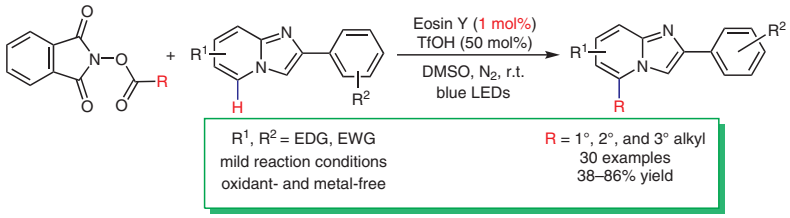
Synlett B. Sun et al. Letter

# Metal-Free Regioselective Alkylation of Imidazo[1,2-*a*]pyridines with *N*-Hydroxyphthalimide Esters under Organic Photoredox Catalysis

**Bin Sun**[a,c]
**Tengwei Xu**[b,c]
**Liang Zhang**[b,c]
**Rui Zhu**[b,c]
**Jin Yang**[b,c]
**Min Xu**[a,c]
**Can Jin***[a,b,c]




[a] Collaborative Innovation Center of Yangtze River Delta Region Green Pharmaceuticals, Zhejiang University of Technology, Hangzhou 310014, P. R. of China
[b] College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. of China
jincan@zjut.edu.cn
[c] National Engineering Research Center for Process Development of Active Pharmaceutical Ingredients, Zhejiang University of Technology, Hangzhou 310014, P. R. of China
jincan@zjut.edu.cn

Received: 14.11.2019
Accepted after revision: 29.12.2019
Published online: 14.01.2020
DOI: 10.1055/s-0039-1691567; Art ID: st-2019-r0617-l

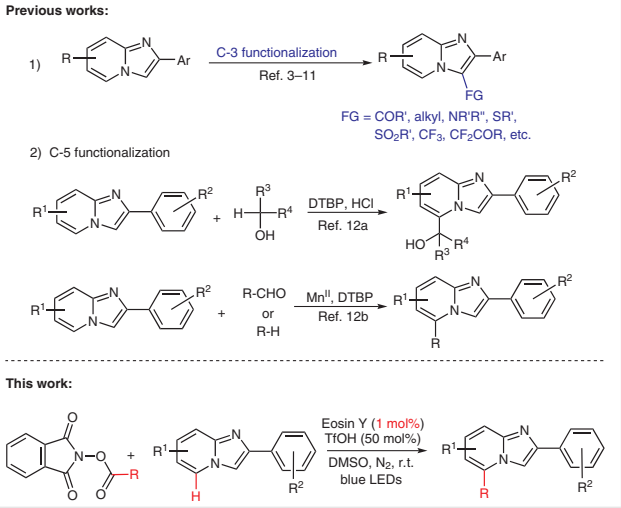
**Abstract** A visible-light-induced direct C–H alkylation of imidazo[1,2-*a*]pyridines has been developed. It proceeds at room temperature by employing inexpensive Eosin Y as a photocatalyst and alkyl *N*-hydroxyphthalimide (NHP) esters as alkylation reagents. A variety of NHP esters derived from aliphatic carboxylic acids (primary, secondary, and tertiary) were tolerated in this protocol, giving the corresponding C-5-alkylated products in moderate to excellent yields. Mechanistic studies indicate that a radical decarboxylative coupling pathway was involved in this process.

**Key words** photocatalysis, C–H alkylation, NHP esters, regioselectivity, metal-free reactions

Among nitrogen-containing fused heterocycles, imidazo[1,2-*a*]pyridine and its derivatives have attracted much attention. They are of special interest in medicinal chemistry and synthetic organic chemistry in terms of their unique structures and diverse pharmacological activities, including antimicrobial, anti-inflammatory, antiviral, antituberculosis, anti-tumor, antipyretic, analgesic, and antidepressant.[1] In addition, a variety of imidazo[1,2-*a*]pyridine moieties exist in several marketed drugs or bioactive molecules. Hence, a significant effort has been dedicated to the synthesis of substituted imidazo[1,2-*a*]pyridine derivatives.[2] To date, the direct C–H functionalization has served as a powerful strategy for the synthesis of imidazo[1,2-*a*]pyridine derivatives, and many successful examples including C–H acylation,[3] dicarbonylation,[4] alkylation,[5] thiolation,[6] sulfonylation,[7] difluoroalkylation,[8] difluorophosphate,[9] amination[10] at C-3 position have been reported (Scheme 1).[11] Though the C–H functionalization at C-3 position of imidazo[1,2-*a*]pyridines has already been extensively explored, the modification of imidazo[1,2-*a*]pyridines at C-5 position has still rarely been investigated. There were only two studies describing the direct C–H functionalization of imidazo[1,2-*a*]pyridines at C-5 position.[12] As pioneering works in this regard, Yan's group firstly developed an effective DTBP-promoted hydroxyalkylation of imidazo[1,2-*a*]pyridines at C-5 position with alcohols.[12a] Very recently, Hajra and coworkers reported a Mn(II)-catalyzed regioselective C–H alkylation of imidazo[1,2-a]pyridines under reflux, which employed aliphatic aldehydes or alkanes as alkylating agents.[12b] To the best of our knowledge, there is lack of effective methods to realise the regioselective C-5 functionalization of imidazo[1,2-*a*]pyridines at room temperature without assistance of chemical oxidants. Therefore, developing greener and more convenient synthetic approaches to C-5-functionalized imidazo[1,2-*a*]pyridines is still of great interest.

