Organic LETTERS

Letter

pubs.acs.org/OrgLett

A New Approach to Nitrones through Cascade Reaction of Nitro Compounds Enabled by Visible Light Photoredox Catalysis

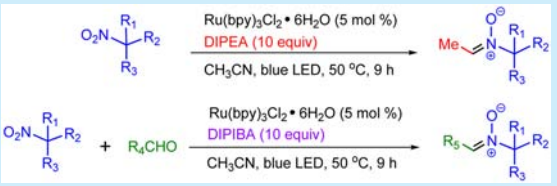
Cheng-Wei Lin,[†] Bor-Cherng Hong,*[,†] Wan-Chen Chang,[†] and Gene-Hsiang Lee[‡]

[†]Department of Chemistry and Biochemistry, National Chung Cheng University, Chia-Yi, 621, Taiwan, R.O.C.

[‡]Instrumentation Center, National Taiwan University, Taipei, 106, Taiwan, R.O.C.

Supporting Information

ABSTRACT: A series of nitroalkanes were efficiently transformed to alkylnitrones using a visible light irradiation photocatalytic process. The mild, efficient, and environmentally benign reaction method, involving dynamic reciprocations of cascade pathways, comprises a mixture of a $Ru(bpy)_3Cl_2$ photoredox catalyst and DIPIBA or Hünig's base in CH_3CN. Notably, DIPIBA was found to be the best additive for the cross condensation reaction of nitroalkanes with aldehydes. The structures of appropriate products were confirmed by X-ray analysis.

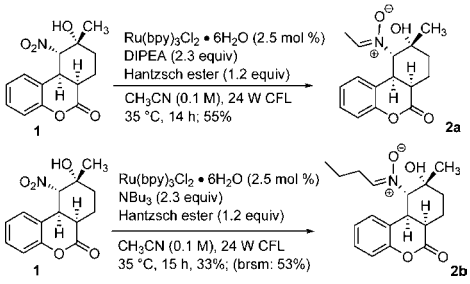


Nitrones have emerged as a key intermediate for the synthesis of naturally occurring compounds and are of medicinal importance.[1,2] The many reported nitrone reactions include 1,3-dipolar cycloadditions, [3 + 3] annulations, [5 + 2] annulations, nucleophilic additions, etc.[3] Alternatively, nitrones are well-known for trapping free radicals in chemical reactions and in biochemical systems. Recently, several nitrones have demonstrated potent biological activity against many diseases of aging, which are known to stem from enhanced levels of free radicals and oxidative stress, including Alzheimer's disease, cancer development, Parkinson disease, and stroke.[4]

Given their value in chemistry and biological systems, efforts have been devoted to the synthesis of nitrones. Nitrones have usually been prepared by condensation reactions between carbonyl compounds and oxidation of amines, imines, or hydroxylamines,[5] as well as by the reduction of nitroalkanes.[6] Other recent preparations include copper-mediated coupling of fluorenone oxime and vinyl boronic acid,[7] reduction of nitro nitriles,[8] and cyclization of β-allenyloximes.[9] Despite the versatility of the syntheses of nitrones, mild, efficient, and convenient approaches to nitrones from nitro compounds have been limited, and the harsh reagents and conditions for the previous methods have limited the application of such advances.[10]

Recently, visible light-induced photoredox catalysis[11] has received much attention and has been used as a key step protocol in organic synthesis. Nevertheless, the visible light photoredox catalyses of nitroalkanes are particularly scarce,[12] and most examples have been conducted on nitroaromatic compounds. During the course of our study in combining organocatalysis with photoredox catalysis,[13] we observed a visible-light-induced photoredox catalyzed reaction of nitroalkanes to efficiently afford the alkylnitrones. To the best of our knowledge, such a photoredox catalytic transformation for the preparation of alkylnitrone from nitroalkane is unprecedented and is a compelling theme of exploration.[14] Therefore, we have extended these studies, and herein we present the visible light photoredox catalysis of nitroalkanes. This reaction method constitutes a new entry to alkylnitrones under mild reaction conditions.

