Organic & Biomolecular Chemistry

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2014, **12**, 3802

Received 17th March 2014,
Accepted 14th April 2014

DOI: 10.1039/c4ob00578c

www.rsc.org/obc

Metal-free aerobic oxidative C–N bond cleavage of tertiary amines for the synthesis of N-heterocycles with high atom efficiency†

Xiuling Chen, Tieqiao Chen, Yongbo Zhou,* Daoqing Han, Li-Biao Han and Shuang-Feng Yin*

An efficient metal-free aerobic oxidative C–N bond cleavage of tertiary amines has been developed to construct N-heterocycles using molecular oxygen as the sole oxidant with high atom efficiency, in which all of the three alkyl groups in tertiary amines can be utilized and transformed into N-heterocycles.

Quinazolinone derivatives (Fig. 1), one kind of important N-heterocyclic compounds, are key components in a variety of synthetic drugs and natural products.[1,2] They are widely used as hypnotic,[2a] sedative,[2b] anti-convulsant,[2c] anti-bacterial,[2d] anti-diabetic,[2e] anti-inflammatory[2f] and anti-tumor agents.[2g] Although many methods for the synthesis of quinazolinone derivatives have been developed,[3–8] transition metals are generally required. A Metal-free conditions are highly desirable especially in the drug and pharmaceutical industry, because transition metal catalysts are toxic and they must be carefully removed from the products. Besides, O_2 is the ideal oxidant due to its abundance and low cost. Thus, metal-free aerobic oxidative synthesis of N-heterocyclic compounds would be a preferable choice.

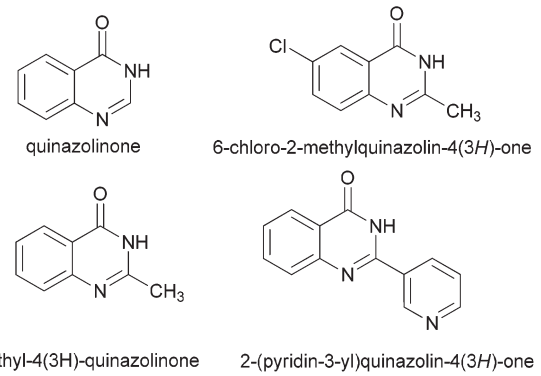
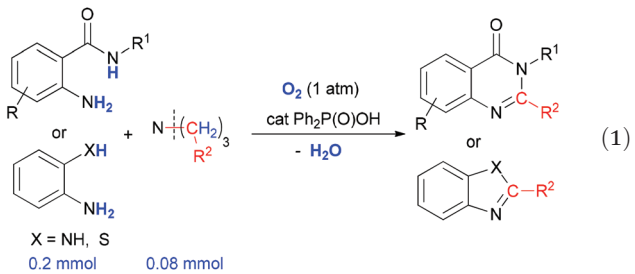


Fig. 1 Structure of natural and synthetic biological quinazolinones.

The cleavage of C–N bonds is of significant synthetic interest since such bonds are common in numerous molecules.[9] Given that tertiary amines contain three C–N bonds and are easily prepared, efficient cleavage of the C–N bonds and further synthetic applications in organic synthesis are very attractive.[8] In the reported work, transition metals and their complexes are generally required as the catalysts for the cleavage of C–N bonds.[9] Herein, we report a metal-free aerobic oxidative C–N bond cleavage of tertiary amines for the synthesis of quinazolinone derivatives in high yields (eqn (1)). *Worth noting is that all of the three alkyl groups in tertiary amines can be utilized and transformed into quinazolinone derivatives under the present conditions*. In addition, this strategy can also be applied to efficient synthesis of benzimidazoles and benzothiazoles *via* similar oxidation–cyclization of tertiary amines with *o*-phenylenediamine or *o*-aminothiophenol, respectively. To the best of our knowledge, there is no precedent on transition-metal-free C–N bond cleavage of tertiary amines for the synthesis of N-heterocycles employing molecular oxygen as the sole oxidant.



