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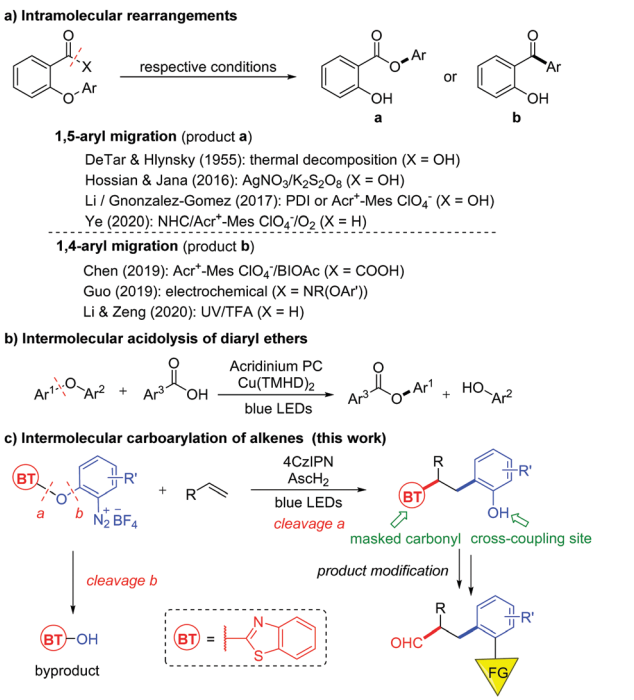
Photocatalytic intermolecular carboarylation of alkenes by selective C–O bond cleavage of diarylethers†

Meishan Ji,[a] Chenyang Chang,[a] Xinxin Wu[a] and Chen Zhu *[ab]

Disclosed herein is a novel radical-mediated intermolecular carboarylation of alkenes by cleaving inert C–O bonds. The strategically designed arylbenzothiazolylether diazonium salts are harnessed as dual-function reagents. A vast array of alkenes are proven to be suitable substrates. The benzothiazolyl moiety in the products serves as the formyl precursor, and the OH residue provides the cross-coupling site for further product elaboration, indicating the robust transformability of the products.

The utilization and transformation of natural aromatic resources, such as lignins, by cleaving arylether C–O bonds has attracted much attention over the past few decades.[1] Nevertheless, the good stability arising from high bond dissociation energies (BDEs $\sim$ 100 kcal mol^{-1}) results in the difficult cleavage of C(Ar)–O bonds, especially diarylether C–O bonds.[2] Many efficient methods involving transition-metal catalysis,[3] hydrogenolyses with the aid of a strong acid/base at high temperature,[4] electrocatalysis[5a,5b] or NHC-organocatalysis[5c] have been disclosed to enable inert C(Ar)–O bond cleavage. Alternatively, radical-mediated *intramolecular* rearrangements including 1,4-/1,5-aryl migration provide an ingenious tactic for the diarylether C–O bond cleavage (Scheme 1a).[6] Notably in 2020, Li and co-workers disclosed a photocatalytic *intermolecular* C–O bond cleavage of diaryl ethers by means of acidolysis, leading to esters and phenols (Scheme 1b).[6i]

Alkenes are ubiquitous in naturally occurring molecules, and also are bulk chemicals extensively used as feedstocks in synthetic chemistry. Radical-mediated functionalization of alkenes supplies a powerful tool for alkene utilization.[7] Notwithstanding the enormous achievements in this area, to the best of our knowledge, the radical-mediated intermolecular carboarylation of alkenes remains underdeveloped.[8] To attain this elusive goal, we attempted to break a diarylether into two parts by cleaving the C(Ar)–O bond and incorporate both fragments into alkenes. Herein, we provide the proof-of-principle studies (Scheme 1c). With the use of the rationally designed arylbenzothiazolylether diazonium salts as a dual-function reagent, the radical carboarylation of alkenes readily proceeds under mild photochemical conditions.[9] The ether bond in the dual-function reagent not only acts as a linker but offers the OH residue as a cross-coupling site for late-stage product elaboration. The incorporated benzothiazolyl in the



Scheme 1 Radical-mediated selective cleavage of diarylether C–O bonds.