In recent years, visible-light-mediated photoredox catalysis has emerged as an efficient and environmentally compatible synthetic strategy for elusive bond construction and challenging chemical transformations.[13] Meanwhile, alkyl NHP esters exhibit specific photochemical properties because they can be reduced under photocatalytic conditions, delivering a variety of alkyl radicals by elimination of $CO_2$ and phthalimide.[14] It could be reasonably hypothesized that the regioselective alkylation of imidazo[1,2-*a*]pyridines could be accomplished through the decarboxylative coupling reaction with alkyl NHP esters. With our ongoing exploration on developing green and efficient methods for direct C–H functionalization,[15] herein we describe a visible-light-induced alkylation of imidazo[1,2-*a*]pyridines with alkyl NHP esters, which firstly employed a photocatalytic sys-

 
Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany




**Scheme 1** Strategies for the synthesis of substituted imidazo[1,2-*a*]pyridine derivatives

tem in the C-5 functionalization of imidazo[1,2-*a*]pyridine. This strategy is metal- and oxidant-free, and shows wide substrate scope, good functional group tolerance, and excellent regioselectivity.

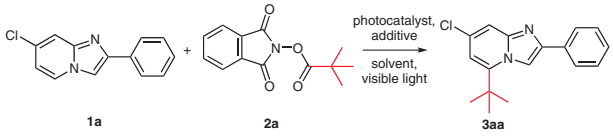
To begin our study, we chose 7-chloro-2-phenylimidazo[1,2-*a*]pyridine **1a** and *tert*-butyl NHP ester **2a** as model substrates to explore and optimize the reaction conditions. The transformation was initially carried out in the presence of *fac*-Ir(ppy)$_3$ in DMSO with the irradiation of blue LEDs under $N_2$ atmosphere at room temperature for 48 hours.

To our delight, the desired product **3aa** was obtained in a yield of 31%. Encouraged by this result, a variety of other photosensitizers such as Eosin Y, Rose Bengal, Methylene Blue, and Rhodamine 6G were also screened. Only Eosin Y exhibited a similar catalytic reactivity compared to that of *fac*-Ir(ppy)$_3$, while no desired product was detected when other photocatalysts were employed (Table 1, entries 2–5). Because of its non-toxicity and easy commercial availability, Eosin Y was chosen as the photocatalyst for further optimization. In order to further enhance the yield of **3aa**, various additives such as trifluoroacetic acid (TFA), TfOH, AcOH, $Et_3N$, and *N*,*N*-diisopropylethylamine (DIPEA) were also studied. Screening revealed that acidic additives had a positive influence on this reaction. The desired product was obtained in yields of 82, 71 and 54% when TfOH, TFA, and AcOH were employed, respectively (Table 1, entries 6–8). However, no desired product was observed when basic additives were added (Table 1, entries 9–10).

Futher investigation of the solvents indicated that except for DMSO, other screened solvents such as acetone, MeCN, $CH_2Cl_2$, DCE, THF, and DMF were all not suitable for this transformation (Table 1, entries 11–16). We then employed 3 W white or green LEDs as a light source and the results revealed that no improvement was obtained (Table 1, entries 17–18). A contrast experiment indicated that both visible light and a photocatalyst were essential for this decarboxylative coupling reaction, and of note, only a trace amount of the desired product was detected when this transformation was carried out under air atmosphere (Table 1, entries 19–21). On the basis of the screening of the reaction conditions, it could be concluded that this decarboxylative coupling reaction should be performed at room temperature in the presence of Eosin Y and TfOH in DMSO with irradiation of blue LEDs under a $N_2$ atmosphere for 48 hours.

Having the optimized reaction conditions in hand, we next turned our attention to probing the scope and generality of these two coupling partners. As summarized in Scheme 2, a broad range of imidazo[1,2-*a*]pyridines **1** with

