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Metal-Free Domino Oligocyclization Reactions of Enynals and Enynones with Molecular Oxygen

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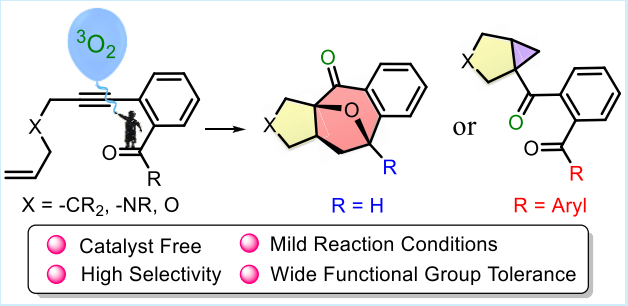
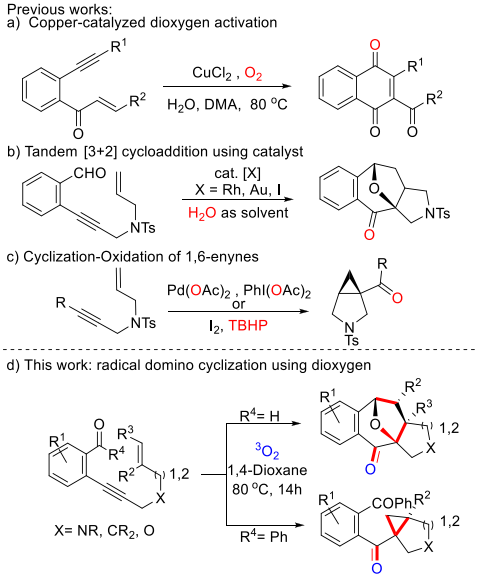
ABSTRACT: A novel metal-free direct addition of molecular oxygen to the C−C triple bond toward benzannulated oxygen-bridged seven-membered ring systems and aza[3.1.0]bicycle skeletons under $^3O_2$ atmosphere has been described. The reaction proceeds through at least three intramolecular C−O and C−C bond forming steps via green, simple, and unprecedented domino radical processes with high selectivity and good yields.



Applications of enynes and related π-precursors have attracted much attention in the generation of cyclic bioactive and complex organic structures as a particularly versatile building block for developing simple, practical, and green synthetic methods in modern organic chemistry.[1] Among these methods, considerable attention has been dedicated to the reaction of enynes with oxygen for regio- and chemoselective synthesis of complex structures as a simple and environmentally benign method.[2] Despite all the remarkable progress in the transition-metal-catalyzed oxygen utilization, an efficient and metal-free addition of molecular oxygen remains a great challenge.[3] To the best of our knowledge, molecular oxygen utilization on enyne scaffolds has been addressed in only a few reports.[4] Li et al. developed a copper-catalyzed cyclization of 1,6-enynes incorporating two oxygen atoms from O_2 and H_2O (Scheme 1a).[5] In another work, Ma et al. presented aerobic coupling−ketooxygenation reaction of enynes with alkynes in the presence of a Pd/Cu catalyst system under atmospheric pressure of O_2.[6]

Molecular oxygen is an ideal and readily available green oxidant that suffers from weak reactivity.[7] Therefore, previous reports have revealed applying various oxidizing reagents and oxygen sources, such as *tert*-butyl hydroperoxide (TBHP), H_2O, and acetate ion.[8] Oh et al. disclosed that domino [3 + 2] cycloaddition of *o*-(1,6-enynyl)benzaldehydes could be performed by using Rh(I) as a catalyst and H_2O as an oxidant for the synthesis of benzannulated oxygen-bridged seven-membered ring systems.[9] The same cycloisomerization through two different catalytic systems (iodine[10a] and gold[10b]) enabled the formation of the same product that has been reported by Liang (Scheme 1b). Also, cyclopropanation of 1,6-enynes using $Pd(OAc)_2$ as a catalyst and acetate ion as an oxygen source has been demonstrated by Sanford et al.[11] Wang et al. developed a

Scheme 1. Formation of C−O Double Bond with Different Oxygen Sources via Cycloisomerization of Enynals/Enynones and Enynes in Various Reports



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radical cascade cyclization reaction of 1,6-enynes that achieved the same aza[3.1.0]bicycles using TBHP as an oxidant and oxygen source (Scheme 1c).[12] After careful deliberation, we noticed that all previous examples involved metal-catalyzed condition or oxidizing reagents.[13] Herein, we present an unprecedented direct addition of molecular oxygen to enynals/enynones scaffolds through a novel metal-free radical domino reaction to synthesize benzannulated oxygen-bridged seven-membered ring systems and aza[3.1.0]bicycle structures (Scheme 1d).