Scheme 1. Photoredox Catalysis of Nitroalkane 1



Initially, irradiation of the nitroalkane **1** in the presence of $Ru(bpy)_3Cl_2{\cdot}6H_2O$ (2.5 mol %), diisopropylethylamine (2.3 equiv), and Hantzsch ester (1.2 equiv) in CH_3CN with a household 24 W white compact florescent light bulb (CFL) at 35 °C for 14 h unexpectedly afforded nitrone **2a** in 55% yield (Scheme 1). Two questions arise from this noteworthy observation: (1) where does the ethyl group come from? and (2) how did the transformation occur and how can it be controlled for a better yield? To answer the first question, the same reaction was conducted with the replacement of DIPEA by NBu_3, followed by a 15 h irradiation to give the corresponding nitrone **2b**, although in lower 33% yield and with recovery of reasonable amounts of starting **1**. These results implied that the alkyl group on the nitrone product came from the alkylamine. In addition, the structure of **2b** was unambiguously assigned by the X-ray analysis of its single crystal (Figure 1).

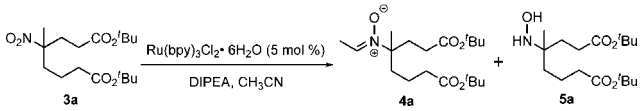
In order to optimize the reaction yield, a series of irradiation conditions were screened (Table 1). Irradiation of **3a** under a 24

Received: March 8, 2015
Published: April 20, 2015

DOI: 10.1021/acs.orglett.5b00684
Org. Lett. 2015, 17, 2314−2317

Figure 1. Stereoplots of the X-ray crystal structures of **2b** and **7m**: C, gray; O, red; N, blue.

Table 1. Screening of the Reaction Conditions for the Photoredoxcatalysis[a]



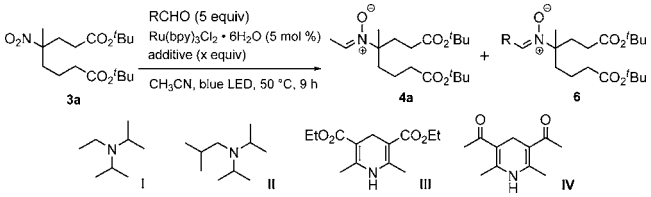
entry	light source	DIPEA (equiv)	time (h)	temp (C)[b]	yield (%)[c] 4a/5a
1	24 W white CFL	10	9	38	72/~0[d]
2[e]	blue LED	10	9	38	83/~0
3[f]	blue LED	10	9	50	90/~0
4[f]	blue LED	10	9	30[g]	87/~0
5[f]	blue LED	5	16	50	81/~0
6[f]	blue LED	2.5	32	50	trace[h]
7[f]	blue LED	10	4	~25[i]	22/41[j]

[a]The reactions were performed in 0.1 M of **3a**. [b]Temperature monitored around the reaction media. [c]Isolated yields. [d]Recovered ~20% starting material **3a**. [e]Under a strip of 24 blue LEDs, located 5 cm away from the reaction vessel. [f]Under a strip of 48 blue LEDs. [g]Temperature controlled by electronic fan. [h]Recovered most of starting material **3a**. [i]Temperature controlled by water bath. [j]Recovered ~30% **3a**.

W white CFL at 38 °C with DIPEA (10 equiv) in CH_3CN for 9 h gave a 72% yield of **4a** with 20% recovery of **3a** (Table 1, entry 1). The same reaction with a strip of 24 blue LEDs, positioned 5 cm away from the reaction vessel, at 38 °C provided an 83% yield of **4a** after 9 h of irradiation (Table 1, entry 2). We increased the light intensity by placing a strip of 48 blue LEDs at the same distance, accompanied by a slight increase of the reaction temperature to 50 °C, and observed the formation of **4a** in 90% yield (Table 1, entry 3). By controlling the reaction temperature at 30 °C with an electronic fan, we obtained a similar yield of **4a** (87%) (Table 1, entry 4). Alternatively, decreasing the DIPEA loading to 5 or 2.5 equiv resulted in a lower yield or only a trace amount of **4a** (Table 1, entries 5−6). Finally, by performing the reaction at ~25 °C for 4 h, a midway reaction time, provided **4a** and **5a** in 22% and 41% yields, respectively, with recovery of 30% of starting **3a** (Table 1, entry 7). The observation of the intermediate hydroxylamine **5a** shed some light on the domino reaction mechanism, vide infra. We also attempted to use different solvents, but acetonitrile was found to be the best choice. Consequently, the best photocatalysis conditions for this transformation were obtained as described in Table 1, entry 3.