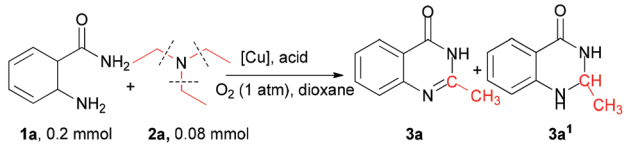
(1)

Initially, 0.2 mmol *o*-aminobenzamide **1a** and 0.08 mmol triethylamine **2a** were used to synthesize quinazolinone **3a** in the presence of 10 mol% $Cu(OAc)_2$ and 20 mol% $Ph_2P(O)OH$ in dioxane at 130 °C. After 13 h, 2-methylquinazolin-4(3*H*)-one **3a** was produced in 82% yield (Table 1, entry 1). By extending the reaction time to 18 h, 88% yield of **3a** was achieved (Table 1, entry 2). Interestingly, in the absence of the copper

State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University, Changsha, 410081, P. R. China. E-mail: zhouyb@hnu.edu.cn, sf_yin@hnu.edu.cn; Fax: (+) 86-731-88821171

†Electronic supplementary information (ESI) available. See DOI: 10.1039/c4ob00578c

Table 1 Optimization of the reaction conditions[a]



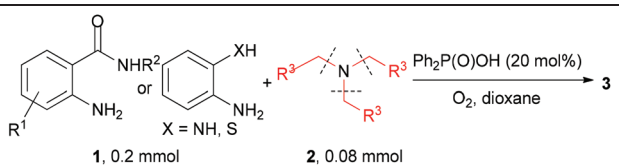
Entry	Catalyst	Additive	Time (h)	Yield **3a**/**3a**^{1} [b] (%)
1	$Cu(OAc)_2$	$Ph_2P(O)OH$	13	82/2
2	$Cu(OAc)_2$	$Ph_2P(O)OH$	18	88/—
3	—	$Ph_2P(O)OH$	13	76/13
4	—	$Ph_2P(O)OH$	18	90/0
5	$Cu(OAc)_2$	—	18	25/5
6	—	—	18	27/4
7[c]	—	$Ph_2P(O)OH$	18	91/—
8[d]	—	$Ph_2P(O)OH$	18	61/8
9[e]	—	$Ph_2P(O)OH$	18	15/6
10[f]	—	$Ph_2P(O)OH$	18	—/—

[a] Reaction conditions: *o*-aminobenzamide **1a** (0.2 mmol), NEt_3 **2a** (0.08 mmol), catalyst (for [Cu], 10 mol%; for acid, 20 mol%) based on **1a**, dioxane (1.0 mL), O_2 (1 atm) in a Schlenk tube (10 mL), 130 °C, 13–18 h, recharging oxygen after 9 h. [b] GC yield based on **1a**, **3a**/**3a**^{1} based on GC. [c] $Ph_2P(O)OH$ (50 mol%). [d] $Ph_2P(O)OH$ (10 mol%). [e] Under air. [f] Under N_2.

salt, the reaction also proceeded to give 76% yield of **3a** and 13% yield of 2-methyl-2,3-dihydroquinazolin-4(1*H*)-one **3a**^{1} (Table 1, entry 3). Compound **3a**^{1} could be further converted to **3a** *via* oxidative dehydrogenation after a prolonged reaction time (Table 1, entry 4). It was noted that the reaction catalyzed by $Cu(OAc)_2$ gave only 25% yield of **3a** (Table 1, entry 5), almost equivalent to that under metal-free and acid-free conditions (Table 1, entry 6), indicating that the copper catalyst was not necessary in the present system (for details, see ESI†). Then, the effect of $Ph_2P(O)OH$ loading was investigated. Obviously, an increase of $Ph_2P(O)OH$ to 50 mol% amount did not improve the yield of **3a** (Table 1, entry 7), whereas a decrease of $Ph_2P(O)OH$ to 10 mol% amount resulted in a much lower yield (Table 1, entry 8). Oxygen was essential for this reaction. For example, a lower yield of **3a** was obtained in air (Table 1, entry 9), while this reaction did not take place at all under an inert atmosphere (Table 1, entry 10).