The benzannulated oxygen-bridged seven-membered ring systems and aza[3.1.0]bicycle scaffolds are prevalent in natural products such as Bruguierol-C,[14] Brussonol,[15] Amitifadine,[16] and Indolizomycin[17] (Figure 1); consequently, the development of new green strategies that enable the rapid construction of such structures are in high demand.

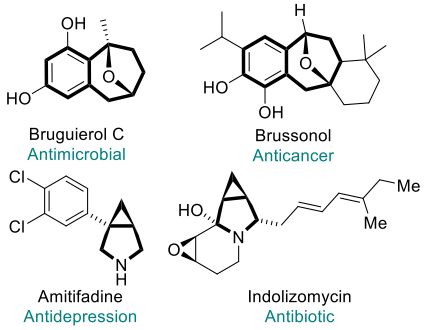
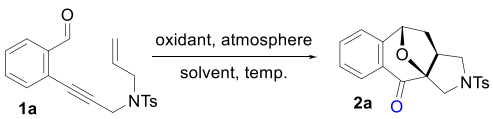


Figure 1. Structure of bioactive benzannulated oxygen-bridged seven-membered ring systems and aza[3.1.0]bicycle skeletons.

The initial reaction was carried out with enynal **1a** in the presence of potassium persulfate ($K_2S_2O_8$) (2.0 equiv) as an inexpensive and convenient oxidant in DCE at 80 °C under aerobic conditions. The desired product **2a** was obtained in 32% yield and with perfect regio- and diastereoselectivity (Table 1, entry 1). Interestingly, by using an oxygen atmosphere, the reaction yields dramatically increased to 70% (Table 1, entry 2). While the reaction could not occur under a nitrogen atmosphere (Table 1, entry 3). This result revealed that the reaction yield is dependent on oxygen concentration. Surprisingly, the control reaction confirmed that $K_2S_2O_8$ does not participate in the reaction yield (Table 1, entry 4). Screening of various solvents showed that DCE is the best solvent provided the desired product in 70% yield (Table 1, entries 4−8). Reducing the reaction temperature from 80 to 60 °C leads to the desired product in 60% yield (Table 1, entry 9), and increasing the reaction temperature from 80 to 100 °C toward the product in 69% yield (Table 1, entry 10).

Table 1. Optimization of the Reaction Conditions[a]

