Visible-Light-Mediated Aerobic Oxidation of *N*-Alkylpyridinium Salts under Organic Photocatalysis

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S *Supporting Information*

ABSTRACT: Quinolones and isoquinolones exhibit diverse biological and pharmaceutical activities, and their synthesis is highly desirable under mild conditions. Here, a highly efficient and environmentally friendly visible light-mediated aerobic oxidation of readily available *N*-alkylpyridinium salts has been developed with Eosin Y as the organic photocatalyst and air as the terminal oxidant, and the reaction provided quinolones and isoquinolones in good yields. The method shows numerous advantages including mild and environmentally friendly conditions, high efficiency, tolerance of wide functional groups and low cost. Furthermore, 4-desoxylonimide with important pharmaceutical activities was effectively prepared by using our method. Therefore, the present method should provide a novel and useful strategy for synthesis and modification of *N*-heterocycles.
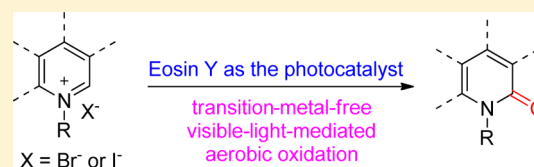
INTRODUCTION

N-Heterocycles are ubiquitous in natural products and biologically active molecules,[1] and they are assigned as privileged motifs in drug development.[2] The diverse functions of nitrogen-containing compounds highly depend on their characteristic structures, so the elaboration of *N*-heterocycles and the late-stage modification of drug candidates with *N*-heterocycles have emerged as an important strategy in organic synthetic chemistry and drug discovery.[3] *N*-Heterocycles containing a pyridine nucleus such as quinolines and isoquinolines are privileged scaffolds, and they occupy key roles in many medicinally related molecules.[4] However, the functionalization on the pyridine ring is a great challenge due to the low reactivity of π-electron-deficient pyridine skeleton.[5] Fortunately, it is easy to get *N*-alkylpyridinium salts via *N*-alkylation of the pyridine ring. On the other hand, quinolones and isoquinolones exhibit diverse biological and pharmaceutical activities. For example, quinolones show anticancer,[6] antibiotic,[7] antiviral, and antihypertensive[8] activities, and they are used as cannabinoid CB2 receptor inverse agonists,[9] neuronal maxi-K channel activators,[10] and AMPA/kainate and glycine antagonists.[11] Isoquinolones are useful antagonists of NK3,[12] agonists of melatonin MT1 and MT2 receptors,[13] and inhibitors of Rho-kinase,[14] JNK,[15] and thymidylate synthase,[16] and the isoquinolin-1(2*H*)-one pharmacophore is used in treatment of stomach tumors and diseases of human brain cells.[17] Therefore, it is highly desirable to develop a convenient, efficient and practical transformation from readily available quinolines and isoquinolines to quinolones and isoquinolones. To the best of our knowledge, the most common method is oxidation of *N*-alkylpyridinium salts using an excess of $K_3Fe(CN)_6$ as the oxidant.[18] Unfortunately, a large amounts of harmful $K_4Fe(CN)_6$ as waste appear together with the products. Recently, copper or iodine-catalyzed oxidative functionalizations of isoquinolines leading to isoquinolones have been reported.[19] However, the substrate scope is very limited. Recently, visible-light photoredox catalysis as an environmentally friendly, sustainable and unique process has received significant attention,[20] in which organic dyes[21] and Ru and Ir complexes[22] have been widely used as the photocatalyts. From an environmental point of view, molecular oxygen (O_2 and air) is an appealing oxidant in sustainable oxidative chemistry, and its advantages include abundance, low cost, and water as main byproduct.[23] As part of our continuing development on the visible-light photoredox organic reactions,[24] we report herein a highly efficient and environmentally friendly visible light-mediated aerobic oxidation of *N*-alkylpyridinium salts with air under organic photocatalysis at room temperature.

RESULTS AND DISCUSSION

First, the visible-light photoredox aerobic oxidation of 1-methylquinolinium iodide (**1c**) was selected as the model to optimize the reaction conditions. As shown in Table 1, several common photocatalysts including Ir and Ru complexes, $Ir(ppy)_2(dtbbpy)(PF_6)$ (**A**), $Ir(dF(CF_3)ppy)_2(dtbbpy)(PF_6)$ (**B**), [*fac*-Ir(ppy)$_3$] (**C**), and [Ru(bpy)$_3$]Cl$_2$ (**D**), and an organic dye, Eosin Y (**E**), were screened with K_3PO_4 as the base and DMF as the solvent under air atmosphere and irradiation of 40 W compact fluorescent light (CFL) for 10 h (entries 1–5), and we found that Eosin Y (**E**) provided the highest yield (entry 5). Only 8% yield was obtained in the absence of photocatalyst (entry 6). Subsequently, other four bases,

