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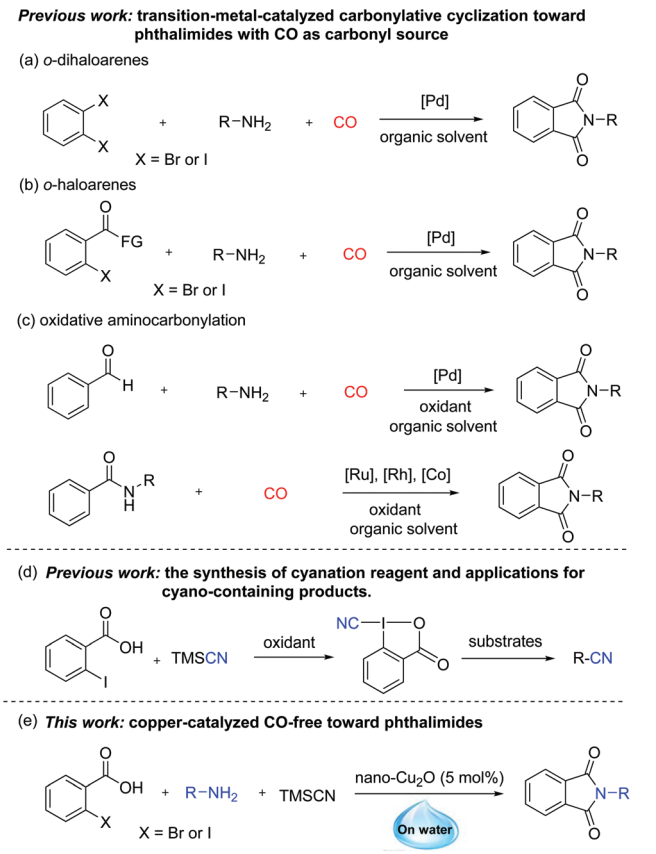
"On water" nano-Cu_2O-catalyzed CO-free one-pot multicomponent cascade cyanation–annulation–aminolysis reaction toward phthalimides†

Xiaowei Wen, Xiaojuan Liu, Zhiqi Yang, Menglan Xie, Yuxi Liu, Lipeng Long and Zhengwang Chen *

An efficient nano-Cu_2O-catalyzed cascade multicomponent reaction of 2-halobenzoic acids and trimethylsilyl cyanide with diverse amines was developed using water as a solvent, affording versatile *N*-substituted phthalimide derivatives in moderate to excellent yields. This novel strategy features carbon monoxide gas-free, environmentally benign, one-pot multistep transformation, commercially available reagents, a cheap catalyst without any additives, wide functional group tolerance, and operational convenience.

The increasing environmental awareness of the chemical community has led to the search for more efficient and environmentally friendly approaches for chemical syntheses.[1] One of the hot research areas has been the replacement of the conventional hazardous organic solvents by safe and green reaction media. Among them, water has attracted great interest from synthetic chemists for its unique physicochemical properties and fascinating advantages, such as its relative abundance, low cost, inherent safety and environmental friendliness.[2] Furthermore, multicomponent reactions (MCRs) have been adopted as a practical and powerful synthetic tool to create a relatively complex heterocyclic skeleton in an atom-economical and straightforward manner by generating multiple bonds in a single reaction vessel.[3] Despite the great achievements, continuing to explore new organic reactions under aqueous conditions involving high efficiency and practicability would be highly desirable.

Phthalimides not only are prevalent in natural products, pharmaceuticals, agrochemicals, polymers, and dyes[4] but also serve as versatile precursors for various organic transformations.[5] Consequently, the development of new and effective methods for their preparation has been stimulated. The traditional protocol of phthalimide synthesis involves condensation between the corresponding phthalic acids or anhydrides and amines.[6] Recently, alternative strategies including oxidation of the C–H bond,[7] coupling of isocyanates,[8] *N*-arylation of phthalimides,[9] transamidation,[10] and transfer-hydrogenation of diols[11] have been reported. Among the various approaches, the most popular methods are the transition-metal-catalyzed carbonylative cyclization of *o*-dihaloarenes (Scheme 1a)[12] or *o*-haloarenes (Scheme 1b)[13] and oxidative



Scheme 1 Synthetic methods for phthalimides.

