OL | Organic Letters

Cite This: Org. Lett. XXXX, XXX, XXX−XXX

Letter

pubs.acs.org/OrgLett

Divergent Conversion of *N*-Acyl-isoxazol-5(2*H*)-ones to Oxazoles and 1,3-Oxazin-6-ones Using Photoredox Catalysis

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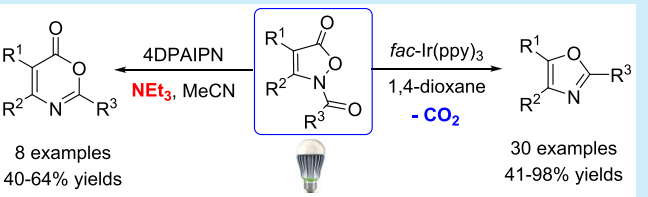
Supporting Information

ABSTRACT: The fragmentation of *N*-acyl-isoxazol-5-ones using visible light photoredox catalysis has been disclosed. The catalyst-controlled divergent mechanisms, namely the oxidative and reductive quenching catalytic cycle, are utilized. Various oxazoles and 1,3-oxazin-6-ones are selectively obtained from the same isoxazol-5-one skeleton under mild conditions.



Isoxazol-5-ones are five-membered heterocycles possessing rich chemical reactivities.[1] They may exist as a mixture of three tautomeric forms, known as CH-form **I**, NH-form **II**, and OH-form **III** (Figure 1).[2] Because of the weak N−O bond

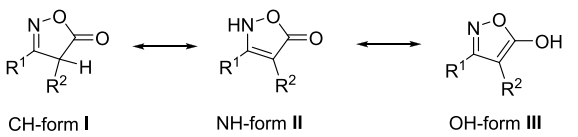
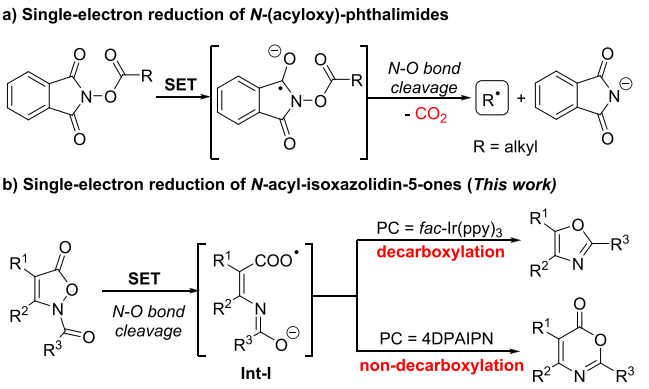


Figure 1. Tautomeric forms of isoxazol-5-ones.

(BDE, D^0_{298} = 151 kcal mol^{-1}) in their architecture,[3] isoxazol-5-ones are versatile building blocks in organic synthesis through N−O bond cleavage and CO_2 extrusion.[4−7] Early reports by Prager indicated that most of the isoxazol-5-ones can be used as the precursors of imino carbene under flash vacuum pyrolysis (FVP) conditions or irradiation with high-energy UV light.[4] Metal-catalyzed decarboxylation of isoxazol-5-ones generates vinylmetal nitrenoid species,[5] which has been applied to prepare diverse aza-heterocycles, such as 1-azabicyclo[3.1.0]hex-2-enes,[5a] pyridines,[5c] and 2*H*-pyrroles.[5g] Nitrosative cleavage of isoxazol-5-ones is a well-established route to access alkynes.[6] The isoxazolone motif has also been developed as a directing group in Rh-catalyzed *ortho* C−H bond activation reaction.[7] Despite these significant advances, the reactivity manifolds of isoxazol-5-ones remain to be explored.

There has been progress using a photoredox strategy to generate alkyl radicals through single-electron reduction of *N*-(acyloxy)-phthalimides (NHPI esters).[8] This reduction results in N−O bond cleavage followed by decarboxylation to release CO_2, an alkyl radical, and a phthalimide anion (Scheme 1a). Due to the highly negative reduction potentials of NHPI esters, reductive conditions are often employed to promote their single electron reduction where the excited photocatalyst is converted into a higher reducing species prior to engaging in SET with *N*-(acyloxy)-phthalimides (reductive quenching of photocatalyst).[9] Recently, the direct electron transfer between excited photocatalyst and NHPI esters has been reported, driven by the formation of hydrogen bonding to increase the electron-acceptor strength of substrates (oxidative quenching of photocatalyst).[10] Stimulated by the structural analogy of *N*-acyl-isoxazol-5-ones with NHPI esters, we wish to investigate the chemical reactivity of isoxazol-5-one derivatives under photoredox conditions. In contrast to numerous reports on the homolytic cleavage of the N−O bond of isoxazol-5-ones,[4] the visible light-driven SET process for their fragmentation has been less explored. If feasible, this new activation mode would expand the applications of isoxazol-5-ones in aza-heterocycles synthesis. Herein, we report a visible light-promoted decarboxylative rearrangement of *N*-acyl-isoxazol-5-ones to oxazoles with *fac*-Ir(ppy)$_3$ as the photocatalyst. By switching the photocatalyst to 4DPAIPN, 1,3-oxazin-6-ones were obtained with complete selectivity from same isoxazol-5-one skeleton (Scheme 1b). Notably, both oxazoles[11] and 1,3-

