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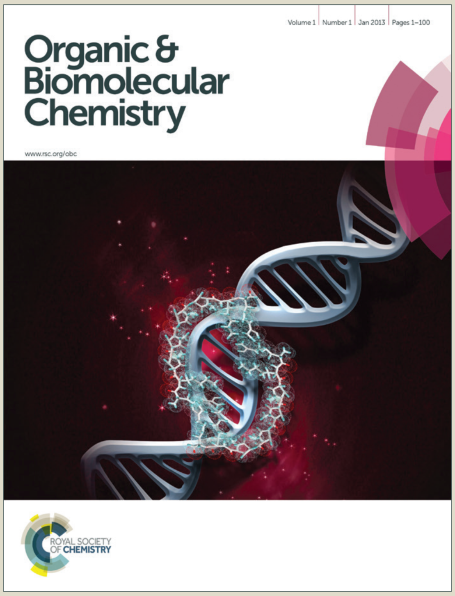

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# Photochemically-Induced C-C Bond Formation between Tertiary Amines and Nitrones

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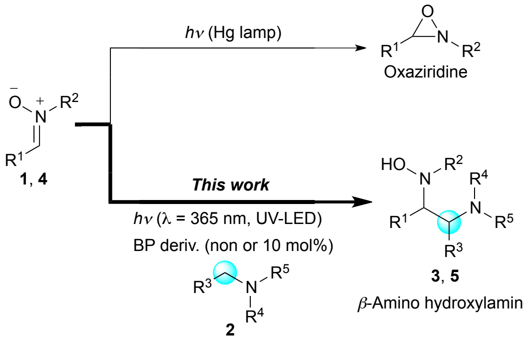
Kennosuke Itoh*[,a,b], Ryo Kato[b], Daito Kinugawa[b], Hideaki Kamiya[b], Ryuki Kudo[a], Masayuki Hasegawa[c], Hideaki Fujii*[,a], and Hiroyuki Suga*[,b]

Photoexcited nitrones served as excellent electron acceptors as well as radical acceptors in the presence of tertiary amines to give $\beta$-amino hydroxylamines via photochemically-induced direct sp$^3$ C-H functionalization of the tertiary amines. The combined use of an organophotosensitizer and photoirradiation was highly effective in accelerating addition reactions. Several nitrones and tertiary amines were successfully utilized to give $\beta$-amino hydroxylamines in good yields. Highly regioselective generation of primary $\alpha$-aminoalkyl radicals based on Lewis's stereoelectronic rule and diastereoselective addition reactions of primary $\alpha$-aminoalkyl radicals with nitrones were successfully achieved. Furthermore, the highly diastereoselective reaction of an $\alpha$-aminoalkyl radical with a chiral (*E*)-geometry-fixed $\alpha$-alkoxycarbonylnitrone was performed.

## Introduction

Direct functionalization of sp$^3$ C-H bonds adjacent to a nitrogen atom has emerged as a particularly attractive synthetic method to construct carbon-carbon bonds. An important method for promoting the reaction is the photosensitized reaction between tertiary amines and a C=X bond (X = C, N, O).[1~8] Benzophenone (BP) derivatives, representative of aromatic carbonyl photosensitizers, have enabled several organic transformations to proceed[1,2,3,5,8] and have been studied in terms of their attractive photophysical properties as well as their photochemical properties from the theoretical point of view.[9,10] BP derivatives have also been investigated as organophotocatalysts that enable several useful organic reactions and for developing greener organic reactions for their attractive properties. BP is excited by absorption of UV light to generate the excited singlet state of BP [$^1$(n, $\pi$)*] ($^1$BP*), and then intersystem crossing (ISC), a very fast process with a picosecond time scale, exerts its effects by the El-Sayed rule to generate the excited triplet state of BP [$^3$($\pi$, $\pi$)*] which then decays to the excited triplet state of BP [$^3$(n, $\pi$)*] ($^3$BP*).[11] On the other hand, when photoirradiation is conducted in the presence of a tertiary amine and BP, a corresponding $\alpha$-aminoalkyl radical and a benzophenone ketyl radical are generated at the same time.