Key Laboratory of Organo-pharmaceutical Chemistry of Jiangxi Province, Gannan Normal University, Ganzhou, 341000, China. E-mail: chenzwang@126.com; Fax: +86 797-8793670; Tel: +86 797 -8793670

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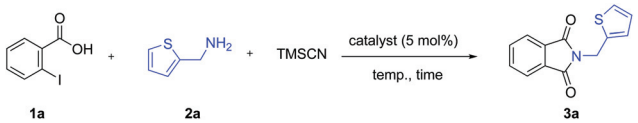
aminocarbonylation (Scheme 1c),[14] in which CO is frequently used as the carbonyl source. However, laboratory use of gaseous CO has been impeded due to its high toxicity and odorless and flammable character. Therefore, further research into a novel route to construct phthalimide frameworks from readily accessible precursors with an inexpensive catalyst under CO-free conditions is still of great challenge.

2-Iodobenzoic acids, as commercially available and versatile building blocks, have been widely employed in many synthetic strategies. In particular, they have attracted a great deal of attention for the preparation of hypervalent iodine reagents used for various organic transformations over the past decades.[15] For example, cyano-1,2-benziodoxol-3(1*H*)-one (CBX) prepared from 2-iodobenzoic acid and trimethylsilyl cyanide (TMSCN) under oxidative conditions has been widely employed for cyano-containing products *via* an umpolung method (Scheme 1d).[16] Herein, we describe the first nano-Cu_2O-catalyzed synthesis of phthalimides from 2-halobenzoic acids and TMSCN with primary aromatic or aliphatic amines through the cascade cyanation–annulation–aminolysis reaction "on water" (Scheme 1e). This protocol is also suitable for the synthesis of a variety of *N*-substituted maleimide derivatives.

We commenced our study with the reaction of 2-iodobenzoic acid **1a** and thiophen-2-ylmethanamine **2a** with TMSCN using water as the reaction medium. As shown in Table 1, a series of common copper salts were investigated. All of the copper catalysts have some effects on the reaction, and Cu_2O gave the best results (Table 1, entries 1–9). To our delight, the isolated yield of the desired product increased to 92% with nano-Cu_2O as the catalyst (Table 1, entry 10). Then the reaction temperatures were evaluated, and it was found that high temperature favored the reaction (Table 1, entries 11–14). When the mixture was stirred in water at room temperature, only a trace amount of the product was observed (Table 1, entry 14). Finally, the reaction time was also examined, and an excellent isolated yield was obtained after 8 h (Table 1, entries 15 and 16). These preliminary experiments showed that the suitable conditions toward phthalimide **3a** are using nano-Cu_2O as the catalyst at 100 °C for 8 h.

With the optimal conditions in hand, we then investigated the scope of this three-component reaction. As presented in Scheme 2, a wide range of aromatic and aliphatic amines were tolerated with 2-iodobenzoic acid to deliver the phthalimide products in moderate to excellent yields (**3b–3ao**). Various aniline derivatives were suitable substrates for this transformation (**3c–3q**). To our delight, the sterically hindered 2,6-diisopropyl substituted **3e** was achieved in a satisfactory yield, which has been approved as an α-tumor necrosis factor (TNF) inhibitor.[17] Noteworthily, the substrates bearing active

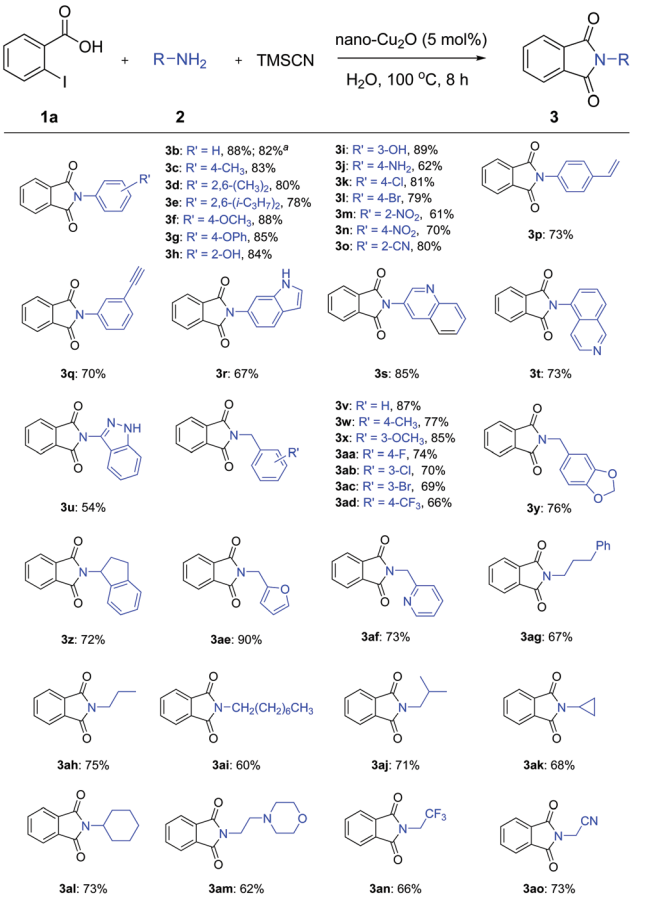
Table 1 Optimization of the reaction conditions[a]



