table 2, entry 17).

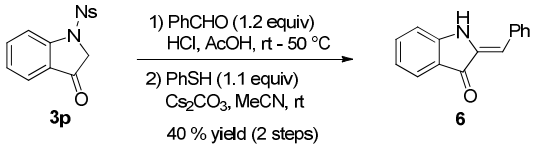
We then considerated the possibilty of extending the reaction to internal alkynes. However, only indole formation could be observed under the above optimized reaction conditions (eq. (4)), and further studies in this direction are currently ongoing.



1r: R = *n*-hexyl **2r**: 72% yield

1s: R = Ph **2s**: 80% yield

These 3-oxyindoles are potentially useful in organic synthesis and will constitute valuable precursors especially for the construction of the corresponding azaaurones, which exist in a number of natural products and bioactive molecules.[1b,1c,12] As outlined in Scheme 2, for example, condensation of 3-oxyindole **3p** with benzaldehyde in acidic conditions, followed by deprotection with PhSH, provided the final azaaurone **6**.



Scheme 2 Synthetic applications.

In summary, we have developed a flexible and general solution for the synthesis of various 3-oxyindoles through a gold-catalyzed intermolecular alkyne oxidation. Most importantly, this gold-catalyzed oxidative process outcompetes the typical indole formation. The use of readily available substrates, a simple procedure, and mild reaction conditions and, in particular, no need to exclude moisture or air ("open flask") render these methods potentially useful in organic synthesis.

We are grateful for the financial support from the National Natural Science Foundation of China (No. 21102119 and 21272191), the Program for Changjiang Scholars and Innovative Research Team in University (PCSIRT) and NFFTBS (No. J1310024).

Notes and references

State Key Laboratory for Physical Chemistry of Solid Surfaces, The Key Laboratory for Chemical Biology of Fujian Province and Department of Chemistry, College of Chemistry and Chemical Engineering, Xiamen University, Xiamen, 361005, Fujian, PR China. Fax: (+86) 592-218-5833; E-mail: longwuye@xmu.edu.cn

† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

1 (a) A. Wetzel and F. Gagosz, *Angew. Chem. Int. Ed.,* 2011, **50**, 7354; (b) T. Mohn, I. Plitzko and M. Hamburger, *Phytochemistry*, 2009, **70**, 924; (c) R. Abonia, P. Cuervo, J. Castillo, B. Insuasty, J. Quiroga, M. Nogueras and J. Cobo, *Tetrahedron Lett.,* 2008**, 49**, 5028; (d) J. D. Perry, K. A. Morris, A. L. James, M. Oliver and F. K. Gould, *J. Appl. Microbiol.,* 2007, 410; (e) P.-L. Wu, Y.-L. Hsu and C.-W. Jao, *J. Nat. Prod.,* 2006, **69**, 1467; (f) A. S. Bourlot, E. Desarbre and J. Y. Mérour, *Synthesis,* 1994, 411; (g) Y. Fukuda, K. Nakatani, Y. Ito and S. Terashima, *Tetrahedron Lett.*, 1990, **31**, 6699; (h) A. Hutchison and Y. Kishi, *J. Am. Chem. Soc.*, 1979, **101**, 6786; (i) M. Hooper and W. N. Pitkethly, *J. Chem. Soc., Perkin Trans. 1,* 1972, 1607.

2 (a) R. V. S. Nirogi, A. D. Deshpande, R. Kambhampati, R. K. Badange, L. Kota, A. V. Daulatabad, A. K. Shinde, I. Ahmad, V. Kandikere, P. Jayarajan and P. K. Dubey, *Bioorg. Med. Chem.,* 2011, **21**, 346; (b) P. N. Wyrembak and A. D. Hamilton, *J. Am. Chem. Soc.,* 2009, **131**, 4566; (c) K. Higuchi, Y. Sato, M. Tsuchimochi, K. Sugiura, M. Hatori and T. Kawasaki, *Org. Lett.,* 2009, **11**, 197; (d) S. Matsumoto, D. Samata, M. Akazome and K. Ogura, *Tetrahedron Lett.,* 2009, **50**, 111; (e) S. Libnow, K. Methling, M. Hein, D. Michalik, M. Harms, K. Wende, A. Flemming, M. Köckerling, H. Reinke, P. J. Bednarski, M. Lalkb and P. Langer, *Bioorg. Med. Chem.,* 2008, **16**, 5570; (f) K. Yamada, T. Kurokawa, H. Tokuyama and T. Fukuyama, *J. Am. Chem. Soc.,* 2003, **125**, 6630; (g) Y. Liu and W. W. McWhorter, Jr., *J. Am. Chem. Soc.,* 2003, **125**, 4240; (h) Y. Liu and W. W. McWhorter, Jr., *J. Org. Chem.,* 2003, **68**, 2618; (i) G.Tommasi, P. Bruni, L. Greci, P. Sgarabotto and L. Righi, *J. Chem. Soc., Perkin Trans. 1,* 1999, 681; (j) A. Asai, S. Nagamura, E. Kobayashi, K. Gomi and H. Saito, *Bioorg. Med. Chem.,* 1996, **6**, 1215; (k) D. L. Boger and T. Nishi, *Bioorg. Med. Chem.,* 1995, **3**, 67; (l) J.-Y. Mérour and A. Mérour, *Synthesis,* 1994, 767.

