OL Organic Letters

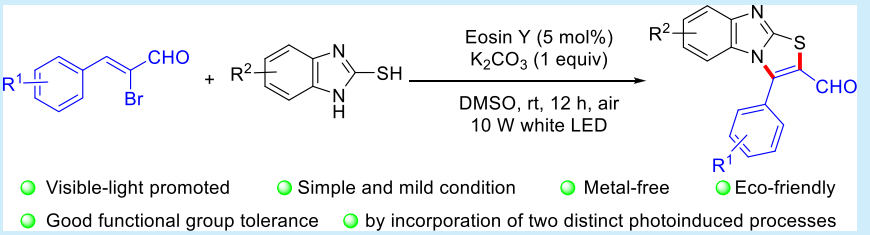
pubs.acs.org/OrgLett Letter

Aminothiolation of α-Bromocinnamaldehydes to Access Imidazo[2,1-*b*]thiazoles by Incorporation of Two Distinct Photoinduced Processes

Ziren Chen, Weiwei Jin, Yu Xia, Yonghong Zhang, Mengwei Xie, Shangchao Ma, and Chenjiang Liu*

Cite This: https://dx.doi.org/10.1021/acs.orglett.0c02907 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information



ABSTRACT: A visible-light-promoted metal-free catalytic system was developed to achieve the aminothiolation of α-bromocinnamaldehydes. This mechanistically novel approach allows the synthesis of diverse imidazo[2,1-*b*]thiazole derivatives in satisfactory yields at room temperature under visible-light irradiation by incorporation of two distinct photoinduced processes. The reaction features readily accessible feedstocks, easy operation, mild reaction conditions, and wide reaction scope.

Fused nitrogen heterocycles[1] and organic sulfur compounds[2] are key structural units, which are frequently encountered in materials, natural products, agrochemicals, and pharmaceutical drugs. Among them, imidazo[2,1-*b*]thiazoles are valuable structural moieties (Figure 1) that are widely

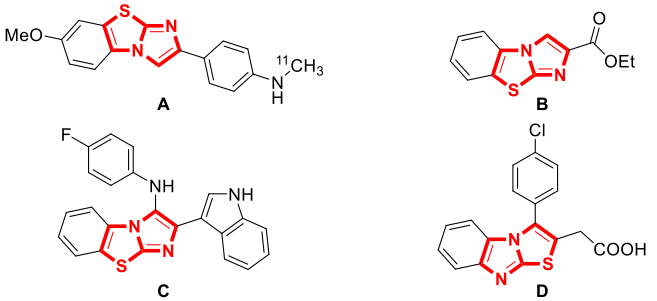
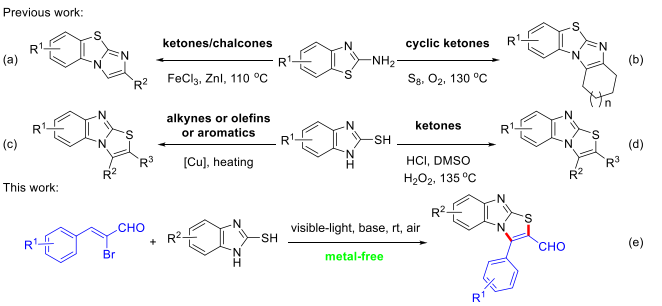


Figure 1. Representative pharmaceuticals containing imidazo[2,1-*b*]thiazoles.

present in biologically active compounds[3] and functional materials.[4] For example, ^{11}C-labeled molecule **A** was used for PET imaging of Alzheimer's patients' brains and β-amyloid plaques.[5] Compounds **B**, **C**, and their derivatives are usually present in antitumor drugs,[6] antimicrobial drugs,[7] antibacterial agents,[8] and antiallergic drugs.[9] Moreover, the compound **D** (tilomisole) has been utilized in the treatment of colon cancer.[10] In the past decades, imidazo[2,1-*b*]thiazoles have attracted much attention, and various protocols for their syntheses have been developed owing to their prominent properties. Typically, it has been reported that imidazo[2,1-*b*]thiazole compounds could be synthesized through the elemental sulfur or iron catalyzed annulation reactions of 2-aminobenzothiazoles with ketones/chalcones or cyclic ketones (Scheme 1a,b).[11] In addition, imidazo[2,1-*b*]thiazole derivatives could be synthesized via the copper-catalyzed cyclization reactions of 2-mercaptobenzoimidazoles with alkynes,[12] nitroalkenes,[13] prefunctionalized olefins, and aromatics (Scheme

Scheme 1. Strategies Related the Construction of Imidazo[2,1-*b*]thiazole Skeletons