Table 1. Optimization of Conditions for Visible-Light Photoredox Aerobic Oxidation of 1-Methylquinolinium Iodide (1c) Leading to 1-Methyl-2-quinolinone (2c)[a]
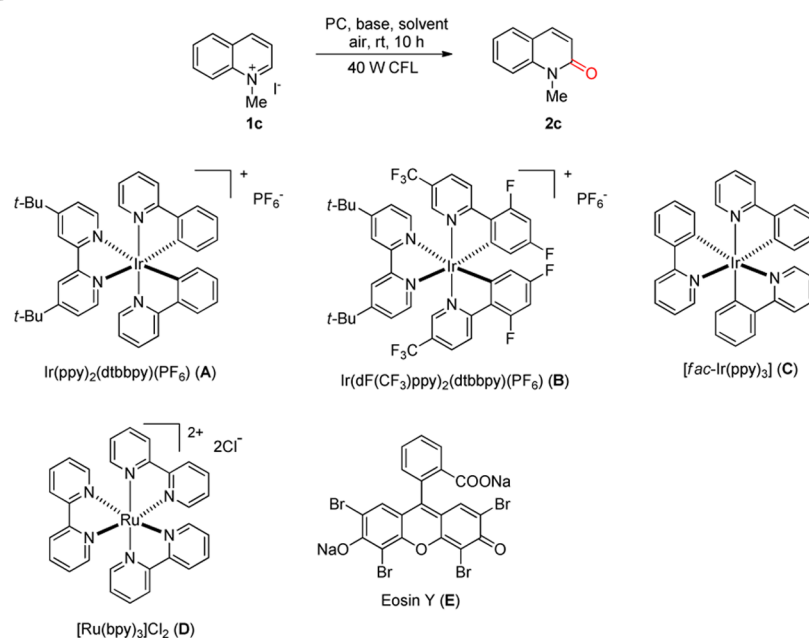

entry	PC	base	solvent	yield (%)[b]
1	A	K_3PO_4	DMF	57
2	B	K_3PO_4	DMF	41
3	C	K_3PO_4	DMF	46
4	D	K_3PO_4	DMF	22
5	E	K_3PO_4	DMF	64
6		K_3PO_4	DMF	8
7	E	Cs_2CO_3	DMF	68
8	E	Na_2CO_3	DMF	33
9	E	$NaHCO_3$	DMF	19
10	E	NEt_3	DMF	trace
11	E		DMF	NR
12	E	Cs_2CO_3	DMSO	80
13	E	Cs_2CO_3	CH_3CN	49
14	E	Cs_2CO_3	THF	87 (84[c])
15	E	Cs_2CO_3	EtOH	63
16	E	Cs_2CO_3	DCE	54
17[d]	E	Cs_2CO_3	THF	NR
18[e]	E	Cs_2CO_3	THF	85
19[f]	E	Cs_2CO_3	THF	86
20[g]	E	Cs_2CO_3	THF	NR

[a]Reaction conditions: air atmosphere and irradiation of visible light with 40 W CFL, 1-methylquinolinium iodide (1c) (0.2 mmol), photocatalyst (PC) (4 μmol), base (0.3 mmol), solvent (2 mL), temperature (rt, ~25 °C), time (10 h) in a 10 mL glass tube. [b]Conversion yields were determined by ¹H NMR using trichloroethylene as the internal standard. [c]Isolated yield. [d]No light. [e]The reaction was performed under irradiation of 3 W green LED instead of CFL for 24 h. [f]Oxygen atmosphere instead of air. [g]Argon atmosphere instead of air. PC = photocatalyst. DCE = 1,2-dichloroethane. CFL = compact fluorescent light. NR = no reaction.

Cs_2CO_3, Na_2CO_3, $NaHCO_3$ and NEt_3, were attempted, and Cs_2CO_3 was found to be a suitable base (compare entries 5, 7–10). No aerobic oxidation occurred in the absence of base (entry 11). Next, effect of solvents was investigated, and THF provided the highest yield (compare entries 7, 12–16) although substrate 1c and photocatalyst E were of low solubility in THF. On the contrary, DMF (entry 7) and DMSO (entry 12) with good solubility gave lower yields. A possible reason is that a low concentration of substrate in the reaction solution is favorable for control of reaction rate, which leads to formation of less byproducts. Furthermore, the reaction did not work without irradiation of visible light (entry 17). A similar yield was obtained when the reaction was performed under irradiation of 3 W green LED instead of CFL for 24 h (entry 18). Finally, influence of atmosphere was surveyed, and reaction under oxygen atmosphere almost provided the same yield as that under air atmosphere (entry 19), but no product was observed under argon atmosphere (entry 20).

With the optimized visible-light photoredox aerobic oxidation conditions in hand, the substrate scope of N-methylpyridinium salts was surveyed (Table 2). First, we attempted different substituted monocyclic N-methylpyridinium salts, and the results showed that the substrates with meta-electron-withdrawing groups provided the corresponding

