

## RESEARCH ARTICLE

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## Cascade cyclization reactions of alkylidenecyclopropanes for the construction of polycyclic lactams and lactones by visible light photoredox catalysis†

Mintao Chen,<sup>a</sup> Yin Wei <sup>\*a</sup> and Min Shi <sup>a,b</sup>

A visible light photocatalytic cascade cyclization reaction of alkylidenecyclopropanes for the rapid construction of seven- and eight-membered ring-containing polycyclic lactams and lactones has been developed. The process is proposed to proceed through a radical pathway, and the suggested radical intermediate was captured by TEMPO successfully. An intermolecular version of the reaction was also achieved, affording a variety of methyl dialinoacetate products.

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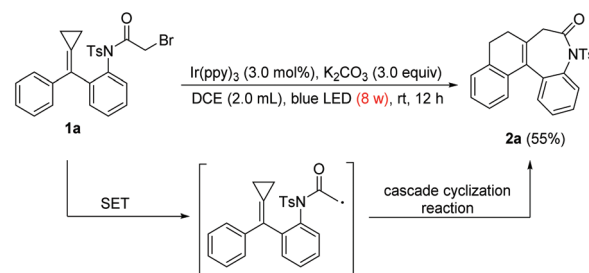
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The past ten years have witnessed a flourish in visible light photocatalysis,<sup>1</sup> and the photocatalytic variants of many important reactions have been achieved, such as cross-coupling reactions, cycloadditions, fluorinations, *etc.*<sup>2</sup> Using light as the driving force in the reaction, the photocatalytic reaction can often proceed under mild reaction conditions. Meanwhile, photocatalysts can serve as both electron donors and acceptors in catalytic reaction cycles<sup>1b,3</sup> and many stoichiometrically used oxidants and reductants in traditional reactions can be replaced by air, oxygen and amines, leading to a more economical and sustainable chemical synthesis.<sup>1a,4</sup>

Alkylidenecyclopropanes are important building blocks due to their high activities and diverse reactivities, and they have been widely used in organic synthesis.<sup>5</sup> To further explore their potential usefulness in organic chemistry, persistent efforts have been made by our group and many other groups, and significant progress and interesting results have been achieved, including some light driven reactions about a decade ago.<sup>6</sup> Considering the immense potential of visible light photocatalysis in organic synthesis, we attempt to combine it with alkylidenecyclopropane chemistry, in order to achieve new and efficient transformations of alkylidenecyclopropanes into useful structural motifs.

Inspired by the previous work,<sup>7</sup> we hypothesized that substrate **1a** having the alkylidenecyclopropane moiety under visible light photocatalysis could produce a radical intermediate by the cleavage of the C–Br bond at the  $\alpha$ -position of the carbonyl group, and a cascade cyclization reaction would probably take place to afford polycyclic compounds. Thus, **1a** was prepared, and we subsequently examined its reactivity under visible light photocatalysis (Scheme 1). To our delight, when **1a** (0.2 mmol) together with Ir(ppy)<sub>3</sub> (3 mol%) and K<sub>2</sub>CO<sub>3</sub> (3.0 equiv.) was exposed to blue LED light for 12 h, polycyclic product **2a** was obtained successfully in a yield of 55% (Scheme 1 and Table 1, entry 6). The structure of **2a** was confirmed by X-ray crystal diffraction. Its ORTEP drawing is shown in Fig. 1 and the CIF data are presented in the ESI.†

Encouraged by the success of the first attempt of this reaction, we tried to optimize the reaction conditions (Table 1). Firstly, we screened several commonly used photocatalysts. Photocatalysts such as eosin Y, fluorescein and Ru(bpy)<sub>3</sub>Cl<sub>2</sub>·6H<sub>2</sub>O could not catalyze this reaction, and the reaction still did not work when we employed white and green



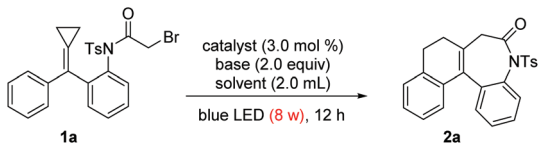
**Scheme 1** Our design and first attempt of the photo-catalyzed reaction.