[a] Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, 199 Ren-Ai Road, Suzhou, Jiangsu 215123, China. E-mail: chzhu@suda.edu.cn
[b] Key Laboratory of Synthetic Chemistry of Natural Substances, Shanghai Institute of Organic Chemistry, Chinese Academy of Science, 345 Lingling Road, Shanghai 200032, China

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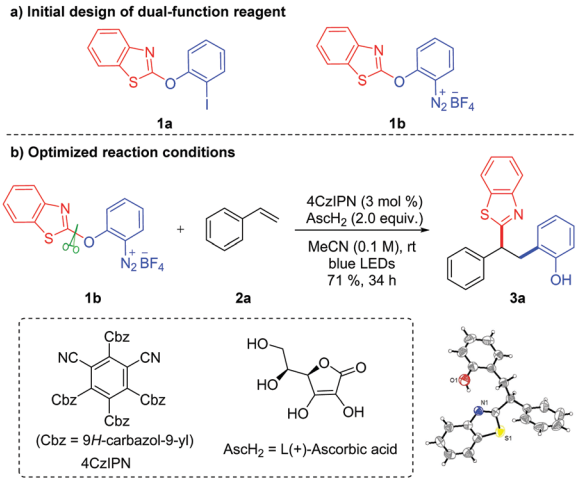
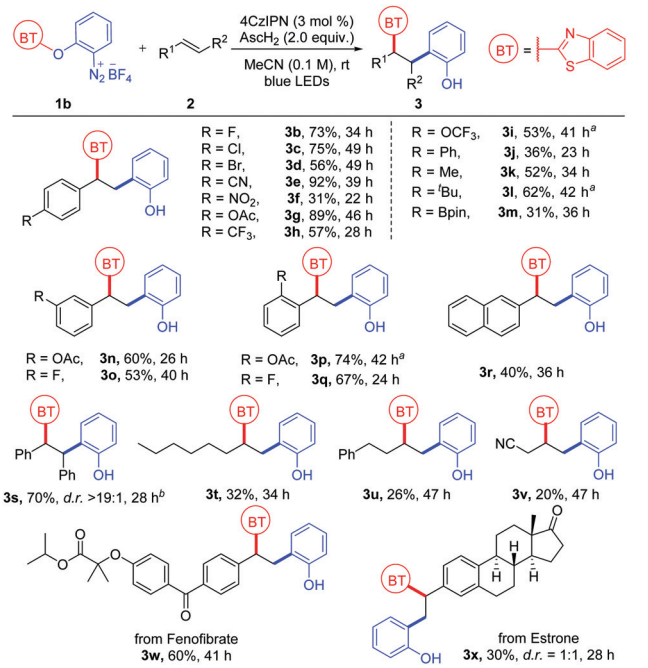


Scheme 2 Optimized reaction conditions.

products serves as a "masked carbonyl", which can be easily converted to a formyl group. Remarkably, the inert C–O bonds are readily cleaved during the heteroaryl migration process.

At the outset, two dual-function reagents **1a** and **1b** with different radical initiators, aryl iodide and diazonium salt, were prepared and examined in the reaction with styrene (Scheme 2a). A systematic survey of reaction parameters was carried out (for details, see ESI†). While the (iodo)phenylbenzothiazolylether **1a** gave rise to the desired carboarylated product in moderate yield, the diazonium surrogate **1b** afforded the same product **3a** in good yield under visible-light-mediated conditions (Scheme 2b). The structure of **3a** was unambiguously assigned by single crystal structure.[10] 4CzIPN was proven to be the most efficient photosensitizer, and ascorbic acid ($AscH_2$) functioned as both the H-source and single-electron reductant. It is worthily mentioned that reagent **1b** is readily accessible by a two-step synthesis, and can be stably stored at −20 °C for a long period.