Received: August 30, 2020

https://dx.doi.org/10.1021/acs.orglett.0c02907
Org. Lett. XXXX, XXX, XXX−XXX

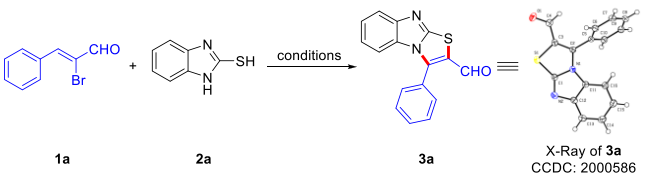
1c).[14] Recently, benzoimidazo[2,1-*b*]thiazoles were constructed via an DMSO/H_2O_2 promoted intermolecular cyclization of 2-mercaptobenzoimidazoles and ketones (Scheme 1d).[15] Although significant achievements have been demonstrated, these available methods have some limitations, such as the requirement of heating and metal catalysts, which are contrary to the concept of green chemistry. Furthermore, due to the strong coordination between metals and heteroatoms, trace transition metals are difficult to remove from heteroaryl compounds.[11a] Therefore, from the perspective of green chemistry and pharmaceutical applications, efficient synthetic methods for imidazo[2,1-*b*]thiazoles employing mild and metal-free conditions are highly desirable.

In recent years, visible-light-induced photoredox catalysis has become a powerful strategy to achieve organic transformations under very mild conditions.[16,17] To date, photoredox catalysis has already been extensively used to construct fused nitrogen heterocycles.[18] In contrast, the preparation of imidazo[2,1-*b*]thiazoles from 2-mercaptobenzimidazoles under visible-light irradiation has not been reported. As part of our continuing interest in the preparation of heterocyclic compounds,[19] herein we report a highly efficient intermolecular cyclization of 2-mercaptobenzimidazoles and *Z*-α-bromocinnamaldehydes for the convenient construction of benzoimidazo[2,1-*b*]thiazole derivatives by incorporation of two distinct visible-light-induced processes under metal-free conditions (Scheme 1e), in which visible light combined with base were found to be the key factors for the success of this cyclization.

For our initial study, we chosen *Z*-α-bromocinnamaldehyde (**1a**) and 2-mercaptobenzimidazole (**2a**) as the model substrates, eosin Y as the photocatalyst, K_2CO_3 as the base, and DMSO as the solvent for demonstrating the practicability of aminothiolation under 10 W white LED irradiation. Delightfully, the expected cyclization product **3a** was obtained in 63% yield after 12 h at room temperature (Table 1, entry 1). The structure of **3a** was further definitely determined by X-ray diffraction. Encouraged by this result, various photocatalysts, including organic dyes and ruthenium/iridium polypyridyl complexes, were examined (Table 1, entries 2−10). However, other organic dyes and Ir(ppy)$_3$ led to lower yields, and ruthenium polypyridyl complexes gave similar yields (Table 1, entries 8 and 9). From the perspective of green and sustainable chemistry, eosin Y was chosen as the best photocatalyst because it is cheap, less toxic, and easier to handle. To our delight, **3a** was obtained in 75% yield by reducing the loading of eosin Y to 5 mol % (Table 1, entry 11). Notably, neither reducing nor increasing the amount of the K_2CO_3 can promote the yield (Table 1, entries 12 and 13). Meanwhile, in the absence of photocatalysts, **1a** also reacted with **2a** to afford **3a** in 46% yield (entry 14). Thus, we speculated that an electron donor−acceptor (EDA) complex may be formed during this novel cyclization reaction.[17] Furthermore, to examine the importance of visible light, the reaction was performed at 100 °C in the dark, providing **3a** in lower yield (entry 15). These results indicate that visible light is an important factor. After a quick screen of other conditions such as visible-light sources, bases, solvents, ratio of reactants, and time (see the Supporting Information for details, Tables S1−S4), the reaction conditions in entry 11 were selected as the optimal conditions.

With the optimized reaction conditions in hand, we started to investigate the substrate scope (Scheme 2). Generally, a variety of *para*-substituted *Z*-α-bromocinnamaldehydes bearing

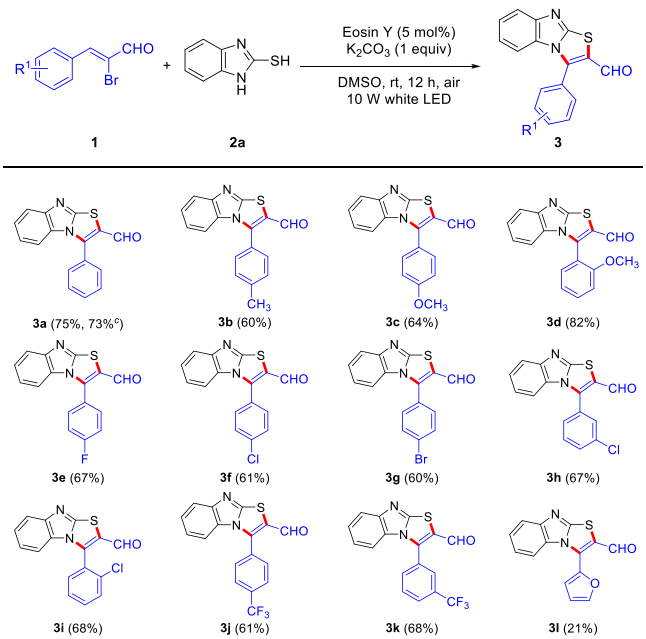
Table 1. Optimization of Reaction Conditions[a]



entry	photocatalyst	yield[b] (%)
1	eosin Y	63
2	eosin B	28
3	rhodamine B	43
4	rose bengal lactone	55
5	acid red	44
6	methylene blue	43
7	indigo	30
8	$[Ru(bpy)_3Cl_2]\cdot 6H_2O$	64
9	$Ru(bpy)_3PF_6$	65
10	$Ir(ppy)_3$	50
11[c]	**eosin Y**	**75**
12[c,d]	eosin Y	62
13[c,e]	eosin Y	72
14[c]		46
15[c,f]	eosin Y	16