Photoredox catalysis involving the α-alkylation of an amine has recently been observed;[15] however, Hünig's base (DIPEA), the common sacrificial electron donor, has rarely been reported to participate in the transformation under visible light photoredox catalysis.[16] Our preliminary observation of the aforementioned photocatalysis clearly demonstrated an unprecedented ethylating ability of DIPEA. To evaluate its competitive ethylation advantage against other aldehydes, the reaction was performed

Table 2. Screening of the Aldehydes and Additives for the Photoredox Catalysis[a]



entry	R	additive (equiv)	ratio[b] 4a/6	yield (%)[c] 4a/6
1	**a**. R = *n*-Pr	**I** (10)	26/74	22/69
2[d]	**a**. R = *n*-Pr	**I** (10)	40/60	32/59
3	**b**. R =Ph	**I** (10)	100/0	88/~0
4	**c**. R = *i*-Pr	**I** (10)	48/52	42/45
5	**a**. R = *n*-Pr	**II** (10)	5/95[e]	4/88[e]
6	**a**. R = *n*-Pr	**II** (5)	5/95[e]	3/65[e]
7	**a**. R = *n*-Pr	**III** (2.1)	0/100	0/27
8	**a**. R = *n*-Pr	**IV** (2.1)	0/100	0/37
9[f]	**a**. R = *n*-Pr	**III** (10)	0/100	0/70
10[f]	**a**. R = *n*-Pr	**IV** (10)	0/100	0/92

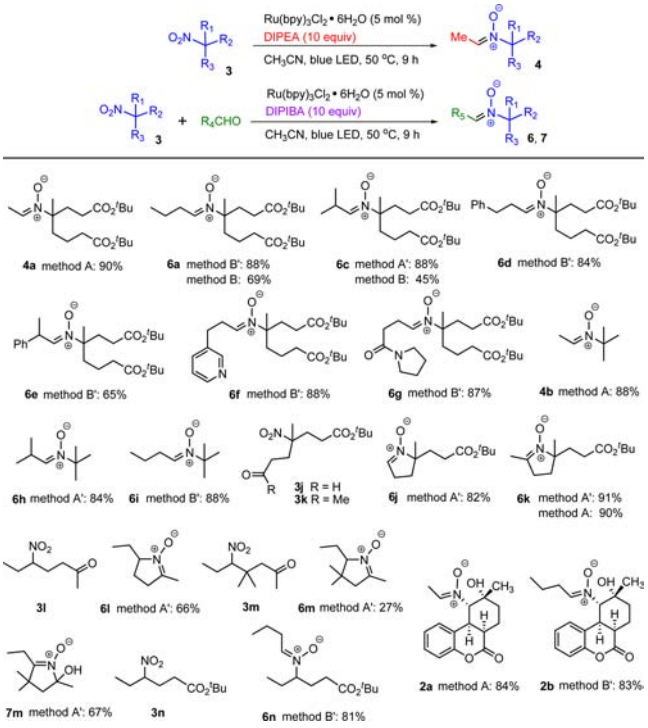
[a]Unless otherwise noted, the reactions were performed in 0.1 M of **3a** and 5 equiv of aldehydes, RCHO. [b]Determined by ^{1}H NMR of the crude product. [c]Isolated yields of **4** and **6**, respectively. [d]1.2 equiv of PrCHO was used. [e]**6c**/**6a**. [f]The reactions were performed in 0.01 M of **3a**.