**Scheme 1** Photochemically-induced addition of an $\alpha$-aminoalkyl radical to a nitrone

The resulting $\alpha$-aminoalkyl radicals are labile species which react with $\alpha,\beta$-unsaturated carbonyl compounds and ketones.[2,3,12] Hoffmann *et al.* have vigorously developed and well established these reactions.[3] Recently, Inoue and Kamijo *et al.* have developed several photoinduced direct functionalizations of sp$^3$ C-H bonds catalyzed by BP derivatives.[8] Several investigations have focused on discovering radical acceptors as well as determining the characteristics and reactivities of $\alpha$-aminoalkyl radicals. However, successful examples of the reaction of $\alpha$-aminoalkyl radicals with a C=N bond under photoirradiation are still rare.[6,7,13,14] Thus, we considered that the development of a novel addition of the $\alpha$-aminoalkyl radical to a C=N bond would be a worthwhile undertaking.

We have focused on the features of nitrone **1** which serves as a good radical acceptor for alkyl radicals to permit generation of aminoxyl radical intermediates. Aminoxyl radicals are known as stable radicals due to spin delocalization

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[a] *Department of Medicinal Chemistry, School of Pharmacy, Kitasato University, 5-9-1 Shirokane, Minato-ku, Tokyo 108-8641, Japan. E-mail: itok@pharm.kitasato-u.ac.jp*
[b] *Department of Chemistry and Material Engineering, Shinshu University, 4-17-1 Wakasato, Nagano 380-8553, Japan.*
[c] *Planning & Coordination Office, Petrochemicals & Plastics Sector, Sumitomo Chemical Co., Ltd., 2-27-1 Shinkawa, Chuo-ku, Tokyo 104-8260, Japan.*

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between the nitrogen-centered radical cations and the aminoxyl radicals.[15] We were also intrigued by the photophysical and photochemical properties of **1**; the use of nitrones as a radical acceptor under photoirradiation has been generally avoided since photoexcited nitrones readily undergo photolysis to give oxaziridines (Scheme 1).[16] Hence, we proposed that if photoinduced electron transfer (PET) from tertiary amines to photoexcited nitrones occurred, photodecomposition of the nitrone would be prohibited and radical carbon-carbon bond formation would be accomplished to afford $\beta$-amino hydroxylamine derivatives.

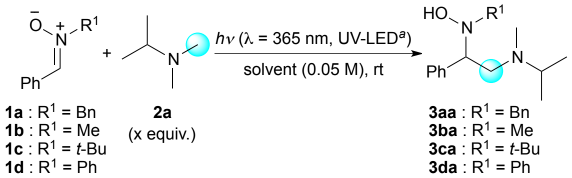
## Results and discussion

We started our investigation of the reaction of *N*-benzylidenebenzylamine *N*-oxide (**1a**) with *N*,*N*-dimethylisopropylamine (**2a**) under photoirradiation [UV-LED light source ($\lambda$ = 365 nm)] by conducting the reaction in several solvents. Desired carbon-carbon bond-forming reactions occurred specifically at the methyl group of **2a** with a C=N bond of **1a** to give $\beta$-amino hydroxylamine **3aa** in each type of solvent with the exception of dichloromethane (DCM) (Table 1, entries 1~6). Acetone was the best solvent for increasing reaction rate and improving chemical yield (entry 1).

We next evaluated the amount of added **2a** within the range of 2 to 10 equivalents (entries 1, 7, 9). We also used a high pressure mercury lamp (100 W) instead of a UV-LED light source, but yield of **3aa** was lower than that observed in entry 7 (entry 8). Consequently, use of 5 equivalents of **2a** led to the optimal result (entry 7). We then tested the effect of the substituent on the nitrogen atom of the *N*-oxide moiety of nitrones. The reaction of *N*-benzylidenemethylamine *N*-oxide (**1b**) gave a complex mixture of products and afforded $\beta$-amino hydroxylamine **3ba** in low yield (entry 10). In the case of *N*-benzylidene *tert*-butylamine *N*-oxide (**1c**), photocyclized product 2-*tert*-butyl-3-phenyl-oxaziridine (**9c**) was obtained in quantitative yield (entry 11). In contrast, *N*-benzylidene aniline *N*-oxide (**1d**) appeared to photodecompose to give a complex mixture (entry 12).

We also used several organophotosensitizers with the aim of increasing reaction rate and chemical yield (Table 2). The rate of reaction was increased by the use of BP (entry 1) in comparison with the result of entry 1 in Table 1. The reaction in the presence of 4,4'-dimethoxybenzophenone (DMBP) was not successful and structurally unknown products were obtained even at low temperature (entries 2~4). We utilized 4,4'-dichlorobenzophenone (DCBP) as a organophotosensitizer instead of DMBP. As a result, the reaction catalyzed by DCBP proceeded reproducibly without notable side reactions to give **3aa** in good yield (entries 5, 6). We used a high pressure mercury lamp (100 W) instead of the UV-LED light source, but yield of **3aa** was lower than that observed in entry 6 (entry 7). When 4,4'-difluorobenzophenone (DFBP) having the strong electron-withdrawing fluorine group was used for the reaction, the result was not an improvement over DCBP (entry 8).

