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Metal-free oxidative cross-dehydrogenative coupling of quinones with benzylic C(sp³)–H bonds†

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A metal-free cross-dehydrogenative coupling of quinones with toluene derivatives has been established. A series of quinones were subjected to reaction with toluene derivatives in the presence of di-tertbutyl peroxide (DTBP) for direct synthesis of benzylquinones. The method exhibits good functional group tolerance, and desired products were obtained in moderate to good yields. Meanwhile, a radical pathway was proposed to describe the cross-dehydrogenative coupling of quinones with toluene derivatives.

Introduction

Cross-dehydrogenative coupling reactions (CDC) via transformations of C–H bond into other bonds are emerging as a subclass of C–H functionalizations which have been established as effective and robust methods for the preparation of valuable fragments of pharmaceuticals and intermediates of natural products.[1] CDC reactions possess the atom- and step-economical nature avoiding the preparation of the prerequisite functional groups (necessary for classical cross-coupling reactions) which have the perspectives of new chemistry development in developing green chemistry and sustainable procedures.[2] Transition-metal (TM)-catalyzed CDC is the most common reaction.[3] However, it suffers from various drawbacks, such as expensive TM catalysts, and heavy metal residues in pharmaceutical products. Thus, TM-free CDC reactions have recently come of age and they offer greener approaches, avoid expensive TM catalysts and the challenges involved in the removal of toxic metal residues.[4] Hence, CDC reactions have attracted the attention of organic chemists for the preparation of C–C bonds under metal-free conditions in academic as well as industrial research.

The quinone is an important type of scaffold found in a number of bioactive natural products and pharmaceutical molecules,[5] which show a wide range of biological activities including anticancer, antifungal, antibacterial, antiprotozoal, antiviral, anti-inflammatory, neurological, antiplasmodial, and trypanocidal activities.[6] Among the derivatives of quinone, 3-benzylmenadiones represent an extremely important type of bioactive compound which the antimalarial activity of 3-benzylmenadiones results from a subtle interplay between bioactivation, fine-tuned redox properties, and interactions with crucial targets of *P. falciparum*.[7] Additionally, 2-benzyl-1,4-naphthoquinone is also important as an intermediate for the synthesis of biologically active compounds. On the other hand, with the rapid development of free radical chemistry, radical oxidative coupling reaction have emerged as a powerful tool in organic synthesis.[8] Hence, the application of the radical oxidative coupling strategy in constructing of quinones derivatives has been attracted much attention by organic chemists. For example, Duan's group reported an efficient and elegant synthesis of 3-benzylcoumarins using a TBPB/Cu(OAc)₂-catalyzed reaction via an intermolecular hydrogen abstraction reaction between the coumarins and toluene (Scheme 1a) in 2014.[9] Nonetheless, only one reaction of 2-methyl-1,4-naphthoquinone with toluene proceeded to afford 2-benzyl-3-methyl-1,4-naphthoquinone in 56% yield. Zhang's group developed the radical alkylation of 1,4-naphthoquinone with various fatty acids in the presence of $(NH_4)_2S_2O_8$ and $AgNO_3$ (Scheme 1b).[10] In 2018, Lee's group discovered a novel route to C–H alkylation of *N*-heteroarenes and quinones with alkylcarboxylic acids employing a $(NH_4)_2S_2O_8$ catalyst under mild conditions (Scheme 1c).[11] Despite the undisputable advance in these papers, there is no mention that organic oxidants oxidized cross-dehydrogenative coupling of quinones with benzylic C(sp³)–H bonds under metal-, photocatalyst-, and light-free conditions.

As we known, benzylic radicals are common intermediates which have been extensively utilized in synthetic organic chemistry.[12] In these processes, a variety of reactions initiated with benzylic radicals were reported.[13] Among the generation of the reactive benzylic radicals, the oxidative activation of sp³ C–H

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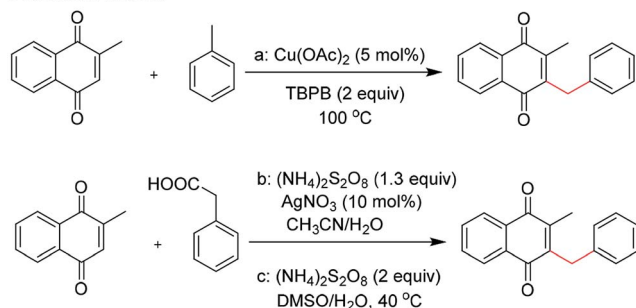
bUniversity of Chinese Academy of Sciences, Beijing 100049, P. R. China

