Organic Letters
Letter
pubs.acs.org/OrgLett

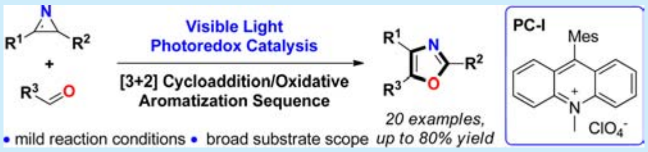
[3 + 2] Cycloaddition/Oxidative Aromatization Sequence via Photoredox Catalysis: One-Pot Synthesis of Oxazoles from 2*H*-Azirines and Aldehydes

Ting-Ting Zeng, Jun Xuan, Wei Ding, Kuan Wang, Liang-Qiu Lu,* and Wen-Jing Xiao*

Key Laboratory of Pesticide and Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University, Wuhan 430079, China

Supporting Information

ABSTRACT: A novel [3 + 2] cycloaddition/oxidative aromatization sequence via visible light-induced photoredox catalysis is disclosed. It provides a general synthetic route to 2,4,5-trisubstituted oxazoles from easily accessible 2*H*-azirines and aldehydes under mild reaction conditions. The potential of this strategy was further demonstrated by the rapid synthesis of a cyclooxygenase-2 inhibitor as well as the success of employing electron-deficient alkenes and imines as the reaction partners.

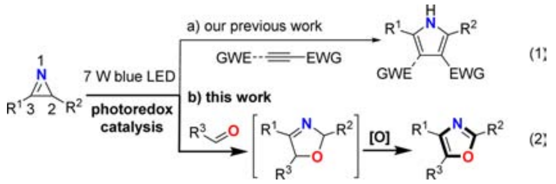


2*H*-Azirines, though a strained three-membered ring, are bench-stable and readily available reagents first reported by Neber and Burgard in 1932.[1] Due to their inherent reactivity, 2*H*-azirines have been extensively used as versatile precursors to prepare diverse *aza*-heterocycles through ring opening reactions.[2] Early reports indicated that cleavage of the C2–N bond can be achieved by treatment with heat[3] or metal salts[4] or through reaction with metal carbenes,[5] delivering nitrene or 1,3-azadiene intermediates for a wide range of cycloaddition reactions. Alternatively, cleavage of the C2–C3 bond is also a viable path to form imino diradicals, nitrile ylides, or 2-azaallenyl radical cations under thermal conditions[6] or irradiation with high-energy UV light.[7] Usually, breaking the C2–C3 bond is more challenging than the C2–N bond because of its slightly higher bond energy than the latter.[8,2c] Recently, our group realized this goal using visible light photocatalysis[9] via a single-electron-transfer process.[10,11] The key to success is the application of a commercially available organic dye photocatalyst.[12] In this work, we expand the success of this strategy to construct other useful *N*-heterocycles.

Oxazole derivatives are frequently found in natural products,[13] pharmaceuticals,[14] and as functional materials[15] and usually display numerous significant bioactivities and unique properties. Encouraged by these findings, numerous strategies have been deveploped to forge this heterocyclic unit, mainly involving oxidation of oxazoline,[16] metal/halogen-promoted intramolecular cyclization,[17] or transition-metal-catalyzed bimolecular annulation.[18] However, known approaches to accessing polysubstituted oxazoles often require poorly accessible starting materials and still face problems such as the need for high temperatures, tedious operations, and/or require transition metal catalysts.

Visible-light-induced photoredox catalysis has been identified as a green and sustainable synthetic method for the assembly of diverse heterocycles under mild reaction conditions.[19] In this regard, we have investigated the photocatalyzed [3 + 2] reaction via amine oxidation for the synthesis of pyrrolo[2,1-*a*]isoquinolines,[20a] imidazoles,[20b] and polysubstituted pyrroles[10] (Scheme 1, eq 1). As a part of our continuing work, herein we disclosed the preparation of 2,4,5-trisubstituted oxazoles from 2*H*-azirines[21] and commercially avaliable aldehydes via a photoredox-catalyzed [3 + 2] cycloaddition/oxidative aromatization sequence (Scheme 1, eq 2).