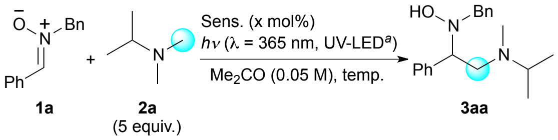
**Table 1** Effects of solvents and of *N*-substituents of nitrones



| entry | Nitrone | solvent | amine/x | time/h | yield/%$^b$ |
|---|---|---|---|---|---|
| 1 | **1a** | $Me_2CO$ | 10 | 2.5 | 63 |
| 2 | **1a** | MeCN | 10 | 4 | 62 |
| 3 | **1a** | $PhCF_3$ | 10 | 3 | 50 |
| 4 | **1a** | MeOH | 10 | 10 | 50 |
| 5 | **1a** | THF | 10 | 4 | 27 |
| 6 | **1a** | DCM | 10 | 12 | $0^c$ |
| 7 | **1a** | $Me_2CO$ | 5 | 2.5 | 61 |
| $8^d$ | **1a** | $Me_2CO$ | 5 | 2.5 | 50 |
| 9 | **1a** | $Me_2CO$ | 2 | 4.5 | 46 |
| 10 | **1b** | $Me_2CO$ | 10 | 24 | 12 |
| 11 | **1c** | $Me_2CO$ | 10 | 24 | $0^e$ |
| 12 | **1d** | $Me_2CO$ | 10 | 24 | $0^c$ |

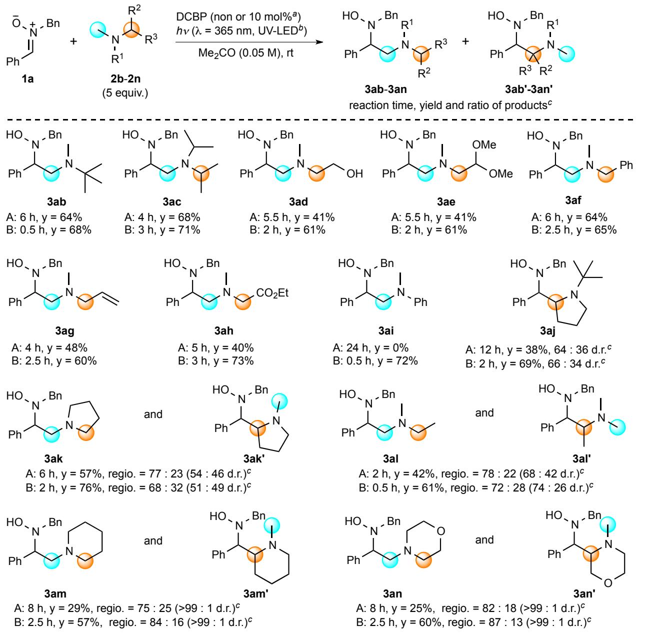
[a] The external irradiation was directed toward the Pyrex test tube with a working distance of 1 cm. Irradiation power of each UV-LED light source was found to be 422 mW/cm$^2$ ± 3 %. All reactions were degassed by argon bubbling for 15 min prior to irradiation. [b] Isolated yield. [c] Complex mixture was obtained. [d] High pressure mercury lamp (100 W) was used for the reaction. [e] 2-*tert*-Butyl-3-phenyl-oxaziridine (**9c**) was obtained in quantitative yield.