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (0.3 mmol), photocatalyst (10 mol %), K_2CO_3 (0.25 mmol), DMSO (1 mL), 10 W white LED, rt, 12 h, air. [b]Isolated yield. [c]5 mol % of eosin Y. [d]0.2 mmol of K_2CO_3. [e]0.3 mmol of K_2CO_3. [f]Without visible-light irradiation, at 100 °C.

Scheme 2. Substrate Scope of *Z*-α-Bromocinnamaldehydes[a,b]



[a]Reaction conditions: **1** (0.25 mmol), **2a** (0.3 mmol), K_2CO_3 (0.25 mmol), DMSO (1 mL), 10 W white LED, rt. [b]Isolated yields. [c]*Z*-α-chlorocinnamaldehyde instead of **1a**.

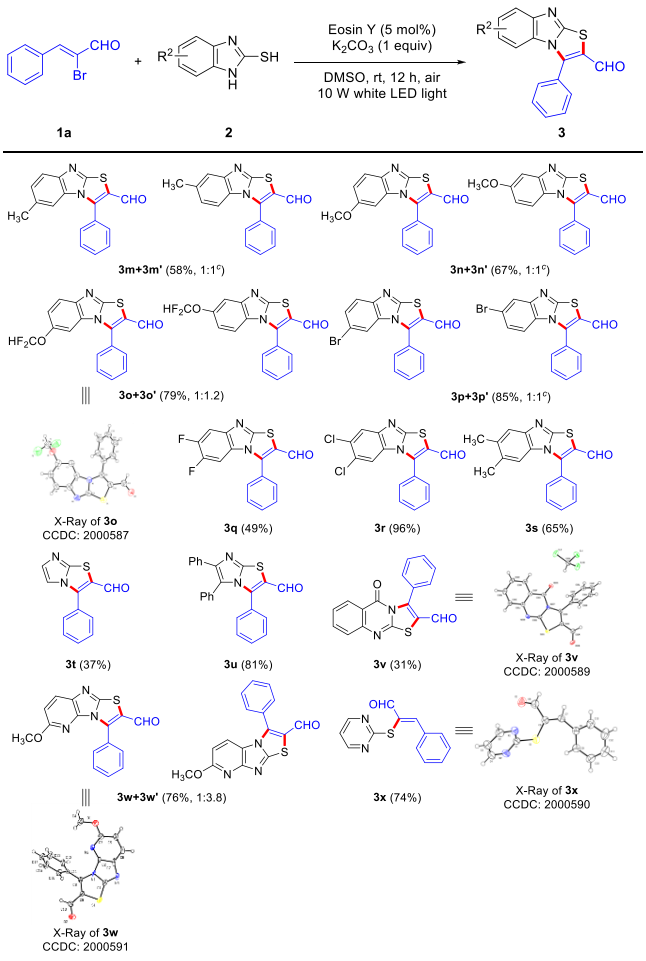
an electron-donating (CH_3 and OCH_3) or electron-withdrawing (F, Cl, Br and CF_3) group could react with 2-mercaptobenzimidazole **2a** smoothly to deliver cyclization products in 60−67% yields (**3b**, **3c**, **3e**, **3f**, **3g**, and **3j**). Subsequently, to explore the effect of steric hindrance on this

https://dx.doi.org/10.1021/acs.orglett.0c02907
Org. Lett. XXXX, XXX, XXX−XXX

reaction, *o*-OCH_3-, *m*-CF_3-, *m*-Cl-, and *o*-Cl-substituted *Z*-*α*-bromocinnamaldehydes were also performed under standard conditions, rendering the corresponding imidazo[2,1-*b*]-thiazoles in good yields (**3d**, **3h**, **3i**, and **3k**, 67−82%). The above results revealed that the reaction is not affected by electronic and steric effects. It is worth noting that the target compound **3l** was also obtained with low yield (21%) when the benzene ring was replaced by a furan ring. To our surprise, the *Z*-*α*-chlorocinnamaldehyde was also an applicable substrate, and the target product **3a** could be isolated in 73% yield.