Under the optimized reaction conditions, we assessed the generality of the protocol (Scheme 3). In general, aryl radicals are highly prone to perform intermolecular addition to electron-deficient alkenes. By using the current method, remarkably, a variety of alkenes bearing either electron-withdrawing or donating substituents were readily converted to the corresponding carboarylated products (**3b–3m**). Of particular note, electron-rich alkenes also delivered the desired products in acceptable yields (**3k** and **3l**). Several susceptible groups, such as NO_2, OAc, and Bpin, remained intact in the transformation. Changing the substitution from *para* to *meta* or *ortho* seemed to have little impact on the reaction outcome (**3n–3q**). An internal alkene, such as stilbene, was also able to afford the tetrasubstituted product **3s** with good yield and unique diastereoselectivity. Compared to aryl alkenes, unactivated alkenes such as aliphatic alkenes delivered relatively lower yields (**3t–3v**). This could be attributed to the highly active phenyl radical arising from **1b** showing a strong propensity of hydrogen abstraction, probably from the solvents, rather than addition to C=C bonds. Besides, previous studies have also revealed a comparatively fast rate constant of $k \sim 10^8\ m^{-1}\ s^{-1}$ for aryl radical additions to activated alkenes and

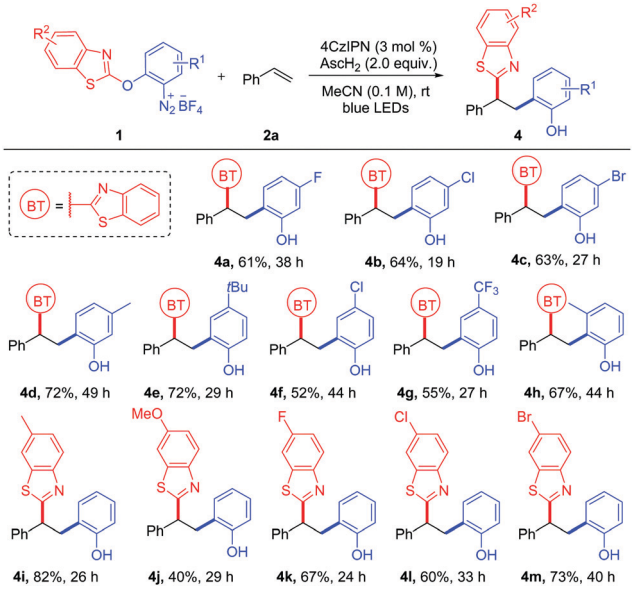


Scheme 3 Scope of alkenes. Reaction conditions: **1b** (1.5 equiv., 0.3 mmol), **2** (0.2 mmol), 4CzIPN (3 mol%), and $AscH_2$ (2.0 equiv., 0.4 mmol) in MeCN (2 mL, 0.1 M), irradiated by 30 W blue LEDs at r.t. under N_2. Yields of isolated products are given. [a]**1b** (2.0 equiv., 0.4 mmol). [b]**1b** (3.0 equiv., 0.6 mmol).

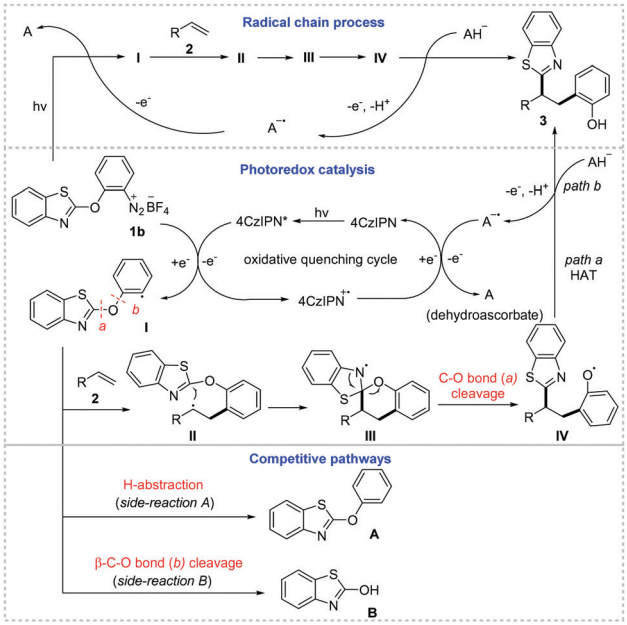
a lower rate constant for aryl radical additions to unactivated alkenes ($k \sim 10^7\ m^{-1}\ s^{-1}$). So undesired side reactions such as hydrogen abstraction are generally difficult to be suppressed.[11] Moreover, this method could be applied to the modification of complex natural products and drug derivatives, *e.g.* fenofibrate and estrone (**3w** and **3x**).