3 For recent examples, see: (a) J.-X. Liu, Q.-Q. Zhou, J.-G. Deng and Y.-C. Chen, *Org. Biomol. Chem.*, 2013, **11**, 8175; (b) M. Rueping, R. Rasappan and S. Raja, *Helv. Chim. Acta*, 2012, **95**, 2296; (c) K. Okuma, N. Matsunaga, N. Nagahora, K. Shioji and Y. Yokomori, *Chem. Commun.,* 2011, 5822; (d) P. Y. Choy, C. P. Lau and F. Y. Kwong, *J. Org. Chem.,* 2011, **76**, 80; (e) Y. Sun and R. Fan, *Chem. Commun.,* 2010, 6834; (f) K. Higuchi, Y. Sato, S. Kojima, M. Tsuchimochi, K. Sugiura, M. Hatori and T. Kawasaki, *Tetrahedron,* 2010, **66**, 1236; (g) P. N. Wyrembak and A. D. Hamilton, *J. Am. Chem. Soc.* 2009, **131**, 4566; (h) Y. Terada, M. Arisawa and A. Nishida, *J. Org. Chem.*, 2006, **71**, 1269.

4 For recent reviews, see: (a) M. Platon, R. Amardeil, L. Djakovitch and J.-C. Hierso, *Chem. Soc. Rev.*, 2012, **41**, 3929; (b) R. Vicente, *Org. Biomol. Chem.*, 2011, **9**, 6469; (c) S. Cacchi, G. Fabrizi and A. Goggiamani, *Org. Biomol. Chem.*, 2011, **9**, 641; (d) K. Krüger A. Tillack,and M. Beller, *Adv. Synth. Catal.*, 2008, **350**, 2153; (e) G. R. Humphrey and J. T. Kuethe, *Chem. Rev.*, 2006, **106**, 2875.

5 For recent selected examples on the internal alkynes, see: (a) L. Yang, Y. Ma, F. Song and J. You, *Chem. Commun.,* 2014, 3024; (b) Q. Wang, L. Huang, X. Wu and H. Jiang, *Org. Lett.,* 2013, **15**, 5940; (c) G. Qiu, C. Chen, L. Yao and J. Wu, *Adv. Synth. Catal.*, 2013, **355**, 1579; (d) W. Yang, T. Wang, Y. Yu, S. Shi, T. Zhang and A. S. K. Hashmi, *Adv. Synth. Catal.*, 2013, **355**, 1523; (e) Z. Hu, D. Liang, J. Zhao, J. Huang and Q. Zhu, *Chem. Commun.*, 2012, 7371; (f) K.

Gray, M. J. Page, J. Wagler and B. A. Messerle, *Organometallics*, 2012, **31**, 6270.

6 For recent selected examples on the terminal alkynes, see: (a) E. Kumaran, W. Y. Fan and W. K. Leong, *Org. Lett.,* 2014, **16**, 1342; (b) A. Varela-Fernández, J. A.Varela and C. Saá, *Synthesis,* 2012, 3285; (c) A. Varela-Fernández, J. A.Varela and C. Saá, *Adv. Synth. Catal.,* 2011*,* **353**, 1933; (d) R. N. Nair, P. J. Lee, A. L. Rheingold and D. B. Grotjahn, *Chem. Eur. J.,* 2010*,* **16**, 7992; (e) B. M. Trost and A. McClory, *Angew. Chem., Int. Ed.,* 2007, **46**, 2074.

7 For reviews, see: (a) M. Rudolph and A. S. K. Hashmi, *Chem. Commun.,* 2011, 6536; (b) R. A. Widenhoefer and X. Han, *Eur. J. Org. Chem.,* 2006, 4555; for recent examples, see: (c) A. Gimeno, A. B. Cuenca, S. Suárez-Pantiga, C. R. de Arellano, M. Medio-Simón and G. Asensio, *Chem. Eur. J.*, 2014, **20**, 683; (d) T. Wang, S. Shi, D. Pflästerer, E. Rettenmeier, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Chem. Eur. J.*, 2014, **20**, 292; (e) J. E. Perea-Buceta, T. Wirtanen, O.-V. Laukkanen, M. K. Mäkelä, M. Nieger, M. Melchionna, N. Huittinen, J. A. Lopez-Sanchez and J. Helaja, *Angew. Chem., Int. Ed.,* 2013, **52**, 11835; (f) M. Chiarucci, R. Mocci, L.-D. Syntrivanis, G. Cera, A. Mazzanti and M. Bandini, *Angew. Chem., Int. Ed.,* 2013, **52**, 10850; (g) A. Arcadi, E. Pietropaolo, A. Alvino and V. Michelet, *Org. Lett.,* 2013, **15**, 2766; (h) X. Zeng, R. Kinjo, B. Donnadieu and G. Bertrand, *Angew. Chem., Int. Ed.,* 2010, **49**, 942.