Scheme 1. Visible Light Photoredox-catalyzed Cycloaddition Reactions of 2*H*-Azirines



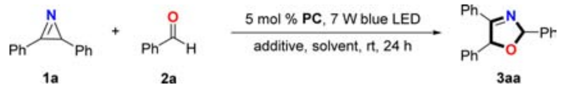
Initially, we tested the formal [3 + 2] cycloaddition of 2*H*-azirine **1a** and benzaldehye **2a** to obtain 2,5-dihydrooxazole **3aa** using 9-mesityl-10-methylacridinium perchlorate (**PC-I**) as the photocatalyst and 1,2-dicloroethane (DCE) as the solvent under the irradiation of a 7 W blue LED. Gratifyingly, the desired [3 + 2] reaction proceeded smoothly, giving 2,5-dihydrooxazole in 37% yield (Table 1, entry 1).[22] By adding desiccant, the yield was improved (Table 1, entries 2–3), especially when 4 Å molecular sieves (MS) were used (Table 1, entry 2: 61% yield). Evaluation of the effect of solvent showed that halogenated solvent and acetonitrile were better than more polar solvents such as MeOH and DMF (Table 1, entries 2 and 4–7), with DCE still being the best solvent. Other reaction parameters such as concentration and substrate ratio were examined, although they did not lead to further improvement

Received: July 12, 2015
Published: August 7, 2015

ACS Publications © 2015 American Chemical Society

DOI: 10.1021/acs.orglett.5b01994
Org. Lett. 2015, 17, 4070–4073

Table 1. Condition Optimization for 2,5-Dihydrooxazole[a]



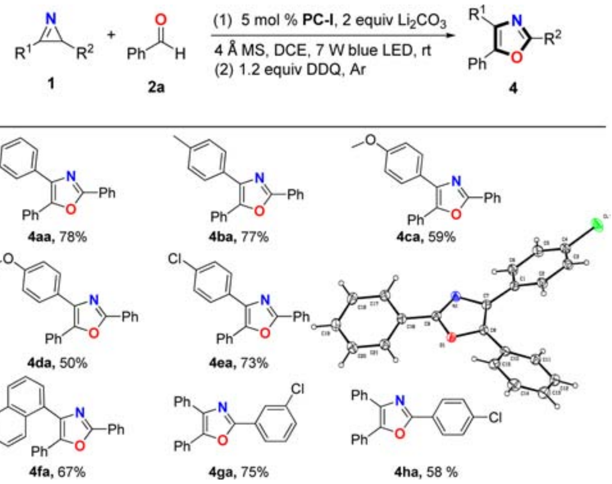
entry	PC	solvent	additive	yield[b] (%)
1	**PC-I**	DCE	–	37
2[c]	**PC-I**	DCE	4 Å MS	61
3[c]	**PC-I**	DCE	$MgSO_4$	45
4[c]	**PC-I**	DCM	4 Å MS	47
5[c]	**PC-I**	MeCN	4 Å MS	45
6[c]	**PC-I**	MeOH	4 Å MS	13
7[c]	**PC-I**	DMF	4 Å MS	0
8[c,d]	**PC-I**	DCE	4 Å MS/K_2CO_3	70
9[c,d]	**PC-I**	DCE	4 Å MS/Li_2CO_3	77
10[c,d]	**PC-I**	DCE	4 Å MS/Na_2CO_3	69
11[c,d]	**PC-II**	DCE	4 Å MS/Li_2CO_3	0
12[c,d]	**PC-III**	DCE	4 Å MS/Li_2CO_3	22
13[c,d,e]	**PC-I**	DCE	4 Å MS/Li_2CO_3	0
14[c,d]	–	DCE	4 Å MS/Li_2CO_3	0