The variation of dual-function reagents was then investigated. A set of arylbenzothiazolylether diazonium salts were synthesized by varying the substitutions on both the benzothiazolyl and aryl parts (Scheme 4). The electronic properties of the substituents on aryl did not dominate the docking step (**4a–4g**). Halides, methyl, *tert*-butyl, and CF_3 groups were well tolerated, leading to the corresponding products in comparable yields. Notably, the case of **4h** also delivered a satisfactory yield regardless of the steric congestion in the dual-function reagent. In contrast, the substitution of benzothiazolyl appreciably influences the migration step (**4i–4m**). The presence of a methoxy group decreased the reaction yield (**4j**), but the reason is not clear so far. The methyl- and halide-decorated reagents resulted in the products with good yields (**4i**, **4k–4m**).

A set of experiments were conducted to probe the mechanistic pathway (for details, see ESI†). The Stern–Volmer study showed that the excited state of 4CzIPN was oxidatively quenched by the diazonium salt **1b**, but not by ascorbic acid. The reduction potential **1b** is −0.15 V *vs.* SCE, indicating that it could be readily reduced by the photo-excited 4CzIPN ($E_{1/2}$ ($PC^{\bullet+}/PC^*$) = −1.18 V *vs.* SCE)[12] to generate the aryl radical. The quantum yield of the reaction (Φ = 1.04) suggested that both photocatalytic and radical-chain pathways might be concurrently



Scheme 4 Variation of dual-function reagents. Reaction conditions: **1** (1.5 equiv., 0.3 mmol), **2a** (0.2 mmol), 4CzIPN (3 mol%), and $AscH_2$ (2.0 equiv., 0.4 mmol) in MeCN (2 mL, 0.1 M), irradiated by 30 W blue LEDs at r.t. under N_2. Yields of isolated products are given.

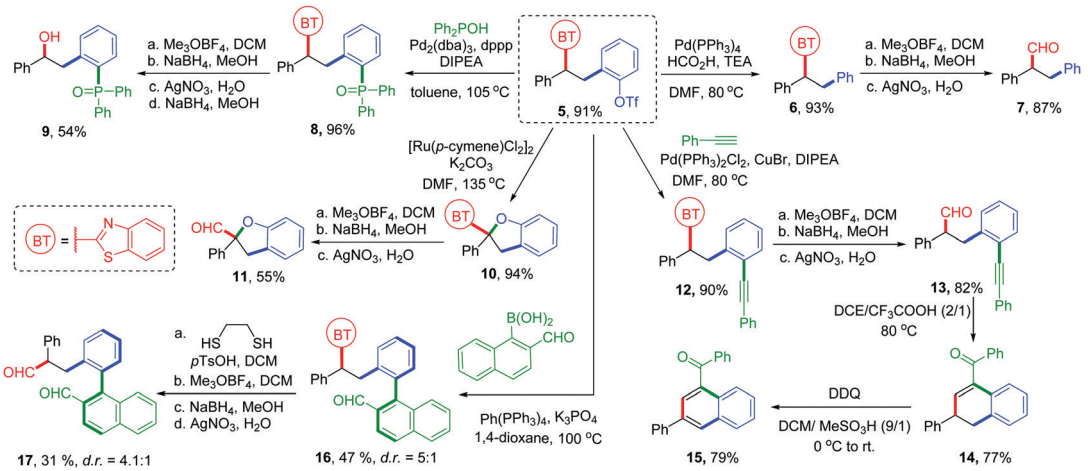


Scheme 5 Proposed reaction mechanism.

present in the reaction. This was also verified by light on–off experiments. After initiating the reaction with light irradiation for a few minutes, a very slow increase of product was still observed by further keeping the reaction in the dark for several hours, suggesting that a radical-chain process might be involved as a subordinary pathway along with the photoredox catalysis.