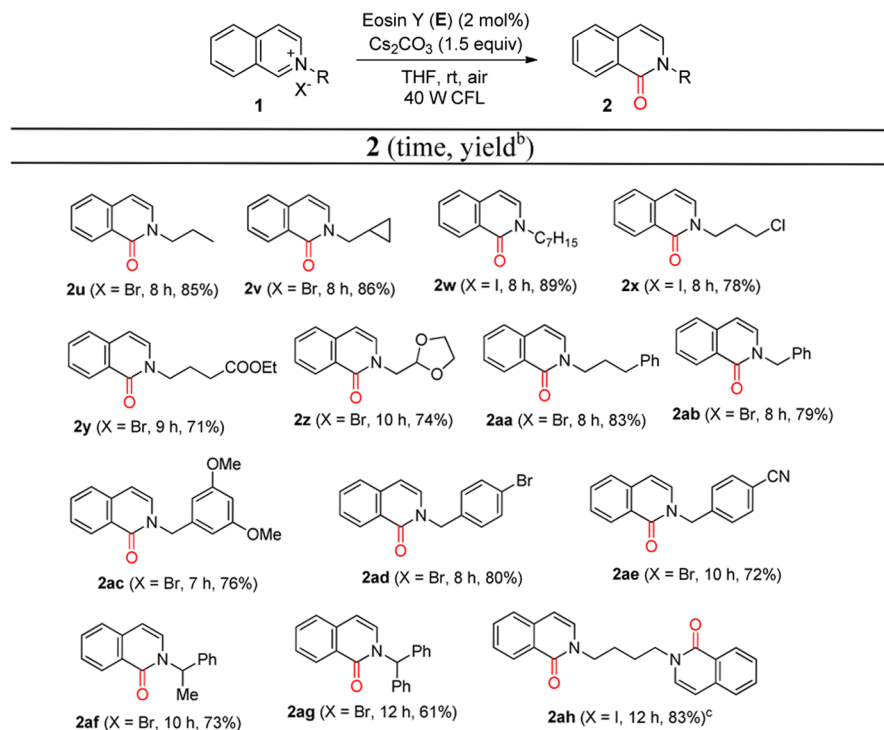## Table 2. Substrate Scope for Visible Light-Mediated Aerobic Oxidation of N-Methylpyridinium Salts[a]
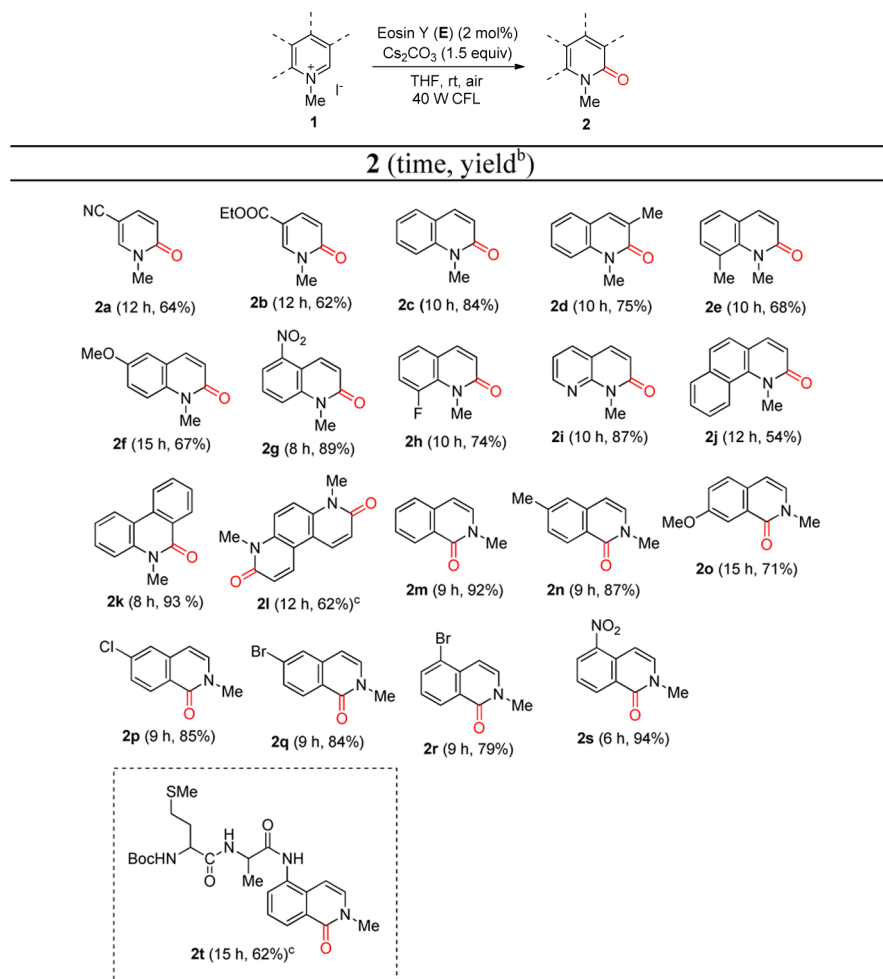
[a]Reaction conditions: air atmosphere and irradiation of visible light with 40 W CFL, N-methylpyridinium salt (**1**) (0.2 mmol), Eosin Y (4 μmol), Cs$_2$CO$_3$ (0.3 mmol), THF (2 mL), temperature (rt, ~25 °C), time (6–15 h) in a 10 mL glass tube. [b]Isolated yield. [c]Using DMSO as the solvent instead of THF. Boc = *tert*-butyloxycarbonyl.

N-methyl pyridones in moderate yields (see **2a** and **2b**). However, other N-methylpyridinium salts were not good substrates. Next, various N-methylquinolinium (see **2c–l**) and N-methylisoquinolinium salts (see **2m–t**) were used as the substrates, and they gave the corresponding quinolones and isoquinolones in good to excellent yields. We found that the substrates containing electron-withdrawing groups on the phenyl rings exhibited higher reactivity than those containing electron-donating groups. The substrate with two N-methyl-pyridinium rings provided a satisfactory result (62% yield) (see **2l**). N-Methylquinolinium salt linking with dipeptide (Met-Ala) also was a good substrate (see **2t**). The present method could tolerate various functional groups including cyano (see **2a**), ester (see **2b**), ether (see **2f** and **2o**), nitro (see **2g** and **2s**), and amide (see **2t**) groups, C−F (see **2h**), C−Cl (see **2p**), and C−Br (see **2q** and **2r**) bonds.

Subsequently, reactivity of different alkyl substituted N-alkylisoquinolinium salts (**1**) was investigated (Table 3), and they showed similar results to the substrates in Table 2 providing the corresponding isoquinolones in good to excellent yields. The substrate with two N-alkylisoquinolinium salts afforded product **2ah** with isoquinolone rings in 83% yield. Some functional group tolerance was also observed including

C−Cl (see **2x**) and C−Br (see **2ad**) bonds, ester (see **2y**), acetal (see **2z**), ether (see **2ac**), and cyano (see **2ae**) groups.