[a] Reaction conditions: **1a** (0.3 mmol), **2a** (1.5 mmol), photocatalyst (5 mol %), solvent (3 mL) at rt for 24 h under the irradiation of a 7 W blue LED. **PC-I**: 9-mesityl-10-methylacridinium perchlorate. **PC-II**: $Ru(bpy)_3Cl_2·6H_2O$. **PC-III**: $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$. [b] Isolated yield. [c] 200 mg of desiccant were added. [d] 2 equiv of base were added. [e] Without visible light.

in efficiency.[23] Since aldehydes are prone to be oxidized to carboxylic acids, we postulated that a weak acidic environment was detrimental to this transformation.[24] Thus, a number of bases were introduced, and increased yields were indeed observed under these conditions (Table 1, entries 8–10). Among them, Li_2CO_3 greatly improved the reaction efficiency, delivering the cycloadduct in 77% yield (Table 1, entry 9). In addition, other transition metal photocatalysts, such as the ruthenium complex **PC-II** or iridium complex **PC-III**, were tested for the photocatalyzed cycloaddition reactions; however, very low yields resulted (Table 1, entries 11–12). Removing the light source or eliminating the photocatalyst from the optimal reaction conditions led to no product, indicating it is a photocatalytic process (Table 1, entries 13–14). To realize the one-pot synthesis of oxazole, an oxidizing agent, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), was added to the reaction system after total consumption of **1a**. After being stirred at room temperature for 14 h, to our delight, the desired oxazole **4aa** was isolated in 78% yield (Scheme 2, **4aa**). Other oxidants such as molecular oxygen and *N*-bromosuccinimide were tried as well, but no desired oxazole product was produced with these reagents.

Having established the optimal conditions, we started to probe the scope of 2,3-disubstituted 2*H*-azirines that partipated in this cycloaddition (Scheme 2). When electron-donating (Me, OMe, OPh) and electron-withdrawing (Cl) groups were introduced to the C3-phenyl ring adjacent to the C═N bond, the reaction worked well, generating the corresponding oxazoles in moderate to good yields (**4ba**–**4ea**, 50%–77%). Moreover, the structure of **4ea** was unambiguously determined by X-ray diffraction analysis.[25] Sterically hindered substrates can also be tolerated by this transformation. For example, when naphthyl-substituted 2*H*-azirine **1f** was applied, the desired oxazole **4fa** was afforded in 67% yield. Modification of the subtitution of the C2-phenyl ring also proved to be viable. 2*H*-Azirines with R^2 possessing Cl at the *meta*- or *para*-positions of the benzene ring underwent this reaction with good efficiency (**4ga**: 75% yield; **4ha**: 58% yield). 2*H*-Azirines with alkyl or heteroaromatic substituents were also examined; however, only a trace amount of products were observed.

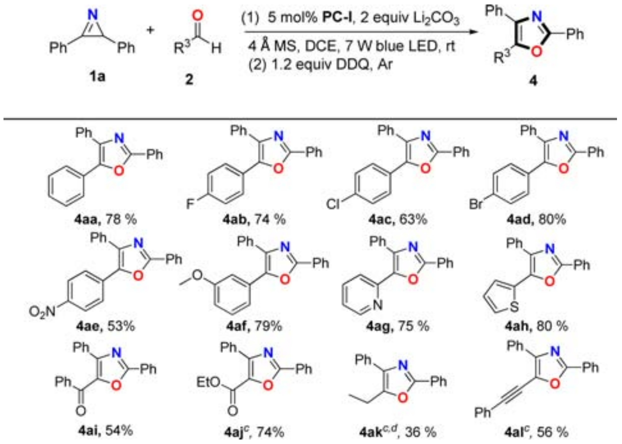
Scheme 2. Substrate Scope of 2*H*-Azirines[a,b]



[a] Reaction conditions: **1** (0.3 mmol), **2a** (1.5 mmol), **PC-I** (5 mol %), DCE (3 mL) at rt under the irradiation of a 7 W blue LED for 24–61 h. DDQ was added after the complete consumption of substrate **1** and stirred at rt for 14–34 h. [b] Isolated yield.