Under the optimized reaction conditions, the substrate scope of this reaction was investigated. As shown in Table 2, *o*-substituted anilines could readily react with aliphatic tertiary amines to produce the corresponding quinazolinone deriva-

Table 2 Substrate scope of *o*-substituted anilines **1** and amines **2**[a]



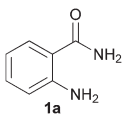
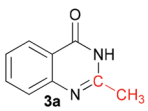
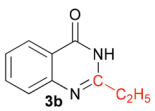
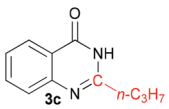
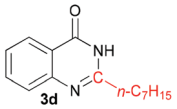
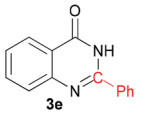
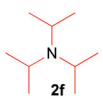
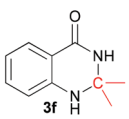
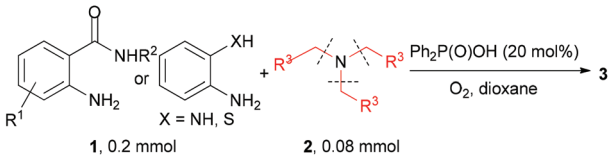
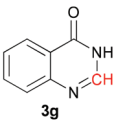
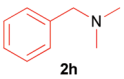
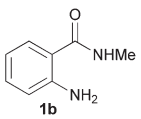
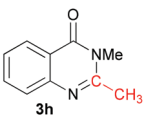
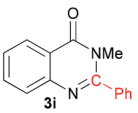
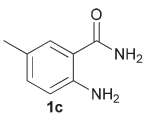
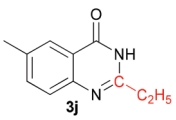
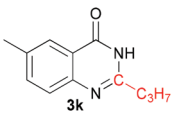
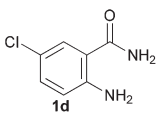
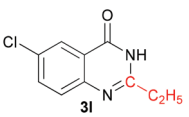
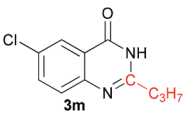
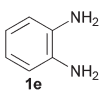
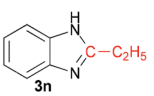
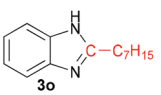
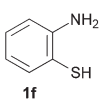
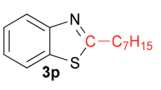
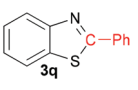
Entry	Aniline **1**	Amine **2**	Product	Yield[b] (%)
1	 **1a**	$N(C_2H_5)_3$ **2a**	 **3a**	87
2	**1a**	$N(n\text{-}C_3H_7)_3$ **2b**	 **3b**	80
3	**1a**	$N(n\text{-}C_4H_9)_3$ **2c**	 **3c**	79
4	**1a**	$N(n\text{-}C_8H_{17})_3$ **2d**	 **3d**	81
5	**1a**	$N(CH_2Ph)_3$ **2e**	 **3e**	86
6	**1a**	 **2f**	 **3f**	82

Table 2 *(Contd.)*



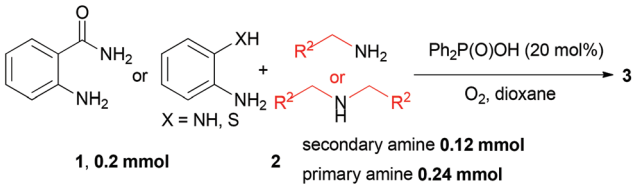
Entry	Aniline **1**	Amine **2**	Product	Yield[b] (%)
7	**1a**	 **2g, 0.04 mmol**	 **3g**	95
8	**1a**	 **2h**	**3g** / **3e**	65 / 26
9	 **1b**	**2a**	 **3h**	91
10	**1b**	**2e**	 **3i**	87
11	 **1c**	**2b**	 **3j**	83
12	**1c**	**2e**	 **3k**	85
13	 **1d**	**2b**	 **3l**	81
14	**1d**	**2e**	 **3m**	82
15[c]	 **1e**	**2b**	 **3n**	85
16[c]	**1e**	**2d**	 **3o**	88
17[c]	 **1f**	**2d**	 **3p**	82
18[c]	**1f**	**2e**	 **3q**	86