**Table 2** Evaluation of several organophotosensitizers

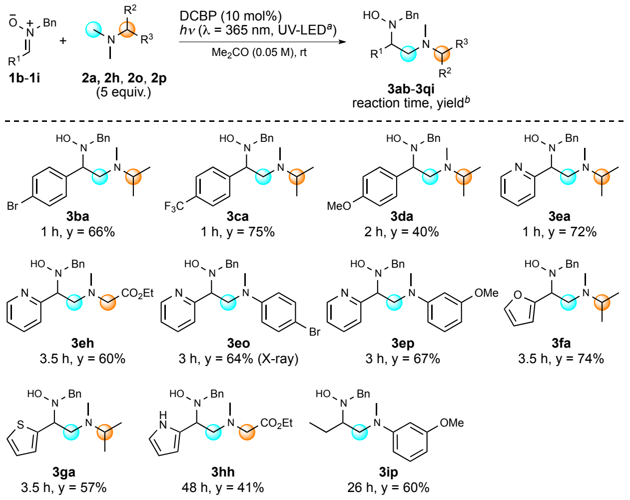


| entry | Sens. | x | Temp./$^o$C | time/h | yield/%$^b$ |
|---|---|---|---|---|---|
| 1 | BP | 10 | rt | 0.7 | 62 |
| 2 | DMBP | 10 | rt | 0.3 | 48 |
| 3 | DMBP | 10 | -40 | 48 | 37 |
| 4 | DMBP | 10 | -78 | 59 | 37 |
| 5 | DCBP | 10 | rt | 1 | $78^c$ |
| 6 | DCBP | 5 | rt | 1.3 | 76 |
| $7^d$ | DCBP | 5 | rt | 1.3 | 66 |
| 8 | DFBP | 10 | rt | 1.3 | 65 |
| 9 | Xanthone | 10 | rt | 6 | 60 |
| 10 | DMABP | 10 | rt | 6 | $0^e$ |
| $11^f$ | Eosin Y | 10 | rt | 24 | $0^e$ |

[a] The same irradiation system as in Table 1 was used for the reaction. [b] Isolated yield. [c] Average of four studies. [d] High pressure mercury lamp (100 W) was used for the reaction. [e] Complex mixture was obtained. [f] Sun light was used for the irradiation source.



**Scheme 2** Exploration of the scope of amine substrates. [a] Conditions A: Reactions in the absence of DCBP. Conditions B: Reactions in the presence of DCBP. [b] The same irradiation system as in Table 1 was used for the reaction. [c] All products were isolated and regioisomer ratios as well as diastereomer ratios were determined by $^1$H NMR.



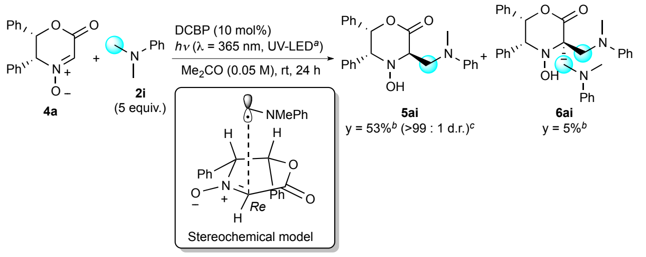
**Scheme 3.** Exploration of the scope of nitrone substrates. [a] The same irradiation system as in Table 1 was used for the reaction. [b] All products were isolated.

Complex mixtures were obtained in the case of 4,4'-bis(dimethylamino)benzophenone (Michler's ketone, DMABP) and Eosin Y (entries 10, 11).

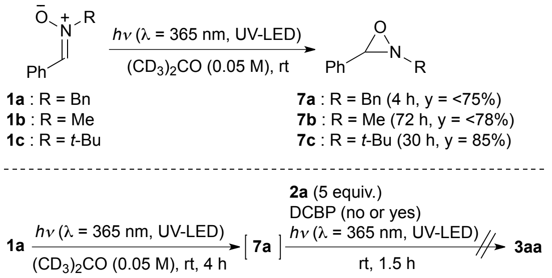
With the optimal reaction conditions in hand, we next evaluated several tertiary amines in the presence or in the absence of DCBP (Scheme 2). In all reactions, DCBP was neccesary to accelerate the reaction. Interestingly, the use of amines containing benzyl (**2f**), allyl (**2g**), or ethoxycarbonylmethyl (**2h**) groups did not lead to formation of any adducts of secondary $\alpha$-aminoalkyl radicals, known as a thermodynamically stable captodative radicals. In our case, primary $\alpha$-aminoalkyl radicals of **2f**, **2g**, and **2h** were predominantly generated rather than the corresponding secondary $\alpha$-aminoalkyl radicals, which were based on Lewis's stereoelectronic rule for a stilbene-amine system.[17] When cyclic amines **2k, 2m**, and **2n** were used as the radical precursor, regioselective formation of primary $\alpha$-aminoalkyl radicals was achieved and the resulting $\alpha$-aminoalkyl radicals added to **1a** gave **3ak**, **3am**, and **3an** as the corresponding major products. The repulsive interaction between concomitantly generated secondary $\alpha$-aminoalkyl radicals of six-membered amines and **1a** was larger than that of five-membered amines, inducing excellent diastereoselectivities observed in **3am'** and **3an'**. In the case of 1-*tert*-butylpyrrolidine (**2j**), inevitable generation of the secondary $\alpha$-aminoalkyl radical followed by the carbon-carbon bond formation were clearly achieved. Interestingly, the reaction of *N*,*N*-dimethylaniline (**2i**) in the absence of DCBP was carried out twice, but **3ai** was not obtained at all. On the contrary, the reaction of **2i** in the presence of DCBP progressed smoothly to give **3ai** in good yield. This result indicated that ET from **2i** to $^3$DCBP* occurred in a more facile manner than with photoexcited nitrone **1***.[18,19]

