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Visible-light-driven photoredox-catalyzed C(sp³)-C(sp³) cross-coupling of *N*-arylamines with cycloketone oxime esters†

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A novel photoredox-catalyzed $C(sp^3)-C(sp^3)$ cross-coupling between N-arylamines and cycloketone oxime esters under mild conditions has been accomplished. The redox-neutral reaction proceeds with good functional group tolerance and excellent regioselectivity without any extra base or ligand control. In addition, this approach was successfully applied for the late-stage modification of short peptides and analogues.

Introduction

Functional amines are regarded as an important class of structural motifs that exist in a large number of pharmaceutically important molecules and natural products. Due to their rich chemical and biological activities, the discovery of a general methodology for the preparation or modification of these compounds has attracted more and more attention. 1,2 Among them, the alkylation of N-arylamines is one of the most efficient pathways to produce N-containing organic compounds, which introduce a C(sp³) moiety to change the spatial conformation, and increase both the lipophilicity and hydrophilicity as drug candidates. A typical method for the alkylation of N-arylamines mainly relies on CDC (cross-dehydrogenative coupling) reactions;3 although significant advances have been made along this line, there are still some considerable limitations: (1) most approaches rely heavily on activated alkyl substrates, whose C(sp³)-H bonds are adjacent to the heteroatom (such as O, S and N) or the electron-withdrawing group (such as a nitrile, an ester, a ketone and an amide) and (2) super-stoichiometric oxidants and high temperatures are usually required, leading to poor chemoselectivity and atom economy. Therefore, the development of mild and sustainable synthetic strategies to accomplish challenging $C(sp^3)-C(sp^3)$

Visible light photocatalysis has been developed as a powerful tool for organic transformation due to its environmental friendliness and sustainability, 4,5 and recently applied in alkylation of N-arylamines.6 In 2017, Yu and co-workers reported a novel visible-light-driven palladium-catalyzed radical alkylation of N-arylamines with alkyl bromides; various tertiary, secondary, and primary unactivated alkyl bromides undergo this simple reaction for the construction of quaternary centers (Scheme 1a).6a Soon after, Cong and co-workers developed the visible light photoredox decarboxylative alkylation of N-arylamines with N-(acyloxy)phthalimides, using erythrosine B sensitized TiO₂ as the photocatalyst. 6b Zhang and co-workers described a similar decarboxylative alkylation through the photoactivation of an electron donor-acceptor (EDA) complex (Scheme 1b).6c In addition to alkyl bromides and N-(acyloxy) phthalimides, Katritzky salts also proved to be efficient, with regard to alkyl radical precursors in the visible-light-mediated deaminative alkylation of N-arylamines (Scheme 1c).6d,e Although these methods provide an efficient way to access alkylation of N-arylamines, they mainly focus on such three active alkyl radical sources, the distal unactive alkyl radical for the alkylation of N-arylamines was still rare.

Recently, redox-active cycloketone oxime esters have been intensively explored as radical precursors under transition-metal or photoredox catalysis *via* C–C bond activation.^{7,8} In 2021, Gong, Lu and co-workers developed a direct C–H cyanoalkylation of glycine derivatives with cyclobutanone oxime esters; the key of this transformation is the combination of Fe (NTf₂)₂ and pyridine-oxazoline ligands as an efficient catalytic system. Moreover, the 2-amino carbonyl moiety was essential to achieve chelation between the catalyst system and glycine

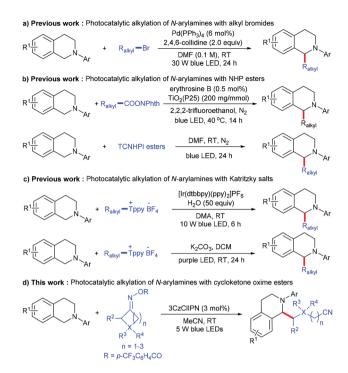
cross-coupling through α-amino C–H functionalization is still highly desirable.

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Scheme 1 Photocatalytic radical alkylation of N-arylamines.

derivatives.9 Inspired by the above work, we wondered whether it would be possible to exploit the radical coupling of N-arylamines and cycloketone oxime esters under photoredox conditions.

Herein, we report a novel metal-free C(sp³)-C(sp³) crosscoupling between N-arylamines and cycloketone oxime esters involving direct C(sp³)-H functionalization; various N-arylamines and cycloketone oxime esters can be transformed into the corresponding products in good to excellent yields under mild conditions (Scheme 1d). This reaction proceeds via a sequence of the iminyl radical generation, C-C bond cleavage to produce a cyanoalkyl radical, single electron transfer to form a nitrogen radical cation, deprotonation and radicalradical coupling.