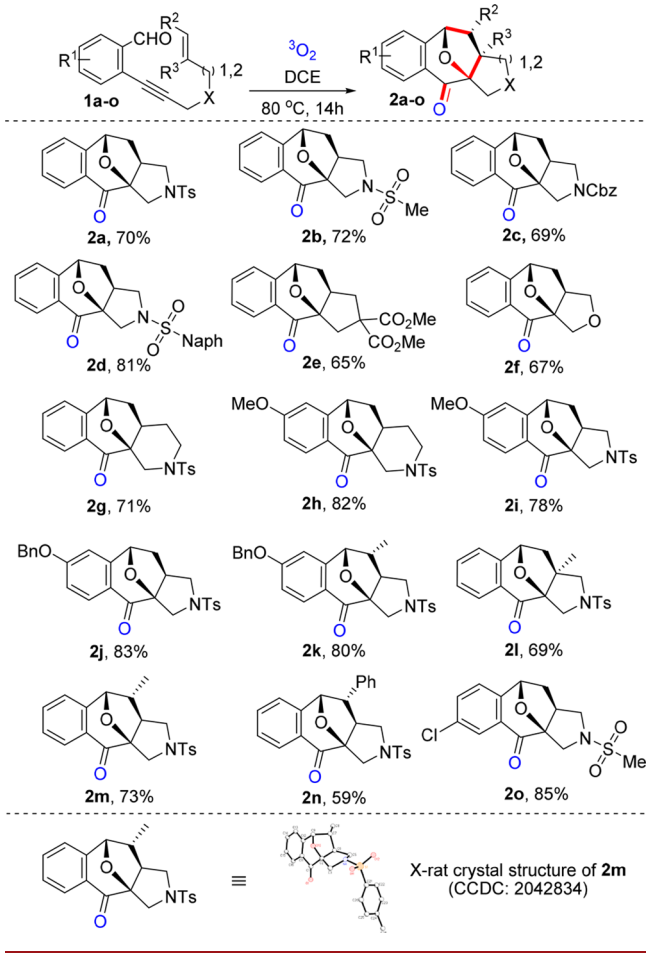


entry	oxidant[b]	atm.	solvent	temp. (°C)	yield[c] (%)
1	$K_2S_2O_8$	Air	DCE	80	32
2	$K_2S_2O_8$	O_2	DCE	80	70
3	$K_2S_2O_8$	N_2	DCE	80	NR[d]
4	–	**O_2**	**DCE**	**80**	**70**
5	–	O_2	1,4-dioxane	80	68
6	–	O_2	EtOH	80	38
7	–	O_2	H_2O	80	35
8	–	O_2	DMF	80	NR
9	–	O_2	DCE	60	60
10	–	O_2	DCE	100	69

[a]Reaction conditions: **1a** (71.0 mg, 0.2 mmol), DCE (1.0 mL), 1 atm of O_2, 80 °C and 14 h. [b]Oxidant (2.0 equiv). [c]Isolated yields, [d]NR = No reaction.

With optimized conditions in hand, the substrate scope was examined (Scheme 2). The reaction was well tolerated by diverse functional groups and provided various benzannulated oxygen-bridged seven-membered ring systems with good to high yields (Scheme 2). The effect of different linker atoms such as nitrogen, carbon, and oxygen (**1a−o**) undergoing the cycloisomerization reaction was first investigated. The reaction of nitrogen linker atom-substituted with sulfonyl and carbamate groups (**1a−d**) proceeded in 69−81% yields. In addition, carbon and oxygen linkers (**2e** and **2f**, respectively) proceeded in good yield. Using higher homologues in substrates (**1g−h**), a different series of products (**2g−h**) were obtained. Different R^1 substituents on the benzene ring were found to be tolerated. Thus, both electron-donating groups (−OMe, −OBn), as well as the electron-withdrawing group (−Cl), provided the cyclization products in 78−85%

Scheme 2. Scope of Benzannulated Oxygen-Bridged Seven-Membered Ring Systems Using Domino Radical Cyclization



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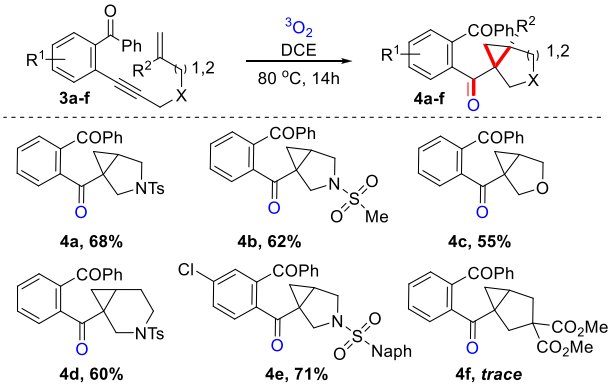
yields (**2h−k**, **2o**). Also, precursors with differently substituted alkene functions (**1k−n**) reacted to the corresponding products in high yields (59−80%) and perfect diastereoselectivities. The configuration of product **2m** was confirmed by X-ray crystallographic analysis.

Searching for a determining factor in the mechanism and to better evaluating the generality of the reaction, we prepared the enynone **3a** and its reaction with O_2 under standard conditions was investigated. Surprisingly, the reaction of enynone under standard conditions led to a cyclopropanation process with the formation of the bicyclic product **4a** in 68% yield (Scheme 3).