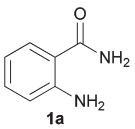
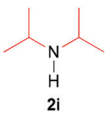
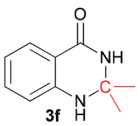
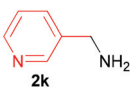
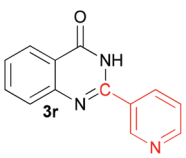
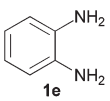
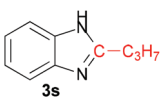
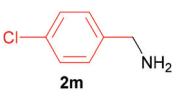
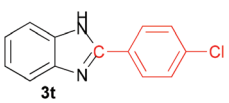
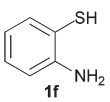
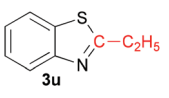
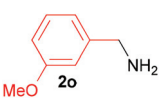
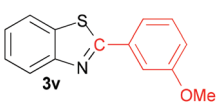
[a] Reaction conditions: **1a–1f** (0.2 mmol), tertiary amine **2a–2h** (0.08 mmol), $Ph_2P(O)OH$ (20 mol%) based on **1**, dioxane (1.0 mL), O_2 (1 atm) in a Schlenk tube (10 mL), 130 °C, 18 h, recharging oxygen after 9 h. [b] Isolated yield. [c] 115 °C, 12 h.

tives. It should be noted that the reactivity of the oxidative cyclocondensation was independent of the alkyl chain length, and different aliphatic tertiary amines could efficiently undergo oxidative cyclocondensation with *o*-substituted anilines, giving the quinazolinone derivatives **3** in high yields with high atom efficiency (Table 2, entries 1–4). Especially, when tribenzylamine **2e** was used as the substrate, the aryl-substituted quinazolinone **3e** was afforded in 86% yield (Table 2, entry 5). When triisopropanolamine **2f** bearing only one α-H was used as the substrate, product **3f** was obtained (Table 2, entry 6). Promoted by $Ph_2P(O)OH$, hexamethylenetetramine also served as an efficient substrate, furnishing a natural product **3g** in 95% yield (Table 2, entry 7). Using *N*,*N*-dimethyl-1-phenylmethanamine **2h** with two kinds of N–C bonds as the substrate, two types of products, **3g** and **3e**, with an almost 2 : 1 ratio were formed (Table 2, entry 8). Under the present reaction conditions, substituted *o*-aminobenzamides **1b**, **1c** and **1d** bearing methyl and chloro functionalities also reacted with tertiary amines to give the corresponding quinazolinone derivatives **3** in good yields (Table 2, entries 9–14). The protocol can also be applied to synthesis of the bioactive benzimidazoles and benzothiazoles. For example, similar oxidative cyclization of *o*-phenylenediamine and *o*-aminothiophenol with tertiary amines readily occurred, giving the corresponding benzimidazoles **3n–3o** and benzothiazoles **3p–3q** in high yields (Table 2, entries 15–18).

Besides tertiary amines, primary and secondary amines are also efficient substrates to afford the corresponding N-heterocyclic compounds in high yields (Table 3, entries 1–7). It is noted that the NC–H bond in tertiary amines is essential for this catalytic oxidative system. For example, there was no product detected using *t*-butylamine **2j** as the substrate, which has no NC–H unit (Table 3, entry 2).