Results and discussion

We started our investigations using 2-phenyl-1,2,3,4-tetrahydroisoquinoline 1a and cyclobutylidenemethyl 4-(trifluoromethyl)benzoate 2a as the model reaction partners to clarify the standard reaction conditions (Table 1). We found that N-arylamine 1a underwent successfully the α-amino C-H functionalization with cycloketone oxime ester 2a, with 3CzClIPN as a photocatalyst and acetonitrile as a solvent at room temperature under irradiation with blue LEDs for 12 h, affording the desired 4-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)butanenitrile 3aa in 86% isolated yield (entry 1). The reaction did not occur in the absence of irradiation or a photocatalyst (entries 2 and 3). The photocatalyst as a crucial factor was investigated; metal photocatalysts such as fac-Ir(ppy)₃ and

Table 1 Screening of the optimal reaction conditions^a

Entry	Variation from the standard conditions	Yield (%)
1	None	86
2	Without blue LEDs	0
3	Without 3CzClIPN	0
4	fac-Ir(ppy) ₃ instead of 3CzClIPN	41
5	Ru(bpy) ₃ Cl ₂ instead of 3CzClIPN	58
6	Eosin Y instead of 3CzClIPN	38
7	[Acr-Mes] ⁺ (ClO ₄) ⁻ instead of 3CzClIPN	40
8	Rhodamine B instead of 3CzClIPN	19
9	Methylene blue instead of 3CzClIPN	58
10	3CzClIPN (1 mol%)	48
11	3CzClIPN (5 mol%)	87
12	DCE instead of MeCN	61
13	MeOH instead of MeCN	65
14	Toluene instead of MeCN	13
15	DMSO instead of MeCN	43
16^b	None	80

^a Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), 3CzClIPN (3 mol%), MeCN (2 mL), RT, 5 W blue LEDs, argon, and 12 h. b 1a (1 g) for 36 h.

Ru(bpy)3Cl2 resulted in good catalytic activity but were less efficient than 3CzClIPN (entries 4 and 5). Other organophotocatalysts including Eosin Y, [Acr-Mes]⁺(ClO₄)⁻, rhodamine B and methylene blue all turned out to be inferior to 3CzClIPN (entries 6–9). Screening of photocatalyst loading revealed that a lower catalytic amount of 3CzClIPN (1 mol%) reduced the yield sharply and a higher catalytic amount (5 mol%) affected the yield slightly (entries 10 and 11). When other solvents such as dichloroethane, methanol, toluene and DMSO were employed to replace acetonitrile, a notable decrease of the yield was observed (entries 12-15). To our delight, the reaction scaled up to 1g of 2-phenyl-1,2,3,4-tetrahydroisoquinoline 1a also smoothly delivered 3aa in 80% yield (entry 16).

With the optimized reaction conditions in hand, we evaluated the generality of this reaction with N-aryl tetrahydroisoquinolines 1 and cycloketone oxime esters 2. As shown in Table 2, the substrates bearing different kinds of groups including methyl 1b, methoxy 1c, fluoro 1d, bromo 1e and tri-

Table 2 Variation of the N-aryl tetrahydroisoquinolines and cycloketone oxime esters (2)

^a Reaction conditions: 1 (0.2 mmol), 2 (0.24 mmol), 3CzClIPN (3 mol%), MeCN (2 mL), RT, 5 W blue LEDs, argon, and 12 h.

fluoromethyl 1f groups at the para position of the N-phenyl ring were well tolerated, affording the C(sp³)-C(sp³) coupling products 3ba-3fa in 48%-84% yields; the ortho and meta position substituents 1g and 1h did not affect the reaction and produced the corresponding products in good yields. Furthermore, substrate 1i with the naphthalene group at the nitrogen atom was also highly active. 2-Methyl-1,2,3,4-tetrahydroisoquinoline 1j was not suitable under the standard conditions; the N-aryl group might be essential for the electron transfer. Several kinds of electron-donating and electron-withdrawing groups 1k-1o at different positions of the benzene ring smoothly transformed into selective alkylation products in 72%–93% yields. A series of cycloketone oxime esters 2b-2i could serve as suitable substrates to afford the desired products 3ab-3ai under mild conditions. Symmetric monosubstituted cyclobutanone oximes bearing various functional groups such as alkyl 2b, ester 2c, and phenyl 2d substituents at the 3-position all underwent ring-opening processes to give the corresponding products 3ab-3ad in 68%-81% yields. The disubstituted cycloketone oxime ester 2e was compatible with the reaction. The heterocyclobutanone oxime esters oxetan-3one 2f and 1-Boc-3-azetidinone 2g also showed comparable reactivity, delivering the corresponding products 3af and 3ag in 82% and 70% yields. To our surprise, this protocol was not only suitable for four-membered ring oxime esters, but other less-strained substrates such as cyclopentanone 2h and cyclohexanone oxime ester 2i were also converted to the desired products in 65% and 53% yields.