<sup>a</sup>State Key Laboratory of Organometallic Chemistry, Center for Excellence in Molecular Synthesis, University of Chinese Academy of Sciences, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China. E-mail: weiyin@sioac.ac.cn

<sup>b</sup>Shenzhen Grubbs Institute, Southern University of Science and Technology, Shenzhen, Guangdong 518000, China

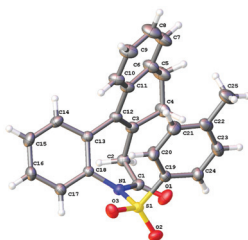
† Electronic supplementary information (ESI) available: Experimental procedures and characterization data of new compounds. CCDC 1842217. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c9qo01360a

Table 1 Optimization of reaction conditions



Entry <sup>a</sup>	Catalyst	Base	Solvent	Yield <sup>b</sup> /%
1 <sup>c</sup>	Eosin Y	K <sub>2</sub> CO <sub>3</sub>	DCE	NR
2 <sup>c</sup>	Fluorescein	K <sub>2</sub> CO <sub>3</sub>	DCE	NR
3 <sup>c</sup>	Ru(bpy) <sub>3</sub> ·Cl <sub>2</sub> ·H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	DCE	NR
4	Ir(ppy) <sub>2</sub> (dtbpy)PF <sub>6</sub>	K <sub>2</sub> CO <sub>3</sub>	DCE	10
5	Ir[dF(CF <sub>3</sub> )ppy] <sub>2</sub> (dtbpy)PF <sub>6</sub>	K <sub>2</sub> CO <sub>3</sub>	DCE	5
6	<b>Ir(ppy)<sub>3</sub></b>	<b>K<sub>2</sub>CO<sub>3</sub></b>	<b>DCE</b>	<b>55</b>
7	Ir(ppy) <sub>3</sub>	Cs <sub>2</sub> CO <sub>3</sub>	DCE	52
8	Ir(ppy) <sub>3</sub>	Pyridine	DCE	10
9	Ir(ppy) <sub>3</sub>	Et <sub>3</sub> N	DCE	15
10	Ir(ppy) <sub>3</sub>	K <sub>2</sub> CO <sub>3</sub>	Toluene	47
11	Ir(ppy) <sub>3</sub>	K <sub>2</sub> CO <sub>3</sub>	CH <sub>3</sub> CN	33
12	Ir(ppy) <sub>3</sub>	K <sub>2</sub> CO <sub>3</sub>	DCM	50
13 <sup>d</sup>	Ir(ppy) <sub>3</sub>	K <sub>2</sub> CO <sub>3</sub>	DCE	54
14 <sup>e</sup>	Ir(ppy) <sub>3</sub>	K <sub>2</sub> CO <sub>3</sub>	DCE	53

<sup>a</sup> Reaction conditions: **1a** (0.2 mmol), photocatalyst (3.0 mol%) and base (3.0 equiv.) were placed in a reaction tube and Ar was charged. Then 2.0 mL solvent was added and the mixture was stirred exposing to blue LED light (8 W) at room temperature for 12 h. NR = no reaction. <sup>b</sup> Isolated yield. All the starting materials had been consumed and instead of forming **2a**, the rest of them might have decomposed into unknown complexes. <sup>c</sup> White light (40 W) and green LED light (8 W) were also employed and no desired product **2a** was obtained. <sup>d</sup> 1.5 mL DCE. <sup>e</sup> 2.5 mL DCE.

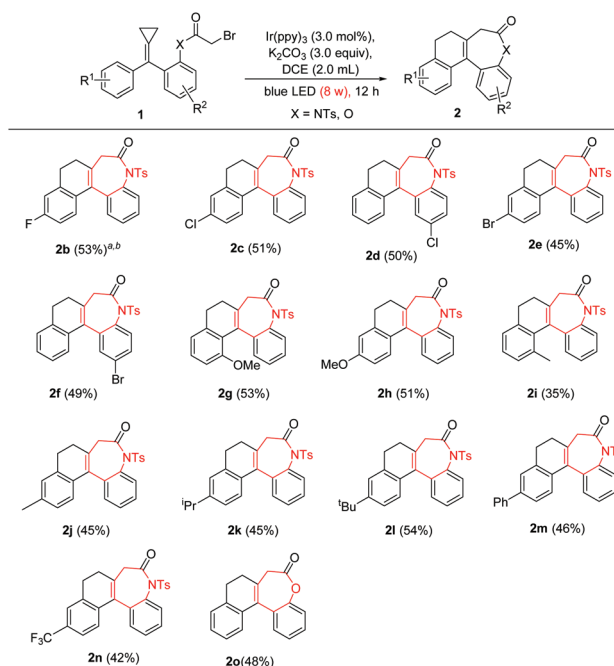
Fig. 1 The X-ray crystal structure of **2a**.