A plausible reaction mechanism is depicted in Scheme 5. Irradiation of 4CzIPN with visible light generates a photo-excited 4CzIPN* that reduces diazonium salt **1b** to aryl radical **I** through a single-electron transfer (SET) and meanwhile is transformed into $4CzIPN^{+\bullet}$. The addition of the aryl radical **I** to alkene forms a new radical intermediate **II**, which is immediately intercepted by the intramolecular benzothiazolyl *via* a six-membered cyclic transition state. The C–O bond homolysis of the spiro-*N*-radical intermediate **III** leads to the benzothiazolyl migration[13] and the formation of phenoxy radical **IV**. Notably, cleavage of the stronger C–O bond (***a***) is exclusive, while the competitive cleavage of the C–S bond does not occur. The H-abstraction by the phenoxy radical **IV** from ascorbic acid results in the final product **3** (*path a*). Alternatively, radical **IV** ($E_{p/2}$ = −0.68 V *vs.* SCE) is readily reduced by the ascorbate monoanion AH^- ($E^{red}_{p/2}$ ($AH^{\bullet}/AH^-$) = −1.38 V *vs.* SCE) to phenolate followed by protonation to give product **3** (*path b*). Meanwhile, oxidation of the *in situ* generated $A^{-\bullet}$ species to dehydroascorbate A ($E^{ox}_{p/2}$ ($A^{-\bullet}/A$) = +0.22 V *vs.* SCE)[14] by $4CzIPN^{+\bullet}$ ($E_{1/2}(PC/PC^{\bullet+})$ = +1.49 V *vs.* SCE)[12] regenerates 4CzIPN and perpetuates the photoredox catalytic cycle. The radical-chain process might be initiated through two routes: the homolysis of **1b** to generate aryl radical **I** under visible-light irradiation, or reduction of **1b** ($E^{red}_{p/2}$ = −0.15 V *vs.* SCE) to **I** by the $A^{-\bullet}$ species ($E^{red}_{p/2}$ ($A/A^{-\bullet}$) = −0.82 V *vs.* SCE). Then the transformation follows the same docking-migration cascade to afford product **3**. It should be noted that the highly reactive aryl radical **I** may be directly terminated through H-abstraction or β-C–O bond (***b***) cleavage. Both the byproducts **A** and **B** were observed in the reaction.

The utility of the protocol was manifested by the product transformations (Scheme 6). In line with the two facts that the OH residue supplies a cross-coupling site and the benzothiazolyl group serves as the precursor of carbonyl, the product **3a** was converted to a diverse range of valuable molecules. Firstly, the phenol moiety of **3a** was smoothly transformed into phenyl triflate by treating with Tf_2O and Et_3N, affording the versatile synthetic intermediate **5**. The triflate could be removed to form the parent product **6** in high yield. The benzothiazolyl group was then converted to a formyl **7** according to the well-established one-pot operation. Palladium-catalyzed phosphonylation of **5** produced phosphine oxide **8** in an excellent yield. Interestingly, the deprotection of benzothiazolyl alternatively unexpectedly yielded alcohol **9**, probably arising from the degradation of the formyl precursor. With the assistance of a ruthenium catalyst, a surprising $C(sp^3)$–H oxidation occurred, leading to the 2,2-diaryl substituted benzotetrafuran **10** in a good yield. The following conversion of benzothiazolyl furnished the corresponding benzotetrafuryl formaldehyde **11**. The Sonogashira coupling of **5** with phenylacetylene produced product **12**, which was then deprotected to give the corresponding aldehyde **13**. Annulation of **13** through the intramolecular alkyne-carbonyl metathesis (IACM) in the presence of DCE/TFA generated **14**, and the ensuing aromatization afforded the multi-functionalized naphthylene **15**. The Suzuki coupling of triflate **5** with naphthylboronic acid gave rise to the axially biaryl compounds **16**. The deprotection of **16** resulted in the biaryldial **17**, which may find use in asymmetric synthesis as an organocatalyst.[15]



Scheme 6 Product transformation.