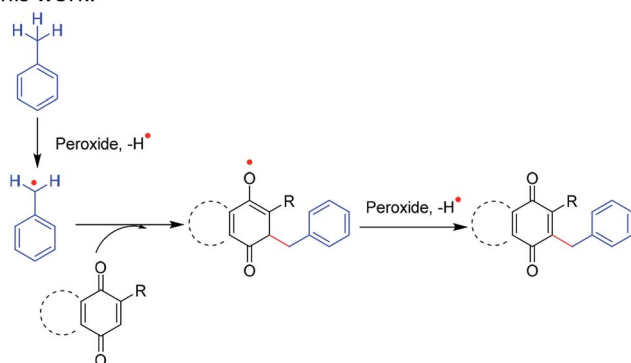*cSouthwest Minzu University, Chengdu 610041, P. R. China*

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Previous work:

This work:

Scheme 1   Methods of direct benzylation of quinones.

bonds of alkylarenes by hydrogen atom abstraction has been considered as one of the most popular methods to access such species. On the basis of the above and previous work,[14] we envisioned that rich electron benzylic radicals[15] could nucleophilic attack the highly electron-deficient double bond of quinones[16] to synthesize 2-benzyl-quinones derivatives without any catalyst (Scheme 1). Herein we reported metal-free oxidative cross-dehydrogenative coupling of quinones with benzylic C(sp^3)–H bonds.

Results and discussion

Following our effort for the construction of a broad range of 2-benzyl-quinones as potential antimalarial agents. Herein we decided to investigate the use of oxidizing reagents for the direct benzylation of quinones with alkylbenzenes. Initially, we evaluated various reaction conditions for the direct coupling of 2-methyl-1,4-naphthoquinone (**1c**) with toluene (**2a**). To our delight, we conducted our investigation by reacting 2-methyl-1,4-naphthoquinone **1c** (0.4 mmol) with toluene **2a** (2 mL) in the presence of 2.0 equiv. of DTBP at 120 °C for 16 h. The reaction proceeded and afforded the expected product of 2-benzyl-3-methylnaphthalene-1,4-dione **3ca** in a good yield (86%, Table 1, entry 1). The reaction could not take place at all if H$_2$O$_2$ (30% aqueous solution), PIFA, DDQ, BQ, K$_2$S$_2$O$_8$, or oxone was employed as the oxidant (Table 1, entries 2–7). And the use of other oxidants such as BPO, PhI(OAc)$_2$, IBX, TBHP (70% aqueous solution), TBPB, or DCP did not provide better results (Table 1, entries 8–13). Almost all of the starting material **1c** remained in the reactions with these examined oxidants

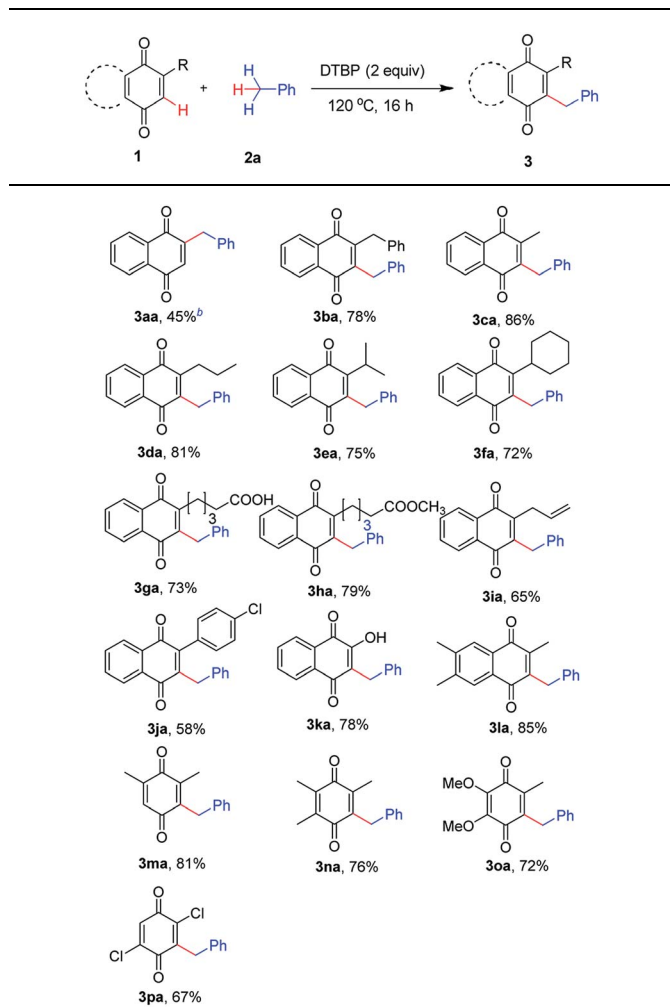Table 1   Optimize the reaction conditions^a