We next attempted to evaluate several nitrones (Scheme 3). As a result, regioselective generations and additions of primary $\alpha$-aminoalkyl radicals were carried out to give desired $\beta$-amino hydroxylamine derivatives in moderate yields. X-Ray crystallographic analysis of **3eo** was successfully achieved to reveal that the predicted carbon-carbon bond formation occurred.[20] We challenged the diastereoselective reaction by using chiral (*E*)-geometry-fixed $\alpha$-alkoxycarbonylnitrone **4a**[21] with **2i** (Scheme 4). The primary $\alpha$-aminoalkyl radical derived from **2i** approached the *re*-face of the reaction site of **4a** by avoiding the phenyl ring to give **5ai** in moderare yield with excellent diastereoselectivity,[22] which was formed concomitantly with a slight amount of double addition product **6ai**.[21c,23]

We carried out photoirradiation for a solution of nitrone **1a**-**1c** to give oxaziridines **7a**-**7c**, respectively. We also performed photoirradiation of a solution of *in situ* generated 2-benzyl-3-phenyl-1,2-oxaziridine (**7a**) and **2a** in acetone-$d_6$, but **3aa** was not obtained at all.



**Scheme 4** Diastereoselective addition of the $\alpha$-aminoalkyl radical to the chiral cyclic nitrone. [a] Irradiation power of UV-LED was 72 mW/cm$^2$. [b] Isolated yield. [c] Diastereomer ratio was determined by $^1$H NMR.



**Scheme 5** Formation of oxaziridines and their photoreactivities.

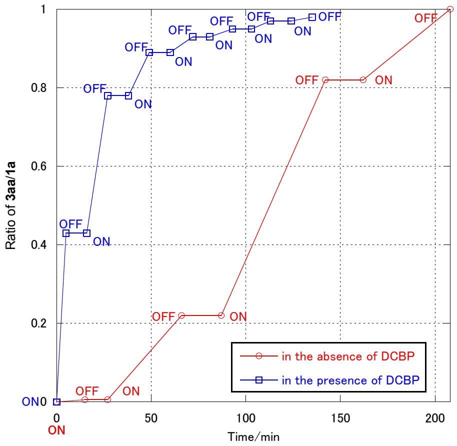
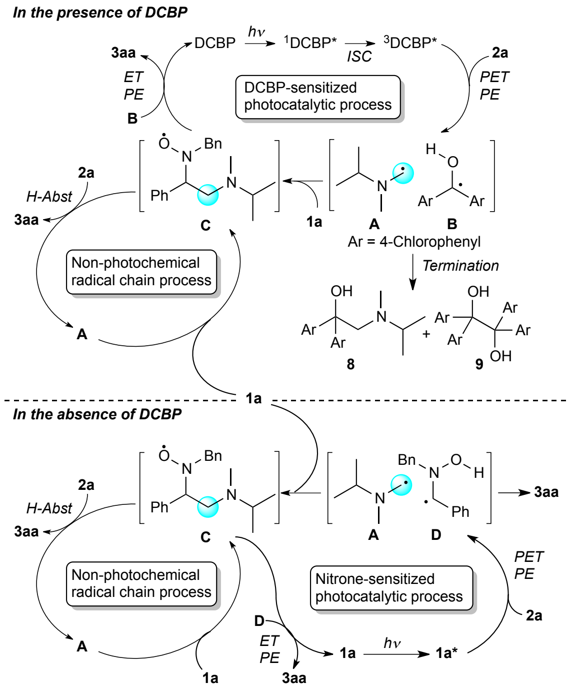


**Figure 1** ON/OFF experiment of UV-LED light source. Conditions : A mixed solution of **1a** (1 eq.) and **2a** (5 eq.) in acetone-$d_6$ (0.05 M) was degassed by argon bubbling for 15 min, then the solution was transferred to an NMR tube and irradiation was conducted at room temperature. Irradiation power of UV-LED was 430 mW/cm$^2$.