Next, the scope of aldehyde components was examined in this [3 + 2] cycloaddition/oxidative aromatization sequence. As highlighted in Scheme 3, benzaldehydes bearing *para*-F/Cl/Br/NO_2 substituents proved to be compatible with this reaction system, giving the desired oxazoles in moderate to good yields (**4ab**–**4ae**, 53%–80% yield). When *meta*-anisaldehyde was applied to the reaction conditions, the corresponding product **4af** was delivered in 79% yield, albeit after an extended reaction time. To our delight, heteroaryl aldehydes reacted well with 2*H*-azirine **1a**. For instance, when pyridyl and thienyl aldehydes were used, the corresponding heterocycle-substituted oxazoles were afforded in 75% (**4ag**) and 80% yields (**4ah**), respectively.

Scheme 3. Substrate Scope of Aldehydes[a,b]



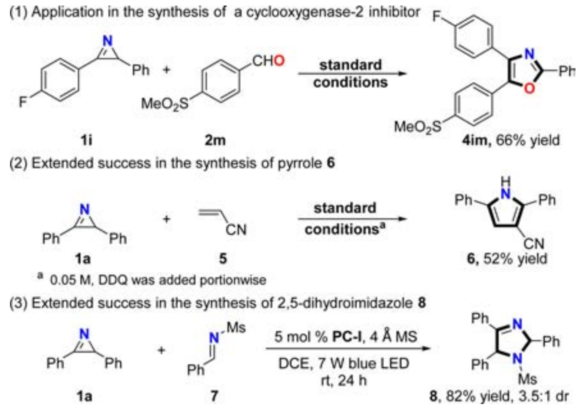
[a] Reaction conditions: **1a** (0.3 mmol), **2** (1.5 mmol), **PC-I** (5 mol %), DCE (3 mL) at rt under the irradiation of a 7 W blue LED for 24–97 h. DDQ was added after complete consumption of substrate **1a** and stirred at rt 14–25 h. [b] Isolated yield. [c] The second step was run at 50 °C. [d] 10 equiv of aldehyde and 0.6 equiv of DDQ were used.

DOI: 10.1021/acs.orglett.5b01994
Org. Lett. 2015, 17, 4070–4073

We expect that this transformation will be very useful in constructing such oxazoles in a regioselective manner.[26] In addition to the aforementioned aldehydes, the reaction went smoothly with phenylglyoxal hydrate (**4ai**: 54% yield) and ethyl glyoxylate (**4aj**: 74% yield) as substrates. Notably, the ester group can be removed to obtain a 2,4-disubstituted oxazole or further transformed to the oxazole analogue of urocanic acid, which shows immunosuppressive activity.[26,27] In addition, after increasing the amount of aldehyde, propanal can also undergo this transformation, affording the desired product **4ak** in an acceptable yield (36%). Lastly, 5-alkynyl substituted oxazole **4al** can be readily prepared in moderate yield (56%) by using alkynyl aldehyde **2l**. Compared with existing methods that use transition-metal-catalyzed cross-coupling reactions or multistep synthesis from arylacrylic acids,[28] this strategy features a simple procedure and mild conditions.

To further explore the potential of this method, the cyclooxygenase-2 inhibitor[29] **4im** was synthesized in a good yield (Scheme 4, eq 1: 66% yield) in a single pot. Apart from aldehydes, the electron-deficient alkene acrylonitrile **5** can be utilized in this reaction, affording pyrrole **6** in moderate yield (Scheme 4, eq 2:52% yield). It is worthy to note that imine **7** can also participate in the visible-light-photocatalyzed [3 + 2] cycloaddition reaction, affording the 2,5-dihydroimidazole product **8** in a good yield and moderate diastereoselectivity (Scheme 4, eq 3:82% yield, 3.5:1 dr),[30] although it did not undergo the oxidative aromatization step under standard conditions.