1a 2a 3a

Entry	Cat.	Temp.	Time	Yield[b] (%)
1	$CuSO_4{\cdot}5H_2O$	100	8	78
2	$Cu(OTf)_2$	100	8	82
3	$Cu(OAc)_2$	100	8	84
4	CuO	100	8	81
5	CuCl	100	8	85
6	CuBr	100	8	79
7	CuI	100	8	78
8	CuCN	100	8	80
9	Cu_2O	100	8	88
10[c]	Nano-Cu_2O	100	8	97 (92)
11	Nano-Cu_2O	80	8	87
12	Nano-Cu_2O	60	8	74
13	Nano-Cu_2O	40	8	56
14	Nano-Cu_2O	25	8	Trace
15	Nano-Cu_2O	100	10	97
16	Nano-Cu_2O	100	6	85

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), TMSCN (0.24 mmol) with catalyst (5 mol%) in 1.0 mL water for 8 h. [b] Determined by GC with mesitylene as an internal standard. The number in parentheses is the isolated yield. [c] Commercially available with 99.9% purity and 4–5 nm mesh size.

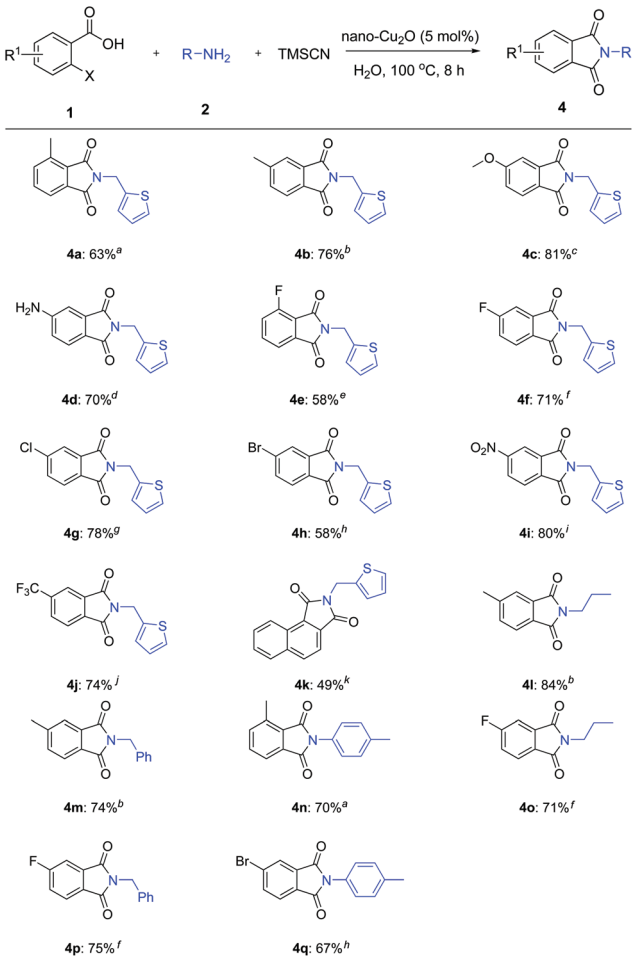


Scheme 2 Substrate scope of amines. Reaction conditions: **1a** (0.2 mmol), **2** (0.2 mmol), TMSCN (0.24 mmol), nano-Cu_2O (5 mol%) and H_2O (1.0 mL) at 100 °C for 8 h. Isolated yield. [a] 2-Bromobenzoic acid was used.