To demonstrate synthetic practicability of the present visible-light photoredox aerobic oxidative protocol, a gram-scale experiment was performed. As shown Scheme 1A, photo-catalytic aerobic oxidation of 2-methyl-5-nitroisoquinolin-2-ium iodide (**1s**) (1.58 g) was performed under the standard conditions, and 2-methyl-5-nitroisoquinolin-1(2H)-one (**2s**) was obtained in 92% yield (0.94 g), which was similar to the small-scale reaction in Table 2 almost without loss of efficiency. 4-Desoxylinomide (**6**) has shown to own antiangiogenic activity and potential in the treatment of autoimmune disease such as rheumatoid arthritis, systemic lupus erythematosis and multiple functions in clinical trials,[25] so it is highly desirable to develop a simple route to **6**. As shown in Scheme 1B, coupling of commercially available quinoline-3-carboxylic acid (**3**) with N-methylaniline provided amide **4** in 85% yield, and N-methylation of **4** gave **5** in almost quantitative yield. Finally, photocatalytic aerobic oxidation of **5** by using our method afforded the desired target product (**6**) in a three-step total yield of 74%. We attempted photocatalytic aerobic oxidation of 1,3-dimethyl-1H-benzo[*d*]imidazol-3-ium iodide (**7**) under the standard conditions (Scheme 1C). To our pleasure, 1,3-dimethyl-1H-benzo[*d*]imidazol-2(3H)-one (**8**) was obtained in

Table 3. Substrate Scope for Visible-Light-Mediated Aerobic Oxidation of *N*-Alkylisoquinolinium Salts[a]

2 (time, yield[b])

2u (X = Br, 8 h, 85%) 2v (X = Br, 8 h, 86%) 2w (X = I, 8 h, 89%) 2x (X = I, 8 h, 78%)

2y (X = Br, 9 h, 71%) 2z (X = Br, 10 h, 74%) 2aa (X = Br, 8 h, 83%) 2ab (X = Br, 8 h, 79%)

2ac (X = Br, 7 h, 76%) 2ad (X = Br, 8 h, 80%) 2ae (X = Br, 10 h, 72%)

2af (X = Br, 10 h, 73%) 2ag (X = Br, 12 h, 61%) 2ah (X = I, 12 h, 83%)[c]

[a]Reaction conditions: air atmosphere and irradiation of visible light with 40 W CFL, *N*-alkylisoquinolinium salt (**1**) (0.2 mmol), Eosin Y (4 μmol), Cs$_2$CO$_3$ (0.3 mmol), THF (2 mL), temperature (rt, ~25 °C), time (7−12 h) in a 10 mL glass tube. [b]Isolated yield. [c]Using DMSO as the solvent instead of THF.
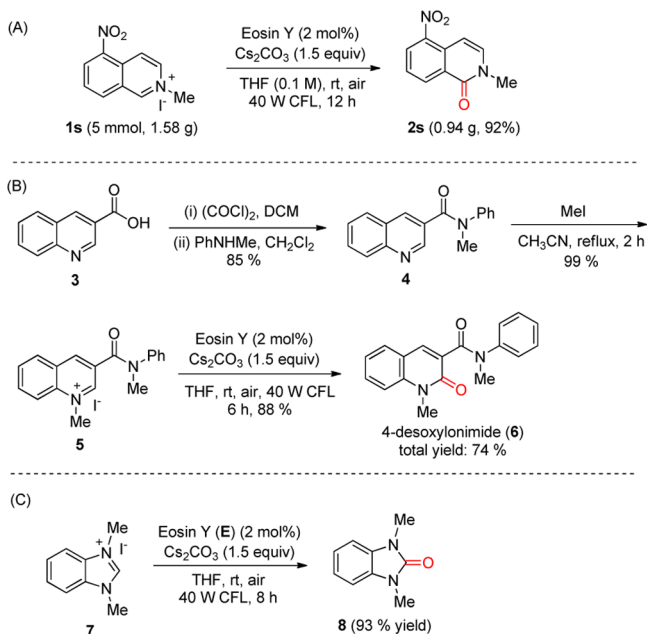
Scheme 1[a]

[a](A) Gram-scale synthesis of 2-methyl-5-nitroisoquinolin-1(2H)-one (**2s**). (B) Synthesis of 4-desoxylonimide (**6**) by using our method. (C) Photocatalytic aerobic oxidation of 1,3-dimethyl-1*H*-benzo[*d*]-imidazol-3-ium iodide (**7**) leading to 1,3-dimethyl-1*H*-benzo[*d*]-imidazol-2(3*H*)-one (**8**).

93% yield. The results above showed that our newly developed method was very effective and practical.

To explore mechanism of the visible light-mediated aerobic oxidation, Stern−Volmer fluorescence quenching experiments were first carried out. As shown in Figure 1A, 576 nm fluorescence launched by Eosin Y was observed when it was excited at 372 nm, and addition of 1-methylquinolinium iodide (**1c**) made the fluorescence intensity dramatically decrease. Meanwhile, the experiments indicated that other reagents such as oxygen in the system did not quench the fluorescence (see Figures S2−S7 in the Supporting Information for the details), which indicated a single electron transfer between Eosin Y and **1c**. Furthermore, the redox potentials of **1c** were measured to be $E_{1/2red}$ (**1c**) = −0.685 V vs SCE (see Figure S8 in the Supporting Information for details) that is higher than $E_{1/2ox}$ (**E***) = −1.15 V vs SCE,[26] and the results showed that **1c** could acquire a single electron from Eosin Y under irradiation of visible light.