Scheme 1. N−O Bond Cleavage Enabled by Visible Light Photoredox Catalysis



Received: March 13, 2019

DOI: 10.1021/acs.orglett.9b00903
Org. Lett. XXXX, XXX, XXX−XXX

oxazin-6-ones[12] are important heterocycles present in a wide range of natural products and bioactive compounds, as exemplified by antidiabetic agent AD-5061,[11d] antimycobacterial texaline,[11e] and salinazinone A (Figure 2).[12d,e] Although

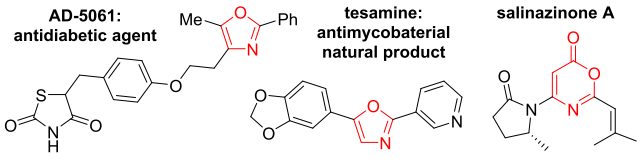


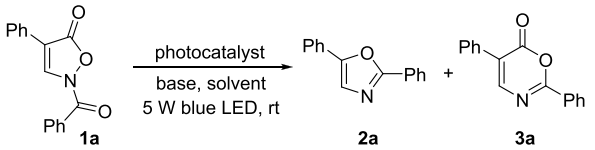
Figure 2. Representative biologically active molecules containing oxazole or 1,3-oxazin-6-one motif.

numerous synthetic methods for the construction of these heterocyclic skeletons have been developed in the past decades,[13,14] processes in which different products can be obtained from identical substrates in synthetically meaningful yields utilizing catalyst rather than substrate control are rare.

At the outset of this investigation, we chose *N*-benzoyl-4-phenyl-isoxazol-5-one **1a** as the model substrate, and its redox potential was measured. Although the cyclic voltammetry experiment indicates that **1a** has a high negative reduction potential (−1.50 V vs SCE), it is still possible to reduce this compound using the strong reducing photoexcited $Ir(ppy)_3$* ($E_{1/2}^{IV/III*} = -1.73$ V vs SCE).[15] To our delight, irradiating the DMSO solution of **1a** in the presence of *fac*-$Ir(ppy)_3$ gave 2,5-diphenyloxazole **2a** in 22% yield (Table 1, entry 1). A brief screen of solvents indicated 1,4-dioxane was the best choice, in which the desired product **2a** was obtained in 91% yields (Table 1, entries 2−6). Because $Ir(ppy)_3^-$ is a higher reducing species ($E_{1/2}^{III/II} = -2.19$ V vs SCE), we also examined the reaction by adding $^iPr_2NEt$ as an electron donor. Interestingly, the yield of oxazole **2a** sharply decreased to 11%, while 1,3-oxazin-6-one **3a** was observed in 15% yield (Table 1, entry 7). Inspired by this result, the reaction conditions toward the formation of **3a** were screened. When $Ru(bpy)_3Cl_2$, $Ir(ppy)_2(dtbbpy)PF_6$, and 4DPAIPN were used as the photocatalysts, oxazole **2a** was completely suppressed, albeit affording 1,3-oxazin-6-one **3a** in low yields (Table 1, entries 8−10). Organic dye Eosin Y was essentially ineffective for the reaction (Table 1, entry 11). We thus sought to further improve the yield of **3a** with 4DPAIPN as the photocatalyst. Several solvents, such as DMSO, DMF, DCE and MeCN, were screened for this transformation, and MeCN was found to be the best one (Table 1, entries 12−15). Triethylamine was the best base in comparison with $^iPr_2NEt$ and N^nBu_3 (Table 1, entries 16, 17), while the use of DBU, 1,4-dihydropyridine (DHP), and inorganic base K_2CO_3 led to no conversion at all (Table 1, entries 18−20). The optimal amounts of NEt_3 were also evaluated. We found the use of 1 equiv of NEt_3 led to **3a** in a slightly diminished yield (Table 1, entry 21). Further increasing the loading of NEt_3 from 1.2 to 2 equiv, the yield was almost identical (Table 1, entry 22). Finally, the control experiments indicated that neither **2a** nor **3a** was detected when the reaction was carried out in the absence of photocatalyst or in the dark, and most of **1a** remained unreacted (Table 1, entries 23−25).