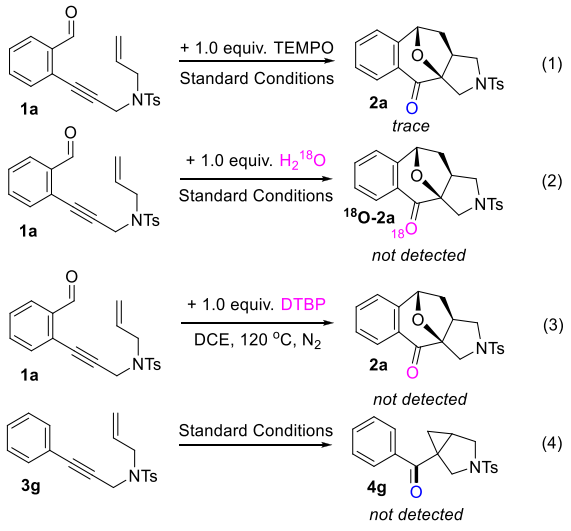
Scheme 3. Scope of Aza[3.1.0]bicycles Skeletons



Then, the scope of substrates **3a−f** was tested in the optimal conditions to achieve a library of diverse aza[3.1.0]bicycles skeletons **4a−f** (Scheme 3). The desired reaction was performed in the presence of different linkers in 55−71% yields. But when dimethylmalonate was used as a linker, the trace amount of the **4f** product was separated. Obtaining the mentioned products would facilitate the achievement of a plausible reaction mechanism.

To elucidate the reaction mechanism, we performed preliminary control experiments, as shown in Scheme 4. On exposure of **1a** to 1.0 equiv of TEMPO as a radical scavenger under the standard conditions, only trace amounts of **2a** were formed. This result suggested that the reaction presumably

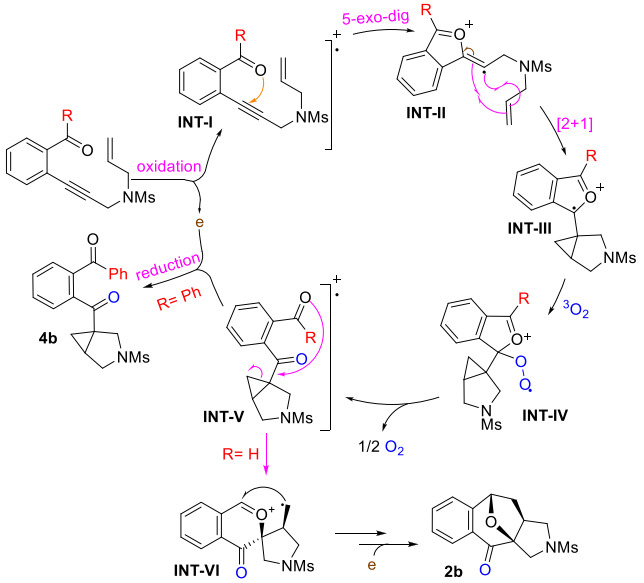
Scheme 4. Control Experiments



proceeds via radical intermediates (Scheme 4, eq 1). Next, the reaction of **1a** was carried out in the presence of ^{18}O-labeled water (under standard conditions), but did not furnish any obvious ^{18}O-labeled products, which ruled out water as an oxygen source (Scheme 4, eq 2). The reaction was tested in the presence of di-*tert*-butyl peroxide (DTBP) as a source of oxyradical, but the conversion has not happened (Scheme 4, eq 3). For investigation of the carbonyl group's role, substrate **3g** has been designed and tested in the optimal conditions, but it did not afford the desired product **4g** (Scheme 4, eq 4), which proved a vital role of the carbonyl group for the reaction to proceed. Finally, we analyzed the reaction in the absence of light, which showed that light has no effect on reaction progress.

As shown in a plausible mechanism (Scheme 5), initial cation radical **INT-I** was formed by one-electron oxidation

Scheme 5. Plausible Reaction Mechanism



with molecular oxygen, which followed subsequent 5-*exo*-dig cyclization to generate intermediate **INT-II**. Intramolecular [2 + 1] cyclization of the vinyl radical provides cation radical **INT-III**. The isobenzofuran cation radical **INT-III** is trapped by triplet dioxygen to obtain the intermediate **INT-IV**.

Next, the intermediate **INT-V** is obtained via cleavage of the O−O bond by the reaction with another radical cation **INT-IV**. This intermediate plays a crucial role in the mechanistic pathways to the two different products depending on whether R is a hydrogen or a phenyl substituent. In the case of R = phenyl, the product **4b** is obtained via electron-accepting from another substrate molecule, and consequently, this electron transfer regenerates another **INT-I**. As for path II, the 6-*exo*-tet cyclization of **INT-V** affords intermediate **INT-VI**.