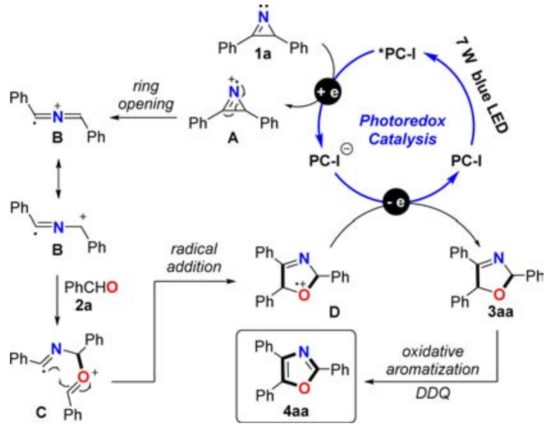
Scheme 4. Synthetic Potentials of this Protocol


(1) Application in the synthesis of a cyclooxygenase-2 inhibitor
(2) Extended success in the synthesis of pyrrole **6**
(3) Extended success in the synthesis of 2,5-dihydroimidazole **8**

^{a} 0.05 M, DDQ was added portionwise

On the basis of our previous work[10] and literature reports,[7] a plausible mechanism for this transformation was proposed as shown in Scheme 5. 2*H*-Azirine **1a** can be converted to 2-azaallenyl radical cation **B** after single-electron oxidation by the excited photocatalyst and homolytic cleavage of the C−C bond. Then, nucleophilic attack of benzaldehyde **2a** on **B** would result in the formation of cation radical **C**, which could undergo subsequent intramolecular radical addition to afford the new cation radical **D**. After that, this transient species would be readily reduced by a low-valent photocatalyst, delivering the cycloadduct **3aa** and regenerating the photocatalyst **PC-I**. Finally, the oxidative aromatization of 2,5-dihydrooxazole **3aa** furnished the desired oxazole product **4aa**.

Scheme 5. Plausible Reaction Mechanism



In summary, we have developed a [3 + 2] cycloaddition/oxidative aromatization sequence through visible-light-induced photoredox catalysis. This process provides a new approach for the one-pot synthesis of multisubstituted oxazoles from readily available 2*H*-azirines and aldehydes. It features a broad substrate scope and mild reaction conditions (i.e., 7 W LED irradiation and organic dye catalyst). Significantly, this strategy enabled the synthesis of a cyclooxygenase-2 inhibitor in one simple operation and can be further applied to the synthesis of biologically important pyrroles and 2,5-dihydroimidazoles.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b01994.

Experimental procedures, characterization data, and NMR spectra (PDF)
Crystallographic data for *cis*-**8** (CIF)
Crystallographic data for **4ea** (CIF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: luliangqiu@mail.ccnu.edu.cn.
*E-mail: wxiao@mail.ccnu.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We acknowledge financial support from the NSFC (Nos. 21272087, 21472058, 21202053, and 21232003) for support of this research.

■ REFERENCES

(1) (a) Neber, P. W.; Burgard, A. *Justus Liebigs Ann. Chem.* **1932**, *493*, 281−294.

(2) For selected reviews, see: (a) Palacios, F.; de Retana, A.; de Marigorta, E. M.; de los Santos, J. M. *Eur. J. Org. Chem.* **2001**, *2001*, 2401−2414. (b) Palacios, F.; de Retana, A. M. O.; de Marigorta, E. M.; de los Santos, J. M. *Org. Prep. Proced. Int.* **2002**, *34*, 219−269. (c) Pinho e Melo, T.; Gonsalves, A. M. R. *Curr. Org. Synth.* **2004**, *1*, 275−292. (d) Khlebnikov, A. F.; Novikov, M. S. *Tetrahedron* **2013**, *69*, 3363−3401. (e) Huang, C.-Y.; Doyle, A. G. *Chem. Rev.* **2014**, *114*, 8153−8198.