light sources instead of blue LED light (Table 1, entries 1–3). However, Ir-relevant photocatalysts smoothly catalyzed this reaction to afford the desired product **2a** (Table 1, entries 4 and 5) and Ir(ppy)<sub>3</sub> used in our first attempt was still the best (Table 1, entry 6). This maybe implied that the redox potentials of Ir-relevant photocatalysts were the most suitable for this reaction. Then, different bases were screened. The use of the inorganic base Cs<sub>2</sub>CO<sub>3</sub> afforded **2a** in a yield of 52% (Table 1, entry 7), which is similar to that obtained using K<sub>2</sub>CO<sub>3</sub>. However, employing organic bases including pyridine and NEt<sub>3</sub> decreased the yield of **2a** to 10% and 15%, respectively (Table 1, entries 8 and 9), which implied that organic bases might hamper the redox cycle of the photocatalyst in the reaction. Different solvents were also screened, and the use of toluene, CH<sub>3</sub>CN and DCM as solvents afforded product **2a** in yields ranging from 30% to 50% (Table 1, entries 10–12). In

comparison, DCE was the most appropriate choice. The adjustment of the volume of solvent did not improve the yield of **2a** (Table 1, entries 13 and 14). The reaction conditions used in the first attempt were still the best reaction conditions.

With the optimal conditions in hand, we then examined the substrate scope (Scheme 2). Generally speaking, the products were obtained in moderate yields; although all the starting materials were consumed, some of them were decomposed to unknown complexes. Substrates **1b–1d** bearing the F/Cl substituent afforded the desired products **2b–2d** in a similar yield of about 50%; substrates **1e** and **1f** bearing the –Br substituent afforded the corresponding products **2e** and **2f** in relatively lower yields of 45% and 49%, respectively. Substrates **1g** and **1h** bearing a methoxy group also afforded the corresponding products **2g** and **2h** in yields of 53% and 51%, respectively. It seemed that the electronic effect of the substituents on the substrates did not have remarkable influence on the yields of the products. Alkyl group substituted substrates **1i–1l** underwent the reaction smoothly, affording products **2i–2l** in yields ranging from 35% to 54%. The phenyl substituted substrate **1m** afforded product **2m** in a yield of 46%. Substrate **1n** having the CF<sub>3</sub> substituent underwent the reaction smoothly, affording product **2n** in a yield of 42%. A polycyclic lactone product **2o** was also obtained in a yield of 48%.

After successfully obtaining a series of polycyclic lactams and lactones containing seven-membered rings, we further proceeded to synthesize polycyclic compounds containing eight-membered rings. With a slight adjustment of the con-



Scheme 2 Substrate scope of **1**. <sup>a</sup> Reaction conditions: **1** (0.2 mmol), Ir(ppy)<sub>3</sub> (3.0 mol%) and K<sub>2</sub>CO<sub>3</sub> (3.0 equiv.) were placed in a reaction tube and Ar was charged. Then 2.0 mL solvent was added and the mixture was stirred upon exposure to blue LED light (8 W) at room temperature for 12 h. <sup>b</sup> Isolated yield.

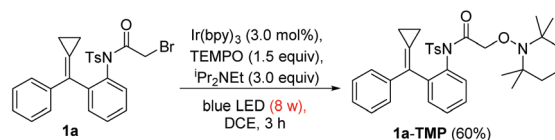
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ditions, we found that when DCE was reduced to 1.0 mL, the temperature was increased to 70 °C and reaction time was prolonged to 24 h (see the ESI†), and product **4a** was also obtained smoothly, though in a relatively lower yield (Scheme 3).

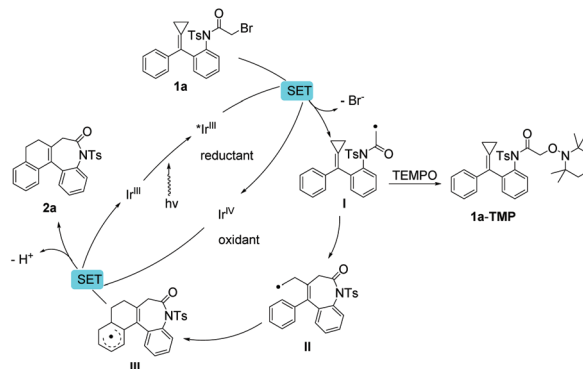
The substrate scope was also examined by employing a variety of alkylidenecyclopropanes **3** bearing  $-Cl/Me^iPr/Ph$  groups. The desired polycyclic lactams and lactones **4b–4j** containing eight-membered rings were obtained in yields ranging from 10% to 30% (Scheme 4). In comparison, the yield of **4** was much lower than that of **2** presumably due to the large size of the eight-membered ring. The reactions of substrates **3d** and **3i** took place, affording products **4d** and **4i** as mixtures of regioisomers in 2.3 : 1 and 2 : 1 ratios, respectively.