To further examine the scope of the visible-light-induced cyclization reaction, various 2-mercaptobenzimidazole derivatives were tested. As illustrated in Scheme 3, the effect of

Scheme 3. Substrate Scope of 2-mercaptobenzimidazoles[a,b]

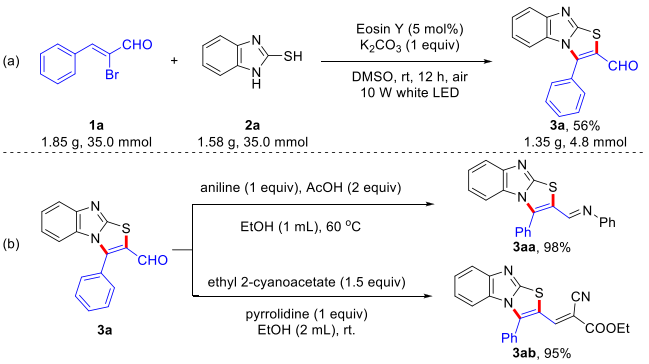


[a]Reaction condition: **1a** (0.25 mmol), **2** (0.3 mmol), eosin Y (5 mol %), K_2CO_3 (0.25 mmol), DMSO (1 mL), 10 W white LED, rt, 12 h, air. [b]Isolated yield. [c]The isomeric ratio was determined by ^{1}H NMR analysis.

substituents on 2-mercaptobenzimidazoles was also investigated. 2-Mercaptobenzimidazoles with an electron-donating substituent (such as Me, OMe, and $OCHF_2$ with special activity) or electron-withdrawing (Br) group on the 5 position proceeded successfully, and the corresponding products as a mixture of two isomers in modest to good yields were obtained (**3m** + **3m′**−**3p** + **3p′**, 58−85%). Interestingly, double substituted 2-mercaptobenzimidazoles also were efficiently transformed into the desired products **3q**, **3r**, and **3s** in 49%, 96% and 65% yields, respectively. Additionally, other nitrogen-containing heterocyclic compounds such as 1*H*-imidazole-2-thiol, 4,5-diphenyl-1*H*-imidazole-2-thiol, and 2-mercaptoquinazolin-4(3*H*)-one with **1a** obtained corresponding products (**3t**−**3v**, 31−81%). We delightedly found that 5-methoxy-3*H*-imidazo[4,5-*b*]pyridine-2-thiol treated with **1a** under standard conditions could also afford the desired cyclized products (**3w** + **3w′**, 76%). Unexpectedly, the reaction of pyrimidine-2-thiol and **1a** under standard conditions could not yield the cyclized product but a substituted product (**3x**). Unfortunately, 2-mercaptobenzothiazole and 2-mercaptobenzoxazole did not give the target compounds under the standard conditions.

The benzoimidazo[2,1-*b*]thiazole **3a** was delivered in 56% yield in a gram-scale reaction (Scheme 4a). Meanwhile, we

Scheme 4. Gram-Scale Reaction and Application of Present Work



evaluated the transformation of **3a** to **3aa** and **3ab** by the derivatization reaction (Scheme 4b). When **3a** was treated with aniline and acetic acid in ethanol at 60 °C, the Schiff base product with potential applications **3aa** was obtained in 98% yield. The Knoevenagel condensation reaction product **3ab** was synthesized in 95% yield when ethyl cyanoacetate was used as the substrate with **3a**. Because the solid of **3ab** emits strong fluorescence, it may have potential to be used as an optoelectronic material.

To gain a preliminary understanding of the cyclization reaction mechanism, several control experiments were carried out. First, the reaction was conducted in the absence of K_2CO_3 or visible-light irradiation; expectedly, only a trace amount of desired product **3a** was observed (Figure 2a). The results indicated that visible-light irradiation and base are all essential to this transformation. The yield of **3a** dropped sharply in the presence of TEMPO, BHT, or 1,1-diphenylethylene (Figure 2b), and the TEMPO-trapped product was detected by ESI-HRMS analysis (see the Supporting Information for details, Figure S3). These results indicate that a radical pathway might be involved. Meanwhile, EPR experiment further confirmed the involvement of the free radical reaction pathway (see the Supporting Information for details, Figure S4). The elimination product 3-phenylprop-2-ynal (**4**) of **1a** was not observed when this reaction proceeded in the absence of **2a** (Figure 2c). Furthermore, the reaction of **4** and **2a** under standard conditions did not yield **3a** (Figure 2d). These results can rule out the way that **1a** is first eliminated by base and then subjected to free radical addition cyclization with **2a**. To further prove the effect of visible-light irradiation, "on/off" experiments were performed, and the result clearly demonstrates that the significant role of the visible-light in the reaction system. (Figure 2e). To further explore the probable