Entry	Oxidant^b (equiv.)	T (°C)	t (h)	Yield^c (%)
1	DTBP (2)	120	16	86
2	H$_2$O$_2$ (2)	120	16	NR
3	PIFA (2)	120	16	NR
4	DDQ (2)	120	16	NR
5	BQ (2)	120	16	NR
6	K$_2$S$_2$O$_8$ (2)	120	16	NR
7	Oxone (2)	120	16	NR
8	BPO (2)	120	16	29
9	PhI(OAc)$_2$ (2)	120	16	46
10	IBX (2)	120	16	17
11	TBHP (2)	120	16	15
12	TBPB (2)	120	16	21
13	DCP (2)	120	16	19
14	DTBP (1)	120	16	55
15	DTBP (4)	120	16	85
16	DTBP (2)	100	16	Trace
17	DTBP (2)	140	16	83
18	DTBP (2)	120	8	67
19	DTBP (2)	120	24	80
20	DTBP (2)	120	16	81^d
21	DTBP (2)	120	16	70^e
22	No^g	120	16	NR^f

^{a} Reaction conditions: unless otherwise noted, the reaction was carried out with **1c** (0.4 mmol), **2a** (2 mL), oxidant (0.8 mmol) under sealed tube. ^{b} DTBP: di-tertbutyl peroxide. H$_2$O$_2$: 30% aqueous solution. PIFA = [Bis(trifluoroacetoxy)iodo] benzene. DDQ: 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. BQ: 1,4-benzoquinone. BPO: benzoyl peroxide. IBX = 2-iodoxybenzoic acid. TBHP: 70% aqueous solution. TBPB: *tert*-butyl peroxybenzoate. DCP: dicumyl peroxide. ^{c} Isolated yields. ^{d} Under a N$_2$ atmosphere. ^{e} Cu(OAc)$_2$ (0.04 mmol) was added. ^{f} NR = no reaction. ^{g} Without oxidant.

(entries 2–13). When the amount of DTBP was reduced to 1.0 equiv., a decrease in the yield of product **3ca** to 55% was observed (Table 1, entry 14). Further increases in the loading of the oxidant did not result in any improvement (Table 1, entry 15). When the reaction was performed at 100 °C, almost no product was obtained (Table 1, entry 16). No significant effect on the yield of **3ca** was found when the reaction was conducted at 140 °C (Table 1, entry 17). Changing the reaction time didn't led to the improvement of the product yield (Table 1, entries 18–19). When the reaction was performed under a N$_2$ atmosphere, it did not result in any improvement of the yield (81%, Table 1, entry 20). Notably, the addition of a metal catalyst, Cu(OAc)$_2$ (10 mol%), suppressed the transformation slightly and the yield reduced (Table 1, entry 21). As per our expectation, no product was detected in the absence of DTBP or other oxidants which the oxidants played a pivotal role in obtaining the desired product (Table 1, entry 22).

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Table 2 Substrate scope for the quinones[a]

3aa, 45%[b]   3ba, 78%   3ca, 86%

3da, 81%   3ea, 75%   3fa, 72%

3ga, 73%   3ha, 79%   3ia, 65%

3ja, 58%   3ka, 78%   3la, 85%

3ma, 81%   3na, 76%   3oa, 72%

3pa, 67%

[a] Reaction conditions: **1** (0.4 mmol), **2a** (2 mL), DTBP (2.0 equiv.), 120 °C, 16 h under sealed tube. Isolated yield based on **1**. [b] The dibenzylnaphthoquinone was obtained in 45% yield when 1,4-naphthoquinone was used as the substrate.