Therefore, this study revealed that **7a** had not participated in promoting the reaction (Scheme 5). We also conducted an ON/OFF experiment of the UV-LED light source. The reaction was not induced at all when UV-LED lighting was OFF (Figure 1).



**Scheme 6** A proposed mechanism for the reaction.

Based on these observations, we conclude that the reaction of $\alpha$-aminoalkyl radicals with nitrones appears to progress by a mechanism that combined a DCBP-sensitized photocalalytic process, a non-photochemical radical chain process, and a nitrone-sensitized photocatalytic process (Scheme 6). In the DCBP-sensitized photocatalytic process, the sequence of DCBP excitation by UV absorption to generate $^3$DCBP*, then PET from **2a** followed by proton exchange (PE) occurred to give the pair of $\alpha$-aminoalkyl radical **A** and ketyl radical **B**. Next, **A** reacted with **1a** to give the aminoxyl radical intermediate **C** which would be subjected to electron transfer (ET) from **B**, followed by PE to give the desired product **3aa** and DCBP. We also identified terminated products aminoalcohol **8** and 4,4',4'',4'''-tetrachlorobenzopinacol (**9**) in the presence of DCBP. Furthermore, we performed photoirradiation for a solution of **1a** and **8** in acetone, but **3aa** was not obtained at all.[24] In the nitrone-sensitized photocatalytic process, nitrone **1a** behaved in the same manner as DCBP to give **3aa** by way of the radical pair of **A** and **D**, which coupled together to give **C**. On the other hand, the aminoxyl radical intermediate **C** could abstract the hydrogen atom adjacent to the nitrogen of **2a** to form **3aa** and $\alpha$-aminoalkyl radical **A** which reacted with **1a** to give **C**. The oxaziridine ring-forming reaction of photoexcited nitrone **1*** was negligibly slow in the presence of tertiary amines. The aminoxyl radical intermediate **C** was the common intermediate for all three processes, *i.e.,* the non-photochemical radical chain process, the nitrone-sensitized photocatalytic process, and the DCBP-sensitized photocatalytic process. On the basis of the initial rate of the reaction in the absence of DCBP, which was extremely slow (Figure 1), and the effect of the amount of added **2a** (entries 1, 7 and 9 in Table 1), the concentration of the aminoxyl radical intermediate **C** might play a critical role in promoting the reaction in the absence of DCBP. Hoffmann *et al.* conducted a thorough study to reveal the mechanism for conjugate addition reactions between $\alpha$-aminoalkyl radicals and $\alpha,\beta$-unsaturated carbonyl compounds catalyzed by BP derivatives under photoirradiation. They successfully determined the value of the quantum yield ($\Phi$) of the reaction to be 4.[3c] In our case, the effect of DCBP on the rate acceleration of the reaction was obvious, but the quantum yield ($\Phi$) of the reaction was unclear. Hence, the non-photochemical radical chain process would not be ruled out in considering the reaction mechanism, even in the presence of DCBP. We also carried out the reaction between **1a** and **2a** by the use of a radical initiator such as di-*tert*-butyl peroxide[25], triethyl borane/O$_2$,[26] and 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) under thermal conditions, but **3aa** was not obtained at all.

## Conclusions

In summary, we have developed the photochemical addition of the $\alpha$-aminoalkyl radical to a nitrone with the following findings and advantages: (1) the nitrone served as a good photosensitizer for generating $\alpha$-aminoalkyl radicals from tertiary amines via PET; (2) BP derivatives accelerated the reactions; (3) regioselective generation of a primary $\alpha$-aminoalkyl radical from a tertiary amine based on Lewis's stereoelectronic rule, followed by its addition to a nitrone was accomplished; (4) wide substrate scope of amines as well as of nitrones was achieved; (5) excellent diastereoselectivity was observed in the reaction with chiral cyclic nitrones. Further studies for elucidating a mechanism of the reaction and for development of a novel organophotocatalysis are ongoing.

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## Notes and references

1 a) H. Rau, *Chem. Rev.* 1983, **83**, 535-547. (b) Y. Inoue, *Chem. Rev.* 1992, **92**, 741-770. (c) K. S. Peters, *Adv. Photochem.* 2002, **27**, 51-82. (d) N. Hoffmann, *Chem. Rev.* 2008, **108**, 1052-1103. (e) T. Bach, J. P. Hehn, *Angew. Chem. Int. Ed.* 2011, **50**, 1000-1045.

2 2a) E. Santiago de Alvarenga, J. Mann, *J. Chem. Soc. Perkin Trans. 1*. 1993, 2141.