Finally, the desired product **2b** is formed through a subsequent 5-*endo*-trig cyclization and one-electron reduction. This mechanism is proposed based on radical cation chain oxidation reactions.[18]

To reveal the detailed mechanism, we conducted the density functional theory (DFT) calculation. Precursors **1b** and **3b** were chosen as the substrates model for aldehydes and ketones. We expanded two possible mechanisms, as shown in Figure 2 and Figure S1. The first mechanism starts with direct

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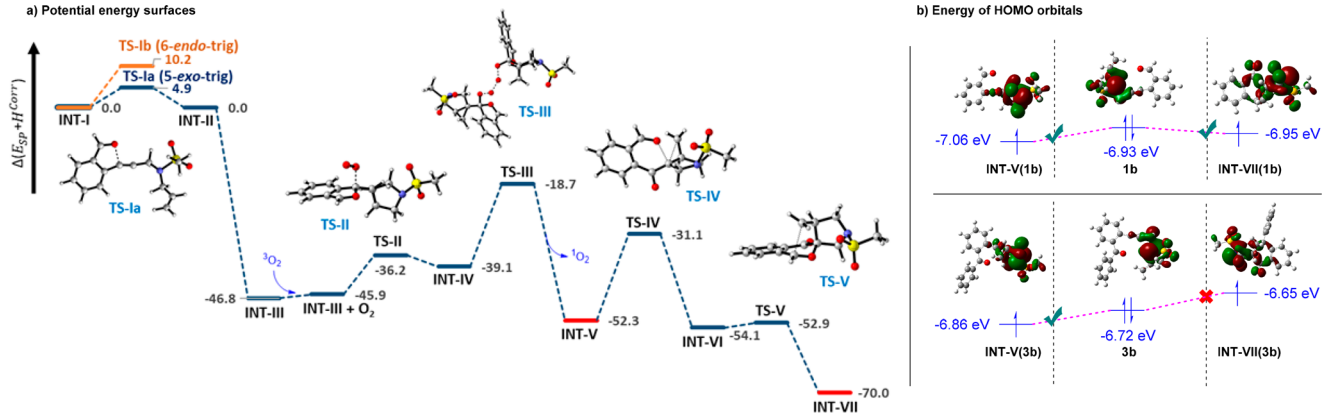

Figure 2. (a) Potential energy surfaces of the radical cation chain oxidation mechanism (for mechanistic details, see the Supporting Information). All energies are in kcal mol^{-1}. (b) HOMO orbitals of starting materials **1b**, **3b**, and related crucial intermediates. All energies are in eV.

dioxygen addition to the alkyne moiety, which the activation barrier is 31.9 kcal/mol, and the overall energy barrier (through **TS2-a**) is 32.5 kcal/mol. In the second proposed mechanism, as illustrated in Scheme 5 and Figure 2, the oxidized **1b** (**INT-I**) undergoes 5-*exo*-dig cyclization through **TS-I** (4.9 kcal/mol) to cation radical **INT-II**, which is immediately cyclized through [2 + 1] cycloaddition reaction to yield **INT-III** barrierlessly (Figure S2). The activation barrier of $^3O_2$ addition to oxidized **1b** (**INT-III**) is 10.6 kcal/mol (through **TS-II**). In other words, the energy barrier of molecular oxygen addition was reduced to 10.6 kcal/mol by starting materials oxidation. The overall energy barrier of this mechanism is 28.1 kcal/mol through **TS-III**, which releases $^1O_2$ via a bimolecular transition state to generate **INT-V**. Then, a stepwise [2 + 1] cycloaddition reaction of cyclopropyl with aldehyde segment leads to **INT-VII**. On the basis of Marcus theory, **INT-V** and **INT-VII** can be reduced to **2b** and **4b′** (is the same as **4b** but R = H) by **1b** (Table 2, and Figure 2b).

Table 2. Internal Reorganization, Activation, and Reaction Free Energies for the Electron Transfer Reactions[a]

Precursor	λ_i	ΔG	ΔG‡
	Nb + INT-V ⟶	INT-I + 4	
1b (Aldehyde)	18.7	-1.2	4.1
3b (Ketone)	16.9	-1.5	3.5
	Nb + INT-VII ⟶	INT-I + 2	
1b	14.9	-2.7	2.5
3b	11.3	-2.8	1.6

[a]All energies are in kcal mol^{-1}.