On the basis of the above results, the best oxidative coupling conditions involved 0.4 mmol of 2-methyl-1,4-naphthoquinone (**1c**), 2 mL of toluene (**2a**), and 2 equiv. of DTBP at 120 °C.

With the optimized reaction conditions in hand, a series of quinones and alkylbenzenes as the substrates were investigated to demonstrate the substrate scope. First, the variation in the quinones part of the reaction was studied (Table 2). The naphthoquinone reacted smoothly to give mono-benzylnaphthoquinone (**3aa**, 45%) and dibenzylnaphthoquinone (**3ba**, 45%), respectively. Alkyl-substituted naphthoquinones with functional groups including benzyl, methyl, *n*-propyl, isopropyl, cyclohexyl and long-chain alkyl groups were proceeded smoothly to afford the corresponding products in moderate to good yields (72–86%, **3ba–3ha**). Pleasingly, the sensitive carboxyl and ester groups at the β-position of naphthoquinone was compatible with the reaction conditions. Notably, naphthoquinone bearing allyl substituent

Table 3 Substrate scope with respect to the toluene derivatives[a]

3ab, 79%   3ac, 84%   3ad, 88%

3ae, 85%   3af, 75%   3ag, 67%

3ah, 62%
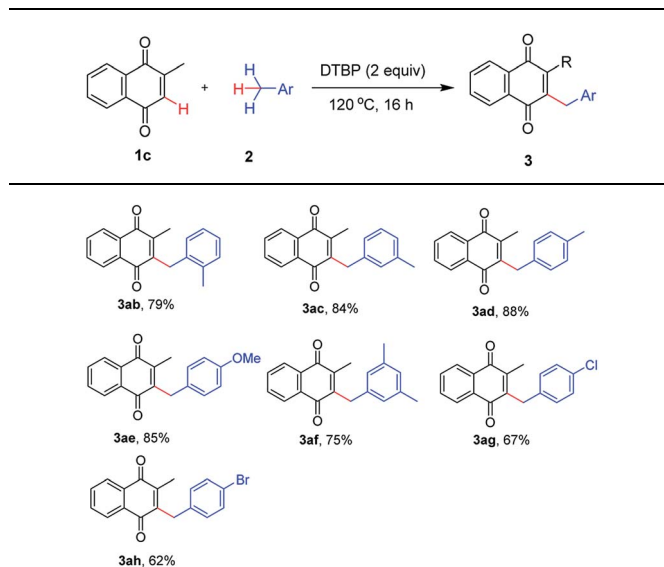
[a] Reaction conditions: **1c** (0.4 mmol), **2** (2 mL), DTBP (2.0 equiv.), 120 °C, 16 h under sealed tube. Isolated yield based on **1c**.

also worked well under this protocol and afforded the desired product **3ia** in moderate yield (65%). Due to steric hindrance caused by the phenyl ring present at the C-2 position, electron-deficient arene substituted naphthoquinone only produced a 58% yield of **3ja**. Although the substrate scope did not explicate decent chemoselectivity, the results with hydroxyl substituted naphthoquinone **1k** was encouraging while considering the radical quenching nature of hydroxy group. The reaction was found to work well with 2,6,7-trimethylnaphthoquinone in the system giving the corresponding products **3la** in good yield. The reaction with 2,6-dimethyl benzoquinone **1m** can be directly to monobenzylation (**3ma**, 81%). Benzoquinones bearing methyl and methoxy groups were also employed, affording corresponding benzylation products **3na** and **3oa** in moderate yield, respectively. The reaction conditions are well-tolerated by chloro (**1p**) substituted benzoquinone which would be vulnerable in Pd catalyzed transformations.

In addition to toluene, we also examined other benzylic hydrocarbons for this transformation. The reaction tolerated a series of toluene derivatives bearing electron-donating or -withdrawing groups, leading to the desired products in moderate to good yields (Table 3, **3ab–3ah**). Remarkably, several functional groups such as chlorine and bromine group were tolerated well under the reaction conditions (**3ag** and **3ah**). More importantly, when substrates with multiple methyl groups were used, such as xylenes and mesitylene, only mono-benzylation products were obtained in good yields with high selectivities (**3ab**, **3ac**, **3ad** and **3af**).