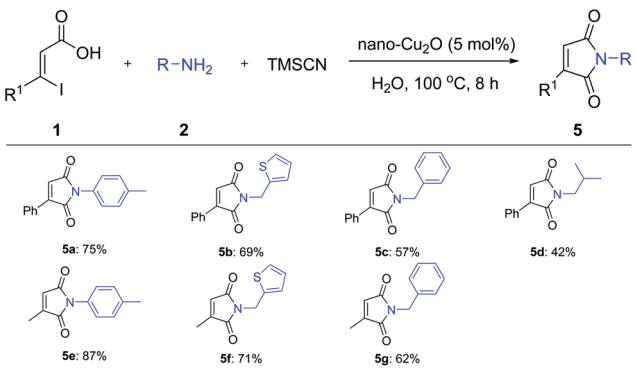
hydroxyl and amino at the *para*, *meta*, and *ortho* positions of the phenyl formed **3h**, **3i**, and **3j** in 84%, 89%, and 62% yields, respectively. Aniline bearing an unsaturated double bond and a triple bond worked well under the standard conditions (**3p** and **3q**). Fortunately, heteroaryl substituted phthalimides could be successfully generated in a good yield (**3r–3u**). Moreover, both electron-donating and electron-withdrawing benzylamines exhibited high reactivity with 2-iodobenzoic acid to lead to the corresponding products in satisfactory yields (**3v–3z**). The reaction was compatible with a set of substituents, such as alkyl, alkoxy, fluoro, chloro, bromo, and trifluoromethyl groups (**3k–3z**). It is noteworthy that arylbromides could be further functionalized in cross-coupling reactions (**3l** and **3ac**). The amines containing different heterocycles underwent the reaction efficiently giving good yields (**3ae** and **3af**). Meanwhile, straight-chain, branched and cyclic amines were all reactive in this multicomponent cascade reaction and converted to phthalimides in good yields (**3ah–3ao**). Notably, **3an** was afforded in 66% yield, which was synthesized through trifluoromethylation reactions in previous work.[18] Unfortunately, the corresponding phthalimide was not obtained when ammonia solution was used as a nucleophilic reagent. Apart from **1a**, 2-bromobenzoic acid was also screened which achieved **3a** in 82% yield. However, 2-chlorobenzoic acid did not afford **3a** under the standard conditions.

Subsequently, we explored a handful of substituted 2-halobenzoic acids with various amines under the optimized conditions. As shown in Scheme 3, it was found that the substituents at the *ortho*- or *meta*-position of 2-halobenzoic acids reacted smoothly to furnish the desired products in moderate to good yields (**4a–4q**). 2-Halobenzoic acid bearing either an electron-rich or an electron-deficient group on the benzene ring favored the reaction, indicating that the electronic effect did not have a significant influence on the reaction (**4a–4j**). The yields were lower when the substituents were at the *ortho*-position as compared to the *meta*-position, suggesting that the steric effect was overwhelming (**4a**, **4b**, **4e** and **4f**). The free amino-substituted substrate was perfectly tolerated under the standard conditions (**4d**). Moreover, 1-bromo-2-naphthoic acid could be successfully converted into polycyclic product **4k** in 49% yield. The representative amines including alkylamine, benzylamine, arylamine and heterocyclic amine were all compatible, and resulted in satisfactory yields under the optimal conditions. These results from Schemes 2 and 3 implied that this cascade multistep transformation can be effective for the phthalimide library.

Maleimide derivatives have found wide applications in pharmaceuticals.[19] Transition-metal-catalyzed annulation reactions containing Ru,[20] Rh,[21] Fe,[22] and Pd[23] complexes from alkynes, CO, and amines or isocyanates have received significant attention for the preparation of maleimides in recent years. Fortunately, the present method can also be applied to the cyclization of β-iodoacrylic acids.[24] Both methyl and phenyl substituted substrates were compatible and rendered the desired products in moderate to good yields (**5a–5g**) (Scheme 4).



Scheme 3 Substrate scope of 2-halobenzoic acids and amines. Reaction conditions: **1** (0.2 mmol), **2** (0.2 mmol), TMSCN (0.24 mmol), nano-Cu_2O (5 mol%) and H_2O (1.0 mL) at 100 °C for 8 h. Isolated yield. [a] 2-Iodo-6-methylbenzoic acid was used. [b] 2-Iodo-5-methylbenzoic acid. [c] 2-Iodo-4-methoxybenzoic acid. [d] 5-Amino-2-bromobenzoic acid. [e] 2-Fluoro-6-iodobenzoic acid. [f] 5-Fluoro-2-iodobenzoic acid. [g] 4-Chloro-2-iodobenzoic acid. [h] 5-Bromo-2-iodobenzoic acid. [i] 2-Bromo-4-nitrobenzoic acid. [j] 2-Iodo-4-(trifluoromethyl)benzoic acid. [k] 1-Bromo-2-naphthoic acid.