In summary, we have achieved a radical-mediated intermolecular carboarylation of alkenes by cleaving inert C–O bonds. A set of dual-function reagents by using the diarylether bond as a linker are harnessed. In the radical cascade, the inert C–O bond is readily cleaved under mild photochemical conditions. A variety of alkenes including both activated and unactivated alkenes are proven to be a suitable substrate. Though in comparatively lower yields, the challenging transformation of unactivated aliphatic alkenes is still noteworthy. The benzothiazolyl moiety in the products functions as the precursor of formyl, and the OH residue offers the cross-coupling site that can be converted into many valuable functionalities, manifesting the robust transformability of the product. This protocol provides an efficient, metal-free approach for the radical intermolecular carboarylation of alkenes.

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Conflicts of interest

There are no conflicts to declare.

Notes and references

1 For selected examples, see: (*a*) F. Kakiuchi, M. Usui, S. Ueno, N. Chatani and S. Murai, *J. Am. Chem. Soc.*, 2004, **126**, 2706; (*b*) B.-T. Guan, Y. Wang, B.-J. Li, D.-G. Yu and Z.-J. Shi, *J. Am. Chem. Soc.*, 2008, **130**, 14468; (*c*) Y. Zhao and V. Snieckus, *J. Am. Chem. Soc.*, 2014, **136**, 11224; (*d*) N. E. S. Tay and D. A. Nicewicz, *J. Am. Chem. Soc.*, 2017, **139**, 16100; (*e*) M. Wang, O. Y. Gutierrez, D. Camaioni and J. A. Lercher, *Angew. Chem., Int. Ed.*, 2018, **57**, 3747; (*f*) W.-Q. Hu, S. Pan, X.-H. Xu, D. A. Vicic and F.-L. Qing, *Angew. Chem., Int. Ed.*, 2020, **59**, 16076.

2 For selected reviews, see: (*a*) J. Zakzeski, P. C. Bruijnincx, A. A. L. Jongerius and B. M. Weckhuysen, *Chem. Rev.*, 2010, **110**, 3552; (*b*) J. Cornella, C. Zarate and R. Martin, *Chem. Soc. Rev.*, 2014, **43**, 8081; (*c*) Z. Zhang, J. Song and B. Han, *Chem. Rev.*, 2017, **117**, 6834; (*d*) W. Schutyser, T. Renders, S. Van den Bosch, S. F. Koelewijn, G. T. Beckham and B. F. Sels, *Chem. Soc. Rev.*, 2018, **47**, 852; (*e*) Z. Qiu and C.-J. Li, *Chem. Rev.*, 2020, **120**, 10454.

3 (*a*) H. Rao and C.-J. Li, *Angew. Chem., Int. Ed.*, 2011, **50**, 8936; (*b*) H. Kinuta, M. Tobisu and N. Chatani, *J. Am. Chem. Soc.*, 2015, **137**, 1593; (*c*) M. Guo, J. Peng, Q. Yang and C. Li, *ACS Catal.*, 2018, **8**, 11174; (*d*) D. Cao, H. Zeng and C.-J. Li, *ACS Catal.*, 2018, **8**, 8873; (*e*) Y.-Y. Kong and Z.-X. Wang, *Adv. Synth. Catal.*, 2019, **361**, 5440; (*f*) X. Zeng, Y. Zhang, Z. Liu, S. Geng, Y. He and Z. Feng, *Org. Lett.*, 2020, **22**, 2950; (*g*) J.-X. Xie, J.-P. Cao, X.-Y. Zhao, W. Jiang, L. Zhao, M. Zhao and H.-C. Bai, *Energy Fuels*, 2021, **35**, 9599.

4 (*a*) V. M. Roberts, R. T. Knapp, X. Li and J. A. Lercher, *ChemCatChem*, 2010, **2**, 1407; (*b*) A. Fedorov, A. A. Toutov, N. A. Swisher and R. H. Grubbs, *Chem. Sci.*, 2013, **4**, 1640; (*c*) L. Yang, Y. Li and P. E. Savage, *Ind. Eng. Chem. Res.*, 2014, **53**, 2633.