Products **2** are thermodynamic products in the reaction of aldehyde precursors. In the case of ketone **3b**, although the energy barriers of electron transfer of **3b** to related **INT-V** and **INT-VII** are 3.5 and 1.6 kcal/mol, respectively (Table 2), it seems that orbital energies are not appropriated for reduction of **INT-VII** (Figure 2b) by **3b**, and this reason probably controlled the chemoselectivity of reaction.

In conclusion, we have established an environmentally benign, novel, and facile method to synthesize benzannulated oxygen-bridged seven-membered ring systems and aza[3.1.0]-bicyclic skeletons through a domino radical cyclization with triplet oxygen. The carbonyl group could act as a vital group to construct the desired compounds. The present method affords a wide diversity of benzannulated oxygen-bridged seven-membered ring systems and novel aza[3.1.0]bicycles skeletons in high chemo- and diastereoselectivity and in good yields. This domino reaction could facilitate the generation of complex skeletons by forming several C−O and C−C bonds in one step.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c04272.

General experimental procedures, computational, characterization details, ^{1}H NMR, ^{13}C NMR, and HR-MS spectra of all compounds (PDF)

Accession Codes

CCDC 2042834 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Méndez, M.; Muñoz, M. P.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2001**, *123*, 10511−10520. (b) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 200−203. (c) Sun, J.; Conley, M. P.; Zhang, L.; Kozmin, S. *J. Am. Chem. Soc.* **2006**, *128*, 9705−9710. (d) Michelet, V.; Toullec, P. Y.; Genêt, J. P. *Angew. Chem., Int. Ed.* **2008**, *47*, 4268−4315. (e) Deng, G.-B.; Wang, Z.-Q.; Xia, J.-D.; Qian, P.-C.; Song, R.-J.; Hu, M.; Gong, L.-B.; Li, J.-H. *Angew. Chem., Int. Ed.* **2013**, *52*, 1535−1538. (f) Qiu, J.-K.; Jiang, B.; Zhu, Y.-L.; Hao, W.-J.; Wang, D.- C.; Sun, J.; Wei, P.; Tu, S.-J.; Li, G. *J. Am. Chem. Soc.* **2015**, *137*, 8928−8931. (g) Xuan, J.; Studer, A. *Chem. Soc. Rev.* **2017**, *46*, 4329−4346. (h) Hu, Y.; Bai, M.; Yang, Y.; Zhou, Q. *Org. Chem. Front.* **2017**, *4*, 2256−2275. (i) Song, L.; Tian, G.; Van Meervelt, L.; Van Der Eycken, E. V. *Org. Lett.* **2020**, *22*, 6537−6542.

(2) (a) Kim, N.; Kim, Y.; Park, W.; Sung, D.; Gupta, A. K.; Oh, C. H. *Org. Lett.* **2005**, *7*, 5289−5291. (b) Oh, C. H.; Ryu, J. H.; Lee, H. I. *Synlett* **2007**, *2007*, 2337−2342. (c) Oh, C. H.; Lee, J. H.; Lee, S. J.; Kim, J. Il; Hong, C. S. *Angew. Chem., Int. Ed.* **2008**, *47*, 7505−7507. (d) Ho Oh, C.; Lee, S. M.; Hong, C. S. *Org. Lett.* **2010**, *12*, 1308−1311. (e) Qian, D.; Zhang, J. *Chem. Commun.* **2011**, *47*, 11152−11154. (f) Han, J. W.; Lee, J. H.; Oh, C. H. *Synlett* **2013**, *24*, 1433−1437. (g) Kim, J. H.; Ray, D.; Hong, C. S.; Han, J. W.; Oh, C. H. *Chem. Commun.* **2013**, *49*, 5690−5692. (h) Liu, B.; Song, R. J.; Ouyang, X. H.; Li, Y.; Hu, M.; Li, J. H. *Chem. Commun.* **2015**, *51*, 12819−12822. (i) Oh, C. H.; Piao, L.; Jung, J.; Kim, J. *Asian J. Org. Chem.* **2016**, *5*, 1237−1241. (j) Zheng, J.; Li, Z.; Wu, W.; Jiang, H. *Org. Lett.* **2016**, *18*, 6232−6235. (k) Kim, K.; Kim, S.; Oh, C. H. *Synlett* **2018**, *29*, 354−358.