with the addition of various aldehydes, e.g., butyraldehyde, benzaldehyde, and isobutyraldehyde (Table 2, entries 1−4). The reaction with 5 equiv of butyraldehyde gave the products of **4a**/**6a** in a ratio of 26/74, favoring the formation of the butyraldehyde-reacted product **6a** along with the non-negligible amount of **4a** (Table 2, entry 1). The reaction with 1.2 equiv of butyraldehyde provided an approximately 2:3 ratio of **4a**/**6a**, while the reaction with 5 equiv of benzaldehyde gave no observable **6b** (Table 2, entries 2−3). Interestingly, the reaction with isobutyraldehyde provided a 48/52 ratio of **4a**/**6c** (Table 2, entry 4). The low reactivity of isobutyraldehyde in this reaction may arise from the sterically encumbered isobutyl substituent. To circumvent the need to eliminate the ethylating ability of DIPEA in this photoreaction, these observations led us to envision a substitute for DIPEA, a replacement which should be a successful electron donor, but with less alkylating capability. In this context, *N*,*N*-diisopropylisobutylamine (**II**), DIPIBA, was selected for the transformation. Promisingly, the reaction with butyraldehyde and **II** under the same reaction conditions afforded a 5/95 ratio of **6c**/**6a** and gave an 88% isolated yield of the corresponding product **6a** (Table 2, entry 5). Reducing the amount of DIPIBA to 5 equiv for the reaction resulted in the formation of **6a** in a lower yield, 65% (Table 2, entry 6). The reaction with other additives, e.g., a Hantzsch ester (**III**) and **IV**, gave **6a** in low yields due to the low solubility of **III** and **IV** in CH_3CN (Table 2, entries 7−8). As a result, a 10-times diluted solution condition (0.01 M) was needed for the reactions of additives **III** and **IV**. The isolated yield of the reaction with **III** gave 70% of **6a**, while a 92% yield was obtained for the condition with **IV**. However, the high yields obtained under highly diluted reaction conditions were offset by the need for tedious purification procedures and by the high cost of **IV** (Table 2, entries 9−10).

Having established the optimal reaction conditions (Table 2, entry 5), we assessed the scope of the photoreaction toward various nitroalkanes with aldehydes and DIPEA or DIPIBA (methods B and B′), or in the absence of aldehyde, for

DOI: 10.1021/acs.orglett.5b00684
Org. Lett. 2015, 17, 2314−2317

Scheme 2. Scope of the Photoredox Transformation of Nitroalkane 3 to Nitrones[a]

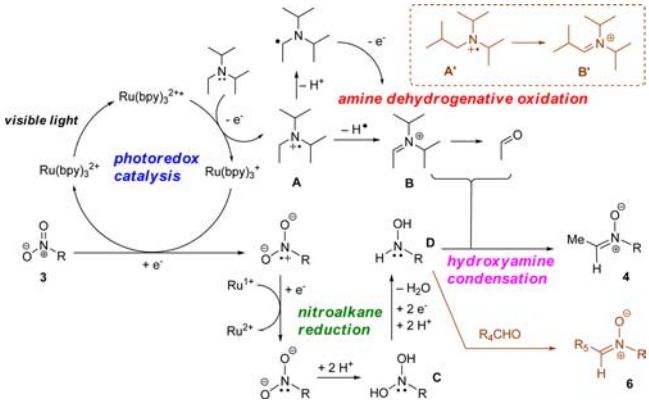


[a]The reactions were performed with catalyst (5 mol %) in 0.1 M of **3**. The yields presented are isolated yields. **Method A**: DIPEA (10 equiv). **Method A′**: DIPIBA (10 equiv). **Method B**: DIPEA (10 equiv), R_4CHO (5 equiv). **Method B′**: DIPIBA (10 equiv), R_4CHO (5 equiv).

introducing the acetyl or isobutyl group (methods A and A′), to give the corresponding nitrones (Scheme 2). All reactions were completed within 9 h and appeared quite general with respect to the nitroalkanes tested, providing the corresponding nitrones in good yields. For these examples, all acyclic nitrones obtained had the *Z*-configuration,[17] whereas the *E*-configuration was preferred with cyclic nitrones. For ethylation of nitroalkanes, the reaction condition with DIPEA (method A) was sufficient enough to achieve the objective (Scheme 2, compounds **4a**, **4b**, **2a**). However, for cross alkylation, in the presence of aldehydes, the reaction condition with DIPIBA (method B′) was superior to DIPEA (method B) and provided higher yields (Scheme 2, compounds **6a**, **2b**). The results demonstrate the proof of concept that DIPIBA can be a superior surrogate for Hünig's base in this photoredox catalysis.