https://dx.doi.org/10.1021/acs.orglett.0c02907
Org. Lett. XXXX, XXX, XXX−XXX

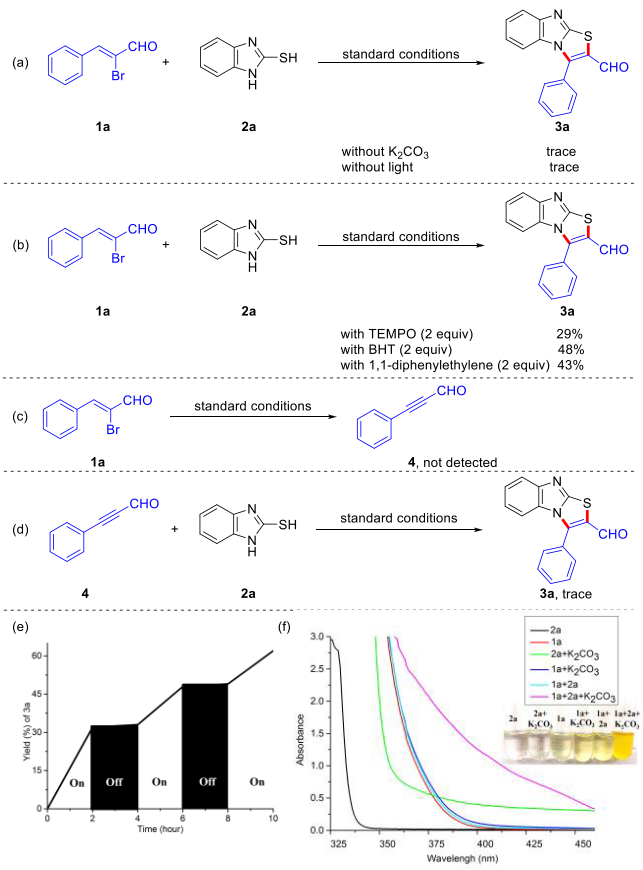
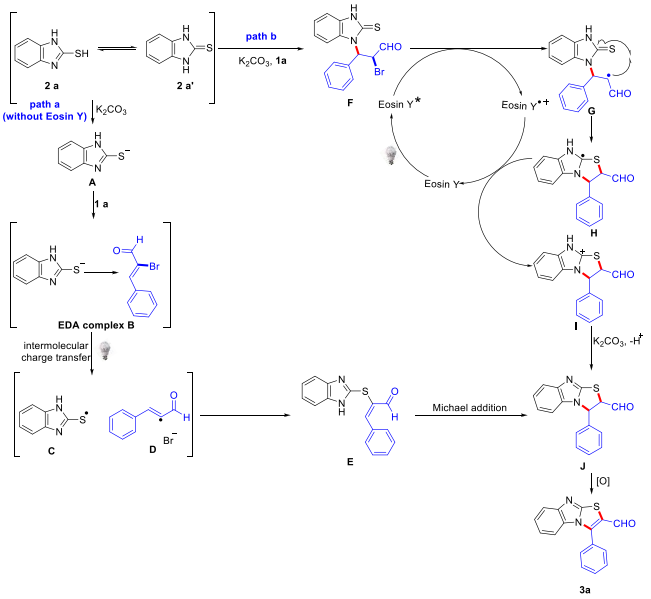


Figure 2. Mechanistic studies: (a) control experiments; (b) radical-trapping experiments; (c) reaction of **1a** under the standard reaction conditions; (d) reaction of **4** and **2a** under the standard reaction conditions; (e) on/off LED irradiation experiments; (f) UV−vis spectroscopic measurements on various combinations of **1a**, **2a**, and K_2CO_3 in DMSO.

mechanism of this aminothiolation process, the UV−vis spectroscopic measurements on various combinations of **1a**, **2a**, and K_2CO_3 in DMSO were conducted (Figure 2f). When **1a**, **2a**, and K_2CO_3 were combined, the solution showed a distinct coloration and its absorption band showed a bathochromic displacement in the visible region; the results indicate that the EDA complex may be formed.[17]

On the basis of the above control experiments and previous reports,[16,17] two possible reaction pathways were proposed in Scheme 5. In path a (without eosin Y), first, an EDA complex **B**[17] was formed between **1a** and thiolate anion **A**. Under visible-light irradiation, this EDA complex **B** undergoes a single-electron transfer (SET) to generate sulfur-centered radical intermediate **C** and vinyl radical **D**. Then these free radicals are coupled to obtain intermediate **E**. Next, intermediate **E** undergoes intramolecular Michael addition to form the intermediate **J**. In path b, initially, the intermediate **F** is formed via the Michael addition of thiol tautomer of **2a** to **1a**.[20] Under visible light irradiation, the photoredox catalyst eosin Y goes to its excited state (eosin Y*), which undergoes a SET with the intermediate **F** to produce an eosin Y radical cation (eosin $Y^{\bullet+}$) and radical intermediate **G**. Subsequently, intermediate **G** undergoes intramolecular cyclization to form the intermediate **H**. Next, **H** reduces eosin $Y^{\bullet+}$ back to the ground state, completing the oxidative quenching cycle and generating a cationic intermediate **I** in the process. The

Scheme 5. Proposed Mechanism



abstraction of an aryl hydrogen in intermediate **I** by base, leading to the intermediate **J**. Finally, aromatization of **J** yields the 3-phenylbenzoimidazo[2,1-*b*]thiazole-2-carbaldehyde **3a** as the final product, but other reaction paths cannot be completely excluded.