(3) For selected examples, see: (a) Padwa, A.; Smolanoff, J.; Tremper, A. *J. Am. Chem. Soc.* **1975**, *97*, 4682−4691. (b) Knittel, D. *Synthesis* **1985**, *1985*, 186−188. (c) Stevens, K. L.; Jung, D. K.; Alberti, M. J.; Badiang, J. G.; Peckham, G. E.; Veal, J. M.; Cheung, M.; Harris, P. A.; Chamberlain, S. D.; Peel, M. R. *Org. Lett.* **2005**, *7*, 4753−4756.

(4) For selected examples, see: (a) Alper, H.; Prickett, J. E.; Wollowitz, S. *J. Am. Chem. Soc.* **1977**, *99*, 4330−4333. (b) Taber, D. F.; Tian, W. *J. Am. Chem. Soc.* **2006**, *128*, 1058−1059. (c) Chiba, S.; Hattori, G.; Narasaka, K. *Chem. Lett.* **2007**, *36*, 52−53. (d) Jana, S.; Clements, M. D.; Sharp, B. K.; Zheng, N. *Org. Lett.* **2010**, *12*, 3736−3739.

(5) For selected examples, see: (a) Rostovskii, N. V.; Novikov, M. S.; Khlebnikov, A. F.; Khlebnikov, V. A.; Korneev, S. M. *Tetrahedron* **2013**, *69*, 4292−4301. (b) Loy, N. S.; Singh, A.; Xu, S.; Park, C.-M. *Angew. Chem., Int. Ed.* **2013**, *52*, 2212−2216. (c) Ryu, T.; Baek, Y.; Lee, P. H. *J. Org. Chem.* **2015**, *80*, 2376−2383. (d) Wang, Y.; Lei, X.; Tang, Y. *Chem. Commun.* **2015**, *51*, 4507−4510. (e) Loy, N. S. Y.; Kim, S.; Park, C.-M. *Org. Lett.* **2015**, *17*, 395−397.

(6) Ghosez, L.; Demoulin, A.; Henriet, M.; Sonveaux, E. *Heterocycles* **1977**, *7*, 895−905.

(7) For selected review, see: (a) Padwa, A. *Acc. Chem. Res.* **1976**, *9*, 371−378. (b) Albrecht, E.; Averdung, J.; Bischof, E. W.; Heidbreder, A.; Kirschberg, T.; Müller, F.; Mattay, J. *J. Photochem. Photobiol., A* **1994**, *82*, 219−232. For selected examples, see: (c) Jackson, B.; Märky, M.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1972**, *55*, 919−921. (d) Müller, F.; Mattay, J. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1336−1337. (e) Müller, F.; Mattay, J.; Steenken, S. *J. Org. Chem.* **1993**, *58*, 4462−4464.

(8) (a) Calvo-Losada, S.; Quirante, J. J.; Suárez, D.; Sordo, T. L. *J. Comput. Chem.* **1998**, *19*, 912−922.

(9) For selected reviews on visible light photoredox catalysis, see: (a) Yoon, T. P.; Ischay, M. A.; Du, J. *Nat. Chem.* **2010**, *2*, 527−532. (b) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* **2011**, *40*, 102−113. (c) Xuan, J.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 6828−6838. (d) Shi, L.; Xia, W. *Chem. Soc. Rev.* **2012**, *41*, 7687−7697. (e) Xi, Y.; Yi, H.; Lei, A. *Org. Biomol. Chem.* **2013**, *11*, 2387−2403. (f) Hari, D. P.; König, B. *Angew. Chem., Int. Ed.* **2013**, *52*, 4734−4743. (g) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322−5363. (h) Schultz, D. M.; Yoon, T. P. *Science* **2014**, *343*, 1239176.

(10) Xuan, J.; Xia, X.-D.; Zeng, T.-T.; Feng, Z.-J.; Chen, J.-R.; Lu, L.-Q.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2014**, *53*, 5653−5656.