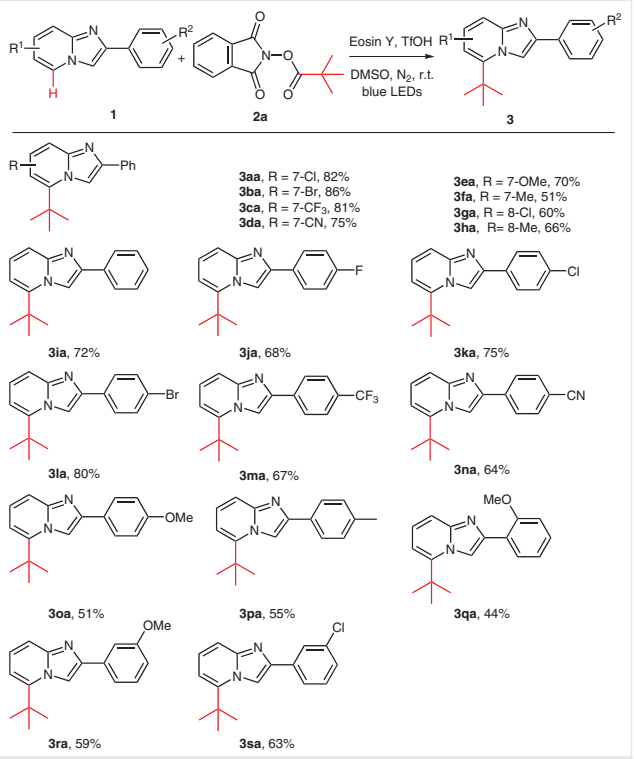
**Table 1** Optimization of the Reaction Conditions[a]




**1a** **2a** **3aa**

| Entry | Photocatalyst | Additive | Solvent | Yield (%)[b] |
|---|---|---|---|---|
| 1 | *fac*-Ir(ppy)$_3$ | – | DMSO | 31 |
| 2 | Eosin Y | – | DMSO | 32 |
| 3 | Rose Bengal | – | DMSO | n.d. |
| 4 | Methylene Blue | – | DMSO | n.d. |
| 5 | Rhodamine 6G | – | DMSO | n.d. |
| 6 | Eosin Y | TFA | DMSO | 71 |
| 7 | Eosin Y | TfOH | DMSO | 82 |
| 8 | Eosin Y | AcOH | DMSO | 54 |
| 9 | Eosin Y | $Et_3N$ | DMSO | n.d. |
| 10 | Eosin Y | DIPEA | DMSO | n.d. |
| 11 | Eosin Y | TfOH | acetone | n.d. |
| 12 | Eosin Y | TfOH | MeCN | n.d. |
| 13 | Eosin Y | TfOH | $CH_2Cl_2$ | n.d. |
| 14 | Eosin Y | TfOH | DCE | n.d. |
| 15 | Eosin Y | TfOH | THF | n.d. |
| 16 | Eosin Y | TfOH | DMF | trace |
| 17[c] | Eosin Y | TfOH | DMSO | 77 |
| 18[d] | Eosin Y | TfOH | DMSO | 72 |
| 19[e] | Eosin Y | TfOH | DMSO | n.d. |
| 20 | – | TfOH | DMSO | n.d. |
| 21[f] | Eosin Y | TfOH | DMSO | trace |

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), photocatalyst (0.005 mmol), additive (0.25 mmol), solvent (2.0 mL), $N_2$, blue LEDs, r.t., 48 h.
[b] Isolated yields; n.d. = not determined.
[c] White LEDs.
[d] Green LEDs.
[e] Without light.
[f] Under air atmosphere.

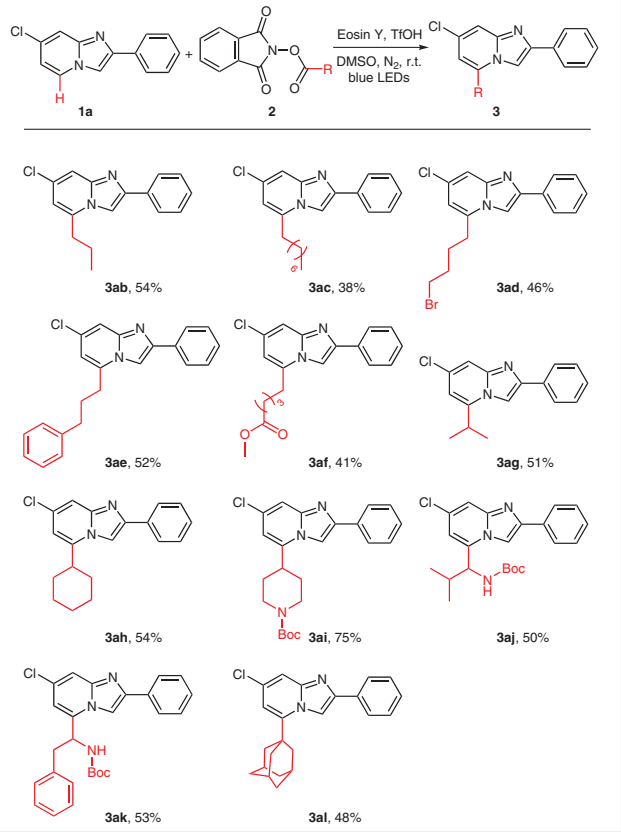



**Scheme 2** Substrate scope of imidazo[1,2-*a*]pyridines. *Reagents and conditions*: **1** (0.5 mmol), **2a** (1.0 mmol), Eosin Y (0.005 mmol), and TfOH (0.25 mmol) in DMSO (2.0 mL) at room temperature with irradiation by blue LEDs under a $N_2$ atmosphere for 48 h.

diverse substituents on the arene moiety or the pyridine ring were examined with *tert*-butyl NHP ester **2a** under the optimized conditions. Expectedly, this transformation was applicable to a variety of imidazo[1,2-*a*]pyridine derivatives **1a–s**, which were all able to undergo this decarboxylative coupling reaction smoothly to give the desired products **3aa–sa** in 44 to 86% yield. For example, the imidazo[1,2-*a*]pyridines possessing various halogens, such as chloro and bromo at the C-7 position of the pyridine rings, were well compatible and gave the desired products **3aa** and **3ba** in 82 and 86% yield, respectively.