In addition, the scalability of this reaction was carried out by using **1c** (6 mmol, 1.03 g) with **2a** under the developed optimal reaction conditions. As expected, the desired product **3ca** was obtained in 82% yields. These results suggested that the
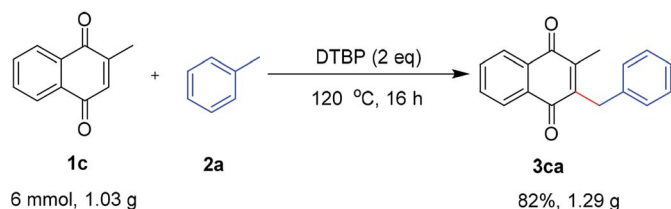
Scheme 2   Gram-scale oxidative coupling reaction.

1c
6 mmol, 1.03 g

2a

3ca
82%, 1.29 g
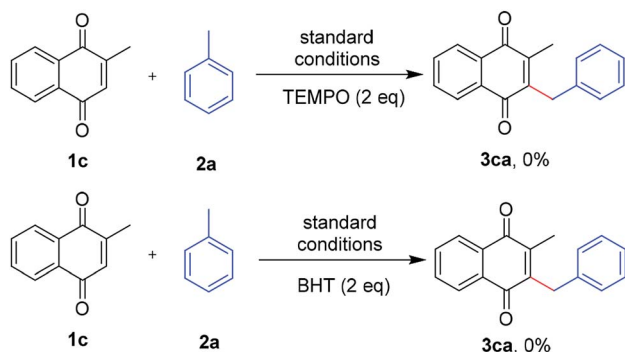
Scheme 3   Control experiments.

1c   2a   3ca, 0%

1c   2a   3ca, 0%

methodology is an economic and practical process for the preparation of benzylquinones (Scheme 2).

To elucidate the mechanism of the coupling reaction, several control experiments were carried out. Initially, when a radical inhibitor, TEMPO (2,2,6,6-tetra-methyl-piperidine-*N*-oxyl) or BHT (2,6-di-*tert*-butyl-4-methylphenol) were added into the reaction, the formation of the desired product was completely suppressed (Scheme 3). These results indicated that this oxidative coupling reaction involved a radical pathway.

On the basis of the literature reports and observations above, a plausible mechanism for the oxidative radical process is illustrated in Scheme 4. At the beginning, homolysis of DTBP gives *tert*-butoxy radical intermediate **A** under the conditions of heating,[17] which could abstract hydrogen from toluene **2a** to afford a benzyl radical **B**.[18] Due to nucleophilic nature of the benzyl radical, it would be attracted to the electrophilic C-2 or C-3 positions of naphthoquinone, and subsequently, addition of

the radical intermediate **B** to the double bond of 2-methyl-1,4-naphthoquinone **1c** afforded the radical intermediate **C**. Product **3ca** can be formed from H radical abstraction by *tert*-butoxy radical.[19]

Conclusions

In summary, we have descried a cross-dehydrogenative coupling reaction of quinones with toluene derivatives using DTBP as the oxidant without any catalyst. The reactions of substrates containing various functional groups proceeded smoothly to give the desired products in moderate to good yields. This protocol provides an efficient and green way for the preparation of compounds containing the benzylquinones structural unit. These compounds have potential in biological and pharmaceutical applications. Further investigations to study the synthetic utility of this reaction are currently in progress.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Notes and references

1 (*a*) K. Yuan, X. Wang and S.-N. Wang, *Org. Lett.*, 2018, **20**, 1617; (*b*) C. Zhang, C. B. Santiago, J. M. Crawford and M. S. Sigman, *J. Am. Chem. Soc.*, 2015, **137**, 15668; (*c*) Y. Ai, Y. Hu, F.-H. Kang, Y.-S. Lai, Y.-J. Jia, Z.-J. Huang, S.-X. Peng, H. Ji, J.-D. Tian and Y.-H. Zhang, *J. Org. Chem.*, 2015, **58**, 4506; (*d*) R. Zhang, S. Jin, Q. Liu, S. Lin and Z. Yan, *J. Org. Chem.*, 2018, **83**, 13030.

2 (*a*) C.-J. Li, *Acc. Chem. Res.*, 2009, **42**, 335; (*b*) C. Liu, H. Zhang, W. Shi and A. Lei, *Chem. Rev.*, 2011, **111**, 1780; (*c*) R. P. Pandit and Y. R. Lee, *Adv. Synth. Catal.*, 2014, **356**, 3171; (*d*) P. T. Parvatkar, R. Manetsch and B. K. Banik, *Chem. Asian J*, 2019, **14**, 6.