(11) 2*H*-Azirines could also participate in reactions via other kinds of intermediates. For selected recent examples, see: (a) Shimada, N.; Ashburn, B. O.; Basak, A. K.; Bow, W. F.; Vicic, D. A.; Tius, M. A. *Chem. Commun.* **2010**, *46*, 3774−3775. (b) Candito, D. A.; Lautens, M. *Org. Lett.* **2010**, *12*, 3312−3315. (c) Prechter, A.; Henrion, G.; Henrion, G.; Faudot dit Bel, P.; Gagosz, F. *Angew. Chem., Int. Ed.* **2014**, *53*, 4959−4963. (d) Jiang, Y.; Park, C.-M.; Loh, T.-P. *Org. Lett.* **2014**, *16*, 3432−3435. (e) Zhu, L.; Yu, Y.; Mao, Z.; Huang, X. *Org. Lett.* **2015**, *17*, 30−33.

(12) For selected reviews or highlight on visible light photoredox catalysis using dyes as catalysts, see: (a) Ravelli, D.; Fagnoni, M. *ChemCatChem* **2012**, *4*, 169−171. (b) Nicewicz, D. A.; Nguyen, T. M. *ACS Catal.* **2014**, *4*, 355−360. (c) Fukuzumi, S.; Ohkubo, K. *Org. Biomol. Chem.* **2014**, *12*, 6059−6071.

(13) (a) Wipf, P. *Chem. Rev.* **1995**, *95*, 2115−2134. (b) Shin-ya, K.; Wierzba, K.; Matsuo, K.; Ohtani, T.; Yamada, Y.; Furihata, K.; Hayakawa, Y.; Seto, H. *J. Am. Chem. Soc.* **2001**, *123*, 1262−1263. (c) Dalisay, D. S.; Rogers, E. W.; Edison, A. S.; Molinski, T. F. *J. Nat. Prod.* **2009**, *72*, 732−738. (d) Wilson, Z. E.; Fenner, S.; Ley, S. V. *Angew. Chem., Int. Ed.* **2015**, *54*, 1284−1288.

(14) (a) Fernandes, E.; Costa, D.; Toste, S. A.; Lima, J. L.F.C.; Reis, S. *Free Radical Biol. Med.* **2004**, *37*, 1895−1905. (b) Wang, W.-L.; Yao, D.-Y.; Gu, M.; Fan, M.-Z.; Li, J.-Y.; Xing, Y.-C.; Nan, F.-J. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 5284−5287. (c) Reddy, B. A.; Hymavathi, R. V.; Swamy, G. N. *J. Chem. Sci.* **2013**, *125*, 495−509.

(15) (a) Baranov, M. S.; Lukyanov, K. A.; Ivashkin, P. E.; Yampolsky, I. V. *Synth. Commun.* **2013**, *43*, 2337−2342. (b) Huong, V. T. T.; Tai, T. B.; Nguyen, M. T. *J. Phys. Chem. A* **2014**, *118*, 3335−3343.

(16) For selected examples, see: (a) Barrish, J. C.; Singh, J.; Spergel, S. H.; Han, W.-C.; Kissick, T. P.; Kronenthal, D. R.; Mueller, R. H. *J. Org. Chem.* **1993**, *58*, 4494−4496. (b) Williams, D. R.; Lowder, P. D.; Gu, Y.-G.; Brooks, D. A. *Tetrahedron Lett.* **1997**, *38*, 331−334. (c) Huang, Y.; Ni, L.; Gan, H.; He, Y.; Xu, J.; Wu, X.; Yao, H. *Tetrahedron* **2011**, *67*, 2066−2071. (d) Li, X.; Li, C.; Yin, B.; Li, C.; Liu, P.; Li, J.; Shi, Z. *Chem. - Asian J.* **2013**, *8*, 1408−1411.