Next, we surveyed types of the radicals produced under different conditions by electron spin resonance (ESR) in the presence of 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO) as the spin trapping agent (Figure 1B). A mixture of Eosin Y (2 mol %), Cs$_2$CO$_3$ (15 mM), and DMPO (10 mM) in DMSO was irradiated with 40 W CFL for 5 min under air atmosphere, and then a small amount of the solution was transferred to a capillary. The ESR spectrum showed that no signal was observed (Figure 1Ba). ESR spectrum for mixture of Eosin Y (2 mol %), **1c** (10 mM), Cs$_2$CO$_3$ (15 mM) and DMPO (10 mM) in DMSO without irradiation of visible light only showed a triplet-signal with a_N = 1.451 mT and g = 1.9996, which was probably attributed to reduction of DMPO by **1c** (Figure 1Bb). After irradiation of 40 W CFL for 5 min, ESR spectrum for mixture of Eosin Y (2 mol %), **1c** (10 mM), Cs$_2$CO$_3$ (15 mM), and DMPO (10 mM) in DMSO exhibited a new sextet-signal
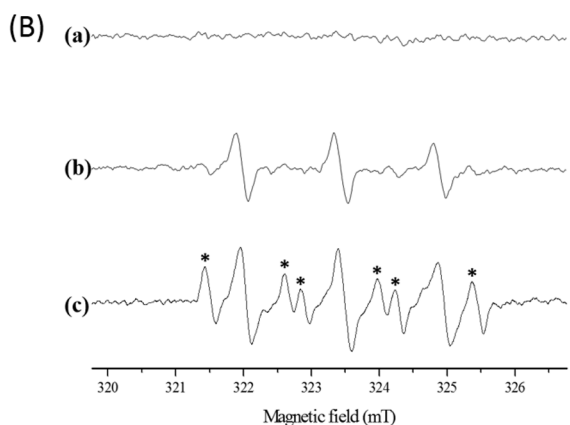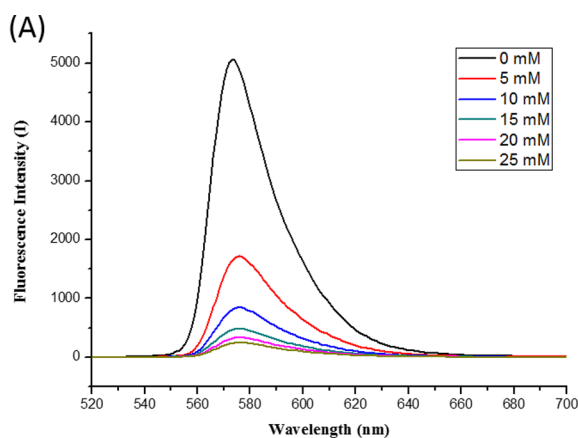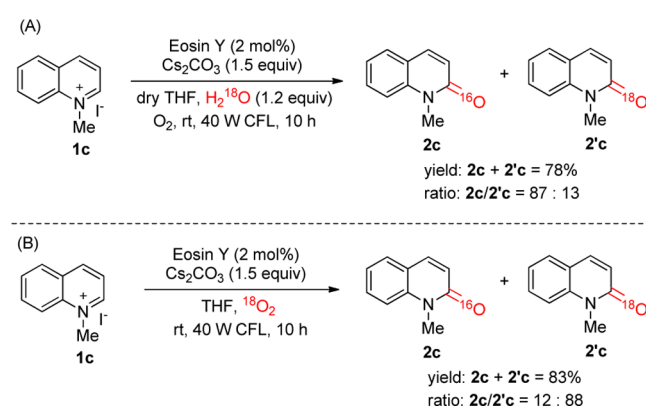
(A)

(B)

Figure 1. (A) Fluorescence emission spectra of Eosin Y (1 mM) with different concentration of **1c** excited at 372 nm. (B) (a) ESR spectrum of mixture of Eosin Y (2 mol %), Cs_2CO_3 (15 mM), and DMPO (10 mM) in DMSO under irradiation of 40 W CFL for 5 min. (b) ESR spectrum of mixture of Eosin Y (2 mol %), **1c** (10 mM), Cs_2CO_3 (15 mM), and DMPO (10 mM) in DMSO in the dark for 5 min. (c) ESR spectrum of mixture of Eosin Y (2 mol %), **1c** (10 mM), Cs_2CO_3 (15 mM), and DMPO (10 mM) in DMSO under irradiation of 40 W CFL for 5 min.

(a_N = 1.373 mT, and a_H = 1.164 mT, g = 1.9994) (Figure 1Bc), which indicated an alkdioxyl DMPO radical adduct occurred[27] (see Figure S1 in the Supporting Information for the details).