We further explored the scope of α-amino carbonyl compounds 4 with cycloketone oxime ester 2a (Table 3). The ethyl 4a, tertiary butyl 4b and benzyl 4c esters of N-aryl glycine were amenable for this catalytic system, giving the corresponding products in 61%-91% yields. Various functional groups 4d-4j on the benzene ring of glycine derivatives were examined; the results showed that electron-donating groups performed better than electron-withdrawing groups, and the position nature had no detrimental effect on the reaction. The dimethyl-substituted and naphthalenyl groups of glycine esters 4k-4m were also tolerated to give the corresponding products 5ka-5ma in 74%–90% yields. Not only glycine esters, other α-amino carbonyl compounds such as amide 4n and ketone 4o could also smoothly transform into the desired products in excellent yields, which indicated that this protocol could be used to modify peptides. Even N-benzylaniline 4p could successfully give the alkylation product 5pa in 41% yield. Unfortunately, N-phenylglycinonitrile 4q was not suitable for this transformation.

Next, the practicability of these mild conditions for the siteselective modification of peptides was tested (Table 4). N-Phenyl protected dipeptide 4r was successfully coupled with cycloketone oxime ester 2a and heterocyclobutanone oxime ester 2f in good yields. Other dipeptides 4s-4u bearing different units also selectively underwent alkylation at the α-position of glycine carbonyl in 71%-75% yields. Even substrate 4v containing the sensitive thiomethyl group could smoothly transform into the corresponding product 5va in a moderate yield.

Table 3 Variation of the α -amino carbonyl compounds (4)^a

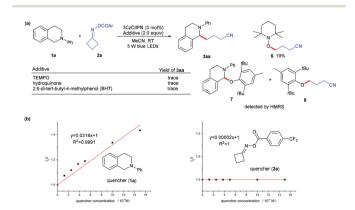
^a Reaction conditions: 4 (0.2 mmol), 2a (0.24 mmol), 3CzClIPN (3 mol%), MeCN (2 mL), RT, 5 W blue LEDs, argon, and 12 h.

Table 4 Site-selective modification of short peptides^a

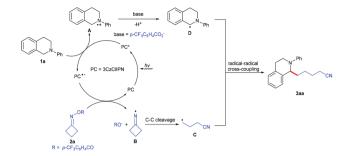
^a Reaction conditions: 4 (0.2 mmol), 2 (0.24 mmol), 3CzClIPN (3 mol%), MeCN (2 mL), RT, 5 W blue LEDs, argon, and 12 h.

To gain insight into this photoredox-catalyzed cross coupling reaction, mechanistic studies were conducted with radical trapping experiments. When TEMPO, hydroquinone and BHT were added into the standard conditions, the reaction was completely suppressed (Scheme 2a), and the radical generated from cycloketone oxime ester 2a was trapped by TEMPO to give product 6 in 19% yield; the radicals from substrates 1a and 2a could be identified through HRMS (see the ESI†). In addition, Stern-Volmer quenching studies indicated that N-aryl tetrahydroisoquinoline 1a quenched the excited state of 3CzClIPN (Scheme 2b). These results implied that the reaction involves a radical process.

Based on the obtained results and previous reports, 6 a plausible mechanism for this visible-light-driven photoredoxcatalyzed C(sp³)-C(sp³) cross-coupling reaction was proposed, as shown in Scheme 3. Firstly, the photocatalyst 3CzClIPN is excited under visible light irradiation to produce its excited state species 3CzClIPN* $(E_{1/2} [PC^*/PC^{*-}] = +1.56 \text{ V } \nu s. \text{ SCE in }$ MeCN), ^{4j} which oxidizes N-arylamine 1a $(E_p^{0/+1}(1a) = +1.04 \text{ V})$ versus SCE in MeCN)^{6p} to give radical cation A and 3CzClIPN'-. 3CzClIPN $^{\bullet}$ ($E_{1/2}$ [PC/PC $^{\bullet}$] = -1.16 V νs . SCE in MeCN) undergoes another SET process with cycloketone oxime ester 2a $(E_p^{0/-1}(2a) = -0.99 \text{ V } \text{ versus SCE in MeCN})^{8j} \text{ to form iminyl}$ radical B and the 4-(trifluoromethyl)benzoate anion, along with the regeneration of 3CzClIPN. Subsequently, iminyl radical B undergoes a ring-opening to give the highly reactive



Scheme 2 Control experiments.



Scheme 3 Possible mechanism.

cyanoalkyl radical C; radical cation A undergoes deprotonation with the 4-(trifluoromethyl)benzoate anion to produce the benzylic radical D. Finally, radical-radical coupling between intermediate C and intermediate D provides the desired product 3aa.