To demonstrate the generality of the present photoredox reactions of *N*-acyl-isoxazol-5-ones, their decarboxylative rearrangement to oxazoles was first examined. As shown in Table 2, a series of *N*-benzoyl-4-phenyl-isoxazol-5-ones **1a−n** were converted to the corresponding 2,5-substituted oxazoles

Table 1. Optimization of Reaction Conditions[a,b]



entry	photocatalyst	base (equiv)	solvent	2a (%)	3a (%)
1	*fac*-$Ir(ppy)_3$	–	DMSO	22	0
2	*fac*-$Ir(ppy)_3$	–	DMF	27	0
3	*fac*-$Ir(ppy)_3$	–	THF	18	0
4	*fac*-$Ir(ppy)_3$	–	DCE	32	0
5	*fac*-$Ir(ppy)_3$	–	MeCN	57	0
6	*fac*-$Ir(ppy)_3$	–	dioxane	91	0
7	*fac*-$Ir(ppy)_3$	$^iPr_2NEt$ (1.2)	dioxane	11	15
8	$Ru(bpy)_3Cl_2$	$^iPr_2NEt$ (1.2)	dioxane	0	11
9	$Ir(ppy)_2(dtbbpy)PF_6$	$^iPr_2NEt$ (1.2)	dioxane	0	14
10	4DPAIPN	$^iPr_2NEt$ (1.2)	dioxane	0	19
11	Eosin Y	$^iPr_2NEt$ (1.2)	dioxane	0	0
12	4DPAIPN	$^iPr_2NEt$ (1.2)	DMSO	0	21
13	4DPAIPN	$^iPr_2NEt$ (1.2)	DMF	0	25
14	4DPAIPN	$^iPr_2NEt$ (1.2)	DCE	0	31
15	4DPAIPN	$^iPr_2NEt$ (1.2)	MeCN	0	58
16	4DPAIPN	NEt_3 (1.2)	MeCN	0	66
17	4DPAIPN	N^nBu_3 (1.2)	MeCN	0	50
18	4DPAIPN	DBU (1.2)	MeCN	0	0
19	4DPAIPN	DHP (1.2)	MeCN	0	0
20	4DPAIPN	K_2CO_3 (1.2)	MeCN	0	0
21	4DPAIPN	NEt_3 (1.0)	MeCN	0	60
22	4DPAIPN	NEt_3 (2.0)	MeCN	0	66
23	–	–	dioxane	0	0
24[c]	*fac*-$Ir(ppy)_3$	–	dioxane	0	0
25[c]	4DPAIPN	NEt_3 (2.0)	MeCN	0	0

[a]Reaction conditions: *N*-benzoyl-4-phenyl-isoxazol-5-one **1a** (0.1 mmol), base (1.2 equiv), 5 mol % of 4DPAIPN or 1 mol % of other photocatalysts, solvent (2 mL), 5 W blue LED, rt, 3 h. [b]Yields were determined using mesitylene as the internal standard. [c]In the dark; DHP = 1,4-dihydropyridine.

2a−n smoothly in 82−97% yields (Table 2, entries 1−14). The reaction was not significantly affected by the substituent on the benzoyl group; both electron-rich groups, such as methyl, *tert*-butyl, methoxyl, phenyl, and electron-deficient groups, such as halogen (F, Cl, Br), trifluoromethyl, ester, on the different positions of the aromatic ring were well-tolerated. 2-Naphthoyl (**1o**), 2-furoyl (**1p**), and 2-thienoyl (**1q**) 4-phenyl-isoxazol-5-ones were also suitable for the reaction, producing oxazoles **2o**, **2p**, and **2q** in the yields of 73%, 85%, and 74%, respectively (Table 2, entries 15−17). For the substrates **1r−t** bearing a substituent (*para*-methyl, *para*- and *meta*-chloro) on the aromatic ring attached to the C−C double bond, the reactions led to 2,5-substituted oxazoles **2r−t** in 81−93% yields (Table 2, entries 18−20). 2,4-Diphenyl oxazole **2u** was successfully synthesized from *N*-benzoyl-3-phenyl-isoxazol-5-one **1u** (Table 2, entry 21). We were delighted to find that the substituent on the 3-position of isoxazol-5-ones was not limited to the aryl group, as exemplified by the formation of 2-alkyl oxazoles **2v−y** (Table 2, entries 22−25). Notably, a cyclopropyl group could survive in this radical-based transformation (Table 2, entry 25). The reaction also allows access to 2,4,5-trisubstituted oxazoles **2z−2ab** in excellent yields via

DOI: 10.1021/acs.orglett.9b00903
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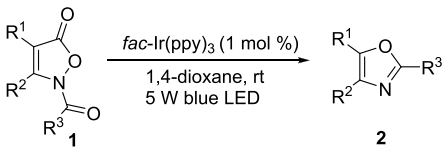
Table 2. Substrate Scope for the Formation of Oxazoles 2[a]