3 (*a*) C.-J. Li, *Acc. Chem. Res.*, 2009, **42**, 335; (*b*) S. A. Girard, T. Knauber and C.-J. Li, *Angew. Chem. Int. Ed*, 2014, **53**, 74; *Angew. Chem.*, 2014, **126**, 76; (*c*) A. Batra, P. Singh and K. N. Singh, *Eur. J. Org. Chem.*, 2016, 4927; (*d*) C. J. Scheuermann, *Chem.–Asian J.*, 2010, **5**, 436; (*e*) L. Lv and Z. Li, *Top. Curr. Chem.*, 2016, **374**, 38.

4 (*a*) X. F. Wu, J. L. Gong and X. Qi, *Org. Biomol. Chem.*, 2014, **12**, 5807; (*b*) C.-L. Sun and Z.-J. Shi, *Chem. Rev.*, 2014, **114**, 9219; (*c*) S. Roscales and A. G. Csaky, *Chem. Soc. Rev.*, 2014, **43**, 8215; (*d*) F. Jafarpour and M. Abbasnia, *J. Org. Chem.*, 2016, **81**, 11982.

5 (*a*) R. H. Thomson, *Naturally Occurring Quinones IV*, Blackie Academic, London, 1997; (*b*) C. Puder, K. Wagner, R. Vettermann, R. Hauptmann and O. Potterat, *J. Nat.*
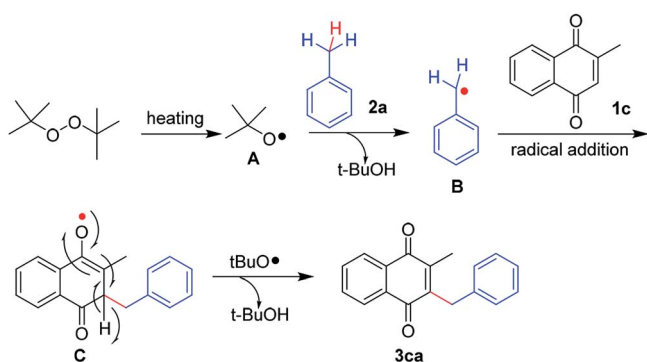
Scheme 4   Proposed reaction mechanism.

Prod., 2005, **68**, 323; (*c*) C. Asche, *Mini-Rev. Med. Chem.*, 2005, **5**, 449; (*d*) J.-K. Liu, *Chem. Rev.*, 2006, **106**, 2209.

6 (*a*) A. Mäntylä, T. Garnier, J. Rautio, T. Nevalainen, J. Vepsaelainen, A. Koskinen, S. L. Croft and T. Järvinen, *J. Med. Chem.*, 2004, **47**, 188; (*b*) J. Grolig and R. Wagner, "Naphthoquinones", *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, 2005; (*c*) A. Baramee, A. Coppin, M. Mortuaire, L. Pelinski, S. Tomavo and J. Brocard, *Bioorg. Med. Chem.*, 2006, **14**, 1294; (*d*) J. M. Finefield, D. H. Sherman, M. Kreitman and R. M. Williams, *Angew. Chem. Int. Ed*, 2012, **51**, 4802; *Angew. Chem.*, 2012, **124**, 4886; (*e*) C. Huo, X. Xu, J. An, X. Jia, X. Wang and C. Wang, *J. Org. Chem.*, 2012, **77**, 8310.

7 (*a*) P. Sidorov, I. Desta, M. Chessé, D. Horvath, G. Marcou, A. Varnek, E. Davioud-Charvet and M. Elhabiri, *ChemMedChem*, 2016, **11**, 1339; (*b*) T. Müller, L. Johann, B. Jannack, M. Brückner, D. A. Lanfranchi, H. Bauer, C. Sanchez, V. Yardley, C. Deregnaucourt, J. Schrével, M. Lanzer, R. H. Schirmer and E. Davioud-Charvet, *J. Am. Chem. Soc.*, 2011, **133**, 11557.