8 (a) C. Shu, L. Li, Y.-F. Yu, S. Jiang and L.-W. Ye, *Chem. Commun.,* 2014, 2522; (b) C. Shu, M.-Q. Liu, S.-S. Wang, L. Li and L.-W. Ye, *J. Org. Chem.,* 2013, **78**, 3292; (c) C. Shu, M.-Q. Liu, Y.-Z. Sun and L.-W. Ye, *Org. Lett.,* 2012, **14**, 4958.

9 For reviews, see: (a) H.-S. Yeom and S. Shin, *Acc. Chem. Res.*, 2014, **47**, 966; (b) L. Zhang, *Acc. Chem. Res.*, 2014, **47**, 877; (c) J. Xiao and X. Li, *Angew. Chem. Int. Ed.*, 2011, **50**, 7226.

10 For recent examples, see: (a) M. D. Santos and P. W. Davies, *Chem. Commun.*, 2014, 6001; (b) J. Li, K. Ji, R. Zheng, J. Nelson and L. Zhang, *Chem. Commun.*, 2014, 4130; (c) G. Wu, R. Zheng, J. Nelson and L. Zhang, *Adv. Synth. Catal.*, 2014, **356**, 1229; (d) K. Ji, L. Zhang, *Org. Chem. Front.*, 2014, **1**, 34; (e) P. Nösel, L. N. dos Santos Comprido, T. Lauterbach, M. Rudolph, F. Rominger and A. S. K. Hashmi, *J. Am. Chem. Soc.*, 2013, **135**, 15662; (f) L. Wang, X. Xie and Y. Liu, *Angew. Chem. Int. Ed.*, 2013, **52**, 13302; (g) S. K. Pawar, C.-D. Wang, S. Bhunia, A. M. Jadhav and R.-S. Liu, *Angew. Chem. Int. Ed.*, 2013, **52**, 7559; (h) K. Ji, Y. Zhao and L. Zhang, *Angew. Chem. Int. Ed.*, 2013, **52**, 6508; (i) G. Henrion, T. E. J. Chava, X. Le Goff and F. Gagosz, *Angew. Chem. Int. Ed.*, 2013, **52**, 6277; (j) S. Ghorpade, M.-D. Su and R.-S. Liu, *Angew. Chem. Int. Ed.*, 2013, **52**, 4229; (k) J. Fu, H. Shang, Z. Wang, L. Chang, W. Shao, Z. Yang and Y. Tang, *Angew. Chem. Int. Ed.*, 2013, **52**, 4198; (l) D. B. Huple, S. Ghorpade and R.-S. Liu, *Chem. Eur. J.*, 2013, **19**, 12965; (m) R. K. Kawade and R.-S. Liu, *Org. Lett.*, 2013, **15**, 4094; (n) H.-H. Hung, Y.-C. Liao and R.-S. Liu, *J. Org. Chem.*, 2013, **78**, 7970; (o) K.-B. Wang, R.-Q. Ran, S.-D. Xiu and C.-Y. Li, *Org. Lett.*, 2013, **15**, 2374; (p) M. Xu, T.-T. Ren, K.-B. Wang and C.-Y. Li, *Adv. Synth. Catal.*, 2013, **355**, 2488.

11 (a) L. Ye, W. He and L. Zhang, *Angew. Chem. Int. Ed.*, 2011, **50**, 3236; (b) L. Ye, W. He and L. Zhang, *J. Am. Chem. Soc.*, 2010, **132**, 8550; (c) L. Ye, L. Cui, G. Zhang and L. Zhang, *J. Am. Chem. Soc.*, 2010, **132**, 3258.

12 (a) M. C. Sharma, S. Sharma, P. Sharma and A. Kumar, *Med. Chem. Res.*, 2014, **23**, 181; (b) H. M. Sim, K. Y. Loh, W. K. Yeo, C. Y. Lee and M. L. Go, *Chem. Med. Chem.*, 2011, **6**, 713; (c) F. Souard, S. Okombi, C. Beney, S. Chevalley, A. Valentin and A. Boumendjel, *Bioorg. Med. Chem.,* 2010, **18**, 5724; (d) B. Gerby, A. Boumendjel, M. Blanc, P. P. Bringuier, P. Champelovier, A. Fortuné, X. Ronot and J. Boutonnat, *Bioorg. Med. Chem.*, 2007, **17**, 208; (e) H. J. Karlsson and G. R. Westman, *Tetrahedron,* 2000, **56**, 8939; (f) A. Buzas and J. Y. Merour, *Synthesis*, 1989, 458.