entry	1	R^1	R^2	R^3	2	yield (%)[b]
1	**1a**	Ph	H	Ph	**2a**	88(85)[c]
2	**1b**	Ph	H	*p*-MeC_6H_4	**2b**	82
3	**1c**	Ph	H	*p*-$^tBuC_6H_4$	**2c**	86
4	**1d**	Ph	H	*p*-$MeOC_6H_4$	**2d**	90
5	**1e**	Ph	H	*p*-PhC_6H_4	**2e**	91
6	**1f**	Ph	H	*p*-FC_6H_4	**2f**	92
7	**1g**	Ph	H	*p*-ClC_6H_4	**2g**	95
8	**1h**	Ph	H	*p*-BrC_6H_4	**2h**	96
9	**1i**	Ph	H	*p*-$CF_3C_6H_4$	**2i**	86
10	**1j**	Ph	H	*p*-$CO_2EtC_6H_4$	**2j**	90
11	**1k**	Ph	H	*m*-MeC_6H_4	**2k**	90
12	**1l**	Ph	H	*o*-MeC_6H_4	**2l**	97
13	**1m**	Ph	H	(2,4-Me_2)C_6H_3	**2m**	95
14	**1n**	Ph	H	(3,4,5-Me_3)C_6H_2	**2n**	91
15	**1o**	Ph	H	2-naphthyl	**2o**	73
16	**1p**	Ph	H	2-furyl	**2p**	85
17	**1q**	Ph	H	2-thienyl	**2q**	74
18	**1r**	*p*-MeC_6H_4	H	Ph	**2r**	82
19	**1s**	*p*-ClC_6H_4	H	Ph	**2s**	81
20	**1t**	*m*-ClC_6H_4	H	Ph	**2t**	93
21	**1u**	H	Ph	Ph	**2u**	60
22	**1v**	H	Me	*p*-MeC_6H_4	**2v**	71
23	**1w**	H	Et	*p*-MeC_6H_4	**2w**	75
24	**1x**	H	^{i}Pr	Ph	**2x**	77
25	**1y**	H	cyclopropyl	Ph	**2y**	87
26	**1z**	benzyl	Me	Ph	**2z**	90
27	**1aa**	Me	Et	Ph	**2aa**	97
28	**1ab**	^{n}pentyl	Me	*p*-$CF_3C_6H_4$	**2ab**	91
29	**1ac**	$(CH_2)_4$		Ph	**2ac**	98
30[d]	**1ad**	Ph	H	Me	**2ad**	36
31[e]	**1ad**	Ph	H	Me	**2ad**	41

[a]All the reactions were carried out using *N*-acyl-isoxazol-5-ones **1** (0.2 mmol), *fac*-Ir(ppy)$_3$ (1 mol %) in 2 mL of 1,4-dioxane under the irradiation of a 5 W blue LED at rt for 3 h. [b]Isolated yields. [c]Isolated yield of 2 mmol scale reaction in the parentheses. [d]20 mol % of HOAc was added. [e]20 mol % of Zn(OTf)$_2$ was added.

the photocatalytic decarboxylative rearrangement of isoxazol-5-ones **1z**−**1ab** (Table 2, entries 26−28). In addition, cyclohexyl fused isoxazol-5-one **1ac** could be converted to 2-phenyl-tetrahydrobenzoxazole **2ac** in 98% yield (Table 2, entry 29). The rearrangement of *N*-acetyl-4-phenyl-isoxazol-5-one **1ad** under the optimal reaction conditions failed, presumably due to its highly negative reduction potential (−1.97 V vs SCE).[16] Therefore, we attempted to increase its electron-acceptor strength by forming stronger hydrogen bonding. To our delight, the desired product **1ad** was obtained in 36% yield when 20 mol % acetic acid was added, which was further improved to 41% with Zn(OTf)$_2$ as the additive (Table 2, entries 30, 31).

Next, the scope of nondecarboxylative rearrangement of *N*-acyl-isoxazol-5-ones for the synthesis of 1,3-oxazin-6-ones **3** was investigated. The generality and efficiency of this transformation are lower than the formation of oxazoles **2**. As shown in Scheme 2, 1,3-oxazin-6-ones **3a**−**f** were isolated in 41−64% yields from the corresponding *N*-benzoyl-4-aryl-isoxazol-5-ones. Switching the products from oxazoles to 1,3-oxazin-6-ones **3g** and **3h** were also viable with 2-furoyl (**1p**) and 2-thienoyl (**1q**) 4-phenyl-isoxazol-5-ones as the substrates. Unfortunately, the attempt to convert 3-ethyl-isoxazol-5-one **1w** to **3i** was unsuccessful.

To understand the limitation of scope and the mechanism of both transformations, the redox profiles of several representative isoxazol-5-ones were evaluated (Scheme 3). Except **1ad**, all of the examined isoxazol-5-ones were expected to undergo SET reduction by Ir(III)* directly. In order to reduce **1ad**, HOAc was added to improve its electron-acceptor strength by forming a stronger hydrogen bond. Due to the low reducibility ($E_{1/2}^{PC^+/PC*}$ = −1.28 V) of excited 4DPAIPN*,[17] it has no ability to reduce any isoxazol-5-ones. In the presence of NEt_3, 4DPAIPN* was reduced to the higher reducing species 4DPAIPN$^-$. Therefore, the SET between 4DPAIPN$^-$ and **1a** was feasible. However, its reducibility is still not sufficient to reduce the isoxazol-5-ones with higher negative reduction potentials, such as **1w**, **1ac**, and **1ad**. Considering the high