In conclusion, we have successfully developed a novel visible-light-promoted intermolecular cyclization reaction between *Z*-*α*-bromocinnamaldehydes and 2-mercaptobenzoimidazoles, rendering a series of compounds containing an imidazo[2,1-*b*]thiazole skeleton in satisfactory isolated yields with one C(sp^2)−S and one C(sp^2)−N bonds formation and one C(sp^2)−Br bond cleavage in one pot. This novel approach features metal-free, mild conditions, readily accessible raw materials, inexpensive catalyst, easy operation, and excellent functional group compatibility.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c02907.

Experimental materials and procedures, NMR of compounds (PDF)

Accession Codes

CCDC 2000586−2000587 and 2000589−2000591 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

Chenjiang Liu − *Urumqi Key Laboratory of Green Catalysis and Synthesis Technology, Key Laboratory of Energy Materials Chemistry, Ministry of Education, Key Laboratory of Advanced Functional Materials, Autonomous Region, College of Chemistry,*

https://dx.doi.org/10.1021/acs.orglett.0c02907
Org. Lett. XXXX, XXX, XXX−XXX

Xinjiang University, Urumqi 830046, P.R. China; orcid.org/0000-0002-8241-0809; Email: pxylcj@126.com

Authors

Ziren Chen − *Urumqi Key Laboratory of Green Catalysis and Synthesis Technology, Key Laboratory of Energy Materials Chemistry, Ministry of Education, Key Laboratory of Advanced Functional Materials, Autonomous Region, College of Chemistry, Xinjiang University, Urumqi 830046, P.R. China*

Weiwei Jin − *Urumqi Key Laboratory of Green Catalysis and Synthesis Technology, Key Laboratory of Energy Materials Chemistry, Ministry of Education, Key Laboratory of Advanced Functional Materials, Autonomous Region, College of Chemistry, Xinjiang University, Urumqi 830046, P.R. China;* orcid.org/0000-0002-5996-3229

Yu Xia − *Urumqi Key Laboratory of Green Catalysis and Synthesis Technology, Key Laboratory of Energy Materials Chemistry, Ministry of Education, Key Laboratory of Advanced Functional Materials, Autonomous Region, College of Chemistry, Xinjiang University, Urumqi 830046, P.R. China*

Yonghong Zhang − *Urumqi Key Laboratory of Green Catalysis and Synthesis Technology, Key Laboratory of Energy Materials Chemistry, Ministry of Education, Key Laboratory of Advanced Functional Materials, Autonomous Region, College of Chemistry, Xinjiang University, Urumqi 830046, P.R. China;* orcid.org/0000-0002-7740-9408

Mengwei Xie − *Urumqi Key Laboratory of Green Catalysis and Synthesis Technology, Key Laboratory of Energy Materials Chemistry, Ministry of Education, Key Laboratory of Advanced Functional Materials, Autonomous Region, College of Chemistry, Xinjiang University, Urumqi 830046, P.R. China*

Shangchao Ma − *Urumqi Key Laboratory of Green Catalysis and Synthesis Technology, Key Laboratory of Energy Materials Chemistry, Ministry of Education, Key Laboratory of Advanced Functional Materials, Autonomous Region, College of Chemistry, Xinjiang University, Urumqi 830046, P.R. China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c02907

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was supported by the National Natural Science Foundation of China (Grant Nos. 21961037, 21702175, and 21572195) and the Graduate Innovation Project of Xinjiang Uygur Autonomous Region (XJ2020G007). We thank Prof. Dr. Guoquan Liu (Peking University) for his generous help with the data processing of EPR.

■ REFERENCES

(1) (a) Eicher, T.; Hauptmann, S. *The Chemistry of Heterocycles*; Wiley-VCH: Weinheim, 2003. (b) Cui, B.; Zheng, B. L.; He, K.; Zheng, Q. Y. *J. Nat. Prod.* **2003**, *66*, 1101−1103. (c) Roué, M.; Domart-Coulon, I.; Ereskovsky, A.; Djediat, C.; Perez, T.; Bourguet-Kondracki, M.-L. *J. Nat. Prod.* **2010**, *73*, 1277−1282. (d) Zhang, L.; Peng, X.-M.; Damu, G. L. V.; Geng, R.-X.; Zhou, C.-H. *Med. Res. Rev.* **2014**, *34*, 340−437.

(2) (a) Feng, M.; Tang, B.; Liang, S. H.; Jiang, X. *Curr. Top. Med. Chem.* **2016**, *16*, 1200−1216. (b) Wang, N.; Saidhareddy, P.; Jiang, X. *Nat. Prod. Rep.* **2020**, *37*, 246−275.