3 (a) S. Bertrand, C. Glapski, N. Hoffmann, J.-P. Pete, *Tetrahedron Lett*. 1999, **40**, 3169-3172. (b) S. Bertrand, N. Hoffmann, S. Humbel, J.-P. Pete, *J. Org. Chem.* 2000, **65**, 8690-8703. (c) S. Bertrand, N. Hoffmann, J.-P. Pete, *Eur. J. Org. Chem*. 2000, 2227-2238. (d) N. Hoffmann, H. Görner, *Chem. Phys. Chem.* 2004, **383**, 451-455. (e) N. Hoffmann, S. Bertrand, S. Marinković, J. Pesch, *Pure Appl. Chem.* 2006, **78**, 2227-2246. (f) R. Jahjah, A. Gassama, V. Bulach, C. Suzuki, M. Abe, N. Hoffmann, A. Martinez, J.-M. Nuzillard, *Chem. Eur. J.* 2010, **16**, 3341-3354.

4 (a) E. Hasegawa, M. A. Brumfield, P. S. Mariano, *J. Org. Chem.* 1988, **53**, 5435-5442. (b) W. Xu, Y. T. Jeon, E. Hasegawa, U. C. Yoon, P. S. Mariano, *J. Am. Chem. Soc.* 1989, **111**, 406-408. (c) W. Xu, X.-M. Zhang, P. S. Mariano, *J. Am. Chem. Soc.* 1991, **113**, 8863-8878. (d) W. Xu, P. S. Mariano, *J. Am. Chem. Soc.* 1991, **113**, 1431-1432.

5 Bauer, F. Westkämper, S. Grimme, T. Bach, *Nature* 2005, **436**, 1139-1140.

6 Yoshimi, K. Kobayashi, H. Kamakura, K. Nishikawa, Y. Haga, K. Maeda, T. Morita, T. Itou, Y. Okada, M. Hatanaka, *Tetrahedron Lett*. 2010, **51**, 2332-2334.

7 Zhou, P. Lu, X. Gu, P. Li, *Org. Lett.* 2013, **15**, 5646-5649.

8 (a) S. Kamijo, T. Hoshikawa, M. Inoue, *Org. Lett.* 2011, **13**, 5928-5931. (b) T. Hoshikawa, S. Kamijo, M. Inoue, *Org. Biomol. Chem.* 2013, **11**, 164-169. (c) Y. Amaoka, M. Nagatomo, M. Watanabe, K. Tao, S. Kamijo, M. Inoue, *Chem. Sci.* 2014, **5**, 4339-4345. (d) S. Kamijo, K. Tao, G. Takao, H. Murooka, T. Murafuji, *Tetrahedron Lett.* 2015, **56**, 1904-1907.

9 (a) S. G. Cohen, R. J. Baumgarten, *J. Am. Chem. Soc.* 1965, **87**, 2996-2997. (b) S. Arimitsu, H. Masuhara, N. Mataga, H. Tsubomura, *J. Phys. Chem.* 1975, **79**, 1255-1259. (c) C. G. Shaefer, K. S. Peters, *J. Am. Chem. Soc.* 1980, **102**, 7567-7568. (d) H. Ohtani, T. Kohyoshi, K. Suzuki, S. Nagakura, *Nippon Kagaku Kaishi* 1984. **10**. 1479-1483. (e) C. Devadoss, R. W. Fessenden, *J. Phys. Chem.* 1991, **95**, 7253-7260. (f) Y. Kajii, H. Itabashi, K. Shibuya, K. Obi, *J. Phys. Chem.* 1992, **96**, 7244-7247. (g) M Dossot, X. Allonas, P. Jacques, *J. Photochem. Photobiol., A: Chem.* 1999, **128**, 47-55.

10 J. Turro, V. Ramamurthy, J. C. Scaiano, *Principles of Molecular Photochemistry: An Introduction*; University Science Books; 1st edition, 2008.

11 (a) M. A. El-Sayd, *J. Chem. Phys.* 1962, **36**, 573-574. (b) M. A. El-Sayd, *J. Chem. Phys.* 1963, **38**, 2834. (c) M. A. El-Sayd, *J. Chem. Phys.* 1964, **41**, 2462-2467.

12 (a) S. G. Cohen, B. Green, *J. Am. Chem. Soc.* 1969, **91**, 6824-6829. (b) S. S. Kim, Y. J. Mah, A. R. Kim, *Tetrahedron Lett.* 2001, **42**, 8315-8317. (c) C. Brulé, N. Hoffmann, *Tetrahedron Lett.* 2002, **43**, 69-72.