The reaction mechanism of this photocatalyzed nitrone formation reaction was proposed to involve dynamic reciprocations of four coupled pathways as depicted in Scheme 3. Upon irradiation by blue LED, Ru^{2+} is excited to Ru^{2+}* and reductively quenched by DIPEA to produce Ru^{+} and the radical cation of DIPEA (**A**) via SET oxidation (photoredox catalysis cycle). Subsequently, the radical cation **A** either releases a hydrogen radical or ejects a proton and is then converted into iminium intermediate **B** or acetaldehyde (amine dehydrogenative oxidation).[18] Alternatively, a series of reductions of nitroalkane (**3**) by Ru^{+} and protonation of intermediates give rise to the dihydroxyamine **C** and the hydroxylamine intermediate **D** (nitroalkane reduction process).[19] The concomitantly generated iminium intermediate **B** or acetaldehyde

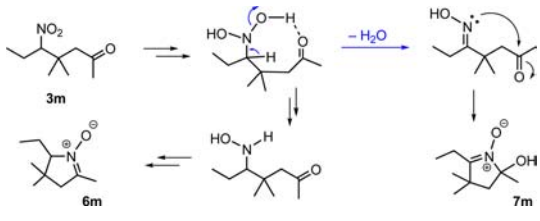
Scheme 3. Proposed Reaction Mechanism



(hydroxylamine condensation process) results in production of the corresponding alkylnitrone product. For the cross condensation reactions, in the case of additive aldehyde (R_4CHO), e.g., **6a**, **6d**, **6e**, **6f**, etc., DIPEA was replaced by DIPIBA (method B′). The aforementioned photoredox catalysis cycle was reductively quenched by DIPIBA (**A′**) to generate the isobutyl aldehyde or its iminium derivative (**B′**). Owing to the steric encumbrance of the isopropyl group and the lower reactivity of isobutyl aldehyde, the additive alkylaldehyde (R_4CHO) was able to compete with isobutyl aldehyde (or its iminium derivative) and reacted faster with hydroxylamine (**D**), thereby rendering the corresponding cross alkylated nitrone in high yields (cross condensation, pathway in brown in Scheme 3).

Intramolecular cyclization of nitroaldehyde (**3j**) or nitroketone (**3k**) gave rise to the corresponding nitroalkane **6j** and **6k** in 82% and 91% yields, respectively (Scheme 2). Such intramolecular reactions are feasible, and the reactions with either DIPEA or DIPIBA additives gave similar yields. In addition, reaction of nitroketone **3l**, the secondary nitroalkane, afforded the corresponding nitrone **6l** in 66% yield, along with a small amount of oxime. Interestingly, the reaction at the nitroalkane derivative **3m** led to the formation of a 27% yield of nitrone **6m** and an unexpected hydroxynitrone **7m** in 67% yield (X-ray stereoplot of **7m** in Figure 1). The disparate reaction pattern of **3m** with **3l** in the formation of **7m** may arise from the influence of the dimethyl group on **3m**, effected by the Thorpe−Ingold effect[20] and the intramolecular H-bonding assisted dehydration of dihydroxyamine (indicated by the blue arrow, Scheme 4),

Scheme 4. Plausible Reaction Mechanism for the Formation of Hydroxynitrone 7m



affording the oxime intermediate, followed by a condensation reaction. Finally, application of the developed photoredox reaction conditions (methods A and B′) on the aforementioned nitroalkane **1** gave substantially improved yields of the nitrone products **2a** and **2b**, 84% vs 55% and 83% vs 33%, respectively (Schemes 2 and 1).

DOI: 10.1021/acs.orglett.5b00684
Org. Lett. 2015, 17, 2314−2317

In summary, we have realized a concise visible-light-induced photocatalytic conversion of nitro compounds with various functionalities to the nitrone derivatives in high yield. The one-pot method not only provides a mild and concise process which adds to the repertoire of nitrone formation methodologies but also demonstrates a proof of concept of the synergistic action of photoredox catalytic cycles and condensation processes. The cross condensation method was not previously achieved by assistance with Hünig's base, but in this case, we achieved this transformation with the addition of DIPBIA as the sacrificial electron donor. The advent of a Hünig base surrogate provides a new pathway for photoredox catalysis which was previously not accessible. The structures of the appropriate products were unambiguously confirmed by single crystal X-ray crystallographic analyses. Given the importance of the nitrone functionality in synthetic and medicinal chemistry, this mild and efficient reaction method could constitute a useful protocol with broad applications in chemical synthesis.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and characterization data for the new compounds and X-ray crystallographic data for compounds **2b** and **7m**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: chebch@ccu.edu.tw.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We acknowledge the financial support for this study from the Ministry of Science and Technology (MOST, Taiwan) and thank the instrument center of MOST for analyses of compounds.