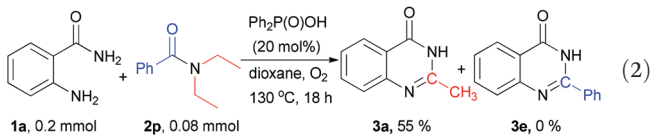
Table 3 Substrate scope of *o*-substituted anilines **1** with primary amines or secondary amines[a]



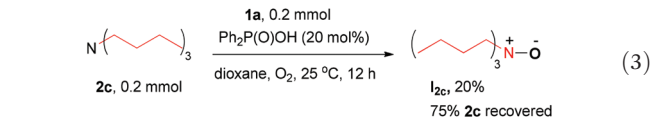
Entry	Aniline **1**	Amine **2**	Product	Yield[b] (%)
1	 **1a**	 **2i**	 **3f**	74
2	**1a**	t-$BuNH_2$ **2j**	—	—
3	**1a**	 **2k**	 **3r**	92
4[c]	 **1e**	$NH(n\text{-}C_4H_9)_2$ **2l**	 **3s**	80
5[c]	**1e**	 **2m**	 **3t**	90
6[c]	 **1f**	$NH(n\text{-}C_3H_7)_2$ **2n**	 **3u**	78
7[c]	**1f**	 **2o**	 **3v**	93

[a] Reaction conditions: *o*-substituted aniline **1a–1f** (0.2 mmol), primary amine (0.24 mmol), secondary amine (0.12 mmol), $Ph_2P(O)OH$ (20 mol%) based on **1**, dioxane (1.0 mL), O_2 (1 atm) in a Schlenk tube (10 mL), 130 °C, 18 h, recharging oxygen after 9 h. [b] Isolated yield. [c] 115 °C, 12 h.

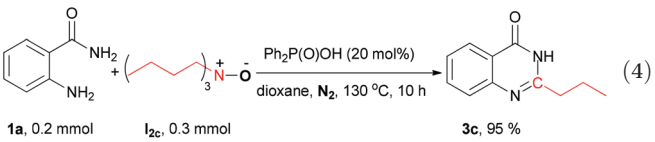
To get insights into the reaction mechanism, several control experiments were carried out. Firstly, the reaction of *o*-aminobenzamide **1a** with *N*,*N*-diethylbenzamide **2p** was performed under similar reaction conditions, **3a** was obtained in 55% yield, whereas **3e** was not detected at all, showing that the amide was not the efficient substrate (eqn (2)). When *o*-aminobenzamide **1a** and 1.0 equiv. tri-*n*-butylamine **2c** were used as substrates at 25 °C, tri-*n*-butylamine *N*-oxide $\mathbf{I_{2c}}$ was obtained (eqn (3)) and the resulting tri-*n*-butylamine *N*-oxide $\mathbf{I_{2c}}$ was found to react with *o*-aminobenzamide **1a** under a N_2 atmosphere, producing the corresponding quinazolinone derivatives **3c** (eqn (4)). Thus, *N*-oxide was probably an intermediate of this reaction.[10] During the reaction of *o*-aminobenzamide with 1.2 equiv. tri-*n*-octylamine, secondary amine and aldehyde were detected by GC-MS (see ESI†). When the radical scavenger TEMPO was loaded under the standard reaction conditions, the desired product **3a** was still obtained in 87% yield, indicating that a free radical perhaps was not involved in the present reaction process (eqn (5)).



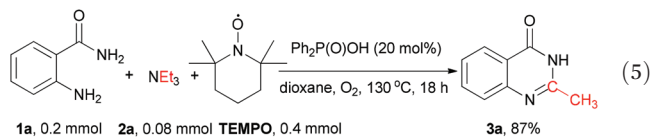
(2)



(3)

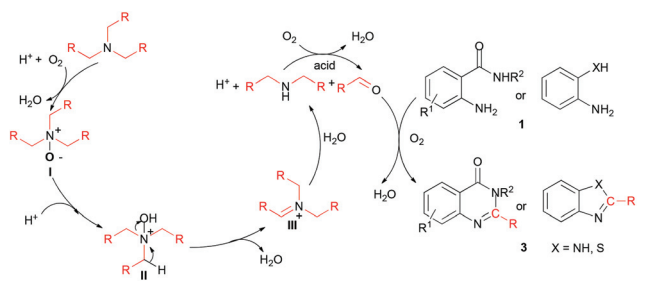


(4)