DOI: 10.1021/acs.orglett.9b00903
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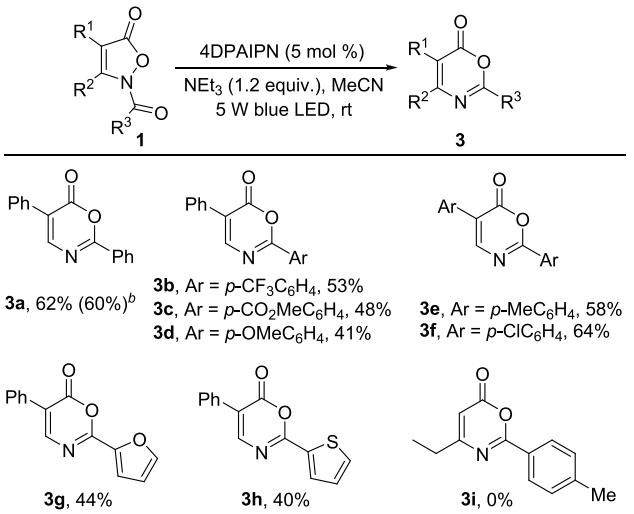
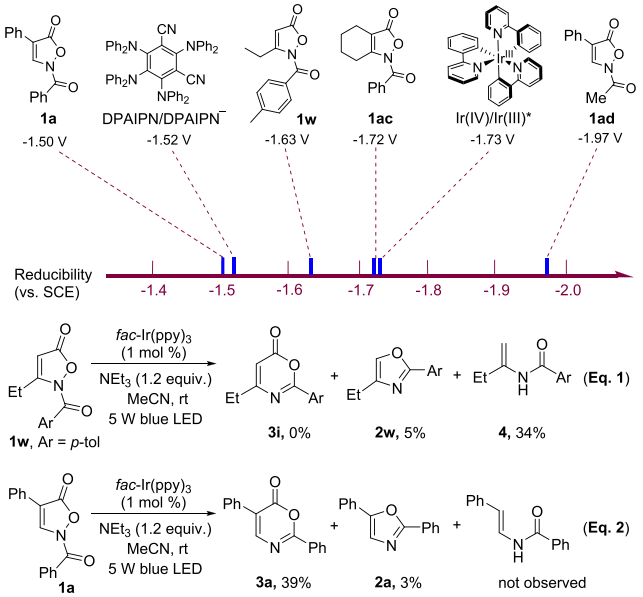
Scheme 2. Substrate Scope for the Formation of 1,3-Oxazin-6-ones 3[a]



[a]All the reactions were carried out using *N*-acyl-isoxazolidin-5-ones **1** (0.2 mmol), 4DPAIPN (5 mol %), and NEt_3 (1.2 equiv) in 2 mL of dry MeCN under the irradiation of a 5 W blue LED at rt for 3 h; isolated yields. [b]Isolated yield of 2 mmol scale reaction in the parentheses.

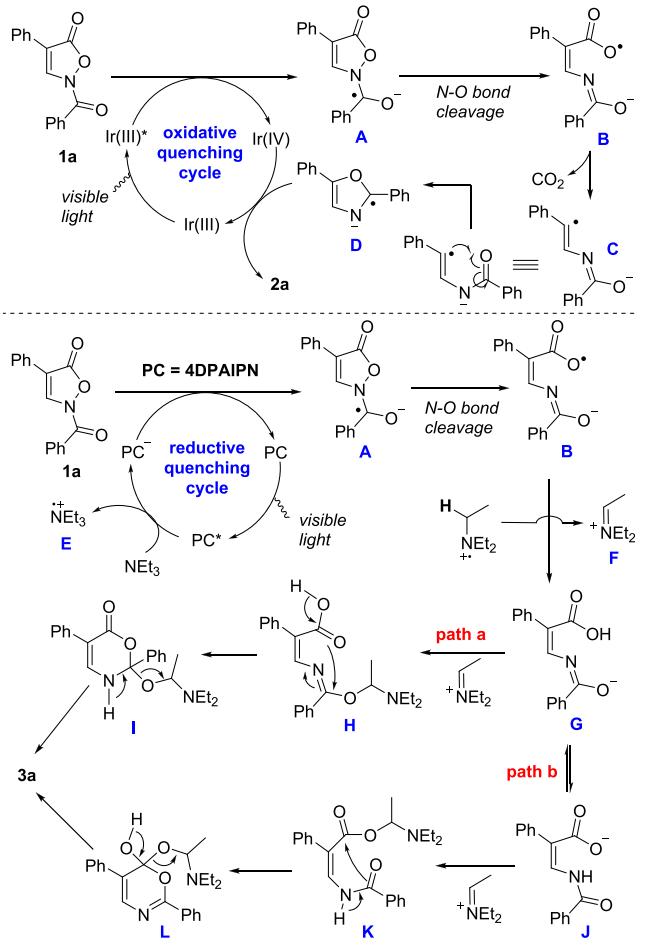
Scheme 3. Redox Profiles of Substrate and Photocatalyst



reducibility of $Ir(ppy)_3^-$ ($E_{1/2}^{III/II}$ = −2.19 V), we examined the rearrangement of 3-ethyl-isoxazol-5-one **1w** with *fac*-$Ir(ppy)_3$ as the photocatalyst and NEt_3 as the electron donor. Instead of the desired 1,3-oxazin-6-one product **3i**, *N*-acyl enamine **4** was obtained in 34% yield, indicating that the decarboxylation of substrates without a phenyl group on the 4-position was much faster than those bearing a phenyl group (Scheme 3, eq 1). As a comparison, nondecarboxylative product **3a** and oxazole **2a** were detected in yields of 39% and 3%, respectively, when the *fac*-$Ir(ppy)_3/NEt_3$ catalytic system was applied to the rearrangement of 4-phenyl-isoxazol-5-one **1a** (Scheme 3, eq 2).