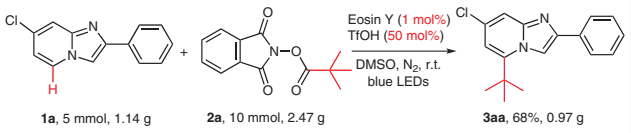
Remarkably, the cyano and trifluoromethyl substituents, which were considered as strong electron-withdrawing groups, also survived well and afforded the coupling products **3ca** and **3da** in 81 and 75% yield, respectively. Imidazo[1,2-*a*]pyridine containing a methyl or methoxy group at the C-7 position was also well tolerated, furnishing the desired products **3ea** and **3fa** in 70 and 51% yield, respectively. In addition, imidazo[1,2-*a*]pyridines containing chloro as an electron-withdrawing group or methyl as an electron-donating group at the C-8 position of the pyridine ring also underwent this decarboxylative coupling smoothly with **2a** to give the corresponding alkylated products **3ga** and **3ha** in yields of 60 and 66%, respectively. The reaction also tolerated the substituent-free imidazo[1,2-*a*]pyridine **1i**, leading to the desired product **3ia** in 72% yield. Further investigation was carried out with respect to the substituents on the C-2 benzene ring, and starting materials with variation of substituents at the *ortho*, *meta*, and *para* positions of benzenes were well compatible to give the corresponding products **3ja–sa** in moderate to good yields. For example, substrates bearing electron-withdrawing groups such as fluoro, chloro, bromo, trifluoromethyl, and cyano at the *para* position of the benzene ring showed good tolerance for this reaction, and provided the corresponding products **3ja–na** in 64 to 80% yield. Moreover, the electron-donating groups at the *para* position of the benzene ring such as methyl and methoxy, also displayed excellent tolerance for this transformation, and the alkylated products **3oa** and **3pa** were obtained in 51 and 55% yield, respectively. Meanwhile, imidazo[1,2-*a*]pyridines bearing substituents at the *ortho* and *meta* positions of the benzene ring were also evaluated. Similarly, the corresponding products **3qa–sa** were obtained in moderate yields whether the benzene ring contained electron-donating or electron-withdrawing groups.

Furthermore, the scope of the alkyl NHP esters was evaluated through the decarboxylative alkylation with 7-chloro-2-phenylimidazo[1,2-*a*]pyridine (**1a**) under the optimized reaction conditions (Scheme 3). Different types of precursors including primary, secondary, and tertiary alkyl NHP esters were all suitable for this reaction and gave the desired coupling products **3ab–al** in 38 to 75% yield. Initially, the primary alkyl NHP esters containing *n*-propyl and *n*-octyl exhibited good tolerance for this protocol and afforded the desired products **3ab** and **3ac** in 54 and 38% yield, respectively. Notably, the primary alkyl NHP esters containing additional functional groups, such as halogen, phenyl, and ester on the aliphatic chain were also well compatible with this transformation, providing the primary alkylated products **3ad–af** in fair yields. Subsequently, we explored whether the secondary alkyl NHP esters could adapt to this reaction. The experimental results indicate that the secondary alkyl NHP esters bearing isopropyl or cyclohexyl also showed good reactivity in this process and produced the desired products **3ag** and **3ah** in satisfactory yields under the optimal conditions. Furthermore, a secondary alkyl NHP ester containing a nitrogen atom on the aliphatic ring also performed well to provide the product **3ai** in good yield. It is worth noting that the derived alkyl NHP esters of natural amino acids were also suitable substrates for this transformation. For example, NHP esters of valine and phenylalanine derivatives were used as radical precursors to deliver the aminoalkylated products **3aj** and **3ak** in synthetically useful yields. Apart from the *tert*-butyl, another tertiary alkyl species, such as adamantyl NHP ester, was also employed in the reaction, and we were pleased to find that this substrate also worked well and gave the desired product **3al** in 48% yield.