(3) (a) Hu, M.; Fan, J. H.; Liu, Y.; Ouyang, X. H.; Song, R. J.; Li, J. H. *Angew. Chem., Int. Ed.* **2015**, *54*, 9577−9580. (b) Biswas, P.; Paul, S.; Guin, J. *Angew. Chem., Int. Ed.* **2016**, *55*, 7756−7760. (c) Li, Y.; Pan, G. H.; Hu, M.; Liu, B.; Song, R. J.; Li, J. H. *Chem. Sci.* **2016**, *7*, 7050−7054. (d) Xu, X. D.; Cao, T. T.; Meng, Y. N.; Zhou, G.; Guo, Z.; Li, Q.; Wei, W. T. *ACS Sustainable Chem. Eng.* **2019**, *7*, 13491−13496. (e) Xia, X. F.; Zhao, M.; He, W.; Zou, L.; San, X.; Wang, D. *Adv. Synth. Catal.* **2020**, *362*, 3621−3626. (f) Qiu, Y. F.; Niu, Y. J.; Song, X. R.; Wei, X.; Chen, H.; Li, S. X.; Wang, X. C.; Huo, C.; Quan, Z. J.; Liang, Y. M. *Chem. Commun.* **2020**, *56*, 1421−1424. (g) Anderson, T. E.; Woerpel, K. A. *Org. Lett.* **2020**, *22*, 5690−5694.

(4) (a) Xia, X. F.; Zhang, G. W.; Wang, D.; Zhu, S. L. *J. Org. Chem.* **2017**, *82*, 8455−8463. (b) Xia, X. F.; He, W.; Zhang, G. W.; Wang, D. *Org. Chem. Front.* **2019**, *6*, 342−346.

(5) Wang, Z.-Q.; Zhang, W.-W.; Gong, L.-B.; Tang, R.-Y.; Yang, X.-H.; Liu, Y.; Li, J.-H. *Angew. Chem., Int. Ed.* **2011**, *50*, 8968−8973.

(6) Ling, F.; Li, Z.; Zheng, C.; Liu, X.; Ma, C. *J. Am. Chem. Soc.* **2014**, *136*, 10914−10917.

(7) (a) Lu, Q.; Zhang, J.; Zhao, G.; Qi, Y.; Wang, H.; Lei, A. J. *J. Am. Chem. Soc.* **2013**, *135*, 11481−11484. (b) Shen, T.; Zhang, Y.; Liang, Y. F.; Jiao, N. *J. Am. Chem. Soc.* **2016**, *138*, 13147−13150. (c) Peng, X.-X.; Wei, D.; Han, W.-J.; Chen, F.; Yu, W.; Han, B. *ACS Catal.* **2017**, *7*, 7830−7834. (d) Liang, Y.-F.; Jiao, N. *Acc. Chem. Res.* **2017**, *50*, 1640−1653.

(8) (a) Tong, X.; Beller, M.; Tse, M. K. *J. Am. Chem. Soc.* **2007**, *129*, 4906−4907. (b) Tsujihara, T.; Takenaka, K.; Onitsuka, K.; Hatanaka, M.; Sasai, H. *J. Am. Chem. Soc.* **2009**, *131*, 3452−3453. (c) Liu, B.; Cheng, J.; Li, Y.; Li, J. H. *Chem. Commun.* **2019**, *55*, 667−670.

(9) Shin, S.; Gupta, A. K.; Rhim, C. Y.; Oh, C. H. *Chem. Commun.* **2005**, 4429−4431.

(10) (a) Xie, Y. X.; Yan, Z. Y.; Qian, B.; Deng, W. Y.; Wang, D. Z.; Wu, L. Y.; Liu, X. Y.; Liang, Y. M. *Chem. Commun.* **2009**, 5451−5453. (b) Song, X. R.; Xia, X. F.; Song, B.; Tian, X.; Zhu, H. T.; Zhou, A. X.; Liu, X. Y.; Liang, Y. M. *Asian J. Org. Chem.* **2013**, *2*, 755−762.

(11) Welbes, L. L.; Lyons, T. W.; Cychosz, K. A.; Sanford, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 5836−5837.

