

pubs.acs.org/OrgLett

Letter

Markovnikov-selectivity

No sacrificial reagents

Mild reaction conditions

Atom-economy

Directing-Group-Assisted Markovnikov-Selective Hydrothiolation of Styrenes with Thiols by Photoredox/Cobalt Catalysis

Qian Xiao, Hong Zhang, Jing-Hong Li, Jing-Xin Jian, Qing-Xiao Tong,* and Jian-Ji Zhong*







the catalytic Markovnikov-selective hydrothiolation of alkenes is very restricted. Because of the catalyst poisoning of metal catalysts by organosulfur compounds, limited examples of transition-metalcatalyzed thiol-ene reactions have been reported. However, in this work, a directing-group-assisted hydrothiolation of styrenes with thiols by photoredox/cobalt catalysis is found to proceed smoothly to afford Markovnikov-type sulfides with excellent regioselectivity.

he incorporation of sulfur into organic molecules is of great importance owing to the fact that organosulfur moieties are widespread in natural products,¹ pharmaceuticals,² and polymer materials.³ In this context, the direct hydrothiolation of alkenes with thiols, well known as the thiol-ene reaction,⁴ represents one of the simplest and most atomeconomical approaches for C-S bond construction.⁵ This reaction can proceed by way of an electrophilic pathway or a radical pathway, leading to the formation of a branched product via Markovnikov addition or a linear product via anti-Markovnikov addition, respectively. Owing to the high reactivity of sulfur, the reaction tends to proceed via a radical pathway. Consequently, the radical thiol-ene reactions⁶ affording anti-Markovnikov products have been well researched by the thermal or UV-light activation of a radical initiator or direct UV-light irradiation or visible-light photoredox catalysis (Scheme 1a).

In contrast, the Markovnikov-selective thiol-ene reaction is far less developed. Traditional methods focus on using stoichiometric Brønsted acids or Lewis acids⁷ to suppress the thiyl radicals and promote the electrophilic pathway for Markovnikov-type adducts (Scheme 1b). However, the research on the catalytic Markovnikov-selective thiol-ene reaction is very restricted.⁸ Transition-metal catalysis offers potential for this transformation; however, because of the inherent challenge of catalyst poisoning of metal catalysts by organosulfur compounds, to date, very limited examples of transition-metal catalytic systems,⁹ including In(OTf)₃,¹⁰ Ph₃PAuOTf,¹¹ AuBr₃,¹² FeCl₃/AgNTf₂,¹³ Pd(OAc)₂,¹⁴ Cu-(OAc)₂,¹⁵ and ZnI₂/TsOH,¹⁶ have been reported for Markovnikov thiol-ene reactions.

Visible-light photoredox catalysis¹⁷ as an alternative for a greener and more sustainable thiol-ene reation has attracted much attention in recent years;¹⁸ however, to the best of our

Scheme 1. Thiol-Ene Reactions

Mes-2,7-Me₂-Acr-Me⁺ClO₄

a) Anti-Markovnikov Addition (well-developed)

$$R_1SH + R_2$$

1) radical initiator (by thermal or light)
2) direct UV light irradiation
3) visible-light photoredox catalysis R_1S

Co(dmgH)₂PyC

-0---

-d

b) Markovnikov Addition (less-developed)



knowledge, all of the reported catalytic systems afforded the anti-Markovnikov-type adducts,¹⁹ and the photoredox-catalyzed Markovnikov-selective thiol-ene reaction has not yet been reported. With our continuous interest in photoredox catalysis, designing a specific and active photocatalytic system to overcome the previously described issues will be appealing and desirable. In this work, we report a directing-group-assisted strategy for the addition of thiols to styrenes with excellent Markovnikov regioselectivity in good yields by photoredox/cobalt catalysis²⁰ (Scheme 1c).

 Received:
 March 23, 2021

 Published:
 April 12, 2021





pubs.acs.org/OrgLett

Organic Letters

One reason for the difficulty of the transition-metalcatalyzed thiol-ene reaction is the poor coordination ability of alkenes to the transition-metal catalyst. Introducing a directing group to the alkenes is a potential solution to address this problem. Thus 2-vinyl aniline **a1** was designed as the model substrate. To our delight, the presence of just a catalytic amount of 9-mesityl-2,7,10-trimethylacridinium perchlorate (**PC**, 5 mol %) as a photocatalyst and Co(dmgH)₂PyCl (20 mol %) as a cocatalyst and the irradiation of 4-chlorothiophenol **b1** with a slight excess **a1** (1.1 equiv) in degassed CH₂Cl₂ by blue light-emitting diodes (LEDs) ($\lambda = 450$ nm) at room temperature resulted in the sole Markovnikov-type adduct **c1** in 88% yield with excellent regioselectivity (Table 1, entry 1).