■ REFERENCES

(1) For reviews: (a) Grigor'ev, I. A. Nitrones: Novel Strategies in Synthesis. In *Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis: Novel Strategies in Synthesis*; Feuer, H., Ed.; Wiley: Hoboken, NJ, 2008; p 129. (b) Frederickson, M. *Tetrahedron* **1997**, *53*, 403. (c) Romeo, G.; Iannazzo, D.; Piperno, A.; Romeo, R.; Corsaro, A.; Rescifina, A.; Chiacchio, U. *Mini. Rev. Org. Chem.* **2005**, *2*, 59. (d) Revuelta, J.; Cicchi, S.; Goti, A.; Brandi, A. *Synthesis* **2007**, 485.

(2) (a) Brandi, A.; Cardona, F.; Cicchi, S.; Cordero, F. M.; Goti, A. *Chem.—Eur. J.* **2009**, *15*, 7808. (b) Merino, P.; Mannucci, V.; Tejero, T. *Eur. J. Org. Chem.* **2008**, 3943. (c) Merino, P.; Delso, I.; Tejero, T.; Cardona, F.; Marradi, M.; Faggi, E.; Parmeggiani, C.; Goti, A. *Eur. J. Org. Chem.* **2008**, 2929. (d) Alcaide, B.; Sáez, E. *Eur. J. Org. Chem.* **2005**, 1680. (e) Cicchi, S.; Marradi, M.; Vogel, P.; Goti, A. *J. Org. Chem.* **2006**, *71*, 1614. (f) Shibue, T.; Hirai, T.; Okamoto, I.; Morita, N.; Masu, H.; Azumaya, I.; Tamura, O. *Chem.—Eur. J.* **2010**, *16*, 11678. (g) Parmeggiani, C.; Cardona, F.; Giusti, L.; Reissig, H.-U.; Goti, A. *Chem.—Eur. J.* **2013**, *19*, 10595. (h) Gilles, P.; Py, S. *Org. Lett.* **2012**, *14*, 1042.

(3) For select reviews: (a) Yang, J. *Synlett* **2012**, *23*, 2293. (b) Torssell, K. B. G. *Nitrile Oxides, Nitrones, and Nitronates in Organic Synthesis*; VCH: Weinheim, 1988; p 75. (c) Confalone, P. N.; Huie, E. M. *The [3 + 2] nitrone-olefin cycloaddition reaction*. In *Organic Reactions*; Kende, A. S., Ed; Wiley: New York, 1988; *Vol 36*; p 1. (d) Breuer, E. Nitrones and nitronic acid derivatives. In *Nitrones, Nitronates and Nitroxides*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1989; p 139.

(4) Floyd, R. A.; Kopke, R. D.; Choi, C.-H.; Foster, S. B.; Doblas, S.; Towner, R. A. *Free Radical Biol. Med.* **2008**, *45*, 1361.

(5) Thiverny, M.; Demory, E.; Baptiste, B.; Philouze, C.; Chavant, P. Y.; Blandin, V. *Tetrahedron: Asymmetry* **2011**, *22*, 1266.

(6) (a) Black, D. S.; Edwards, G. L.; Evans, R. H.; Keller, P. A.; Laaman, S. M. *Tetrahedron* **2000**, *56*, 1889. (b) Gautheron-Chapoulaud, V.; Pandya, S. U.; Cividino, P.; Masson, G.; Py, S.; Vallée, Y. *Synlett* **2001**, 1281.

(7) Mo, D.-L.; Wink, D. A.; Anderson, L. L. *Org. Lett.* **2012**, *14*, 5180.

(8) Grela, K.; Konopski, L. *Tetrahedron* **2010**, *66*, 3608.

(9) Man, S.; Buchlovič, M.; Potáček, M. *Tetrahedron Lett.* **2006**, *47*, 6961.

(10) The nitro group, recognized as a "synthetic chameleon", can be further transformed to various functionalities. Therefore, the nitro group has been widely applied in asymmetric organocatalysis; for a recent review, see: (a) Aitken, L. S.; Arezki, N. R.; Dell'Isola, A.; Cobb, A. J. A. *Synthesis* **2013**, *45*, 2627. For a recent review of naturally occurring nitro compounds, see: (b) Parry, R.; Nishino, S.; Spain, J. *Nat. Prod. Rep.* **2011**, *28*, 152.