Conclusions

In summary, we have developed a new site selective photoredox-catalyzed $C(sp^3)-C(sp^3)$ cross-coupling N-arylamines and cycloketone oxime esters without employing any extra base or ligand control. A variety of N-aryl tetrahydroisoquinolines, glycine derivatives and cycloketone oxime esters can be transformed into the corresponding products in good to excellent yields. In addition, this protocol is also successfully applied in the alkylated modification of short peptides, which is highly attractive for medicinal chemistry and organic synthesis.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

1 For selected examples, see: (a) A. Cabré, X. Verdaguer and A. Riera, Recent Advances in the Enantioselective Synthesis of Chiral Amines via Transition Metal-Catalyzed Asymmetric Hydrogenation, Chem. Rev.,2022, 122, (b) S. France, D. J. Guerin, S. J. Miller and T. Lectka, Nucleophilic Chiral Amines as Catalysts in Asymmetric Synthesis, Chem. Rev., 2003, 103, 2985-3012; (c) G. Guillena, D. J. Ramón and M. Yus, Hydrogen Autotransfer in the N-Alkylation of Amines and Related Compounds using

Alcohols and Amines as Electrophiles, Chem. Rev., 2010, 110, 1611-1641; (d) P. Kalck and M. Urrutigoïty, Tandem Hydroaminomethylation Reaction to Synthesize Amines from Alkenes, Chem. Rev., 2018, 118, 3833-3861; (e) T. E. Müller, K. C. Hultzsch, M. Yus, F. Foubelo and M. Tada, Hydroamination: Direct Addition of Amines to Alkenes and Alkynes, Chem. Rev., 2008, 108, 3795-3892; (f) A. Trowbridge, S. M. Walton and M. J. Gaunt, New Strategies for the Transition-Metal Catalyzed Synthesis of Aliphatic Amines, Chem. Rev., 2020, 120, 2613-2692.