To further investigate mechanism of the photoredox aerobic oxidation, some control experiments were carried out. First, two ^{18}O-labeling experiments were handled as follows: (a) Visible-light photoredox aerobic oxidation of 1-methylquinolinium iodide (**1c**) was performed in the presence of ^{18}O-labeling water, and high resolution positive ion electrospray mass spectrum showed that **2c** was main product with minor ^{18}O-labeling product **2′c** appearing (Scheme 2A) (see Figure S9 in the Supporting Information for details). (b) When ^{18}O-labeling oxygen replaced common oxygen as atmosphere, ^{18}O-labeling product **2′c** was major (Scheme 2B) (see Figure S10 in the Supporting Information for details). The experimental results showed that the added oxygen atoms in the obtained products (**2**) in Tables 2 and 3 were mainly from molecular oxygen rather than water. When 2,2,6,6-tetramethylpiperidinooxy (TEMPO) or 2,6-di-*tert*-butyl-4-methylphenol (BHT) was added to the reaction system of **1c**, yields of **2c** obviously decreased, which indicated that the reaction could involve a radical process (see Figure S11a,b in the Supporting Information for details). The single oxygen pathway was

Scheme 2[a]

(A)

yield: **2c** + **2′c** = 78%
ratio: **2c/2′c** = 87 : 13

(B)

yield: **2c** + **2′c** = 83%
ratio: **2c/2′c** = 12 : 88

[a] (A) Visible-light photoredox aerobic oxidation of 1-methylquinolinium iodide (**1c**) in the presence of ^{18}O-labeling water. (B) Visible-light photoredox aerobic oxidation of 1-methylquinolinium iodide (**1c**) under ^{18}O-labeling oxygen atmosphere.

ruled out in the visible-light photoredox aerobic oxidation through the experiments in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) or THF-d_8 (see Figure S11c,d in the Supporting Information for details). In previous research, the electron donor−acceptor (EDA) complexes between Eosin Y (**E**) and pyridinium salts were found,[28] so we also investigated interaction between **1c** and **E** in DMSO or DMSO-d_6 by UV−vis and NMR spectroscopies, and the results showed that no EDA complex was observed in our reaction system (see Figures S12−S15 in the Supporting Information for details). In addition, quantum yield of the reaction using **1c** as the substrate was detected by following Yoon's method,[29] and the experiments implied the involvement of radical chain processes (see Figures S16 and S17 in the Supporting Information for details).

According to the results above, a possible mechanism for the visible light-mediated aerobic oxidation is proposed in Scheme 3. First, organic photocatalyst, Eosin Y, transforms into its excited state **E*** under irradiation of visible light. Next, a single electron transfer (SET) from **E*** to **1c** (here, **1c** is selected as an *example*) provides two radicals **I** and **E**[·+] (confirmed by fluorescence quenching experiments). Sequentially, coupling of

Scheme 3. Possible Mechanism for the Visible-Light Photoredox Aerobic Oxidation of *N*-Alkylpyridinium Salts
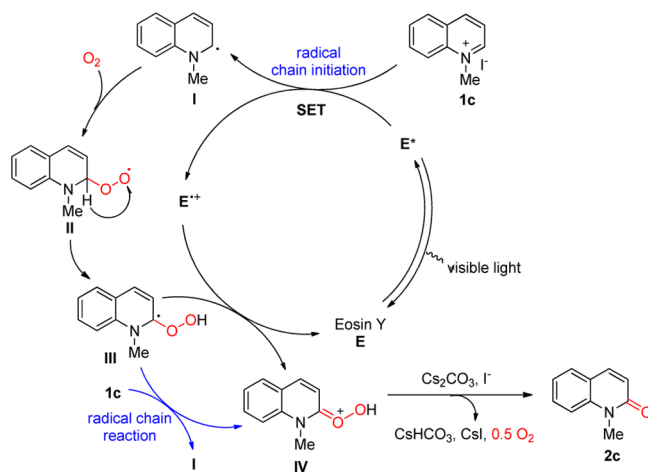
radical **I** with oxygen produces alkdioxyl radical **II** (detected by ESR).[27] Migration of a hydrogen radical in **II** forms carbon radical **III**, and another SET from **III** to **E**[.+] affords an oxygen-centered cation **IV** with regenerating the photocatalyst (**E**). Meanwhile, a radical chain reaction between **III** and **1c** through SET gives **I** and **IV**. Finally, treatment of **IV** with Cs_2CO_3 and I^- gets the target product (**2c**) with leaving $CsHCO_3$, CsI and 0.5 equiv of oxygen.[30]

CONCLUSIONS

We have developed a highly efficient and environmentally friendly visible light-mediated aerobic oxidation of N-alkylpyridinium salts with air under organic photocatalysis at room temperature. The corresponding N-methyl pyridones, quinolones, and isoquinolones were obtained in good yields, and 4-desoxylonimide with important pharmaceutical value was prepared in a high yield by using our method. The present method exhibits some advantages including mild and environmentally friendly conditions, high efficiency, tolerance of wide functional groups, and low cost. We believe that the method will find wide application in synthesis and modification of N-heterocycles.

ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b07883.

> Synthetic procedures, mechanism investigations, characterization data and ^1H, ^{13}C NMR spectra of these synthesized compounds (PDF)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

REFERENCES

(1) (a) *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: New York, 1984. (b) DeSimone, R. W.; Currie, K. S.; Mitchell, S. A.; Darrow, J. W.; Pippin, D. A. *Comb. Chem. High Throughput Screening* 2004, 7, 473.

(2) Leeson, P. D.; Springthorpe, B. *Nat. Rev. Drug Discovery* 2007, 6, 881.

(3) (a) Dyker, G. *Angew. Chem., Int. Ed.* 1999, 38, 1698. (b) Wencel-Delord, J.; Glorius, F. *Nat. Chem.* 2013, 5, 369.

(4) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* 2006, 4, 2337.

(5) Smith, D. M. In *Rodd's Chemistry of Carbon Compounds*; Coffey, S., Ed.; Elsevier: Amsterdam, 1976; Vol. 4, Part F, pp 27−229.