(3) (a) Raeymaekers, A. H. M.; Allewijn, F. T. N.; Vandenberk, J.; Demoen, P. J. A.; Offenwert, T. T. T. V.; Janssen, P. A. J. *J. Med. Chem.* **1966**, *9*, 545−551. (b) Budriesi, R.; Ioan, P.; Locatelli, A.; Cosconati, S.; Leoni, A.; Ugenti, M. P.; Andreani, A.; Toro, R. D.; Bedini, A.; Spampinato, S.; Marinelli, L.; Novellino, E.; Chiarini, A. *J. Med. Chem.* **2008**, *51*, 1592−1600. (c) Vu, C. B.; Bemis, J. E.; Disch, J. S.; Ng, P. Y.; Nunes, J. J.; Milne, J. C.; Carney, D. P.; Lynch, A. V.; Smith, J. J.; Lavu, S.; Lambert, P. D.; Gagne, D. J.; Jirousek, M. R.; Schenk, S.; Olefsky, J. M.; Perni, R. B. *J. Med. Chem.* **2009**, *52*, 1275−1283. (d) Ali, A. R.; El-Bendary, E. R.; Ghaly, M. A.; Shehata, I. A. *Eur. J. Med. Chem.* **2014**, *75*, 492−500.

(4) Cui, L.-S.; Kim, J. U.; Nomura, H.; Nakanotani, H.; Adachi, C. *Angew. Chem., Int. Ed.* **2016**, *55*, 6864−6868.

(5) (a) Yousefi, B. H.; Manook, A.; Drzezga, A.; Reutern, B.; Schwaiger, M.; Wester, H.-J.; Henriksen, G. *J. Med. Chem.* **2011**, *54*, 949−956. (b) Alagille, D.; DaCosta, H.; Baldwin, R. M.; Tamagnan, G. D. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 2966−2968. (c) Yousefi, B. H.; Drzezga, A.; Reutern, B.; Manook, A.; Schwaiger, M.; Wester, H.-J.; Henriksen, G. *ACS Med. Chem. Lett.* **2011**, *2*, 673−677.

(6) (a) Andreani, A.; Burnelli, S.; Granaiola, M.; Leoni, A.; Locatelli, A.; Morigi, R.; Rambaldi, M.; Varoli, L.; Calonghi, N.; Cappadone, C.; Farruggia, G.; Zini, M.; Stefanelli, C.; Masotti, L.; Radin, N. S.; Shoemaker, R. H. *J. Med. Chem.* **2008**, *51*, 809−816. (b) Trapani, G.; Franco, M.; Latrofa, A.; Reho, A.; Liso, G. *Eur. J. Pharm. Sci.* **2001**, *14*, 209−216. (c) Andreani, A.; Granaiola, M.; Locatelli, A.; Morigi, R.; Rambaldi, M.; Varoli, L.; Calonghi, N.; Cappadone, C.; Farruggia, G.; Stefanelli, C.; Masotti, L.; Nguyen, T. L.; Hamel, E.; Shoemaker, R. H. *J. Med. Chem.* **2012**, *55*, 2078−2088.

(7) Al-Tel, T. H.; Al-Qawasmeh, R. A.; Zaarour, R. *Eur. J. Med. Chem.* **2011**, *46*, 1874−1881.

(8) Palkar, M.; Noolvi, M.; Sankangoud, R.; Maddi, V.; Gadad, A.; Nargund, L. V. G. *Arch. Pharm.* **2010**, *343*, 353−359.

(9) Ager, I. R.; Barnes, A. C.; Danswan, G. W.; Hairsine, P. W.; Kay, D. P.; Kennewell, P. D.; Matharu, S. S.; Miller, P.; Robson, P.; Rowlands, D. A.; Tully, W. R.; Westwood, R. *J. Med. Chem.* **1988**, *31*, 1098−1115.

(10) (a) Fenichel, R. L.; Dheer, S. K.; Grant, N. H.; Scott, D. P.; Bloom, R.; Gregory, F. J. *J. Immunopharmacol.* **1983**, *5*, 333−340. (b) Fenichel, R. L.; Alburn, H. E.; Schreck, P. A.; Bloom, R.; Gregory, F. J. *J. Immunopharmacol.* **1980**, *2*, 491−508.

(11) (a) Xie, Y.; Chen, X.; Wang, Z.; Huang, H.; Yi, B.; Deng, G.-J. *Green Chem.* **2017**, *19*, 4294−4298. (b) Mishra, S.; Monir, K.; Mitra, S.; Hajra, A. *Org. Lett.* **2014**, *16*, 6084−6087.

(12) (a) Kuang, J.; Xia, Y.; Yang, A.; Zhang, H.; Su, C.; Lee, D. *Chem. Commun.* **2019**, *55*, 1813−1816. (b) Xiao, D.; Han, L.; Sun, Q.; Chen, Q.; Gong, N.; Lv, Y.; Suzenet, F.; Guillaumet, G.; Cheng, T.; Li, R. *RSC Adv.* **2012**, *2*, 5054−5057. (c) Omar, M. A.; Frey, W.; Conrad, J.; Beifuss, U. *J. Org. Chem.* **2014**, *79*, 10367−10377.

(13) Jana, S.; Chakraborty, A.; Shirinian, V. Z.; Hajra, A. *Adv. Synth. Catal.* **2018**, *360*, 2402−2408.