(17) For selected examples, see: (a) Beccalli, E. M.; Borsini, E.; Broggini, G.; Palmisano, G.; Sottocornola, S. *J. Org. Chem.* **2008**, *73*, 4746−4749. (b) Weyrauch, J. P.; Hashmi, A. S. K.; Schuster, A.; Hengst, T.; Schetter, S.; Littmann, A.; Rudolph, M.; Hamzic, M.; Visus, J.; Rominger, F.; Frey, W.; Bats, J. W. *Chem. - Eur. J.* **2010**, *16*, 956−963. (c) Senadi, G. C.; Hu, W.-P.; Hsiao, J.-S.; Vandavasi, J. K.; Chen, C.-Y.; Wang, J.-J. *Org. Lett.* **2012**, *14*, 4478−4481. (d) Hu, Y.; Yi, R.; Wang, C.; Xin, X.; Wu, F.; Wan, B. *J. Org. Chem.* **2014**, *79*, 3052−3059.

(18) For selected examples, see: (a) Wan, C.; Zhang, J.; Wang, S.; Fan, J.; Wang, Z. *Org. Lett.* **2010**, *12*, 2338−2341. (b) Zheng, J.; Zhang, M.; Huang, L.; Hu, X.; Wu, W.; Huang, H.; Jiang, H. *Chem. Commun.* **2014**, *50*, 3609−3611. (c) Zheng, M.; Huang, L.; Huang, H.; Li, X.; Wu, W.; Jiang, H. *Org. Lett.* **2014**, *16*, 5906−5909. (d) Luo, W.; Zhao, J.; Yin, C.; Liu, X.; Lin, L.; Feng, X. *Chem. Commun.* **2014**, *50*, 7524−7526. (e) Zhang, L.; Zhao, X. *Org. Lett.* **2015**, *17*, 184−186.

(19) Xuan, J.; Lu, L.-Q.; Chen, J.-R.; Xiao, W.-J. *Eur. J. Org. Chem.* **2013**, *2013*, 6755−6770.

(20) (a) Zou, Y.-Q.; Lu, L.-Q.; Fu, L.; Chang, N.-J.; Rong, J.; Chen, J.-R.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2011**, *50*, 7171−7175. (b) Deng, Q.-H.; Zou, Y.-Q.; Lu, L.-Q.; Tang, Z.-L.; Chen, J.-R.; Xiao, W.-J. *Chem. - Asian J.* **2014**, *9*, 2432−2435.

(21) For selected examples on oxazole synthesis from 2*H*-azirines, see: (a) Sá, M. C. M.; Kascheres, A. *J. Org. Chem.* **1996**, *61*, 3749−3752. (b) Palacios, F.; de Retana, A. M. O.; Gil, J. I.; Alonso, J. M. *Tetrahedron: Asymmetry* **2002**, *13*, 2541−2552. (c) Brahma, S.; Ray, J. K. *J. Heterocycl. Chem.* **2008**, *45*, 311−317.

(22) The diastereoselectivity was determined to be 1.4:1 by ^{1}H NMR of the crude product.

(23) Please see the Supporting Information for details.

(24) By adding 0.1 equiv of benzoic acid, the yield of 2,5-dihyrooxazole was decreased to 55% yield under the reaction conditions described in Table 1, entry 2.

(25) CCDC number: 1408700.

(26) Verrier, C.; Martin, T.; Hoarau, C.; Marsais, F. *J. Org. Chem.* **2008**, *73*, 7383−7386.

(27) Millan, D. S.; Prager, R. H.; Brand, C.; Hart, P. H. *Tetrahedron* **2000**, *56*, 811−816.

(28) For selected examples on the synthesis of alkynyloxazoles, see: (a) Langille, N. F.; Dakin, L. A.; Panek, J. S. *Org. Lett.* **2002**, *4*, 2485−2488. (b) Pankova, A. S.; Stukalov, A. Y.; Kuznetsov, M. A. *Org. Lett.* **2015**, *17*, 1826−1829.

(29) Roniker, B., LaChapell, R. J.; Connolly, D. T.; Seibert, K.; Needleman, P. US 2002/0035156 A1. Mar. 21, 2002.

(30) The structure of the major isomer has been determined by X-ray diffraction analysis. Please see the Supporting Information for details.