(6) (a) Claassen, G.; Brin, E.; Crogan-Grundy, C.; Vaillancourt, M. T.; Zhang, H. Z.; Cai, S. X.; Drewe, J.; Tseng, B.; Kasibhatla, S. *Cancer Lett.* 2009, 274, 243. (b) Ni, Z.-J.; Barsanti, P.; Brammeier, N.; Diebes, A.; Poon, D. J.; Ng, S.; Pecchi, S.; Pfister, K.; Renhowe, P. A.;

(7) Forbis, R. M.; Rinehart, K. L., Jr *J. Am. Chem. Soc.* 1973, 95, 5003.

(8) Afonso, A.; Weinstein, J.; Gentles, M. J. (Schering Corp.) Patent WO 9203327, 1992.

(9) Raitio, K. H.; Savinainen, J. R.; Vepsäläinen, J.; Laitinen, J. T.; Poso, A.; Järvinen, T.; Nevalainen, T. *J. Med. Chem.* 2006, 49, 2022.

(10) Hewawasam, P.; Fan, W.; Knipe, J.; Moon, S. L.; Boissard, V. C. G.; Gribkoff, K.; Starrett, J. E. *Bioorg. Med. Chem. Lett.* 2002, 12, 1779.

(11) (a) Cordi, A. A.; Desos, P.; Randle, J. C. R.; Lepagnol, J. *Bioorg. Med. Chem.* 1995, 3, 129. (b) Desos, P.; Lepagnol, J. M.; Morain, P.; Lestage, P.; Cordi, A. A. *J. Med. Chem.* 1996, 39, 197.

(12) Simonsen, K. B.; Kehler, J.; Juhl, K.; Khanzhin, N.; Nielsen, S. M. Patent WO2008131779 A1, 2008.

(13) Wong, Y. H.; Ho, M. K. C.; Hu, Y. Q.; New, D. C.; He, X. X.; Pang, H. H. Patent WO2008092292 A1, 2008.

(14) Plettenburg, O.; Lorenz, K.; Goerlitzer, J.; Loehn, M. Patent WO2008077555 A2.

(15) Asano, Y.; Kitamura, S.; Ohra, T.; Itoh, F.; Kajino, M.; Tamura, T.; Kaneko, M.; Ikeda, S.; Igata, H.; Kawamoto, T.; Sogabe, S.; Matsumoto, S.; Tanaka, T.; Yamaguchi, M.; Kimura, H.; Fukumoto, S. *Bioorg. Med. Chem.* 2008, 16, 4699.

(16) Li, S. W.; Nair, M. G.; Edwards, D. M.; Kisliuk, R. L.; Gaumont, Y.; Dev, I. K.; Duch, D. S.; Humphreys, J.; Smith, G. K.; Ferone, R. *J. Med. Chem.* 1991, 34, 2746.

(17) Glushkov, V. A.; Shklyaev, Y. V. *Chem. Heterocycl. Compd.* 2001, 37, 663.

(18) For selected papers, see: (a) González-Bello, C.; Abell, C.; Leeper, F. J. *J. Chem. Soc., Perkin Trans. 1* 1997, 1, 1017. (b) Youte, J.-J.; Barbier, D.; Al-Mourabit, A.; Gnecco, D.; Marazano, C. *J. Org. Chem.* 2004, 69, 2737. (c) Khalil, I. M.; Barker, D.; Copp, B. R. *J. Org. Chem.* 2016, 81, 282. (d) Ishi-i, T.; Hirashima, R.; Tsutsumi, N.; Amemori, S.; Matsuki, S.; Teshima, Y.; Kuwahara, R.; Mataka, S. *J. Org. Chem.* 2010, 75, 6858. (e) Fan-Chiang, T.-T.; Wang, H.-K.; Hsieh, J.-C. *Tetrahedron* 2016, 72, 5640.

(19) (a) Wang, D.; Zhang, R.; Deng, R.; Lin, S.; Guo, S.; Yan, Z. *J. Org. Chem.* 2016, 81, 11162. (b) Luo, W.-K.; Shi, X.; Zhou, W.; Yang, L. *Org. Lett.* 2016, 18, 2036.

(20) For selected reviews on visible-light photoredox catalysis, see: (a) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* 2013, 113, 5322. (b) Yoon, T. P.; Ischay, M. A.; Du, J. *Nat. Chem.* 2010, 2, 527. (c) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* 2011, 40, 102. (d) Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* 2012, 77, 1617. (e) Shi, L.; Xia, W. *Chem. Soc. Rev.* 2012, 41, 7687. (f) Xuan, J.; Xiao, W.-J. *Angew. Chem., Int. Ed.* 2012, 51, 6828. (g) Hari, D. P.; König, B. *Angew. Chem., Int. Ed.* 2013, 52, 4734. (h) Zeitler, K. *Angew. Chem., Int. Ed.* 2009, 48, 9785. (i) Xuan, J.; Zhang, Z.-G.; Xiao, W.-J. *Angew. Chem., Int. Ed.* 2015, 54, 15632. (j) Jin, Y.; Fu, H. *Asian J. Org. Chem.* 2017, 6, 368.

(21) For selected recent examples, see: (a) Romero, N. A.; Margrey, K. A.; Tay, N. E.; Nicewicz, D. A. *Science* 2015, 349, 1326. (b) Griffin, J. D.; Zeller, M. A.; Nicewicz, D. A. *J. Am. Chem. Soc.* 2015, 137, 11340. (c) Romero, N. A.; Nicewicz, D. A. *J. Am. Chem. Soc.* 2014, 136, 17024. (d) Wilger, D. J.; Grandjean, J.-M.; Lammert, T. R.; Nicewicz, D. A. *Nat. Chem.* 2014, 6, 720.