To gain some insights into the mechanism, TEMPO was used to capture radical intermediates involved in the reaction. Fortunately, compound **1a-TMP** was successfully obtained in a yield of 60% (Scheme 5). This provided evidence for the proposed radical pathway.

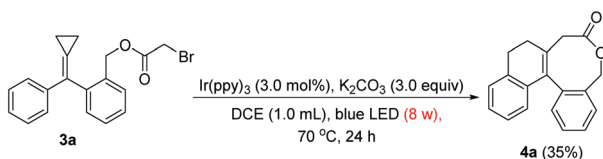
Based on the previous reports<sup>7b,c,8</sup> and the above experimental results, we proposed a radical reaction mechanism for



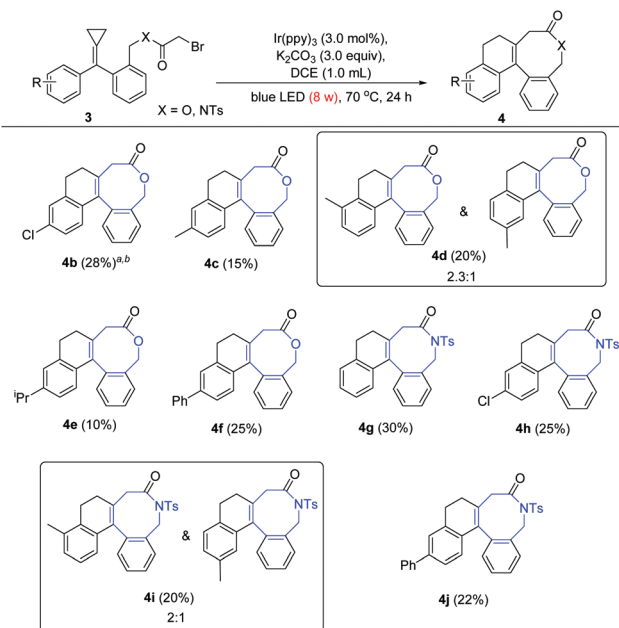
Scheme 5 Capture of the radical intermediate with TEMPO.



Scheme 6 A plausible pathway for the reaction.



Scheme 3 Attempt to construct polycyclic compound **4a** using substrate **3a**.

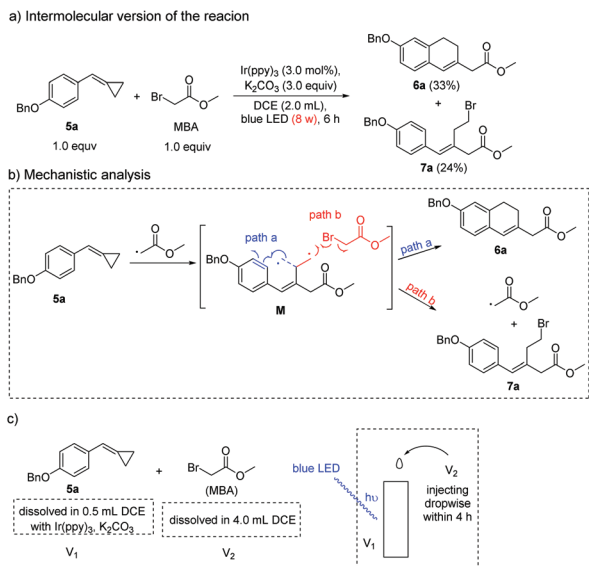


Scheme 4 Substrate scope of **3**. <sup>a</sup> Reaction conditions: **3** (0.2 mmol), Ir(ppy)<sub>3</sub> (3.0 mol%) and K<sub>2</sub>CO<sub>3</sub> (3.0 equiv.) were placed in a reaction tube and Ar was charged. Then 2.0 mL solvent was added and the mixture was stirred upon exposure to blue LED light (8 W) at 70 °C for 12 h. <sup>b</sup> Isolated yield.