Research Article

- 2 For selected reviews and examples, see: (a) W. Ding, L.-Q. Lu, J. Liu, D. Liu, H.-T. Song and W.-J. Xiao, Visible Photocatalytic Radical-Radical Cross-Coupling Reactions of Amines and Carbonyls: A Route to 1,2-Amino Alcohols, J. Org. Chem., 2016, 81, 7237-7243; (b) X. Li, M. Chen, X. Xie, N. Sun, S. Li and Y. Liu, Synthesis of Multiple-Substituted Pyrroles via Gold(1)-Catalyzed Hydroamination/Cyclization Cascade, Org. Lett., 2015, 17, 2984-2987; (c) J. Liu, Y. Song, X. Wu and L. Ma, N-Dimethylation and N-Functionalization of Amines Using Ru Nanoparticle Catalysts and Formaldehyde or Functional Aldehydes as the Carbon Source, ACS Omega, 2021, 6, 22504-22513; (d) H. T. Ten Brink, J. T. Meijer, R. V. Geel, M. Damen, D. W. P. M. Löwik and J. C. M. van Hest, Solid-Phase Synthesis of C-Terminally Modified Peptides, J. Pept. Sci., 2006, 12, 686-692; (e) W.-T. Wei, F. Teng, Y. Li, R.-J. Song and J.-H. Li, Oxidative [4+2] Cycloaddition of α-(N-Arylamino) Carbonyls with Aryl Alkenes by Multiple C-H Functionalizations and [1,2]-Aryl Shifts, Org. Lett., 2019, 21, 6285–6288; (f) H. Deng, H. Li, W. Zhang and L. Wang, Rh^{III}-Catalyzed Site-Selective Amidation with Nitrone as a Traceless Directing Group: An Approach to Functionalized Arylaldehydes, Chem. Commun., 2017, 53, 10322-10325; (g) Z.-W. Hou, L. Li and L. Wang, Organocatalytic Electrochemical Amination of Benzylic C-H Bonds, Org. Chem. Front., 2021, 8, 4700-4705.
- 3 For selected reviews, see: (a) J. Chen, Y.-J. Liang, P.-Z. Wang, G.-Q. Li, B. Zhang, H. Qian, X.-D. Huan, W. Guan, W.-J. Xiao and J.-R. Chen, Photoinduced Copper-Catalyzed Asymmetric C-O Cross-Coupling, J. Am. Chem. Soc., 2021, 143, 13382-13392; (b) X. Liu, J. Pu, X. Luo, X. Cui, Z. Wu and G. Huang, CBr₄-Mediated Cross-Coupling Reactions of α-Amino Carbonyl Compounds with Alcohols and Thiols to Build C-O and C-S Bonds, Respectively, Org. Chem. Front., 2018, 5, 361-365; (c) X.-X. Liu, Z.-Y. Wu, Y.-Q. He, X.-Q. Zhou, T. Hu, C.-W. Ma and G.-S. Huang, Copper-Catalyzed C-N Bond Formation via Oxidative Cross-Coupling of Amines with α-Aminocarbonyl Compounds, Adv. Synth. Catal., 2016, 358, 2385–2391; (d) M. R. Mutra, G. K. Dhandabani and J.-J. Wang, Mild Access to N-Formylation of Primary Amines using Ethers as C1 Synthons under Metal-Free Conditions, Adv. Synth. Catal., 2018, 360, 3960-3968; (e) H. Peng, J.-T. Yu, Y. Jiang, H. Yang and J. Cheng, Di-tert-butyl Peroxide-Promoted α-Alkylation of α-Amino Carbonyl Compounds by Simple Alkanes, J. Org. Chem., 2014, 79, 9847–9853; (f) M. San Segundo and A. Correa, Site-Selective
- Cu-Catalyzed Alkylation of α-Amino Acids and Peptides toward the Assembly of Quaternary Centers, ChemSusChem, 2018, 11, 3893-3898; (g) D. Tang, X. Guo, Y. Wang, J. Wang, J. Li, Q. Huang and B. Chen, Metal Free, I₂-Catalyzed [3+1+1] Cycloaddition Reactions to Synthesize 1,2,4-Trisubstituted Imidazoles, Tetrahedron Lett., 2015, 56, 5982-5985; (h) H. Tian, W. Xu, Y. Liu and Q. Wang, Unnatural α-Amino Acid Synthesized through α-Alkylation of Glycine Derivatives by Diacyl Peroxides, Org. Lett., 2020, 22, 5005-5008; (i) G.-Z. Wang, M.-C. Fu, B. Zhao and R. Shang, Photocatalytic Decarboxylative Alkylations of C(sp³)-H and C(sp²)-H Bonds Enabled by Ammonium Iodide in Amide Solvent, Sci. China: Chem., 2021, 64, 439-444; (*j*) Z.-H. Wang, P.-S. Gao, X. Wang, J.-O. Gao, X.-T. Xu, Z. He, C. Ma and T.-S. Mei, TEMPO-Enabled Electrochemical Enantioselective Oxidative Coupling of Secondary Acyclic Amines with Ketones, J. Am. Chem. Soc., 2021, 143, 15599-15605; (k) W.-T. Wei, H.-B. Li, R.-J. Song and J.-H. Li, Copper-Catalyzed Oxidative Oxyalkylation of Enol ethers with α-Amino Carbonyl Compounds and Hydroperoxides, Chem. Commun., 2015, 51, 11325-11328; (l) W.-T. Wei, R.-J. Song and J.-H. Li, Copper-Catalyzed Oxidative α-Alkylation of α-Amino Carbonyl Compounds with Ethers via Dual C(sp³)-H Oxidative Cross-Coupling, Adv. Synth. Catal., 2014, 356, 1703-1707; (m) X.-H. Wei, G.-W. Wang and S.-D. Yang, Enantioselective Synthesis of Arylglycine Derivatives by Direct C-H Oxidative Cross-Coupling, Chem. Commun., 2015, 51, 832-835; (n) J.-C. Wu, R.-J. Song, Z.-Q. Wang, X.-C. Huang, Y.-X. Xie and J.-H. Li, Copper-Catalyzed C-H Oxidation/Cross-Coupling of α-Amino Carbonyl Compounds, Angew. Chem., Int. Ed., 2012, 51, 3453-3457; (o) L. Yang, Z. Qiu, J. Wu, J. Zhao, T. Shen, X. Huang and Z.-Q. Liu, Molecular Oxygen-Mediated Radical Alkylation of C(sp³)-H Bonds with Boronic Acids, Org. Lett., 2021, 23, 3207-3210; (p) M. Zhu, D. Chen, S. Zeng, C. Xing, W. Deng, J. Xiang and R.-J. Wang, Synthesis of (Z)-Nitroalkene Derivatives through Oxidative Dehydrogenation coupling of α-Aminocarbonyl Compounds with Nitromethane by Copper Catalysis, Tetrahedron Lett., 2018, 59, 3214-3219; (q) Y. Li, B. Liu, H.-B. Li, Q. Wang and J.-H. Li, Oxidative Radical 1,2-Alkylarylation of Alkenes with α -C(sp³)-H Bonds of Acetonitriles Involving 1,2-Aryl Migration, Chem. Commun., 2015, **51**, 1024–1026; (r) B. Wei, J.-H. Qin, Y.-Z. Yang, Y.-X. Xie, X.-H. Ouyang and R.-J. Song, Electrochemical Radical C(sp³)-H Arylation of Xanthenes with Electron-Rich
- 4 For selected examples, see: (a) R. Asahi, T. Morikawa, H. Irie and T. Ohwaki, Nitrogen-Doped Titanium Dioxide as Visible-Light-Sensitive Photocatalyst: Designs, Developments, and Prospects, Chem. Rev., 2014, 114, 9824-9852; (b) F. Juliá, T. Constantin and D. Leonori, Applications of Halogen-Atom Transfer (XAT) for the Generation of Synthetic Photochemistry and Carbon Radicals in Photocatalysis, Chem. Rev., 2022, 122, 2292-2352; (c) K. Kwon, R. T. Simons, M. Nandakumar and J. L. Roizen, Strategies to Generate Nitrogen-Centered Radicals That May

Arenes, Org. Chem. Front., 2022, 9, 816-821.