(5)

Based on above results and the reported literature,[11] the reaction possibly takes place as shown below (Scheme 1). Initially, in the presence of molecular oxygen, the tertiary amine is oxidized to *N*-oxide **I**, followed by protonation to form **II** under suitable pH conditions. Dehydration of **II** affords the immonium ion **III**, which is readily hydrolyzed to produce a secondary amine and an aldehyde.[12] Finally, N-heterocyclic compound **3** is produced by condensation/oxidative dehydrogenation of *in situ* aldehyde[13] with *o*-substituted aniline. The resulting secondary amine and primary amine can react with *o*-substituted aniline readily and be further converted to N-heterocyclic compound **3**.[7] The fact that the amine bearing no α-H cannot be converted to **3** also supports this mechanism, in which the immonium salt **III** cannot be formed.



Scheme 1 Possible mechanism for the aerobic oxidative C–N bond cleavage and cyclization reaction.

In summary, a metal-free aerobic oxidative C–N bond cleavage of tertiary amines with *o*-substituted anilines for the preparation of N-heterocyclic derivatives has been developed. We believe that this environmentally benign and highly atom-efficient protocol will find wide potential application in organic synthesis.

This work was supported by the NSFC (U1162109, 21273066, 21172062, 21273067), Program for Changjiang Scholars and Innovative Research Team in University (IRT1238), the Program for New Century Excellent Talents in Universities (NCET-10-0371), and the Fundamental Research Funds for the Central Universities (Hunan University).

Notes and references

1 (*a*) S. I. Murahashi and D. Zhang, *Chem. Soc. Rev.*, 2008, **37**, 1490; (*b*) S. B. Mhaske and N. P. Argade, *Tetrahedron*, 2006, **62**, 9787.

2 (*a*) S. L. Cao, Y. P. Feng, Y. Y. Jiang, S. Liu, Y. G. Ding and R. T. Li, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 1915; (*b*) D. J. Connolly, D. Cusack, T. P. O'Sullivan and P. J. Guiry, *Tetrahedron*, 2005, **61**, 10153; (*c*) A. Witt and J. Bergman, *Curr. Org. Chem.*, 2003, **7**, 659; (*d*) P. P. Kung, M. D. Casper, K. L. Cook, L. Wilson-Lingardo, L. M. Risen, T. A. Vickers, R. Ranken, L. B. Blyn, J. R. Wyatt and P. D. Cook, *J. Med. Chem.*, 1999, **42**, 4705; (*e*) S. E. De Laszlo, C. S. Quagliato, W. J. Greenlee, A. A. Patchett, V. J. Lotti, T. B. Chen, S. A. Scheck and A. Faust, *J. Med. Chem.*, 1993, **36**, 3207; (*f*) M. S. Malamas and J. Millen, *J. Med. Chem.*, 1991, **34**, 1492; (*g*) J. F. Wolfe, T. L. Rathman, M. C. Sleevi, J. A. Campbell and T. D. Greenwood, *J. Med. Chem.*, 1990, **33**, 161.

3 For reviews, see: (*a*) D. A. Horton, G. T. Bourne and M. L. Smythe, *Chem. Rev.*, 2003, **103**, 893; (*b*) D. J. Connolly, D. Cusack, T. P. O'Sullivan and P. J. Guiry, *Tetrahedron*, 2005, **61**, 10153; (*c*) L. He, H. Li, J. Chen and X. Wu, *RSC Adv.*, 2014, **4**, 12065.

4 Traditional methods for the preparation of quinazolin-4(3*H*)-one derivatives, see: (*a*) J. Bergman and A. Witt, *Curr. Org. Chem.*, 2003, **7**, 659; (*b*) A. Patil, O. Patil, B. Patil and J. Surana, *Mini-Rev. Med. Chem.*, 2011, **11**, 633; (*c*) R. J. Abdel-Jalila, W. Voelterb and M. Saeed, *Tetrahedron Lett.*, 2004, **45**, 3475; (*d*) C. Zhang, L. Zhang and N. Jiao, *Green Chem.*, 2012, **14**, 3273.