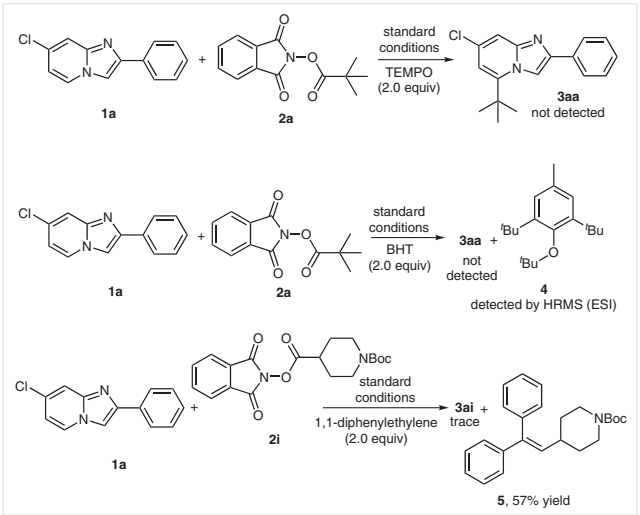

**Scheme 3** Substrate scope of alkyl NHP esters. *Reagents and conditions*: **1a** (0.5 mmol), **2** (1.0 mmol), Eosin Y (0.005 mmol), and TfOH (0.25 mmol) in DMSO (2.0 mL) at room temperature with irradiation by blue LEDs under a $N_2$ atmosphere for 48 h.

To evaluate the potential synthetic utility of this decarboxylative coupling strategy, a gram-scale reaction was carried out between 7-chloro-2-phenylimidazo[1,2-*a*]pyridine (**1a**) and *tert*-butyl NHP ester **2a** under the optimized conditions, and the desired product **3aa** was finally isolated in a yield of 68% (Scheme 4).




**Scheme 4** Gram-scale synthetic experiment

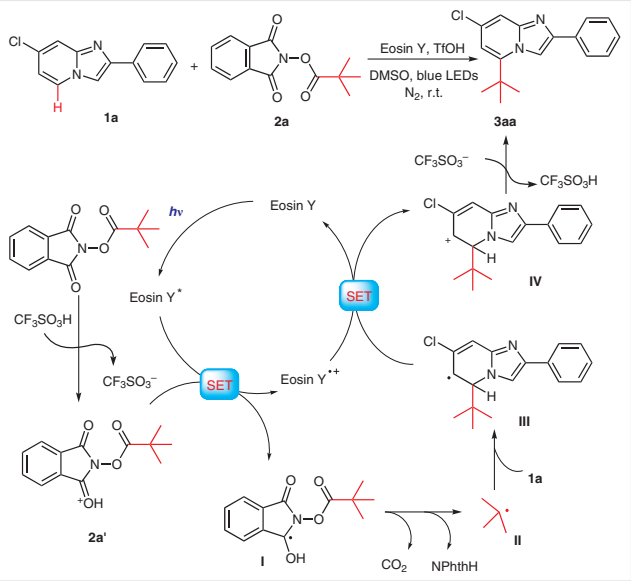
In order to gain a deeper insight into the reaction mechanism, several control experiments were carried out as shown in Scheme 5. When the radical scavenger TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) was added to the model reaction, this decarboxylative coupling process was completely suppressed. Subsequently, a similar result was observed when another radical scavenger BHT (butylated hydroxytoluene) was employed in same reaction system, and the corresponding radical-trapping product (**4**) was detected by HRMS.




**Scheme 5** Control experiments

These results indicate that the reaction might involve a radical pathway. The hypothesis was further confirmed by the addition of another milder radical scavenger, 1,1-diphenylethylene, and the radical adduct **5** of alkyl with diphenylethylene was isolated in 57% yield. In addition, Stern–Volmer experiments (for details, see Supporting Information) revealed that the excited state of Eosin Y could be quenched by alkyl NHP esters, suggesting that the reaction might proceed through an oxidative quenching pathway.

According to the above experimental results and previous literature reports,[14i,16] a plausible mechanism for this decarboxylative coupling reaction is proposed in Scheme 6. Initially, the organic dye Eosin Y was irradiated to its excited state (Eosin Y*), which underwent a single electron transfer (SET) process with **2a'** that was generated by protonation of substrate **2a** to afford a radical intermediate **I** and a radical cation (Eosin Y$^{\bullet+}$). The radical **I** was then converted into *tert*-butyl radical **II** after the elimination of $CO_2$ and phthalimide. Subsequently, the radical **II** regioselectively attacked at the C-5 position of **1a** to produce radical **III**, which could be further oxidized by Eosin Y$^{\bullet+}$ to give the corresponding cation intermediate and regenerate the photocatalyst. After deprotonation, **IV** was finally transformed into the desired product **3aa**.




**Scheme 6** Proposed mechanism

In summary, we have successfully developed a green and efficient method for the C($sp^2$)–C($sp^3$) bond formation through the decarboxylative coupling process between imidazo[1,2-*a*]pyridines and alkyl NHP esters under visible-light irradiation at room temperature.[17] This protocol exhibits a broad substrate scope with respect to both the two coupling partners, and a series of C-5-alkylated imidazo[1,2-*a*]pyridine derivatives were obtained in moderate to good yields. Employing the commercially available and low cost Eosin Y as the photocatalyst made this protocol environmentally friendly and practical. The advantages of this reaction involve the avoidance of transition-metal and stoichiometric oxidants, easy availability of substrates, and mild conditions.