^{*a*}Reaction conditions: **a1** (0.22 mmol), **b1** (0.20 mmol), **PC** (5 mol %), $Co(dmgH)_2PyCl$ (20 mol %), CH_2Cl_2 (3.0 mL), under N₂, room temperature, 450 nm LED irradiation for 24 h. ^{*b*}Isolated yields.

Other photocatalysts such as Mes-Acr-Me⁺ClO₄⁻, 4CzIPN, and Ru(bpy)₃Cl₂ were also investigated, but just moderate yields were provided (Table 1, entries 2-4). The reaction yield decreased to 70% when $Co(dmgBF_2)_2(H_2O)_2$ instead of Co(dmgH)₂PyCl was used (Table 1, entry 5). No reaction was observed when $CoCl_2$ or $Co(OAc)_2$ acted as the cocatalyst (Table 1, entries 6 and 7), indicating that the ligand around the cobalt center plays an important role in the catalytic activity. Furthermore, the solvent examination revealed that besides CH₂Cl₂, toluene also proved to be a good choice, with an 89% yield (Table 1, entries 8-12). When diphenyl disulfide d1 replaced thiol b1 in the optimized reaction, only the disulfidation product el rather than the hydrothiolation product c1 was obtained (Scheme S1). Further control experiments indicated that a photocatalyst, cobaloxime catalyst, and light were essential parameters for the success

of this highly selective and atom-economical thiol-ene reaction (Table 1, entries 13-15).

To investigate the functional group tolerance of the photoredox/cobalt-catalyzed Markovnikov-selective thiol-ene reaction, we first examined a variety of different substituted 2-vinyl anilines under standard conditions, and some representative results are shown in Scheme 2. For various substituents on

Scheme 2. Scope of 2-Vinyl Anilines⁴



^{*a*}Reaction conditions: **a** (0.22 mmol), **b1** (0.20 mmol), **PC** (5 mol %), $Co(dmgH)_2PyCl$ (20 mol %), CH_2Cl_2 (3.0 mL), under N₂, room temperature, 450 nm LED irradiation for 24 h. ^{*b*}Isolated yields.

the phenyl ring of 2-vinyl anilines, regardless of the position of the electron-withdrawing group or the electron-donating group, the desired Markovnikov-type adducts were obtained in good to excellent yields (Scheme 2, c1-c12). Notably, to demonstrate the scalability of this protocol, a gram-scale reaction of a1 and b1 was conducted and proceeded smoothly to give the desired Markovnikov-type product c1 in 70% yield (Scheme 2, c1). Unfortunately, when the unactivated alkene a13 was attempted, no desired product was observed (Scheme 2, a13). As previously stated, the transition-metal-catalyzed thiol-ene reaction of alkenes is a challenging task owing to its poor coordination ability to the metal center. Indeed, when the directing group of the tosyl-protected amine group was removed, the reaction could not happen (Scheme 2, a14), and the unprotected 2-vinyl aniline was also proved to be ineffective in the reaction (Scheme 2, a15). Therefore, we next investigated the N-substituents of 2-vinyl anilines, Various

Organic Letters

functional groups such as methyl, methoxyl, fluoride, chloride, and bromide were introduced to the phenyl ring of the arylsulfone moiety in 2-vinyl anilines, and the desired products were obtained in good to excellent yields (Scheme 2, c16–c21). Further experiments found that, besides arylsulfone moieties, the substrates equipped with quinoline sulfonyl, naphthalene sulfonyl, and trifluoroacetyl as the *N*-protected group were also compatible with the reaction to give yields of 86, 71, and 73%, respectively (Scheme 2, c22–c24). Regrettably, when *N*-Boc 2-vinyl aniline was used, no desired product was observed (Scheme 2, c25). It is noteworthy that the structure of c23 has been confirmed by single-crystal X-ray diffraction analysis.²¹

We further explored the variety of thiols. It is known that the formation of thiyl radicals from aryl thiols is faster than that of alkyl thiols, leading to the addition of aryl thiols to styrene preferentially affording anti-Markovnikov-type adducts via a radical pathway. Notably, in this photoredox/cobalt-catalytic system, the anti-Markovnikov-type adducts were completely suppressed, and the Markovnikov-type adducts were exclusively obtained with excellent regioselectivity, no matter whether the phenyl ring of the aryl thiols was substituted with electron-withdrawing groups or electron-donating groups (Scheme 3, c26-c30). Moreover, various commercially