8 (*a*) S. Guo, P. S. Kumar and M. Yang, *Adv. Synth. Catal.*, 2017, **359**, 2; (*b*) J. Sun, Y. Zhang, S. Mathan, Y. Wang and Y. Pan, *J. Org. Chem.*, 2016, **81**, 3380; (*c*) N. Okugawa, K. Moriyama and H. Togo, *J. Org. Chem.*, 2017, **82**, 170; (*d*) S. Liu, A. Liu, Y. Zhang and W. Wang, *Chem. Sci.*, 2017, **8**, 4044; (*e*) L. Wang, J. Cao, Q. Chen and M. He, *J. Org. Chem.*, 2015, **80**, 4743; (*f*) Q. Xia, W. Chen and H. Qiu, *J. Org. Chem.*, 2011, **76**, 7577; (*g*) Q. Yang, P. Y. Choy, W. C. Fu, B. Fan and F. Y. Kwong, *J. Org. Chem.*, 2015, **80**, 11193; (*h*) M. K. Singh, H. K. Akula, S. Satishkumar, L. Stahl and M. K. Lakshman, *ACS Catal.*, 2016, **6**, 1921; (*i*) Z. Luo, Z. Jiang, W. Jiang and D. Lin, *J. Org. Chem.*, 2018, **83**, 3710; (*j*) L.-Y. Xie, L.-L. Jiang, J.-X. Tan, Y. Wang, X.-Q. Xu, B. Zhang, Z. Cao and W.-M. He, *ACS Sustainable Chem. Eng.*, 2019, **7**, 14153; (*k*) L.-Y. Xie, S. Peng, T.-G. Fan, Y.-F. Liu, M. Sun, L.-L. Jiang, X.-X. Wang, Z. Cao and W.-M. He, *Sci. China. Chem*, 2019, **62**, 460.

9 S.-L. Zhou, L.-N. Guo and X.-H. Duan, *Eur. J. Org. Chem.*, 2014, **2014**, 8094.

10 B. Liu, L. Gu and J. Zhang, *Recl. Trav. Chim. Pays-Bas*, 1991, **110**, 99.

11 D. R. Sutherland, M. Veguillas, C. L. Oates and A.-L. Lee, *Org. Lett.*, 2018, **20**, 6863.

12 (*a*) H. Togo, in *Advanced Free Radical Reactions for Organic Synthesis*, Elsevier, Amsterdam, 1st edn, 2004; (*b*) H. Yi, G. Zhang, H. Wang, Z. Huang, J. Wang, A. K. Singh and A. Lei, *Chem. Rev.*, 2017, **117**, 9016; (*c*) W. Liu and J. T. Groves, *Acc. Chem. Res.*, 2015, **48**, 1727; (*d*) H. Yu, B. Hu and H. Huang, *Chem.–Asian J.*, 2018, **24**, 7114.

13 For selected examples: (*a*) G. Qin, X. Chen, L. Yang and H. Huang, *ACS Catal.*, 2015, **5**, 2882; (*b*) K. Li, Q. Wu, J. Lan and J. You, *Nat. Commun.*, 2015, **6**, 8404; (*c*) X. Huang, T. Bergsten and J. T. Groves, *J. Am. Chem. Soc.*, 2015, **137**, 5300; (*d*) W. Zhang, F. Wang, S. D. McCann, D. Wang, P. Chen, S. S. Stahl and G. Liu, *Science*, 2016, **353**, 1014; (*e*) W. Zhang, P. Chen and G. Liu, *J. Am. Chem. Soc.*, 2017, **139**, 7709; (*f*) G. Qin, Y. Wang and H. Huang, *Org. Lett.*, 2017, **19**, 6352; (*g*) W. Liu, M.-J. Cheng, R. J. Nielsen, W. A. Goddard III and J. T. Groves, *ACS Catal.*, 2017, **7**, 4182; (*h*) M. Rafiee, F. Wang, D. P. Hruszkewycz and S. S. Stahl, *J. Am. Chem. Soc.*, 2018, **140**, 22; (*i*) S.-h. Hao, L.-X. Li, D.-Q. Dong, Z.-L. Wang and X.-Y. Yu, *Tetrahedron Lett.*, 2018, **59**, 4073.