5 (*a*) T. A. Thornton, N. F. Woolsey and D. E. Bartak, *J. Am. Chem. Soc.*, 1986, **108**, 6497; (*b*) W. B. Wu and J. M. Huang, *J. Org. Chem.*, 2014, **79**, 10189; (*c*) D. Janssen-Mgller, S. Singha, F. Lied, K. Gottschalk and F. Glorius, *Angew. Chem., Int. Ed.*, 2017, **56**, 6276.

6 (*a*) D. F. DeTar and A. Hlynsky, *J. Am. Chem. Soc.*, 1955, **77**, 4411; (*b*) A. Hossian and R. Jana, *Org. Biomol. Chem.*, 2016, **14**, 9768; (*c*) S.-F. Wang, X.-P. Cao and Y. Li, *Angew. Chem., Int. Ed.*, 2017, **56**, 13809; (*d*) J. C. Gonzalez-Gomez, N. P. Ramirez, T. Lana-Villarreal and P. Bonete, *Org. Biomol. Chem.*, 2017, **15**, 9680; (*e*) X. Chang, Q. Zhang and C. Guo, *Org. Lett.*, 2019, **21**, 10; (*f*) J. Li, Z. Liu, S. Wu and Y. Chen, *Org. Lett.*, 2019, **21**, 2077; (*g*) Q. Dou, C.-J. Li and H. Zeng, *Chem. Sci.*, 2020, **11**, 5740; (*h*) Z.-H. Xia, L. Dai, Z.-H. Gao and S. Ye, *Chem. Commun.*, 2020, **56**, 1525; (*i*) F.-F. Tan, X.-Y. He, W.-F. Tian and Y. Li, *Nat. Commun.*, 2020, **11**, 6126.

7 (*a*) T. Pintauer and K. Matyjaszewski, *Chem. Soc. Rev.*, 2008, **37**, 1087; (*b*) W. T. Eckenhoff and T. Pintauer, *Catal. Rev.*, 2010, **52**, 1.

8 (*a*) Y.-Y. Ma, D.-C. Zhang, Z.-Y. Yan, M.-F. Wang, C.-L. Bian, X.-L. Gao, E. E. Bunel and A.-W. Lei, *Org. Lett.*, 2015, **17**, 2174; (*b*) X.-H. Ouyang, J. Cheng and J.-H. Li, *Chem. Commun.*, 2018, **54**, 8745; (*c*) J.-H. Qin, M.-J. Luo, D.-L. An and J.-H. Li, *Angew. Chem., Int. Ed.*, 2021, **60**, 1861.

9 (*a*) T. P. Yoon, M. A. Ischay and J. Du, *Nat. Chem.*, 2010, **2**, 527; (*b*) J. M. R. Narayanam and C. R. J. Stephenson, *Chem. Soc. Rev.*, 2011, **40**, 102; (*c*) C. K. Prier, D. A. Rankic and D. W. MacMillan, *Chem. Rev.*, 2013, **113**, 5322.

10 DOI: 10.5517/ccdc.csd.cc28l5tw.

11 S. J. Garden, D. V. Avila, A. L. J. Beckwith, V. W. Bowry, K. U. Ingold and J. Lusztyk, *J. Org. Chem.*, 1996, **61**, 805.

12 E. Speckmeier, T. G. Fischer and K. Zeitler, *J. Am. Chem. Soc.*, 2018, **140**, 15353.

13 (*a*) X. Wu and C. Zhu, *Acc. Chem. Res.*, 2020, **53**, 1620; (*b*) Z. Wu, D. Wang, Y. Liu, L. Huan and C. Zhu, *J. Am. Chem. Soc.*, 2017, **139**, 1388; (*c*) X. Wu, M. Wang, L. Huan, D. Wang, J. Wang and C. Zhu, *Angew. Chem., Int. Ed.*, 2018, **57**, 1640; (*d*) J. Yu, Z. Wu and C. Zhu, *Angew. Chem., Int. Ed.*, 2018, **57**, 17156.

14 D. Njus, P. M. Kelley, Y.-J. Tu and H. B. Schlegel, *Free Radical Biol. Med.*, 2020, **159**, 37.

15 G. Liao, H. Chen, Y. Xia, B. Li, Q. Yao and B. Shi, *Angew. Chem., Int. Ed.*, 2019, **58**, 11464.