(12) Mutra, M. R.; Dhandabani, G. K.; Li, J.; Wang, J. J. *Chem. Commun.* **2020**, *56*, 2051−2054.

(13) (a) Yin, G.; Liu, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 5442−5445. (b) Oh, C. H.; Lee, S. J.; Lee, J. H.; Na, Y. J. *Chem. Commun.* **2008**, 5794−5796. (c) Kusama, H.; Ishida, K.; Funami, H.; Iwasawa, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 4903−4905. (d) Oh, C. H.; Yi, H. J.; Lee, J. H.; Lim, D. H. *Chem. Commun.* **2010**, *46*, 3007−3009. (e) Feng, J.-J.; Zhang, J. *J. Am. Chem. Soc.* **2011**, *133*, 7304−7307. (f) Peng, H.; Liu, G. *Org. Lett.* **2011**, *13*, 772−775. (g) Song, X. R.; Xia, X. F.; Song, Q. B.; Yang, F.; Li, Y. X.; Liu, X. Y.; Liang, Y. M. *Org. Lett.* **2012**, *14*, 3344−3347. (h) Wang, K. B.; Ran, R. Q.; Xiu, S. D.; Li, C. Y. *Org. Lett.* **2013**, *15*, 2374−2377. (i) Toh, K. K.; Biswas, A.; Wang, Y. F.; Tan, Y. Y.; Chiba, S. *J. Am. Chem. Soc.* **2014**, *136*, 6011−6020. (j) Jiao, Z.-W.; Tu, Y.-Q.; Zhang, Q.; Liu, W.-X.; Zhang, S.-Y.; Wang, S.-H.; Zhang, F.-M.; Jiang, S. *Nat. Commun.* **2015**, *6*, 7332. (k) Luo, C.; Wang, Z.; Huang, Y. *Nat. Commun.* **2015**, *6*, 10041−10046. (l) Lanzi, M.; Santacroce, V.; Balestri, D.; Marchiò, L.; Bigi, F.; Maggi, R.; Malacria, M.; Maestri, G. *Angew. Chem., Int. Ed.* **2019**, *58*, 6703−6707. (m) Xu, T.; Wang, D.; Tong, X. *Org. Lett.* **2019**, *21*, 5368−5372. (n) Murai, M.; Taniguchi, R.; Takai, K. *Org. Lett.* **2020**, *22*, 3985−3988. (o) Huang, X.; Nguyen, M. H.; Pu, M.; Zhang, L.; Chi, Y. R.; Wu, Y. D.; Zhou, J. S. *Angew. Chem., Int. Ed.* **2020**, *59*, 10814−10818.

(14) (a) Solorio, D. M.; Jennings, M. P. *J. Org. Chem.* **2007**, *72*, 6621−6623. (b) Fañanás, F. J.; Fernández, A.; Çevic, D.; Rodriguez, F. *J. Org. Chem.* **2009**, *74*, 932−934.

(15) (a) Martinez-Solorio, D.; Jennings, M. P. *Org. Lett.* **2009**, *11*, 189−192. (b) Ahmad, A.; Burtoloso, A. C. B. *Org. Lett.* **2019**, *21*, 6079−6083.

(16) (a) Xu, F.; Murry, J. A.; Simmons, B.; Corley, E.; Fitch, K.; Karady, S.; Tschaen, D. *Org. Lett.* **2006**, *8*, 3885−3888. (b) Xu, F.; Simmons, B.; Reamer, R. A.; Corley, E.; Murry, J.; Tschaen, D. *J. Org. Chem.* **2008**, *73*, 312−315.

(17) (a) Kim, G.; Chu-Moyer, M. Y.; Danishefsky, S. J.; Schulte, G. K. *J. Am. Chem. Soc.* **1993**, *115*, 30−39. (b) Kim, G.; Chu-Moyer, M. Y.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 2003−2005.

(18) (a) Pickett, J. E. *Non-Free Radical Oxidation Mechanisms in InService Life Prediction of Polymers and Plastics Exposed to Outdoor Weathering*; White, C. C, White, K. M, Pickett, J. E., Eds.; William Andrew Publishing: Norwich, 2018; pp 283−300. (b) Rostami, A.; Wang, Y.; Arif, A. M.; McDonald, R.; West, F. G. *Org. Lett.* **2007**, *9*, 703−706.