## Funding Information

This work was supported by the National Natural Science Foundation of China (21606202) and Natural Science Foundation of Zhejiang Province (LY15B060007). We are also grateful to the College of Pharmaceutical Sciences, Zhejiang University of Technology and Collaborative Innovation Center of Yangtze River Delta Region Green Pharmaceuticals for the financial help.

## Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1691567.

## References and Notes

(1) (a) Enguehard-Gueiffier, C.; Gueiffier, A. *Mini-Rev. Med. Chem.* **2007**, *7*, 888. (b) Almirante, L.; Polo, L.; Mugnaini, A.; Provinciali, E.; Rugarli, P.; Biancotti, A.; Gamba, A.; Murmann, W. *J. Med. Chem.* **1965**, *8*, 305. (c) Dymińska, L. *Bioorg. Med. Chem.* **2015**, *23*, 6087. (d) Deep, A.; Bhatia, R. K.; Kaur, R.; Kumar, S.; Jain, U. K.; Singh, H.; Batra, S.; Kaushik, D.; Deb, P. K. *Curr. Top. Med. Chem.* **2017**, *17*, 238.

(2) (a) Bagdi, A. K.; Santra, S.; Monir, K.; Hajra, A. *Chem. Commun.* **2015**, *51*, 1555. (b) Ma, L.; Wang, X.; Yu, W.; Han, B. *Chem. Commun.* **2011**, *47*, 11333. (c) Gao, Y.; Yin, M.; Wu, W.; Huang, H.; Jiang, H. *Adv. Synth. Catal.* **2013**, *355*, 2263. (d) Zeng, J.; Tan, Y. J.; Leow, M. L.; Liu, X.-W. *Org. Lett.* **2012**, *14*, 4386. (e) Huang, H.; Ji, X.; Tang, X.; Zhang, M.; Li, X.; Jiang, H. *Org. Lett.* **2013**, *15*, 6254. (f) Palani, T.; Park, K.; Kumar, M. R.; Jung, H. M.; Lee, S. *Eur. J. Org. Chem.* **2012**, 5038.

(3) (a) Cao, H.; Lei, S.; Li, N.; Chen, L.; Liu, J.; Cai, H.; Qiu, S.; Tan, J. *Chem. Commun.* **2015**, *51*, 1823. (b) Nitha, P. R.; Joseph, M. M.; Gopalan, G.; Maiti, K. K.; Radhakrishnan, K. V.; Das, P. *Org. Biomol. Chem.* **2018**, *16*, 6430.

(4) (a) Samanta, S.; Mondal, S.; Santra, S.; Kibriya, G.; Hajra, A. *J. Org. Chem.* **2016**, *81*, 10088. (b) Shakoor, S. M. A.; Agarwal, D. S.; Kumar, A.; Sakhuja, R. *Tetrahedron* **2016**, *72*, 645.

(5) (a) Naresh, G.; Lakkaniga, N. R.; Kharbanda, A.; Yan, W.; Frett, B.; Li, H. *Eur. J. Org. Chem.* **2019**, 770. (b) Patel, O. P. S.; Nandwana, N. K.; Sah, A. K.; Kumar, A. *Org. Biomol. Chem.* **2018**, *16*, 8620. (c) Mondal, S.; Samanta, S.; Singsardar, M.; Hajra, A. *Org. Lett.* **2017**, *19*, 3751. (d) Kibriya, G.; Bagdi, A. K.; Hajra, A. *J. Org. Chem.* **2018**, *83*, 10619. (e) Zhu, M.; Han, X.; Fu, W.; Wang, Z.; Ji, B.; Hao, X.-Q.; Song, M.-P.; Xu, C. *J. Org. Chem.* **2016**, *81*, 7282. (f) Su, H.; Wang, L.; Rao, H.; Xu, H. *Org. Lett.* **2017**, *19*, 2226. (g) Kim, H.; Byeon, M.; Jeong, E.; Baek, Y.; Jeong, S. J.; Um, K.; Han, S. H.; Han, G. U.; Ko, G. H.; Maeng, C.; Son, J.-Y.; Kim, D.; Kim, S. H.; Lee, K.; Lee, P. H. *Adv. Synth. Catal.* **2019**, *361*, 1. (h) Yang, Q.; Li, S.; Wang, J. *Org. Chem. Front.* **2018**, *5*, 577. (i) Lu, S.; Zhu, X.; Li, K.; Guo, Y.-J.; Wang, M.-D.; Zhao, X.-M.; Hao, X.-Q.; Song, M.-P. *J. Org. Chem.* **2016**, *81*, 8370.

(6) (a) Yuan, Y.; Cao, Y.; Qiao, J.; Lin, Y.; Jiang, X.; Weng, Y.; Tang, S.; Lei, A. *Chin. J. Chem.* **2019**, *37*, 49. (b) Gao, Y.-C.; Huang, Z.-B.; Xu, L.; Li, Z.-D.; Lai, Z.-S.; Tang, R.-Y. *Org. Biomol. Chem.* **2019**, *17*, 2279. (c) Zhang, J.-R.; Zhan, L.-Z.; Wei, L.; Ning, Y.-Y.; Zhong, X.-L.; Lai, J.-X.; Xu, L.; Tang, R.-Y. *Adv. Synth. Catal.* **2018**, *360*, 533. (d) Zhang, J.-R.; Liao, Y.-Y.; Deng, J.-C.; Feng, K.-Y.; Zhang, M.; Ning, Y.-Y.; Lin, Z.-W.; Tang, R.-Y. *Chem. Commun.* **2017**, *53*, 7784.