13 Kamon, Y. Irifune, T. Tanaka, T. Yoshimitsu, *Org. Lett*. 2011, **13**, 2674-2677.

14 We also cite additions of $\alpha$-oxyalkyl radicals to a C=N bond. (a) S. Torrente, R. Alonso, *Org. Lett.* 2001, **3**, 1985-1987. (b) M. Fernández, R. Alonso, *Org. Lett.* 2003, **5**, 2461-2464. (c) M. Fernández-González, R. Alonso, *J. Org. Chem.* 2006, **71**, 6767-6775.

15 (a) P. S. Taylor, P. Ghalsasi, P. M. Lahti, *Tetrahedron Lett.* 2004, **45**, 6295-6298. (b) V. Mugnaini, C. Punta, R. Liantonio, P. Metrangolo, F. Recupero, G. Resnati, G. F. Pedulli, M. Lucarini, *Tetrahedron Lett.* 2006, **47**, 3265-3269.

16 (a) K. Koyano, H. Suzuki, Y. Mori, I. Tanaka, *Bull. Chem. Soc. Jpn.* 1970, **43**, 3582-3587. (b) J. S. Splitter, T.-M. Su, H. Ono, M. Calvin, *J. Am. Chem. Soc.* 1971, **93**, 4705-4706. (c) H. Suginome, N. Sato, T. Masamune, *Tetrahedron* 1971, **27**, 4863-4881. (d) D. R. Cyr, T. Mathew, K. Ashok, P. K. Das, M. V. George, *J. Photochem. Photobiol. A: Chem.* 1991, **60**, 161-174. (e) Y. Zeng, B. T. Smith, J. Hershberger, J. Aubé, *J. Org. Chem.* 2003, **68**, 8065-8067. (f) Y. Zhang, M. L. Blackman, A. B. Leduc, T. F. Jamison, *Angew. Chem. Int. Ed.* 2013, **52**, 4251-4255.

17 (a) F. D. Lewis, T.-I. Ho, *J. Am. Chem. Soc.* 1977, **99**, 7991-7996. (b) F. D. Lewis, T.-I. Ho, *J. Am. Chem. Soc.* 1980, **102**, 1751-1752. (c) F. D. Lewis, T.-I. Ho, J. T. Simpson, *J. Org. Chem.* 1981, **46**, 1077-1082. (d) F. D. Lewis, T.-I. Ho, J. T. Simpson, *J. Am. Chem. Soc.* 1982, **104**, 1924-1929. (e) F. D. Lewis, *Acc. Chem. Res.* 1986, **19**, 401-405. (f) F. D. Lewis, G. D. Reddy, D. M. Bassani, *J. Am. Chem. Soc.* 1993, **115**, 6468-6469.

18 The molar extinction coefficients ($\varepsilon$) of DCBP and **1a** at 365 nm in MeCN were 93.2 and 0.768 ($M^{-1}cm^{-1}$) respectively. See Supporting Information for experimental details and results.

19 When $\alpha$-aminoalkyl radical precursors having an electron-withdrawing group and trimethylsilyl group on a nitrogen atom were used for the reaction, no desired products were obtained at all. See Supporting Information for results.

20 See Supporting Information for results.

21 (a) O. Tamura, K. Gotanda, R. Terashima, M. Kikuchi, T. Miyawaki, M. Sakamoto, *Chem. Commun.* 1996, 1861-1862. (b) S. W. Baldwin, B. G. Young, A. T. McPhail, *Tetrahedron Lett*. 1998, **39**, 6819-6822. (c) M. Ueda, H. Miyabe, M. Teramachi, O. Miyata, T. Naito, *Chem. Commun.* 2003, 426-427.

22 The absolute configuration of **5ai** was assigned to be 3*R, 5R, 6S* by 1D differential NOE experiment. See Supporting Information for spectra.

23 The formation of **6ai** was specifically observed in the reaction of **4a**.

24 See Supporting Information for experimental details and results.

25 H. Urry, O. O. Juveland, *J. Am. Chem. Soc.* 1958, **80**, 3322-3328.

26 (a) K. Nozaki, K. Oshima, K. Utimoto, *J. Am. Chem. Soc.* 1987, **109**, 2547-2548-3328. (b) T. Yoshimitsu, Y. Arano, H. Nagaoka, *J. Am. Chem. Soc.* 2005, **127**, 11610-11611.