(11) For recent reviews: (a) Yoon, T. P.; Ischay, M. A.; Du, J. *Nat. Chem.* **2010**, *2*, 527. (b) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* **2011**, *40*, 102. (c) Xuan, J.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 6828. (d) Shi, L.; Xia, W. *Chem. Soc. Rev.* **2012**, *41*, 7687. (e) Ravelli, D.; Fagnoni, M.; Albini, A. *Chem. Soc. Rev.* **2013**, *42*, 97. (f) Reckenthäler, M.; Griesbeck, A. G. *Adv. Synth. Catal.* **2013**, *355*, 2727. (g) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322. (h) Schultz, D. M.; Yoon, T. P. *Science* **2014**, *343*, 1239176. (i) Xi, Y.; Yi, H.; Lei, A. *Org. Biomol. Chem.* **2013**, *11*, 2387.

(12) (a) Zhu, H.; Ke, X.; Yang, X.; Sarina, S.; Liu, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 9657. (b) Cai, S.; Zhang, S.; Zhao, Y.; Wang, D. Z. *Org. Lett.* **2013**, *15*, 2660. (c) Cismesia, M. A.; Ischay, M. A.; Yoon, T. P. *Synthesis* **2013**, *45*, 2699. (d) Yang, X. J.; Chen, B.; Zheng, L. Q.; Wu, L. Z.; Tung, C. H. *Green Chem.* **2014**, *16*, 1082.

(13) For a previous study in this series: Hong, B.-C.; Lin, C.-W.; Liao, W.-K.; Lee, G.-H. *Org. Lett.* **2013**, *15*, 6258.

(14) (a) For a recent independent study in the visible-light photoredox-catalyzed synthesis of nitrones: Hou, H.; Zhu, S.; Pan, F.; Rueping, M. *Org. Lett.* **2014**, *16*, 2872. (b) For a new approach to oximes via the visible light photoredox-catalyzed reaction of nitro compounds, see ref 12b.

(15) (a) Prier, C. K.; MacMillan, D. W. C. *Chem. Sci.* **2014**, *5*, 4173. (b) Pandey, G.; Jadhav, D.; Tiwari, S. K.; Singh, B. *Adv. Synth. Catal.* **2014**, *356*, 2813.

(16) (a) Singh, A.; Arora, A.; Weaver, J. D. *Org. Lett.* **2013**, *15*, 5390. (b) Dai, X.; Cheng, D.; Guan, B.; Mao, W.; Xu, X.; Li, X. *J. Org. Chem.* **2014**, *79*, 7212.

(17) Energy barriers of *E*-,*Z*-isomerizations of nitrones are high and the equilibration required higher temperature, and thus, the nitrones favored the more stable *Z*-configuration. (a) Hassan, A.; Wazeer, M. I. M.; Saeed, M. T.; Siddiqui, M. N.; Ali, S. A. *J. Phys. Org. Chem.* **2000**, *13*, 443. (b) Boyle, L. W.; Peagram, M. J.; Whitham, G. H. *J. Chem. Soc. B* **1971**, 1728.

(18) Alternatively, the initially formed DIPEA radical cation **A** could release a hydrogen radical and/or eject a proton toward the isopropyl substituent, instead of toward the ethyl group. However, such a contribution would not lead to the formation of an ethyl substituted nitrone product, but could provide the proton arsenal for the subsequent nitroalkane reduction process.

(19) (a) Hydroxyamine **5a** was isolated as described in Table 1, entry 7. (b) In a separate reaction, photocatalysis of (2-nitroethyl)benzene, a primary nitroalkane, under condition A′ gives a 58% yield of the corresponding oxime. Presumably, prior to further processing into hydroxylamine, primary dihydroxyamine tends to undergo dehydration to give the oxime product; see ref 12b.

(20) Levine, M. N.; Raines, R. T. *Chem. Sci.* **2012**, *3*, 2412.

■ NOTE ADDED AFTER ASAP PUBLICATION

On April 21, 2015 the structures of the nitrones were corrected in all graphics and the Supporting Information.

DOI: 10.1021/acs.orglett.5b00684
Org. Lett. 2015, 17, 2314−2317