Rely on Photoredox Catalysis: Development in Reaction Methodology and Applications in Organic Synthesis, Chem. Rev., 2022, 122, 2353–2428; (d) S. P. Pitre and L. E. Overman, Strategic Use of Visible-Light Photoredox Catalysis in Natural Product Synthesis, Chem. Rev., 2022, 122, 1717-1751; (e) 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, 5322-5363; (f) K. P. S. Cheung, S. Sarkar and V. Gevorgyan, Visible Light-Induced Transition Metal Catalysis, Chem. Rev., 2022, 122, 1543-1625; (g) X.-Y. Yu, J.-R. Chen and W.-J. Xiao, Visible Light-Driven Radical-Mediated C-C Bond Cleavage/Functionalization in Organic Synthesis, Chem. Rev., 2021, 121, 506-561; (h) J.-Y. Chen, Y.-H. Li, L. Mei and H.-Y. Wu, Application of Photosensitizer 2,4,5,6-Tetrakis(carbazol-9-yl)-1,3-dicyanobenzene in Photo-Induced Transition-Metal-Free Organic Synthesis, Chin. J. Org. Chem., 2019, 39, 3040-3050; (i) Y. Chen, L.-Q. Lu, D.-G. Yu, C.-J. Zhu and W.-J. Xiao, Visible Light-Driven Organic Photochemical Synthesis in China, Sci. China: Chem., 2019, 62, 24-57; (j) E. Speckmeier, T. G. Fischer and K. Zeitler, A Toolbox Approach to Construct Broadly Applicable Metal-Free Catalysts for Photoredox Chemistry: Deliberate Tuning of Redox Potentials and Importance of Halogens in Donor-Acceptor Cyanoarenes, J. Am. Chem. Soc., 2018, 140, 15353-15365.

5 For selected examples, see: (a) T. Chatterjee, J. Y. Cho and E. J. Cho, Synthesis of Substituted Oxazoles by Visible-Light Photocatalysis, J. Org. Chem., 2016, 81, 6995-7000; (b) Y. Pan, S. Wang, C. W. Kee, E. Dubuisson, Y. Yang, K. P. Loh and C.-H. Tan, Graphene Oxide and Rose Bengal: Oxidative C-H Functionalisation of Tertiary Amines Using Visible Light, Green Chem., 2011, 13, 3341-3344; (c) B. Sun, J. Deng, D. Li, C. Jin and W. Su, Photocatalytic Aerobic Cross-Coupling Reaction of N-Substituted Anilines with N-Aryl Glycine Esters: Synthesis of α-Aryl α-Amino Esters, Tetrahedron Lett., 2018, 59, 4364-4369; (d) C. Wang, R. Qi, H. Xue, Y. Shen, M. Chang, Y. Chen, R. Wang and Z. Xu, Visible-Light-Promoted $C(sp^3)$ -H Alkylation Intermolecular Charge Transfer: Preparation of Unnatural α-Amino Acids and Late-Stage Modification of Peptides, Angew. Chem., Int. Ed., 2020, 59, 7461-7466; (e) H. Xue, M. Guo, C. Wang, Y. Shen, R. Qi, Y. Wu, Z. Xu and M. Chang, Photo-Induced Preparation of Unnatural α-Amino Acids: Synthesis and Characterization of Novel Leu⁵-Enkephalin Analogues, Org. Chem. Front., 2020, 7, 2426-2431; (f) J. Wang, Y. Su, Z. Quan, J. Li, J. Yang, Y. Yuan and C. Huo, Visible-Light Promoted α-Alkylation of Glycine Derivatives with Alkyl Boronic Acids, Chem. Commun., 2021, 57, 1959–1962; (g) Y.-X. Chen, Z.-J. Wang, J.-A. Xiao, K. Chen, H.-Y. Xiang and H. Yang, Visible-Light-Driven Sulfonation of α-Trifluoromethylstyrenes: Access to Densely Functionalized CF₃-Substituted Tertiary Alcohol, Org. Lett., 2021, 23, 6558-6562; (h) X.-J. Liu, S.-Y. Zhou, Y. Xiao, Q. Sun, X. Lu, Y. Li and J.-H. Li, Photocatalytic Decarboxylative [3+2] and [4+2] Annulation of Enynals and γ,σ-Unsaturated N-(Acyloxy)