Scheme 4 Reaction of β-iodoacrylic acids with amines. Reaction conditions: **1** (0.2 mmol), **2** (0.2 mmol), TMSCN (0.24 mmol), nano-Cu_2O (5 mol%) and H_2O (1.0 mL) at 100 °C for 8 h. Isolated yield.

Most importantly, the reaction could be conducted on a large scale and provided the product in a good yield (Fig. 1). Before the reaction, 2-iodobenzoic acid was only partially dissolved in water. When reacting at 100 °C, the reaction mixture became clear. After reaction for 1 h, a great amount of precipitate appeared in the reaction mixture. After the reaction, the desired product was obtained through extraction and column chromatography with 81% yield.

Some control experiments were carried out to elucidate the mechanism (Scheme 5). First, considering that the phthalimide products may be formed by the cyanation of substituted 2-iodobenzamide, the reaction of 2-iodobenzoic acid **1a** and thiophen-2-ylmethanamine **2a** was performed under the standard conditions. However, they could not form the corresponding intermediate **6a** (Scheme 5a). Then, the reaction of **1a** and TMSCN could smoothly form *o*-phthalic anhydride **7a** (Scheme 5b). Subsequently, the reaction of *o*-phthalic anhydride **7a** or 2-cyanobenzoic acid **8a** with **2a** generated the desired product **3a** in 98% or 93% yield, respectively (Scheme 5c and d). The results indicated that **8a** and **7a** may be the intermediates of the reaction. In addition, **8a** leads to *o*-phthalic anhydride **7a** in an excellent yield (Scheme 5e). Furthermore, the reaction of 2-iodobenzoic acid **1a** with an excess of CuCN gave the corresponding aryl nitrile **8a** in a trace yield; this result inferred that TMSCN was indispensible for this transformation and excluded the Rosenmund–von Braun mechanism for the cyanation process (Scheme 5f).

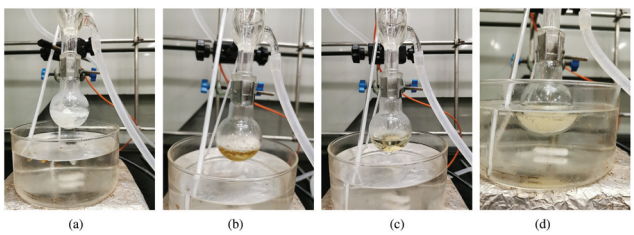
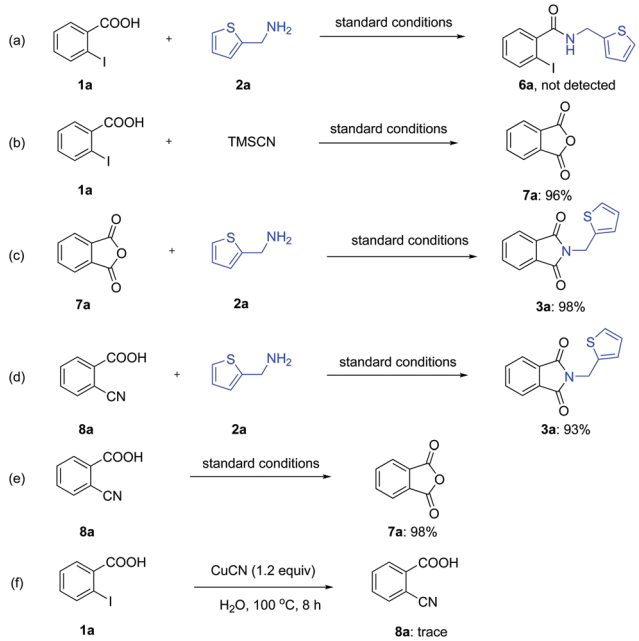
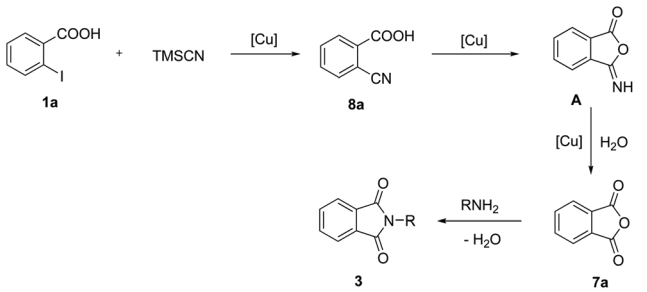


Fig. 1 Gram-scale synthesis of **3a**: (a) before the reaction, 20 mL of water and 2-iodobenzoic acid (10 mmol) were added; (b) before the reaction, a mixture of 20 mL of water, TMSCN (12 mmol), 2-iodobenzoic acid (10 mmol), thiophen-2-ylmethanamine (10 mmol), and nano-Cu_2O (2 mol%) was added; (c) reacted at 100 °C; and (d) reacted for 1 h.