According to the above observations and previous reports in literature, a possible pathway for the overall processes was proposed in Scheme 4. Visible-light-promoted decarboxylative

Scheme 4. Plausible mechanism



rearrangement of *N*-acyl-isoxazol-5-ones to oxazoles is supposed to proceed through the oxidative quenching of excited photocatalyst *fac*-$Ir(ppy)_3$*. Single electron reduction of **1a** by Ir(III)* generates radical ion **A**, followed by *β*-scission of the N−O bond to give intermediate **B**. The extrusion of a CO_2 molecule from **B** leads to vinyl radical **C**, which subsequently undergoes intramolecular addition to form oxazole radical anion **D**.[18] Finally, single electron oxidation of **D** by Ir(IV) gives oxazole **2a** with regeneration of the photocatalyst. In contrast, the formation of 1,3-oxazin-6-one **3a** is initiated by the reductive quenching of 4DPAIPN*. As described in Scheme 3, the reductive potential of 4DPAIPN* ($E_{1/2}^{PC^+/PC*}$= −1.28 V vs SCE) is not sufficient to reduce **1a** ($E_{1/2}$ = −1.50 V vs SCE) directly. Therefore, it has to be reduced to higher reducing species $4DPAIPN^-$ ($E_{1/2}^{PC/PC^-}$ = −1.52 V vs SCE) by NEt_3 prior to engaging in SET with **1a**. Instead of direct decarboxylation, intermediate **B** undergoes hydrogen abstraction from **E** to give carboxylic acid **G** and iminium ion **F**. Nucleophilic attack of iminium ion **F** by the carbonyl oxygen of the amide ion **G** leads to intermediate **H**, which undergoes a fast cyclization reaction to produce product **3a** with elimination of a molecule of *α*-OH amine (path a).[19] Alternatively, intramolecular proton transfer of **G**, followed by

DOI: 10.1021/acs.orglett.9b00903
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nucleophilic attack of the resulting carboxylate **J** to iminium ion **F**, and cyclization also afford the desired 1,3-oxazin-6-one **3a** (path b). Because carboxylate **J** is a more stable anion than **G** and the conversion of the carboxyl OH to a good leaving group is more common in organic synthesis, path b is probably a major route to form **3a**. As shown in Table 1, entry 19, the use of 1,4-dihydropyridine (DHP) is essentially ineffective for the reaction because its oxidation product pyridine is stable to intermediate **G**. Therefore, we assume that NEt_3 plays a threefold role for the formation of 1,3-oxazin-6-ones: (1) as an electron donor; (2) as a hydrogen donor; and (3) as the precursor of the iminium ion to promote the cyclization.

In conclusion, we have developed a mild and convenient approach to oxazoles and 1,3-oxazin-6-ones via visible-light-promoted decarboxylative and nondecarboxylative rearrangement of isoxazol-5-ones, respectively. The photocatalyst-controlled divergent mechanisms, namely oxidative and reductive quenching catalytic cycle, are utilized, and various oxazoles and 1,3-oxazin-6-ones are selectively obtained from the same isoxazol-5-one skeleton. Since isoxazol-5-ones are readily prepared from β-keto esters and their equivalents,[20] such a catalyst-controllable methodology is an important addition to those previous reports on diversity-oriented synthesis of *N*-heterocycles.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b00903.

Experimental details, characterization data, NMR spectra of all new products (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for the funds from the National Basic Research Program of China (Grant 2016YFA0602900), the National Natural Science Foundation of China (Grant No. 21871300), and the Natural Science Funds of Guangdong Province for Distinguished Young Scholars (Grant 2016A030306029).

■ REFERENCES

(1) da Silva, A. F.; Fernandes, A. A. G.; Thurow, S.; Stivanin, M. L.; Jurberg, I. D. *Synthesis* **2018**, *50*, 2473−2489.

(2) (a) Wollweber, H.-J.; Wentrup, C. *J. Org. Chem.* **1985**, *50*, 2041−2047. (b) Woodcock, S.; Green, D. V. S.; Vincent, M. A.; Hillier, I. H.; Guest, M. F.; Sherwood, P. *J. Chem. Soc., Perkin Trans. 2* **1992**, 2151−2154. (c) Cramer, C. J.; Truhlar, D. G. *J. Am. Chem. Soc.* **1993**, *115*, 8810−8817.

(3) Benson, S. W. *J. Chem. Educ.* **1965**, *42*, 502−518.