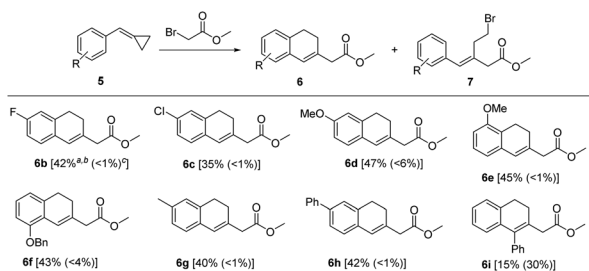
this photo-catalyzed reaction (Scheme 6). Firstly, substrate **1a** produces an active radical intermediate **I** through a SET process, and then intermediate **I** undergoes cascade cyclization to afford intermediates **II** and **III**. Afterwards, through another SET process and deprotonation, the desired polycyclic product **2a** can be generated. It should be noted here that K<sub>2</sub>CO<sub>3</sub> as the auxiliary base is also critical for this reaction; without the base, the substrate will be quickly decomposed in the presence of HBr generated during the reaction process and the yield will be dramatically decreased.

Furthermore, we developed an intermolecular version of the visible light photocatalyzed reaction on the basis of the above results. The reaction of **5a** and methyl bromoacetate (MBA) occurred under the same conditions, and the desired product **6a** was obtained in a yield of 33%, together with a radical chain product **7a** in a yield of 24% (Scheme 7a). Based on the proposed mechanism (Scheme 6), we proposed that the key radical intermediate **M** probably underwent either cyclization (*via* path a) to give product **6** or a chain reaction with MBA (*via* path b) to generate product **7**. We hypothesized that if the concentration of MBA was kept low enough, intermediate **M** would be favorably transformed into **6a** through path a while path b would be greatly suppressed (Scheme 7b). Thus, MBA was injected dropwise into the reaction system through a syringe pump within 4 h and the yield of **6a** successfully increased to 54% while the yield of **7a** decreased to 10% (Scheme 7c; for details, see the ESI†).

We also investigated the substrate scope of **5** for this reaction (Scheme 8). Substrates **5b–5h** bearing  $-F/Cl/Me/MeO/Ph/OBn$  groups underwent this reaction to afford products **6b–6h** in yields ranging from 35% to 47% while the radical chain products **7b–7h** were obtained in dramatically suppressed yields.



**Scheme 7** Intermolecular reaction of **5a** with MBA.

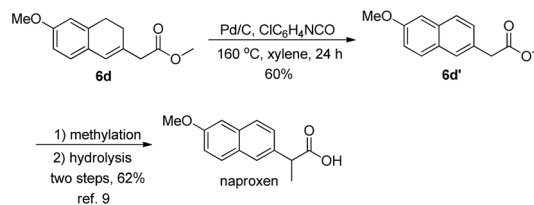


**Scheme 8** Substrate scope for the intermolecular reaction. <sup>a</sup> Reaction conditions: **5** (0.2 mmol), Ir(ppy)<sub>3</sub> (3.0 mol%) and K<sub>2</sub>CO<sub>3</sub> (3.0 equiv.) were placed in a reaction tube. Ar was charged and 0.5 mL DCE was added. Then upon exposure to blue LED light (8 W), MBA (0.2 mmol) dissolved in 4.0 mL DCE was injected dropwise through a syringe pump within 4 h. <sup>b</sup> Isolated yields of product **6**. <sup>c</sup> Yields of **7** determined by <sup>1</sup>H NMR spectroscopy with 1,3,5-trimethoxybenzene as an internal standard.

As for substrate **5e**, it transformed regioselectively into product **6e**. For substrate **5i**, the corresponding product **6i** was only obtained in a yield of 15% while the yield of **7i** increased to 30%, presumably due to the electronic effect (see the ESI†).

Products **6** can be used as precursors of many valuable compounds. For example, **6d** can be dehydrogenated to form **6'd** (available at a high price on the market) and then naproxen (non-steroidal anti-inflammatory drug) after further methylation and hydrolysis (Scheme 9).<sup>9</sup>

In summary, a facile method for the synthesis of polycyclic lactams and lactones containing seven-membered or eight-membered rings by visible light photocatalysis has been developed and a plausible radical pathway is proposed. An intermolecular version of the reaction was also achieved which could afford various substituted methyl dialinoacetate products used as valuable precursors for further transformations.



**Scheme 9** Synthetic transformation of **6d**.

## Conflicts of interest

There are no conflicts of interest to declare.