(14) (a) Shen, G.; Yang, B.; Huang, X.; Hou, Y.; Gao, H.; Cui, J.; Cui, C.; Zhang, T. *J. Org. Chem.* **2017**, *82*, 3798−3805. (b) Zhang, X.; Jia, J.; Ma, C. *Org. Biomol. Chem.* **2012**, *10*, 7944−7948. (c) Xu, H.; Zhang, Y.; Huang, J.; Chen, W. *Org. Lett.* **2010**, *12*, 3704−3707.

(15) Xu, J.; Deng, R.; Chen, J.; Tang, X.; Zhao, J. *Adv. Synth. Catal.* **2019**, *361*, 5144−5148.

(16) For selected references, see: (a) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322−5363. (b) Shi, L.; Xia, W. *Chem. Soc. Rev.* **2012**, *41*, 7687−7697. (c) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* **2011**, *40*, 102−113. (d) Fabry, D. C.; Rueping, M. *Acc. Chem. Res.* **2016**, *49*, 1969−1979. (e) Margrey, K. A.; Nicewicz, D. A. *Acc. Chem. Res.* **2016**, *49*, 1997−2006. (f) Xie, J.; Jin, H.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2017**, *46*, 5193−5203. (g) Shaw, M. H.; Twilton, J.; MacMillan, D. W. C. *J. Org. Chem.* **2016**, *81*, 6898−6926. (h) Zhou, Q.-Q.; Zou, Y.-Q.; Lu, L.-Q.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2019**, *58*, 1586−1604. (i) Lv, Y.; Bao, P.; Yue, H.; Li, J.-S.; Wei, W. *Green Chem.* **2019**, *21*, 6051−6055. (j) Yan, D.-M.; Chen, J.-R.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2019**, *58*, 378−380. (k) Geng, X.; Lin, F.; Wang, X.; Jiao, N. *Org. Lett.* **2017**, *19*, 4738−4741. (l) Xie, L.-Y.; Jiang, L.-L.; Tan, J.-X.; Wang, Y.; Xu, X.-Q.; Zhang, B.; Cao, Z.; He, W.-M. *ACS Sustainable Chem. Eng.*

2019, *7*, 14153−14160. (m) Li, Y.; Rizvi, S. A.; Hu, D.; Sun, D.; Gao, A.; Zhou, Y.; Li, J.; Jiang, X. *Angew. Chem., Int. Ed.* **2019**, *58*, 13499−13506. (n) Marzo, L.; Pagire, S. K.; Reiser, O.; König, B. *Angew. Chem., Int. Ed.* **2018**, *57*, 10034−10072. (o) Wang, D.; Zhu, N.; Chen, P.; Lin, Z.; Liu, G. *J. Am. Chem. Soc.* **2017**, *139*, 15632−15635. (p) Liu, Q.; Wu, L.-Z. *Natl. Sci. Rev.* **2017**, *4*, 359−380. (q) Chen, B.; Wu, L.-Z.; Tung, C.-H. *Acc. Chem. Res.* **2018**, *51*, 2512−2523.

(17) (a) Crisenza, G. E. M.; Mazzarella, D.; Melchiorre, P. *J. Am. Chem. Soc.* **2020**, *142*, 5461−5476. (b) Wei, Y.; Zhou, Q.-Q.; Tan, F.; Lu, L.-Q.; Xiao, W.-J. *Synthesis* **2019**, *51*, 3021−3054. (c) Li, G.; Yan, Q.; Gan, Z.; Li, Q.; Dou, X.; Yang, D. *Org. Lett.* **2019**, *21*, 7938−7942. (d) Liu, B.; Lim, C.-H.; Miyake, G. M. *J. Am. Chem. Soc.* **2017**, *139*, 13616−13619.

(18) For selected references, see: (a) Chen, J.-R.; Hu, X.-Q.; Lu, L.-Q.; Xiao, W.-J. *Chem. Soc. Rev.* **2016**, *45*, 2044−2056. (b) Natarajan, P.; Chuskit, D.; Priya. *Green Chem.* **2019**, *21*, 4406−4411. (c) Yang, X.-L.; Guo, J.-D.; Lei, T.; Chen, B.; Tung, C.-H.; Wu, L.-Z. *Org. Lett.* **2018**, *20*, 2916−2920. (d) Qi, X.-K.; Zhang, H.; Pan, Z.-T.; Liang, R.-B.; Zhu, C.-M.; Li, J.-H.; Tong, Q.-X.; Gao, X.-W.; Wu, L.-Z.; Zhong, J.-J. *Chem. Commun.* **2019**, *55*, 10848−10851.

(19) Li, H.; Liu, C.; Zhang, Y.; Sun, Y.; Wang, B.; Liu, W. *Org. Lett.* **2015**, *17*, 932−935.

(20) Liu, Y.; Yu, Y.; Fu, Y.; Liu, Y.; Shi, L.; Li, H.; Wang, W. *Org. Chem. Front.* **2017**, *4*, 2119−2123.

https://dx.doi.org/10.1021/acs.orglett.0c02907
Org. Lett. XXXX, XXX, XXX−XXX