phthalimides by NaI/PPh3 Catalysis, Org. Lett., 2021, 23, 7839-7844; (i) P.-Z. Wang, Y. Gao, J. Chen, X.-D. Huan, W.-J. Xiao and J.-R. Chen, Asymmetric Three-Component Olefin Dicarbofunctionalization Enabled by Photoredox and Copper Dual Catalysis, Nat. Commun., 2021, 12, 1815; (i) C. Zhu, S. Zhumagazy, H. Yue and M. Rueping, Metal-Free C-Se Cross-Coupling Enabled by Photoinduced Inter-Molecular Charge Transfer, Chem. Commun., 2022, 58, 96-

6 (a) W.-J. Zhou, G.-M. Cao, G. Shen, X.-Y. Zhu, Y.-Y. Gui, J.-H. Ye, L. Sun, L.-L. Liao, J. Li and D.-G. Yu, Visible-Light-Driven Palladium-Catalyzed Radical Alkylation of C-H Bonds with Unactivated Alkyl Bromides, Angew. Chem., Int. Ed., 2017, 56, 15683-15687; (b) L. Ren and H. Cong, Visible-Light-Driven Decarboxylative Alkylation of C-H Bond Catalyzed by Dye-Sensitized Semiconductor, Org. Lett., 2018, **20**, 3225–3228; (c) P. Ma, Y. Liu, L. Chen, X. Zhao, B. Yang and J. Zhang, Photocatalystand Additive-Free Decarboxylative Alkylation of N-Aryl Tetrahydroisoquinolines Induced by Visible Light, Org. Chem. Front., 2021, 8, 2473-2479; (d) Y. Xu, Z.-J. Xu, Z.-P. Liu and H. Lou, Visible-Light-Mediated De-Aminative Alkylation of N-Arylamines with Alkyl Katritzky Salts, Org. Chem. Front., 2019, 6, 3902-3905; (e) Q. Xia, Y. Li, X. Wang, P. Dai, H. Deng and W.-H. Zhang, Visible Light-Driven α-Alkylation of N-Arvl Tetrahydroisoquinolines Initiated by Electron Donor-Acceptor Complexes, Org. Lett., 2020, 22, 7290-7294; (f) J. Dhineshkumar, M. Lamani, K. Alagiri and K. R. Prabhu, A Versatile C-H Functionalization of Tetrahydroisoquinolines Catalyzed by Iodine at Aerobic Conditions, Org. Lett., 2013, 15, 1092-1095; (g) Z. Džambaski and B. P. Bondžić, Dehydrogenative C(sp³)-H Bond Functionalization of Tetrahydroisoquinolines Mediated by Organic Oxidants under Mild Conditions, Org. Biomol. Chem., 2019, 17, 6420-6425; (h) H. E. Ho, Y. Ishikawa, N. Asao, Y. Yamamoto and T. Jin, Highly Efficient Heterogeneous Aerobic Cross-Dehydrogenative Coupling via C-H Functionalization of Tertiary Amines Using a Nanoporous Gold Skeleton Catalyst, Chem. Commun., 2015, 51, 12764-12767; (i) Z. Li and C.-J. Li, CuBr-Catalyzed Direct Indolation of Tetrahydroisoquinolines via Dehydrogenative Coupling between sp³ C-H and sp² C-H Bonds, J. Am. Chem. Soc., 2005, 127, 6968-6969; (j) W. Liang, T. Zhang, Y. Liu, Y. Huang, Z. Liu, Y. Liu, B. Yang, X. Zhou and J. Zhang, Polydimethylsiloxane Sponge-Supported Nanometer Gold: Highly Efficient Recyclable Catalyst for Cross-Dehydrogenative Coupling in Water, ChemSusChem, 2018, 11, 3586-3590; (k) H. Tian, W. Xu, Y. Liu and Q. Wang, Radical Alkylation of C(sp³)-H Bonds with Diacyl Peroxides under Catalyst-Free Conditions, Chem. Commun., 2019, 55, 14813-14816; (l) C. Wang, M. Guo, R. Qi, Q. Shang, Q. Liu, S. Wang, L. Zhao, R. Wang Visible-Light-Driven, Xu, Copper-Catalyzed Decarboxylative C(sp³)-H Alkylation of Glycine and Peptides, Angew. Chem., Int. Ed., 2018, 57, 15841-15846; (m) J. Xuan, T.-T. Zeng, Z.-J. Feng, Q.-H. Deng, J.-R. Chen, L.-Q. Lu,