(4) (a) Prager, R. H.; Singh, Y. *Tetrahedron* **1993**, *49*, 8147−8158. (b) Ang, K. H.; Prager, R. H.; Smith, J. A.; Weber, B.; Williams, C. M. *Tetrahedron Lett.* **1996**, *37*, 675−678. (c) Prager, R. H.; Smith, J. A.; Weber, B.; Williams, C. M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2665−2672. (d) Clark, A. D.; Ha, U. T.; Prager, R. H.; Smith, J. A. *Aust. J. Chem.* **1999**, *52*, 1029−1033. (e) Clark, A. D.; Janowski, W. K.; Prager, R. H. *Tetrahedron* **1999**, *55*, 3637−3648. (f) Cox, M.; Heidarizadeh, F.; Prager, R. H. *Aust. J. Chem.* **2000**, *53*, 665−671. (g) Cox, M.; Prager, R. H.; Riessen, D. M. *Arkivoc* **2001**, *20*, 88−103. (h) Cox, M.; Dixon, M.; Lister, T.; Prager, R. H. *Aust. J. Chem.* **2004**, *57*, 455−460. (i) Abel, S.-A. G.; Eglinton, M. O.; Howard, J. K.; Hunt, D. J.; Prager, R. H.; Smith, J. A. *Aust. J. Chem.* **2014**, *67*, 1228−1233.

(5) (a) Okamoto, K.; Oda, T.; Kohigashi, S.; Ohe, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 11470−11473. (b) Okamoto, K.; Shimbayashi, T.; Tamura, E.; Ohe, K. *Chem. - Eur. J.* **2014**, *20*, 1490−1494. (c) Rieckhoff, S.; Hellmuth, T.; Peters, R. *J. Org. Chem.* **2015**, *80*, 6822−6830. (d) Okamoto, K.; Shimbayashi, T.; Yoshida, M.; Nanya, A.; Ohe, K. *Angew. Chem., Int. Ed.* **2016**, *55*, 7199−7202. (e) Rieckhoff, S.; Titze, M.; Frey, W.; Peters, R. *Org. Lett.* **2017**, *19*, 4436−4439. (f) Rieckhoff, S.; Frey, W.; Peters, R. *Eur. J. Org. Chem.* **2018**, *2018*, 1797−1805. (g) Shimbayashi, T.; Matsushita, G.; Nanya, A.; Eguchi, A.; Okamoto, K.; Ohe, K. *ACS Catal.* **2018**, *8*, 7773−7780.

(6) For a review see: (a) Zard, S. Z. *Chem. Commun.* **2002**, 1555−1563. For selected examples, see: (b) Jurberg, I. D. *Chem. - Eur. J.* **2017**, *23*, 9716−9720. (c) Capreti, N. M. R.; Jurberg, I. D. *Org. Lett.* **2015**, *17*, 2490−2493. (d) Huppé, S.; Rezaei, H.; Zard, Z. S. *Chem. Commun.* **2001**, 1894−1895. (e) Dias-Jurberg, I.; Gagosz, F.; Zard, S. Z. *Org. Lett.* **2010**, *12*, 416−419. (f) Boivin, J.; Elkaim, L.; Ferro, P. G.; Zard, S. Z. *Tetrahedron Lett.* **1991**, *32*, 5321−5324.

(7) Too, P. C.; Wang, Y.-F.; Chiba, S. *Org. Lett.* **2010**, *12*, 5688−5691.

(8) Murarka, S. *Adv. Synth. Catal.* **2018**, *360*, 1735−1753.

(9) (a) Okada, K.; Okamoto, K.; Morita, N.; Okubo, K.; Oda, M. *J. Am. Chem. Soc.* **1991**, *113*, 9401−9402. (b) Schnermann, M. J.; Overman, L. E. *Angew. Chem., Int. Ed.* **2012**, *51*, 9576−9580. (c) Pratsch, G.; Lackner, G. L.; Overman, L. E. *J. Org. Chem.* **2015**, *80*, 6025−6036. (d) Hu, C.; Chen, Y. *Org. Chem. Front.* **2015**, *2*, 1352−1355. (e) Yang, J.; Zhang, J.; Qi, L.; Hu, C.; Chen, Y. *Chem. Commun.* **2015**, *51*, 5275−5278. (f) Schwarz, J.; Konig, B. *Green Chem.* **2016**, *18*, 4743−4749. (g) Jiang, M.; Yang, H.; Fu, H. *Org. Lett.* **2016**, *18*, 1968−1971. (h) Xu, K.; Tan, Z.; Zhang, H.; Liu, J.; Zhang, S.; Wang, Z. *Chem. Commun.* **2017**, *53*, 10719−10722.

(10) (a) Tlahuext-Aca, A.; Garza-Sanchez, R. A.; Glorius, F. *Angew. Chem., Int. Ed.* **2017**, *56*, 3708−3711. (b) Sha, W.; Ni, S.; Han, J.; Pan, Y. *Org. Lett.* **2017**, *19*, 5900−5903. (c) Zhang, J.-J.; Yang, J.-C.; Guo, L.-N.; Duan, X.-H. *Chem. - Eur. J.* **2017**, *23*, 10259−10263. (d) Zhao, Y.; Chen, J.-R.; Xiao, W.-J. *Org. Lett.* **2018**, *20*, 224−227. (e) Kong, W.; Yu, C.; An, H.; Song, Q. *Org. Lett.* **2018**, *20*, 349−352. (f) Cheng, W.-M.; Shang, R.; Fu, Y. *ACS Catal.* **2017**, *7*, 907−911.