14 (*a*) B. R. Ai, X. L. Chen, Y. Dong, L. Tang and J. Y. Wang, *Synthesis*, 2017, **49**, 4017; (*b*) X. L. Chen, Y. Dong, S. He, R. Zhang and J. Y. Wang, *Synlett*, 2019, **30**, 615; (*c*) L.-Y. Xie, T.-G. Fang, J.-X. Tan, B. Zhang, Z. Cao, L.-H. Yang and W.-M. He, *Green Chem.*, 2019, **21**, 3858; (*d*) F.-L. Zeng, X.-L. Chen, S.-Q. He, K. Sun, Y. Liu, R. Fu, L.-B. Qu, Y.-F. Zhao and B. Yu, *Org. Chem. Front.*, 2019, **6**, 1476; (*e*) Z. Li, W. Wang, H. Jian, W. Li, B. Dai and L. He, *Chin. Chem. Lett.*, 2019, **30**, 386; (*f*) L.-Y. Xie, Y. Duan, L.-H. Lu, Y.-J. Li, S. Peng, C. Wu, K.-J. Liu, Z. Wang and W.-M. He, *ACS Sustainable Chem. Eng.*, 2017, **5**, 10407; (*g*) L.-Y. Xie, S. Peng, J.-X. Tan, R.-X. Sun, X. Yu, N.-N. Dai, Z.-L. Tang, X. Xu and W.-M. He, *ACS Sustainable Chem. Eng.*, 2018, **6**, 16976; (*h*) C. Wu, X. Xin, Z.-M. Fu, L.-Y. Xie, K.-J. Liu, Z. Wang, W. Li, Z.-H. Yuan and W.-M. He, *Green Chem.*, 2017, **19**, 1983.

15 V. F. De, S. V. Van, M. Waroquier, P. Geerlings and P. F. De, *Org. Lett.*, 2007, **9**, 2721.

16 (*a*) J. Aleman, B. Richter and K. A. Jørgensen, *Angew. Chem., Int. Ed.*, 2007, **46**, 5515; (*b*) J. Aleman, S. Cabrera, E. Maerten, J. Overgaard and K. A. Jørgensen, *Angew. Chem., Int. Ed.*, 2007, **46**, 5520; (*c*) J. Aleman, C. B. Jacobsen, K. Frisch, J. Overgaard and K. A. Jørgensen, *Chem. Commun.*, 2008, 632; (*d*) Z. He, T. Liu, H. Tao and C.-J. Wang, *Org. Lett.*, 2012, **14**, 6230; (*e*) Ł. Albrecht, C. V. Gomez, C. B. Jacobsen and K. A. Jørgensen, *Org. Lett.*, 2013, **15**, 3010; (*f*) T. K. Johansen, C. V. Gomez, J. R. Bak, R. L. Davis and K. A. Jørgensen, *Chem. - Eur. J*, 2013, **19**, 16518; (*g*) C. Martín-Santos, C. Jarava-Barrera, S. delPozo, A. Parra, S. Díaz-Tendero, R. MasBalleste, S. Cabrera and J. Alema, *Angew. Chem., Int. Ed*, 2014, **53**, 8184; (*h*) J. Blom, T. K. Johansen, F. Jensen and K. A. Jørgensen, *Chem. Commun.*, 2016, 52; (*i*) A. Skrzyńska, M. Romaniszyn, D. Pomikło and Ł. Albrecht, *J. Org. Chem.*, 2018, **83**, 5019.

17 (*a*) Z.-Q. Xu, C. Wang, L. Li, L. Duan and Y.-M. Li, *J. Org. Chem.*, 2018, **83**, 9718; (*b*) X.-H. Ouyang, R.-J. Song, B. Liu and J.-H. Li, *Adv. Synth. Catal.*, 2016, **358**, 1903; (*c*) J. Zhao, H. Fang, P. Qian, J. Han and Y. Pan, *Org. Lett.*, 2014, **16**, 5342.

18 (*a*) H. Yang, H. Yan, P. Sun, Y. Zhu, L. Lu, D. Liu, G. Rong and J. Mao, *Green Chem.*, 2013, **15**, 976; (*b*) S.-L. Zhou, L.-N. Guo, S. Wang and X.-H. Duan, *Chem. Commun.*, 2014, **50**, 3589; (*c*) Z. Li, L. Cao and C.-J. Li, *Angew. Chem. Int. Ed*, 2007, **46**, 6505.

19 (*a*) P. Patil, A. Nimonkar and K. G. Akamanchi, *J. Org. Chem.*, 2014, **79**, 2331; (*b*) A. Ilangovan, S. Saravanakumar and S. Malayappasamy, *Org. Lett.*, 2013, **15**, 4968; (*c*) See ref. 11.