## Acknowledgements

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## Notes and references

- (a) X. Sala, I. Romero, M. Rodríguez, L. Escriche and A. Llobet, Molecular catalysts that oxidize water to dioxygen, *Angew. Chem., Int. Ed.*, 2009, **48**, 2842; (b) K. Zeitler, Photoredox catalysis with visible light, *Angew. Chem., Int. Ed.*, 2009, **48**, 9785; (c) T. P. Yoon, M. A. Ischay and J. Du, Visible light photocatalysis as a greener approach to photochemical synthesis, *Nat. Chem.*, 2010, **2**, 527; (d) J. M. R. Narayanam and C. R. J. Stephenson, Visible light photoredox catalysis: applications in organic synthesis, *Chem. Soc. Rev.*, 2011, **40**, 102; (e) J. Xuan and W.-J. Xiao, Visible-light photoredox catalysis, *Angew. Chem., Int. Ed.*, 2012, **51**, 6828; (f) X. Dai, X. Xu and X. Li, Applications of visible light photoredox catalysis in organic synthesis, *Chin. J. Org. Chem.*, 2013, **33**, 2046; (g) C. K. Prier, D. A. Rankic and D. W. C. MacMillan, Visible light photoredox catalysis with transition metal complexes: Applications in organic synthesis, *Chem. Rev.*, 2013, **113**, 5322; (h) M.-Y. Cao, X. Ren and Z. Lu, Visible-light-induced direct alpha-C(sp<sup>3</sup>)-H thiocyanation of tertiary amines, *Tetrahedron Lett.*, 2015, **56**, 3732; (i) N. Corrigan, S. Shanmugam, J. T. Xu and C. Boyer, Photocatalysis in organic and polymer synthesis, *Chem. Soc. Rev.*, 2016, **45**, 6165; (j) X. Li, J. G. Yu and M. Jaroniec, Cooperative photoredox catalysis, *Chem. Soc. Rev.*, 2016, **45**, 2603; (k) N. A. Romero and D. A. Nicewicz, Organic photoredox catalysis, *Chem. Rev.*, 2016, **116**, 10075; (l) K. L. Skubi,