(22) For selected recent examples, see: (a) Zuo, Z.; Cong, H.; Li, W.; Choi, J.; Fu, G. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* 2016, 138, 1832. (b) Jin, J.; MacMillan, D. W. C. *Nature* 2015, 525, 87. (c) Cuthbertson, J. D.; MacMillan, D. W. C. *Nature* 2015, 519, 74. (d) Amador, A. G.; Sherbrook, E. M.; Yoon, T. P. *J. Am. Chem. Soc.* 2016, 138, 4722.

(23) For selected papers, see: (a) Shi, Z.; Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* 2012, 41, 3381. (b) Yuan, G.; Zheng, J.; Gao, X.; Li, X.; Huang, L.; Chen, H.; Jiang, H. *Chem. Commun.* 2012, 48, 7513. (c) Kang, Q.; Zhang, Y. *Green Chem.* 2012, 14, 1016. (d) Gao, W.; He, Z.; Qian, Y.; Zhao, J.; Huang, Y. *Chem. Sci.* 2012, 3, 883. (e) Yang, D.; Yang, H.; Fu, H. *Chem. Commun.* 2011, 47, 2348. (f) Wang, Y.; Zhu, X.; Chiba, S. *J. Am. Chem. Soc.* 2012, 134, 3679. (g) Zhang, G.; Ma, Y.; Wang, S.; Zhang, Y.; Wang, R. *J. Am. Chem. Soc.* 2012, 134, 12334.

Ramurthy, S.; Wagman, A. S.; Bussiere, D. E.; Le, V.; Zhou, Y.; Jansen, J. M.; Ma, S.; Gesner, T. G. *Bioorg. Med. Chem. Lett.* 2006, 16, 3121.

(h) Wendlandt, A. E.; Suess, A. M.; Stahl, S. S. *Angew. Chem., Int. Ed.* **2011**, *50*, 11062.

(24) (a) Jin, Y.; Jiang, M.; Wang, H.; Fu, H. *Sci. Rep.* **2016**, *6*, 20068. (b) Jiang, M.; Jin, Y.; Yang, H.; Fu, H. *Sci. Rep.* **2016**, *6*, 26161. (c) Jin, Y.; Yang, H.; Fu, H. *Chem. Commun.* **2016**, *52*, 12909. (d) Li, J.; Tian, H.; Jiang, M.; Yang, H.; Zhao, Y.; Fu, H. *Chem. Commun.* **2016**, *52*, 8862. (e) Gao, C.; Li, J.; Yu, J.; Yang, H.; Fu, H. *Chem. Commun.* **2016**, *52*, 7292. (f) Zhang, H.; Zhang, P.; Jiang, M.; Yang, H.; Fu, H. *Org. Lett.* **2017**, *19*, 1016. (g) Jin, Y.; Yang, H.; Fu, H. *Org. Lett.* **2016**, *18*, 6400. (h) Jiang, M.; Yang, H.; Fu, H. *Org. Lett.* **2016**, *18*, 1968. (i) Jiang, M.; Yang, H.; Fu, H. *Org. Lett.* **2016**, *18*, 5248. (j) Li, J.; Zhang, P.; Jiang, M.; Yang, H.; Zhao, Y.; Fu, H. *Org. Lett.* **2017**, *19*, 1994. (k) Yang, J.; Jiang, M.; Jin, Y.; Yang, H.; Fu, H. *Org. Lett.* **2017**, *19*, 2758. (l) Jiang, M.; Li, H.; Yang, H.; Fu, H. *Angew. Chem., Int. Ed.* **2017**, *56*, 874.

(25) (a) Muscia, G. C.; Bollini, M.; Bruno, A. M.; Asis, S. E. *J. Chil. Chem. Soc.* **2006**, *51*, 859. (b) Shi, J.; Xiao, Z.; Ihnat, M. A.; Kamat, C.; Pandit, B.; Hu, Z.; Li, P.-K. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 1187.

(26) Shen, T.; Zhao, Z.-G.; Yu, Q.; Xu, H.-J. *J. Photochem. Photobiol., A* **1989**, *47*, 203.

(27) (a) Zhang, Z.; Su, J.; Zha, Z.; Wang, Z. *Chem. Commun.* **2013**, *49*, 8982. (b) Qian, P.; Su, J.-H.; Wang, Y.; Bi, M.; Zha, Z.; Wang, Z. *J. Org. Chem.* **2017**, *82*, 6434.

(28) (a) Willner, I.; Eichen, Y.; Rabinovitz, M.; Hoffman, R.; Cohen, S. *J. Am. Chem. Soc.* **1992**, *114*, 637. (b) Willner, I.; Marx, S.; Eichen, Y. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1243. (c) Quint, V.; Morlet-Savary, F.; Lohier, J.-F.; Lalevee, J.; Gaumont, A.-C.; Lakhdar, S. J. *J. Am. Chem. Soc.* **2016**, *138*, 7436.

(29) Cismesia, M. A.; Yoon, T. P. *Chem. Sci.* **2015**, *6*, 5426.

(30) (a) Suzuki, N.; Kazui, Y.; Tsukamoto, T.; Kato, M.; Izawa, Y. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1519. (b) Motoyoshiya, J.; Inoue, H.; Takaguchi, Y.; Aoyama, H. *Heteroat. Chem.* **2002**, *13*, 252.