(7) Guo, Y.-J.; Lu, S.; Tian, L.-L.; Huang, E.-L.; Hao, X.-Q.; Zhu, X.; Shao, T.; Song, M.-P. *J. Org. Chem.* **2018**, *83*, 338.

(8) Yin, G.; Zhu, M.; Fu, W. *J. Fluorine Chem.* **2017**, *199*, 14.

(9) Singsardar, M.; Mondal, S.; Laru, S.; Hajra, A. *Org. Lett.* **2019**, *21*, 5606.

(10) (a) Mondal, S.; Samanta, S.; Jana, S.; Hajra, A. *J. Org. Chem.* **2017**, *82*, 4504. (b) Yu, Y.; Yuan, Y.; Liu, H.; He, M.; Yang, M.; Liu, P.; Yu, B.; Dong, X.; Lei, A. *Chem. Commun.* **2019**, *55*, 1809.

(11) (a) Liu, P.; Gao, Y.; Gu, W.; Shen, Z.; Sun, P. *J. Org. Chem.* **2015**, *80*, 11559. (b) Fu, H. Y.; Chen, L.; Doucet, H. *J. Org. Chem.* **2012**, *77*, 4473. (c) Xue, C.; Han, J.; Zhao, M.; Wang, L. *Org. Lett.* **2019**, *21*, 4402. (d) Rafique, J.; Saba, S.; Rosário, A. R.; Braga, A. L. *Chem. Eur. J.* **2016**, *22*, 11854. (e) Ren, Y.; Xu, B.; Zhong, Z.; Pittman, C. U.; Zhou, A. *Org. Chem. Front.* **2019**, *6*, 2023. (f) Kim, Y. J.; Kim, D. Y. *Tetrahedron Lett.* **2019**, *60*, 739.

(12) (a) Jin, S.; Xie, B.; Lin, S.; Min, C.; Deng, R.; Yan, Z. *Org. Lett.* **2019**, *21*, 3436. (b) Samanta, S.; Hajra, A. *J. Org. Chem.* **2019**, *84*, 4363.



(13) (a) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* **2011**, *40*, 102. (b) Chen, J.-R.; Hu, X.-Q.; Lu, L.-Q.; Xiao, W.-J. *Chem. Soc. Rev.* **2016**, *45*, 2044. (c) Chen, J.-R.; Hu, X.-Q.; Lu, L.-Q.; Xiao, W.-J. *Acc. Chem. Res.* **2016**, *49*, 1911. (d) Marzo, L.; Pagire, S. K.; Reiser, O.; König, B. *Angew. Chem. Int. Ed.* **2018**, *57*, 10034. (e) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322. (f) Romero, N. A.; Nicewicz, D. A. *Chem. Rev.* **2016**, *116*, 10075. (g) Shi, L.; Xia, W. J. *Chem. Soc. Rev.* **2012**, *41*, 7687. (h) Zhao, Y.; Xia, W. J. *Chem. Soc. Rev.* **2018**, *47*, 2591. (i) Wang, J.; Huang, B.; Yang, C.; Xia, W. J. *Chem. Commun.* **2019**, *55*, 11103. (j) Cai, S.; Xiao, Z.; Shi, Y.; Gao, S. H. *Chem. Eur. J.* **2014**, *20*, 8677. (k) Xiao, Z.; Cai, S.; Shi, Y.; Yang, B.; Gao, S. H. *Chem. Commun.* **2014**, *50*, 5254. (l) Cai, S.; Xiao, Z.; Ou, J.; Shi, Y.; Gao, S. H. *Org. Chem. Front.* **2016**, *3*, 354.