5 Many transition-metal-catalyzed systems for the synthesis of N-heterocycles have been developed. For examples of using aldehydes as the starting material, see: (*a*) R. J. Abdel-Jalil, H. M. Aldoqum, M. T. Ayoub and W. Voelter, *Heterocycles*, 2005, **65**, 2061; (*b*) C. Balakumar, P. Lamba, D. P. Kishore, B. L. Narayana, K. V. Rao, K. Rajwinder, A. R. Rao, B. Shireesha and B. Narsaiah, *Eur. J. Med. Chem.*, 2010, **45**, 4904; (*c*) D. Zhan, T. Li, H. Wei, W. Weng, K. Ghandic and Q. Zeng, *RSC Adv.*, 2013, **3**, 9325; (*d*) R. G. Mahesh and P. S. N. Reddy, *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.*, 1998, **37**, 689; (*e*) R. G. Mahesh and P. S. N. Reddy, *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.*, 1997, **36**, 166; (*f*) K. S. Deepthi, D. S. Reddy, P. P. Reddy and P. S. N. Reddy, *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.*, 2000, **39**, 220; (*g*) D. Zhan, T. Li, X. Zhang, C. Dai, H. Wei, Y. Zhang and Q. Zeng, *Synth. Commun.*, 2013, **43**, 2493; (*h*) J. G. Kettle, S. Brown, C. Crafter, B. R. Davies, P. Dudley, G. Fairley, P. Faulder, S. Fillery, H. Greenwood, J. Hawkins, M. James, K. Johnson, C. D. Lane, M. Pass, J. H. Pink, H. Plant and S. C. Cosuliche, *J. Med. Chem.*, 2012, **55**, 1261; For examples of Ullmann-type N-arylation, see: (*i*) X. Liu, H. Fu, Y. Jiang and Y. Zhao, *Angew. Chem., Int. Ed.*, 2009, **48**, 348; (*j*) C. Wang, S. Li, H. Liu, Y. Jiang and H. Fu, *J. Org. Chem.*, 2010, **75**, 7936; (*k*) W. Xu and H. Fu, *J. Org. Chem.*, 2011, **76**, 3846; (*l*) W. Xu, Y. B. Jin, H. X. Liu, Y. Y. Jiang and H. Fu, *Org. Lett.*, 2011, **13**, 1274; (*m*) K. S. Devanga, R. Nagarajan and N. Rajagopal, *Org. Biomol. Chem.*, 2012, **10**, 3417; (*n*) D. S. Yang, Y. Y. Wang, H. J. Yang, T. Liu and H. Fu, *Adv. Synth. Catal.*, 2012, **354**, 477; (*o*) M. A. McGowan, C. Z. McAvoy and S. L. Buchwald, *Org. Lett.*, 2012, **14**, 3800; (*p*) X. Zhang, D. Ye, H. Sun, D. Guo, J. Wang, H. Huang, X. Zhang, H. Jiang and H. Liu, *Green Chem.*, 2009, **11**, 1881; for examples of using alcohol as a starting material, see: (*q*) J. Zhou and J. Fang, *J. Org. Chem.*, 2011, **76**, 7730; (*r*) A. J. A. Watson, A. C. Maxwell and J. M. Williams, *Org. Biomol. Chem.*, 2012, **10**, 240; (*s*) H. Hidemasa, Y. Ino, H. Suzuki and Y. Yokoyama, *J. Org. Chem.*, 2012, **77**, 7046; (*t*) W. Ge, X. Zhu and Y. Wei, *RSC Adv.*, 2013, **3**, 10817; (*u*) M. Sharif, J. Opalach, P. Langer, M. Bellerb and X. Wu, *RSC Adv.*, 2014, **4**, 8; for CO insertion and intramolecular cyclization, see: (*v*) B. Ma, Y. Wang, J. L. Peng and Q. Zhu, *J. Org. Chem.*, 2011, **76**, 6362; (*w*) F. Zeng and H. Alper, *Org. Lett.*, 2010, **12**, 3642; (*x*) F. Zeng and H. Aiper, *Org. Lett.*, 2010, **12**, 1188; (*y*) Z. Y. Zheng and H. Alper, *Org. Lett.*, 2008, **10**, 829; (*z*) M. Costa, N. Della Cà, B. Gabriele, C. Massera, G. Salerno and M. Soliani, *J. Org. Chem.*, 2004, **69**, 2469.