Scheme 5 Control experiments.



Scheme 6 Possible reaction mechanism.

On the basis of the results described above and the literature procedure, a plausible mechanism is proposed for this cascade reaction (Scheme 6). Initially, intermediate **8a** was generated from 2-iodobenzoic acid **1a** and TMSCN *via* a copper-catalyzed cyanation reaction.[25] Then intramolecular nucleophilic addition took place to generate intermediate **A**, followed by hydrolysis of **A** to obtain *o*-phthalic anhydride **7a**. Finally, the fast reaction of *o*-phthalic anhydride with an amine formed the phthalimide product **3**. Probably, Cu_2O catalyzed the cyanation reaction and accelerated the cyclization and hydrolysis process.

In conclusion, we have developed the first nano-Cu_2O-catalyzed, ligand- and additive-free cascade multicomponent reaction for the synthesis of *N*-substituted phthalimide and maleimide derivatives. A variety of amines were compatible and afforded the products in moderate to excellent yields. The reaction circumvents the use of carbon monoxide gas with an additional advantage of the application of water as a reaction solvent towards valuable phthalimide and maleimide products. Moreover, readily available substrates, excellent functional group compatibilities, and operational simplicity make this approach practical to the synthetic community. Further synthetic utilization and mechanistic studies are currently ongoing in our laboratory.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

1 (*a*) C.-J. Li and B. M. Trost, *Proc. Natl. Acad. Sci. U. S. A.*, 2008, **105**, 13197; (*b*) I. T. Horváth and P. T. Anastas, *Chem. Rev.*, 2007, **107**, 2169.

2 (*a*) T. Kitanosono, K. Masuda, P. Xu and S. Kobayashi, *Chem. Rev.*, 2018, **118**, 679; (*b*) B. H. Lipshutz and S. Ghorai, *Green Chem.*, 2014, **16**, 3660; (*c*) M.-O. Simon and C.-J. Li, *Chem. Soc. Rev.*, 2012, **41**, 1415; (*d*) R. N. Butler and A. G. Coyne, *Chem. Rev.*, 2010, **110**, 6302.

3 (*a*) B. H. Rotstein, S. Zaretsky, V. Rai and A. K. Yudin, *Chem. Rev.*, 2014, **114**, 8323; (*b*) C. de Graaff, E. Ruijter and R. V. A. Orru, *Chem. Soc. Rev.*, 2012, **41**, 3969; (*c*) N. Isambert, M. d. M. S. Duque, J.-C. Plaquevent, Y. Génisson, J. Rodriguez and T. Constantieux, *Chem. Soc. Rev.*, 2011, **40**, 1347; (*d*) M. González-López and J. T. Shaw, *Chem. Rev.*, 2009, **109**, 164.

4 (*a*) G. E. Winter, D. L. Buckley, J. Paulk, J. M. Roberts, A. Souza, S. Dhe-Paganon and J. E. Bradner, *Science*, 2015, **348**, 1376; (*b*) Y. Wu and W. Zhu, *Chem. Soc. Rev.*, 2013, **42**, 2039; (*c*) X. Guo, F. S. Kim, S. A. Jenekhe and M. D. Watson, *J. Am. Chem. Soc.*, 2009, **131**, 7206.

5 (*a*) Y.-C. Yuan, C. Bruneau, V. Dorcet, T. Roisnel and R. Gramage-Doria, *J. Org. Chem.*, 2019, **84**, 1898; (*b*) X. Wu, G. Ding, L. Yang, W. Lu, W. Li, Z. Zhang and X. Xie, *Org. Lett.*, 2018, **20**, 5610; (*c*) Y.-C. Yuan, R. Kamaraj, C. Bruneau, T. Labasque, T. Roisnel and R. Gramage-Doria, *Org. Lett.*, 2017, **19**, 6404; (*d*) J. R. Cabrero-Antonino, R. Adam, V. Papa, M. Holsten, K. Junge and M. Beller, *Chem. Sci.*, 2017, **8**, 5536; (*e*) G. Ding, C. Li, Y. Shen, B. Lu, Z. Zhang and X. Xie, *Adv. Synth. Catal.*, 2016, **358**, 1241; (*f*) G. Ding, B. Lu, Y. Li, J. Wan, Z. Zhang and X. Xie, *Adv. Synth. Catal.*, 2015, **357**, 1013.