(14) (a) Cheng, W.-M.; Shang, R.; Fu, M.-C.; Fu, Y. *Chem. Eur. J.* **2017**, *23*, 2537. (b) Wang, G.-Z.; Shang, R.; Fu, Y. *Org. Lett.* **2018**, *20*, 888. (c) Wang, C.; Guo, M.; Qi, R.; Shang, Q.; Liu, Q.; Wang, S.; Zhao, L.; Wang, R.; Xu, Z. *Angew. Chem. Int. Ed.* **2018**, *57*, 15841. (d) Yao, S.; Zhang, K.; Zhou, Q.-Q.; Zhao, Y.; Shi, D.-Q.; Xiao, W.-J. *Chem. Commun.* **2018**, *54*, 8096. (e) Ouyang, X.-H.; Li, Y.; Song, R.-J.; Li, J.-H. *Org. Lett.* **2018**, *20*, 6659. (f) Yu, L.; Tang, M.-L.; Si, C.-M.; Meng, Z.; Liang, Y.; Han, J.; Sun, X. *Org. Lett.* **2018**, *20*, 4579. (g) Xia, Z.-H.; Zhang, C.-L.; Gao, Z.-H.; Ye, S. *Org. Lett.* **2018**, *20*, 3496. (h) Ren, L.; Cong, H. *Org. Lett.* **2018**, *20*, 3225. (i) Yang, J.-C.; Zhang, J.-Y.; Zhang, J.-J.; Duan, X.-H.; Guo, L.-N. *J. Org. Chem.* **2018**, *83*, 1598. (j) Zhao, Y.; Chen, J.-R.; Xiao, W.-J. *Org. Lett.* **2018**, *20*, 224. (k) Hu, D.; Wang, L.; Li, P. *Org. Lett.* **2017**, *19*, 2770. (l) Liu, L.; Pan, N.; Sheng, W.; Su, L.; Liu, L.; Dong, J.; Zhou, Y.; Yin, S.-F. *Adv. Synth. Catal.* **2019**, *361*, 4126. (m) Lyu, X-L.; Huang, S.-S.; Song, H.-J.; Liu, Y.-X.; Wang, Q.-M. *Org. Lett.* **2019**, *21*, 5728.

(15) (a) Sun, B.; Wang, Y.; Li, D.; Jin, C.; Su, W. *Org. Biomol. Chem.* **2018**, *16*, 2902. (b) Sun, B.; Yin, S.; Zhuang, X.; Jin, C.; Su, W. *Org. Biomol. Chem.* **2018**, *16*, 6017. (c) Sun, B.; Yan, Z.; Jin, C.; Su, W. *Synlett* **2018**, *29*, 2432. (d) Jin, C.; Yan, Z.; Sun, B.; Yang, J. *Org. Lett.* **2019**, *21*, 2064. (e) Sun, B.; Deng, J.; Li, D.; Jin, C.; Su, W. *Tetrahedron Lett.* **2018**, *59*, 4364. (f) Jin, C.; Zhuang, X.; Sun, B.; Li, D.; Zhu, R. *Asian J. Org. Chem.* **2019**, *8*, 1490. (g) Jin, C.; Zhang, X.; Sun, B.; Yan, Z.; Xu, T. *Synlett* **2019**, *30*, 1585. (h) Yan, Z.; Sun, B.; Zhang, X.; Zhuang, X.; Yang, J.; Su, W.; Jin, C. *Chem. Asian J.* **2019**, *14*, 3344. (i) Wang, J.; Sun, B.; Zhang, L.; Xu, T.; Xie, Y.; Jin, C. *Asian J. Org. Chem.* **2019**, *8*, 1942. (j) Sun, B.; Yang, J.; Zhang, L.; Shi, R.; Zhang, X.; Xu, T.; Zhuang, X.; Zhu, R.; Yu, C.; Jin, C. *Asian J. Org. Chem.* **2019**, *8*, 2058.

(16) (a) Pirenne, V.; Kurtay, G.; Voci, S.; Bouffier, L.; Sojic, N.; Robert, F.; Bassani, D. M.; Landais, Y. *Org. Lett.* **2018**, *20*, 4521. (b) Wang, H.; Zhang, D.; Bolm, C. *Chem. Eur. J.* **2018**, *24*, 14942. (c) Tiwari, D. P.; Dabral, S.; Wen, J.; Wiesenthal, J.; Terhorst, S.; Bolm, C. *Org. Lett.* **2017**, *19*, 4295. (d) Sun, D.; Yin, K.; Zhang, R. *Chem. Commun.* **2018**, *54*, 1335.

(17) **5-(*tert*-Butyl)-7-chloro-2-phenylimidazo[1,2-*a*]pyridine (3aa); Typical Procedure**

A 10 mL Schlenk-tube was charged with 7-chloro-2-phenylimidazo[1,2-*a*]pyridine (**1a**) (114 mg, 0.5 mmol), *tert*-butyl NHP ester **2a** (247 mg, 1.0 mmol), Eosin Y (3 mg, 0.005 mmol), DMSO (2 mL), and TfOH (37 mg, 0.25 mmol). The tube was evacuated and backfilled with $N_2$ (3×). The mixture was then irradiated by 3 W blue LEDs at r.t. for 48 h. The reaction mixture was then quenched with 1 M NaOH aq (15 mL) and extracted with $CH_2Cl_2$ (3 × 10 mL). The organic layer was dried with anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE, 1:20) to afford **3aa** as a white solid. Yield: 116 mg (82%); mp 141.6–142.4 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ = 8.07 (s, 1 H), 7.96 (d, *J* = 7.2 Hz, 2 H), 7.58 (s, 1 H), 7.45 (t, *J* = 7.6 Hz, 2 H), 7.35 (t, *J* = 7.2 Hz, 1 H), 6.71 (s, 1 H), 1.57 (s, 9 H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 147.1, 146.5, 145.7, 133.6, 131.5, 128.8, 128.2, 126.2, 114.3, 110.7, 108.9, 35.6, 27.6. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{18}ClN_2$: 285.1153; found: 285.1163.