- T. R. Blum and T. P. Yoon, Dual catalysis strategies in photochemical synthesis, *Chem. Rev.*, 2016, **116**, 10035.
- 2 (a) M. Fagnoni, D. Dondi, D. Ravelli and A. Albini, Photocatalysis for the formation of the C–C bond, *Chem. Rev.*, 2007, **107**, 2725; (b) M. A. Ischay, M. E. Anzovino, J. Du and T. P. Yoon, Efficient visible light photocatalysis of [2+2] enone cycloadditions, *J. Am. Chem. Soc.*, 2008, **130**, 12886; (c) D. A. Nicewicz and D. W. C. MacMillan, Merging photoredox catalysis with organocatalysis: the direct asymmetric alkylation of aldehydes, *Science*, 2008, **322**, 77; (d) J. R. Chen, X. Q. Hu, L. Q. Lu and W. J. Xiao, Exploration of visible-light photocatalysis in heterocycle synthesis and functionalization: reaction design and beyond, *Acc. Chem. Res.*, 2016, **49**, 1911; (e) Y. Liu, R. Song and J. Li, The cycloaddition reaction using visible light photoredox catalysis, *Sci. China: Chem.*, 2016, **59**, 161; (f) S. Poplata, A. Troster, Y. Q. Zou and T. Bach, Recent advances in the synthesis of cyclobutanes by olefin 2+2 photocycloaddition reactions, *Chem. Rev.*, 2016, **116**, 9748; (g) J. Xie, T. Zhang, F. Chen, N. Mehrkens, F. Rominger, M. Rudolph and A. S. K. Hashmi, Gold-catalyzed highly selective photoredox C(sp<sup>2</sup>)-H difluoroalkylation and perfluoro-alkylation of hydrazones, *Angew. Chem., Int. Ed.*, 2016, **55**, 2934; (h) C.-Y. He, J.-W. Gu and X. Zhang, Visible-light-mediated direct perfluoroalkylation and trifluoro-methylation of free anilines, *Tetrahedron Lett.*, 2017, **58**, 3939; (i) J. H. Kou, C. H. Lu, J. Wang, Y. K. Chen, Z. Z. Xu and R. S. Varma, Selectivity enhancement in heterogeneous photocatalytic transformations, *Chem. Rev.*, 2017, **117**, 1445; (j) Q. Qin, H. Jiang, Z. Hu, D. Ren and S. Yu, Functionalization of C-H bonds by photoredox catalysis, *Chem. Rec.*, 2017, **17**, 754; (k) J. Twilton, C. Le, P. Zhang, M. H. Shaw, R. W. Evans and D. W. C. MacMillan, The merger of transition metal and photocatalysis, *Nat. Rev. Chem.*, 2017, **1**, 1; (l) X.-K. He, B.-G. Cai, Q.-Q. Yang, L. Wang and J. Xuan, Visible-light-promoted cascade radical cyclization: synthesis of 1,4-diketones containing chroman-4-one skeletons, *Chem. – Asian J.*, 2019, **14**, 3269; (m) X. Yi, F. Huang, J. B. Baell, H. Huang and Y. Yu, The formation of C(sp<sup>3</sup>)-C(sp<sup>3</sup>) by visible-light photocatalysis, *Prog. Chem.*, 2019, **31**, 505.
- 3 (a) M. D. Kaerkaes, B. S. Matsuura and C. R. J. Stephenson, Enchained by visible light-mediated photoredox catalysis, *Science*, 2015, **349**, 1285; (b) W. Yu, X.-H. Xu and F.-L. Qing, Photoredox catalysis mediated application of methyl fluorosulfonyldifluoroacetate as the CF<sub>2</sub>CO<sub>2</sub>R radical source, *Org. Lett.*, 2016, **18**, 5130.
- 4 (a) X. Lang, J. Zhao and X. Chen, Cooperative photoredox catalysis, *Chem. Soc. Rev.*, 2016, **45**, 3026; (b) X. Cheng, X. Hu and Z. Lu, Visible-light-promoted aerobic homogenous oxygenation reactions, *Chin. J. Org. Chem.*, 2017, **37**, 251.
- 5 (a) A. Goti, F. M. Cordero and A. Brandi, Cycloadditions onto methylene- and alkylidenecyclopropane derivatives, in *Small Ring Compounds in Organic Synthesis V*, ed. A. deMeijere, 1996, vol. 178, p. 1; (b) M. Lautens, W. Klute and W. Tam, Transition metal-mediated cycloaddition reactions, *Chem. Rev.*, 1996, **96**, 49; (c) I. Nakamura and Y. Yamamoto, Transition metal-catalyzed reactions of methylene-cyclopropanes, *Adv. Synth. Catal.*, 2002, **344**, 111; (d) A. Brandi, S. Cicchi, F. M. Cordero and A. Goti, Heterocycles from alkylidenecyclopropanes, *Chem. Rev.*, 2003, **103**, 1213; (e) L.-X. Shao and M. Shi, Lewis and Brønsted acid mediated ring-opening reactions of methylenecyclopropanes and further transformation of the ring-opened products, *Curr. Org. Chem.*, 2007, **11**, 1135; (f) A. Masarwa and I. Marek, Selectivity in metal-catalyzed carbon–carbon bond cleavage of alkylidenecyclopropanes, *Chem. – Eur. J.*, 2010, **16**, 9712; (g) L.-Z. Yu, K. Chen, Z.-Z. Zhu and M. Shi, Recent advances in the chemical transformations of functionalized alkylidene-cyclopropanes (FACPs), *Chem. Commun.*, 2017, **53**, 5935; (h) M. Shi, J.-M. Lu, Y. Wei and L.-X. Shao, Rapid generation of molecular complexity in the Lewis or Brønsted acid-mediated reactions of methylenecyclopropanes, *Acc. Chem. Res.*, 2012, **45**, 641; (i) A. Brandi, S. Cicchi, F. M. Cordero and A. Goti, Progress in the synthesis and transformations of alkylidenecyclopropanes and alkylidenecyclobutanes, *Chem. Rev.*, 2014, **114**, 7317; (j) H. Pellissier, Recent developments in the synthesis and reactivity of methylene- and alkylidene-cyclopropane derivatives, *Tetrahedron*, 2014, **70**, 4991; (k) J. Liu, R. Liu, Y. Wei and M. Shi, Recent developments in cyclopropane cycloaddition reactions, *Trends Chem.*, 2019, **1**, 779; (l) I. Marek, A. Masarwa, P.-O. Delaye and M. Leibelng, Selective carbon–carbon bond cleavage for the stereo-selective synthesis of acyclic systems, *Angew. Chem., Int. Ed.*, 2015, **54**, 414; (m) H. G. Cao, F. L. Chen, C. L. Su and L. Yu, Construction of carbocycles from methylenecyclopropanes, *Adv. Synth. Catal.*, 2019, DOI: 10.1002/adsc.201900615.
- 6 (a) L. Yu, M. Liu, F. Chen and Q. Xu, Heterocycles from methylenecyclopropanes, *Org. Biomol. Chem.*, 2015, **13**, 8379; (b) D. Nishikawa, R. Sakae, Y. Miki, K. Hirano and M. Miura, Copper-catalyzed regioselective ring-opening hydro-amination of methylenecyclopropanes, *J. Org. Chem.*, 2016, **81**, 12128; (c) L.-Z. Yu and M. Shi, The construction of molecular complexity from functionalized alkylidene-cyclopropanes (FACPs), *Chem. – Eur. J.*, 2019, **25**, 7591; (d) L. Yu, F. Chen and Y. Ding, Organoselenium-catalyzed oxidative ring expansion of methylenecyclopropanes with hydrogen peroxide, *ChemCatChem*, 2016, **8**, 1033; (e) Y.-C. Yuan, H.-B. Yang, X.-Y. Tang, Y. Wei and M. Shi, Unprecedented oxycyanation of methylenecyclopropanes for the facile synthesis of benzoxazine compounds containing a cyano group, *Chem. – Eur. J.*, 2016, **22**, 5146; (f) A. Dey, N. Thrimurtulu and C. M. R. Volla, Cobalt-catalyzed annulation reactions of alkylidenecyclopropanes: access to spiro-cyclopropanes at room temperature, *Org. Lett.*, 2019, **21**, 3871; (g) H. Clavier and G. Buono, 2+1 cycloaddition affording methylene- and vinylidenecyclopropane derivatives: a Journey around the reactivity of metal-phosphinito-phosphinous acid complexes, *Chem. Rec.*, 2017, **17**, 399; (h) L. Tao and M. Shi, Pd(II)-catalyzed cyclization oxidation of urea-tethered alkylidenecyclopropanes, *Org. Lett.*, 2018, **20**, 3017; (i) W.-D. Liu, G.-Q. Xu, X.-Q. Hu and P.-F. Xu, Visible-light-induced aza-