W.-J. Xiao and H. Alper, Redox-Neutral α-Allylation of Amines by Combining Palladium Catalysis and Visible-Light Photoredox Catalysis, Angew. Chem., Int. Ed., 2015, 54, 1625-1628; (n) W. Zhang, S. Yang and Z. Shen, Copper-Catalyzed Cyanomethylation of Substituted Tetrahydroisoquinolines with Acetonitrile, Adv. Synth. Catal., 2016, 358, 2392-2397; (o) S.-S. Zhu, Y. Liu, X.-L. Chen, L.-B. Qu and B. Yu, Polymerization-Enhanced Photocatalysis Functionalization of C(sp³)-H Bonds, ACS Catal., 2022, 12, 126-134; (p) S.-S. Zhu, Y. Liu, X.-L. Chen, L.-B. Ou and B. Yu, Polymerization-Enhanced Photocatalysis Functionalization of C(sp³)-H Bonds, ACS Catal., 2022, 12, 126-134.

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- 7 W. Xiao and J. Wu, Recent Advances for the Photoinduced C-C Bond Cleavage of Cycloketone Oximes, Chin. Chem. Lett., 2020, 31, 3083-3094.
- 8 (a) J. Chen, Y.-J. Liang, P.-Z. Wang, G.-Q. Li, B. Zhang, H. Qian, X.-D. Huan, W. Guan, W.-J. Xiao and J.-R. Chen, Photoinduced Copper-Catalyzed Asymmetric C-O Cross-Coupling, J. Am. Chem. Soc., 2021, 143, 13382-13392; (b) H. Qian, J. Chen, B. Zhang, Y. Cheng, W.-J. Xiao and J.-R. Chen, Visible-Light-Driven Photoredox-Catalyzed Three-Component Radical Cyanoalkylfluorination of Alkenes with Oxime Esters and a Fluoride Ion, Org. Lett., 2021, 23, 6987-6992; (c) B. Shuai, P. Fang and T.-S. Mei, Nickel-Catalyzed Favorskii-Type Rearrangement of Cyclobutanone Oxime Esters to Cyclopropanecarbonitriles, Synlett, 2021, 32, 1637-1641; (d) P.-Z. Wang, X. Wu, Y. Cheng, M. Jiang, W.-J. Xiao and J.-R. Chen, Photoinduced Copper-Catalyzed Asymmetric Three-Component Coupling of 1,3-Dienes: An Alternative to
- Kharasch-Sosnovsky Reaction, Angew. Chem., Int. Ed., 2021, 60, 22956-22962; (e) X.-Y. Yu, J.-R. Chen, P.-Z. Wang, M.-N. Yang, D. Liang and W.-J. Xiao, A Visible-Light-Driven Iminyl Radical-Mediated C-C Single Bond Cleavage/Radical Addition Cascade of Oxime Esters, Angew. Chem., Int. Ed., 2018, 57, 738-743; (f) X.-Y. Yu, O.-O. Zhao, J. Chen, J.-R. Chen and W.-J. Xiao, Copper-Catalyzed Radical Cross-Coupling of Redox-Active Oxime Esters, Styrenes, and Boronic Acids, Angew. Chem., Int. Ed., 2018, 57, 15505-15509; (g) B.-Q. He, X.-Y. Yu, P.-Z. Wang, J.-R. Chen and W.-J. Xiao, A Photoredox Catalyzed Iminyl Radical-Rriggered C-C Bond Cleavage/Addition/Kornblum Oxidation Cascade of Oxime Esters and Styrenes: Synthesis of Ketonitriles, Chem. Commun., 2018, 54, 12262-12265; (h) Y.-X. Jiang, L. Chen, C.-K. Ran, L. Song, W. Zhang, L.-L. Liao and D.-G. Yu, Visible-Light Photoredox-Catalyzed Ring-Opening Carboxylation of Cyclic Oxime Esters with CO₂, ChemSusChem, 2020, 13, 6312-6317; (i) C.-K. Ran, H. Huang, X.-H. Li, W. Wang, J.-H. Ye, S.-S. Yan, B.-Q. Wang, C. Feng and D.-G. Yu, Cu-Catalyzed Selective Oxy-Cyanoalkylation of Allylamines with Cycloketone Oxime Esters and CO₂, Chin. J. Chem., 2020, 38, 69-76; (j) L. Li, H. Chen, M. Mei and L. Zhou, Visible-Light Promoted γ-Cyanoalkyl Radical Generation: Three-Component Cyanopropylation/ Etherification of Unactivated Alkenes, Chem. Commun., 2017, 53, 11544-11547.
- 9 D. Lu, J. Cui, S. Yang and Y. Gong, Iron-Catalyzed Cyanoalkylation of Glycine Derivatives Promoted by Pyridine-Oxazoline Ligands, ACS Catal., 2021, 11, 4288-4293.