6 (*a*) L. Wan, X. Sun, S. Shi, J. Zhang, X. Li, Z. Li and K. Guo, *Catal. Commun.*, 2017, **88**, 30; (*b*) J. Fraga-Dubreuil, G. Comak, A. W. Taylor and M. Poliakoff, *Green Chem.*, 2007, **9**, 1067; (*c*) A. A. M. Abdel-Aziz, *Eur. J. Med. Chem.*, 2007, **42**, 614.

7 (*a*) M. Wang, J. Lu, J. Ma, Z. Zhang and F. Wang, *Angew. Chem., Int. Ed.*, 2015, **54**, 14061; (*b*) X. Yan, K. Fang, H. Liu and C. Xi, *Chem. Commun.*, 2013, **49**, 10650.

8 (*a*) X.-F. Dong, J. Fan, X.-Y. Shi, K.-Y. Liu, P.-M. Wang and J.-F. Wei, *J. Organomet. Chem.*, 2015, **779**, 55; (*b*) X.-Y. Shi, A. Renzetti, S. Kundu and C.-J. Li, *Adv. Synth. Catal.*, 2014, **356**, 723; (*c*) S. De Sarkar and L. Ackermann, *Chem. – Eur. J.*, 2014, **20**, 13932; (*d*) J.-C. Hsieh and C.-H. Cheng, *Chem. Commun.*, 2005, 4554.

9 (*a*) L. J. Allen, P. J. Cabrera, M. Lee and M. S. Sanford, *J. Am. Chem. Soc.*, 2014, **136**, 5607; (*b*) H. J. Kim, J. Kim, S. H. Cho and S. Chang, *J. Am. Chem. Soc.*, 2011, **133**, 16382; (*c*) A. A. Kantak, S. Potavathri, R. A. Barham, K. M. Romano and B. DeBoef, *J. Am. Chem. Soc.*, 2011, **133**, 19960.

10 (*a*) K. P. Patel, E. M. Gayakwad, V. V. Patil and G. S. Shankarling, *Adv. Synth. Catal.*, 2019, **361**, 2107; (*b*) H. Sheng, R. Zeng, W. Wang, S. Luo, Y. Feng, J. Liu, W. Chen, M. Zhu and Q. Guo, *Adv. Synth. Catal.*, 2017, **359**, 302; (*c*) J.-W. Wu, Y.-D. Wu, J.-J. Dai and H.-J. Xu, *Adv. Synth. Catal.*, 2014, **356**, 2429; (*d*) S. N. Rao, D. C. Mohan and S. Adimurthy, *Green Chem.*, 2014, **16**, 4122.

11 (*a*) J. Kim and S. H. Hong, *Org. Lett.*, 2014, **16**, 4404; (*b*) J. Zhang, M. Senthilkumar, S. C. Ghosh and S. H. Hong, *Angew. Chem., Int. Ed.*, 2010, **49**, 6391.

12 (*a*) P. Wojcik and A. M. Trzeciak, *Appl. Catal., A*, 2018, **560**, 73; (*b*) S. Liu, Q. Deng, W. Fang, J.-F. Gong, M.-P. Song, M. Xu and T. Tu, *Org. Chem. Front.*, 2014, **1**, 1261; (*c*) J. Chen, K. Natte, A. Spannenberg, H. Neumann, M. Beller and X.-F. Wu, *Org. Biomol. Chem.*, 2014, **12**, 5578; (*d*) H. Cao and H. Alper, *Org. Lett.*, 2010, **12**, 4126.

13 (*a*) M. V. Khedkar, A. R. Shinde, T. Sasaki and B. M. Bhanage, *J. Mol. Catal. A: Chem.*, 2014, **385**, 91; (*b*) M. V. Khedkar, S. R. Khan, K. P. Dhake and B. M. Bhanage, *Synthesis*, 2012, **44**, 2623; (*c*) M. V. Khedkar, S. R. Khan, D. N. Sawant, D. B. Bagal and B. M. Bhanage, *Adv. Synth. Catal.*, 2011, **353**, 3415; (*d*) S. A. Worlikar and R. C. Larock, *J. Org. Chem.*, 2008, **73**, 7175.