6 For transition-metal-catalyzed synthesis of N-heterocycles using amines as substrates, see: (*a*) M. Pizzetti, E. De Luca, E. Petricci, A. Porcheddu and M. Taddei, *Adv. Synth. Catal.*, 2012, **354**, 2453; (*b*) L. De Luca and A. Porcheddu, *Eur. J. Org. Chem.*, 2011, 5791; (*c*) T. B. Nguyen, J. L. Bescont, L. Ermolenko and A. Al-Mourabit, *Org. Lett.*, 2013, **15**, 6218.

7 T. B. Nguyen, L. Ermolenko and A. Al-Mourabit, *Green Chem.*, 2013, **15**, 2713.

8 Metal-free C–N bond cleavage of amines using sulfur as an oxidizing agent to synthesize N-heterocycles represents an attractive approach, whereas H_2S is generated. T. B. Nguyen, L. Ermolenko, W. A. Dean and A. Al-Mourabit, *Org. Lett.*, 2012, **14**, 5948.

9 For selected examples, see: (*a*) N. J. Turner, *Chem. Rev.*, 2011, **111**, 4073; (*b*) A. Roglans, A. Pla-Quintana and M. Moreno-Mañas, *Chem. Rev.*, 2006, **106**, 4622; (*c*) M. Gandelman and D. Milstein, *Chem. Commun.*, 2000, 1603; (*d*) S. Guo, B. Qian, Y. Xie, C. Xia and H. Huang, *Org. Lett.*, 2011, **13**, 522; (*e*) R. D. Patil and S. Adimurthy, *Adv. Synth. Catal.*, 2011, **353**, 1695; (*f*) Z. Ling, L. Yun, L. Liu, B. Wu and X. Fu, *Chem. Commun.*, 2013, **49**, 4214.

10 According to the referees' comments, peroxyacids are well known to oxidize tertiary amines to *N*-oxides, so the oxidative cyclocondensation of *o*-aminobenzamide **1a** with tri-*n*-butylamine **2c** was performed using *m*-cpba (3-chloroperbenzoic acid) as an oxidant instead of dioxygen. It was found that this reaction took place smoothly and the corresponding product 2-propylquinazolin-4(3*H*)-one **3c** was obtained in 93% yield.

11 (*a*) J. P. Ferris, R. D. Gerwe and G. R. Gapski, *J. Org. Chem.*, 1968, **33**, 3493; (*b*) J. C. Craig, N. Y. Mary and L. Wolf, *J. Org. Chem.*, 1964, **29**, 2868; (*c*) P. A. Bather, J. R. L. Smith and R. O. C. Norman, *J. Chem. Soc., C*, 1971, 3060; (*d*) M. B. Smith and J. March, *March's Advanced Organic Chemistry*, John Wiley & Sons, Hoboken, New Jersey, 6th edn, 2007; (*e*) Y. Li, L. Ma and Z. Li, *Chin. J. Org. Chem.*, 2013, **33**, 704.

12 Aldehydes were formed in the absence of the substrate **1** under similar reaction conditions. For example, in the presence of 20 mol% $Ph_2P(O)OH$, tri-*n*-octylamine and tribenzylamine could be readily oxidized by dioxygen and the corresponding aldehydes were obtained in 56% and 50% yields, respectively.

13 In the absence of $Ph_2P(O)OH$, the reaction of benzaldehyde with *o*-aminobenzamide **1a** took place smoothly under similar reaction conditions and the product 2-phenylquinazolin-4(3*H*)-one was produced in 97% yield.