(11) (a) Jin, Z.; Li, Z.; Huang, R. *Nat. Prod. Rep.* **2002**, *19*, 454−476. (b) Lewis, J. R. *Nat. Prod. Rep.* **2002**, *19*, 223−258. (c) Jin, Z. *Nat. Prod. Rep.* **2011**, *28*, 1143−1191. (d) Momose, Y.; Maekawa, T.; Yamano, T.; Kawada, M.; Odaka, H.; Ikeda, H.; Sohda, T. *J. Med. Chem.* **2002**, *45*, 1518−1534. (e) Giddens, A. C.; Boshoff, H. I. M.; Franzblau, S. G.; Barry, C. E., III; Copp, B. R. *Tetrahedron Lett.* **2005**, *46*, 7355−7357.

(12) (a) Jarvest, R. L.; Parratt, M. J.; Debouck, C. M.; Gorniak, J. G.; Jennings, L. J.; Serafinowska, H. T.; Strickler, J. E. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2463−2466. (b) Gütschow, M.; Neumann, U. *Bioorg. Med. Chem.* **1997**, *5*, 1935−1942. (c) Neumann, U.; Schechter, N. M.; Gütschow, M. *Bioorg. Med. Chem.* **2001**, *9*, 947−954. (d) Kim, M. C.; Lee, J. H.; Shin, B.; Subedi, L.; Cha, J. W.; Park, J.-S.; Oh, D.-C.; Kim, S. Y.; Kwon, H. C. *Org. Lett.* **2015**, *17*, 5024−5027. (e) Fu, P.; La, S.; MacMillan, J. B. *J. Nat. Prod.* **2016**, *79*, 455−462.

(13) For reviews on the synthesis of oxazoles, see: (a) Yeh, V. S. C. *Tetrahedron* **2004**, *60*, 11995−12042. (b) Bresciani, S.; Tomkinson, N. C. O. *Heterocycles* **2014**, *89*, 2479−2453. (c) Ibrar, A.; Khan, I.; Abbas, N.; Farooq, U.; Khan, A. *RSC Adv.* **2016**, *6*, 93016−93047.

(14) For selected examples on 1,3-oxazin-6-one synthesis, see: (a) Chen, M.; Ren, Z.-H.; Wang, Y.-Y.; Guan, Z.-H. *Angew. Chem., Int. Ed.* **2013**, *52*, 14196−14199. (b) Liu, Q.; Chen, P.; Liu, G. *ACS Catal.* **2013**, *3*, 178−181. (c) Li, W.; Wu, X. F. *J. Org. Chem.* **2014**, *79*,

DOI: 10.1021/acs.orglett.9b00903
Org. Lett. XXXX, XXX, XXX−XXX

10410−10416. (d) Karad, S. N.; Chung, W.-K.; Liu, R.-S. *Chem. Sci.* **2015**, *6*, 5964−5968. (e) Liu, K.; Zou, M.; Lei, A. *J. Org. Chem.* **2016**, *81*, 7088−7092. (f) Verma, A.; Kumar, S. *Org. Lett.* **2016**, *18*, 4388−4291. (g) Song, P.; Yu, P.; Lin, J.-S.; Li, Y.; Yang, N.-Y.; Liu, X.-Y. *Org. Lett.* **2017**, *19*, 1330−1333. (h) Niu, B.; Jiang, B.; Yu, L.-Z.; Shi, M. *Org. Chem. Front.* **2018**, *5*, 1267−1271.

(15) Flamigni, L.; Barbieri, A.; Sabatini, C.; Ventura, B.; Barigelletti, F. *Top. Curr. Chem.* **2007**, *281*, 143−203.

(16) See Figures S1−S4 in the Supporting Information for cyclic voltammograms.

(17) Luo, J.; Zhang, J. *ACS Catal.* **2016**, *6*, 873−877.

(18) (a) Wang, H.; Yu, S. *Org. Lett.* **2015**, *17*, 4272−4275. (b) Jiang, H.; Cheng, Y.; Zhang, Y.; Yu, S. *Org. Lett.* **2013**, *15*, 4884−4887.

(19) Nikpour, F.; Bahmani, A.; Havasi, F.; Sharafi-Kolkeshvandi, M. *J. Heterocyclic Chem.* **2014**, *51*, 34−37.

(20) (a) Katritzky, A. R.; Barczynski, P.; Ostercamp, D. L.; Yousaf, T. I. *J. Org. Chem.* **1986**, *51*, 4037−4042. (b) Jacobsen, N.; Kolind-Andersen, H.; Christensen, J. *Can. J. Chem.* **1984**, *62*, 1940−1944. (c) Abignente, E.; de Caprariis, P. *J. Heterocycl. Chem.* **1983**, *20*, 1597−1599.

DOI: 10.1021/acs.orglett.9b00903
Org. Lett. XXXX, XXX, XXX−XXX