14 (*a*) R. Shi, F. Liao, H. Niu and A. Lei, *Org. Chem. Front.*, 2018, **5**, 1957; (*b*) F. Ji, J. Li, X. Li, W. Guo, W. Wu and H. Jiang, *J. Org. Chem.*, 2018, **83**, 104; (*c*) L. Grigorjeva and O. Daugulis, *Org. Lett.*, 2014, **16**, 4688; (*d*) Y. Du, T. K. Hyster and T. Rovis, *Chem. Commun.*, 2011, **47**, 12074; (*e*) S. Inoue, H. Shiota, Y. Fukumoto and N. Chatani, *J. Am. Chem. Soc.*, 2009, **131**, 6898.

15 (*a*) A. Yoshimura and V. V. Zhdankin, *Chem. Rev.*, 2016, **116**, 3328; (*b*) V. V. Zhdankin and P. J. Stang, *Chem. Rev.*, 2008, **108**, 5299.

16 (*a*) N. Declas, F. Le Vaillant and J. Waser, *Org. Lett.*, 2019, **21**, 524; (*b*) F. Le Vaillant, M. D. Wodrich and J. Waser, *Chem. Sci.*, 2017, **8**, 1790; (*c*) R. Frei, T. Courant, M. D. Wodrich and J. Waser, *Chem. – Eur. J.*, 2015, **21**, 2662.

17 H. Miyachi, A. Azuma, E. Hioki, S. Iwasaki, Y. Kobayashi and Y. Hashimoto, *Biochem. Biophys. Res. Commun.*, 1996, **224**, 426.

18 (*a*) P. J. Sarver, V. Bacauanu, D. M. Schultz, D. A. DiRocco, Y.-h. Lam, E. C. Sherer and D. W. C. MacMillan, *Nat. Chem.*, 2020, **12**, 459; (*b*) X. Tan, Z. Liu, H. Shen, P. Zhang, Z. Zhang and C. Li, *J. Am. Chem. Soc.*, 2017, **139**, 12430.

19 (*a*) N. Matuszak, G. G. Muccioli, G. Labar and D. M. Lambert, *J. Med. Chem.*, 2009, **52**, 7410; (*b*) C. Peifer, T. Stoiber, E. Unger, F. Totzke, C. Schächtele, D. Marmé, R. Brenk, G. Klebe, D. Schollmeyer and G. Dannhardt, *J. Med. Chem.*, 2006, **49**, 1271; (*c*) M. C. Jaye, J. A. Krawiec, N. Campobasso, A. Smallwood, C. Qiu, Q. Lu, J. J. Kerrigan, M. De Los Frailes Alvaro, B. Laffitte, W.-S. Liu, J. P. Marino, C. R. Meyer, J. A. Nichols, D. J. Parks, P. Perez, L. Sarov-Blat, S. D. Seepersaud, K. M. Steplewski, S. K. Thompson,

P. Wang, M. A. Watson, C. L. Webb, D. Haigh, J. A. Caravella, C. H. Macphee, T. M. Willson and J. L. Collins, *J. Med. Chem.*, 2005, **48**, 5419.

20 T. Kondo, M. Nomura, Y. Ura, K. Wada and T.-a. Mitsudo, *J. Am. Chem. Soc.*, 2006, **128**, 14816.

21 (*a*) F. Zhu, Y. Li, Z. Wang and X.-F. Wu, *ChemCatChem*, 2016, **8**, 3710; (*b*) S. Inoue, Y. Fukumoto and N. Chatani, *J. Org. Chem.*, 2007, **72**, 6588.

22 (*a*) P. Mathur, R. K. Joshi, D. K. Rai, B. Jha and S. M. Mobin, *Dalton Trans.*, 2012, **41**, 5045; (*b*) K. M. Driller, H. Klein, R. Jackstell and M. Beller, *Angew. Chem., Int. Ed.*, 2009, **48**, 6041.

23 J. Yang, J. Liu, R. Jackstell and M. Beller, *Chem. Commun.*, 2018, **54**, 10710.

24 A.-u.-H. A. Shah, Z. A. Khan, N. Choudhary, C. Lohölter, S. Schäfer, G. P. L. Marie, U. Farooq, B. Witulski and T. Wirth, *Org. Lett.*, 2009, **11**, 3578.

25 (*a*) G. P. Ellis and T. M. Romney-Alexander, *Chem. Rev.*, 1987, **87**, 779; (*b*) P. Anbarasan, T. Schareina and M. Beller, *Chem. Soc. Rev.*, 2011, **40**, 5049.