- pinacol rearrangement: ring expansion of alkylidenecyclopropanes, *Org. Lett.*, 2017, **19**, 6288; (j) F. Verdugo, L. Villarino, J. Duran, M. Gulas, J. L. Mascarenas and F. Lopez, Enantioselective palladium-catalyzed 3C+2C and 4C+3C intramolecular cycloadditions of alkylidenecyclopropanes, *ACS Catal.*, 2018, **8**, 6100; (k) L.-Z. Yu, Y. Wei and M. Shi, Synthesis of polysubstituted polycyclic aromatic hydrocarbons by gold-catalyzed cyclization-oxidation of alkylidenecyclopropane-containing 1,5-enynes, *ACS Catal.*, 2017, **7**, 4242; (l) D. Bai, T. Xu, C. Ma, X. Zheng, B. Liu, F. Xie and X. Li, Rh(III)-catalyzed mild coupling of nitrones and azomethine imines with alkylidenecyclopropanes via C-H activation: facile access to bridged cycles, *ACS Catal.*, 2018, **8**, 4194; (m) Y. Liu, Z. Chen, Q.-L. Wang and K.-W. Tang, Synthesis of 2-acyl-3,4-dihydronaphthalenes by silver-promoted oxidative C-C sigma-bond acylation/arylation of alkylidenecyclopropanes with alpha-ketoacids, *J. Org. Chem.*, 2019, **84**, 9984; (n) L. Yu and X. Huang, Reaction of methylenecyclopropanes and diphenyl diselenide under visible-light, *Synlett*, 2006, 2136; (o) L. Yu and X. Huang, Copper(II) acetate mediated reactions of methylenecyclopropane and diphenyl diselenide, *Synlett*, 2007, 1371.
- 7 (a) J. M. R. Narayanam, J. W. Tucker and C. R. J. Stephenson, Electron-transfer photoredox catalysis: development of a tin-free reductive dehalogenation reaction, *J. Am. Chem. Soc.*, 2009, **131**, 8756; (b) J. W. Tucker, J. M. R. Narayanam, S. W. Krabbe and C. R. J. Stephenson, Electron transfer photo-redox catalysis: intramolecular radical addition to indoles and pyrroles, *Org. Lett.*, 2010, **12**, 368; (c) J. Li, J. Z. Chen, W. Jiao, G. Q. Wang, Y. Li, X. Cheng and G. G. Li, Difluoro-alkylation/C-H annulation cascade reaction induced by visible-light photoredox catalysis, *J. Org. Chem.*, 2016, **81**, 9992.
- 8 J. Li, J. Z. Chen and G. G. Li, Difluoroalkylation/C-H Annulation Cascade Reaction Induced by Visible-Light Photoredox Catalysis, *J. Org. Chem.*, 2016, **81**, 9992.
- 9 Y. Tsukamoto, S. Itoh, M. Kobayashi and Y. Obora, Iridium-catalyzed  $\alpha$ -methylation of  $\alpha$ -aryl esters using methanol as the C1 source, *Org. Lett.*, 2019, **21**, 3299.