Scheme 3. Scope of Thiols^a



^{*a*}Reaction conditions: **a1** (0.22 mmol), **b** (0.20 mmol), **PC** (5 mol %), $Co(dmgH)_2PyCl$ (20 mol %), CH_2Cl_2 (3.0 mL), under N_2 , room temperature, 450 nm LED irradiation for 24 h. ^{*b*}Isolated yields.

available alkyl thiols were examined. The results revealed that primary thiols such as 2-phenyl ethyl mercaptan (b31), ethyl thioglycolate (b32), 2-methy butyl mercaptan (b33), *n*-octyl mercaptan (b34), and furan-2-yl methanethiol (b35) reacted well with a1 to generate the corresponding Markovnikov-type products in good yields (Scheme 3, c31–c35). Regrettably, secondary and tertiary thiols were ineffective in this transformation, probably due to the steric hindrance effect (Scheme 3, c36–c39).

To gain more insights into the reaction mechanism, a series of control experiments were carried out. Quenching experiments showed that the excited photocatalyst *PC could be effectively quenched by thiol **b1**, indicating an electron-transfer process between **b1** and *PC (Figure S1). Furthermore, when a radical inhibitor (2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO)) was added, the desired product was completely inhibited, and the TEMPO-trapped thiyl radical adduct was detected by high-resolution mass spectrometry (HRMS), revealing that a thiyl radical is involved in the reaction (Scheme 4a). It is commonly known that once a sulfur radical

Scheme 4. Reaction Mechanism Investigations



is generated, it is preferential to access the anti-Markovnikovtype product via a radical pathway. However, in this catalytic system, Markovnikov-type products were exclusively obtained. We assume that this is attributed to the fact that the rate of the addition of the thiyl radical to the cobaloxime catalyst is faster than that of alkene, which could suppress the generation of an anti-Markovnikov-type adduct. The deuterium labeling experiment indicated that the hydrogen source in the product c1 mainly originated from the thiol substrate b1 (Scheme 4b). Recently, Chen, Xiao, and coworkers²² reported a nitrogenradical-mediated difunctionalization of 2-vinyl anilines. To confirm the possibility of a nitrogen radical's involvement in this reaction, we designed several control experiments. 3-Vinyl aniline a40 and 4-vinyl aniline a41 were exposed to the standard conditions, and no reaction occurred (Scheme 4c,d). Furthermore, when the N-H moiety of al was methylated, the reaction still proceeded smoothly in 70% yield (Scheme 4e). These results suggest that a nitrogen-radical-mediated pathway could be excluded in this reaction. Nevertheless, when the N-H moiety was protected by bulky groups such as benzyl (a43), isopropyl (a44), and tert-butyl (a45), the reaction could not happen (Scheme S2). We speculate that the steric hindrance would affect the coordination ability of nitrogen.

On the basis of the above observations, a reasonable mechanism is proposed in Scheme 5. The protected amine group as a directing group for activating the alkene is coordinated to a cobalt catalyst to generate the species I-1.

Scheme 5. Proposed Reaction Pathway



A thiol is oxidized by the excited photocatalyst ***PC** to generate the thiyl radical cation and the one-electron-reduced photocatalyst $PC^{\bullet-}$. Then, single-electron transfer from $PC^{\bullet-}$ to I-1 regenerates the photoredox cycle and leads to the formation of Co(II) species I-2. Deprotonation of the thiyl radical cation generates a thiyl radical, which is added to I-2 to form the cobalt sulfide intermediates I-3. The subsequent migration insertion of cobalt sulfide to the alkene produces intermediate I-4 with exclusive Markovnikov selectivity. The final protonation of I-4 furnishes the desired product and regenerates the cobalt-catalyzed cycle.

In summary, we have described a photoredox/cobaltcatalyzed strategy for the challenging catalytic Markovnikovtype thiol-ene reaction with excellent regioselectivity. The protected amine group as the directing group plays an important role in this reaction. This catalytic system shows mild reaction conditions, good functional group tolerance, and excellent atom economy. The gram-scale synthesis demonstrates the practicability of the strategy. Applications of this strategy to the hydrothiolation of more challenging alkenes are ongoing in our laboratory.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c00999.

Experimental procedures, methods, characterization data, and copies of the NMR spectra (PDF)

Accession Codes

CCDC 2041016 contains 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 Authors

Jian-Ji Zhong – Department of Chemistry, Key Laboratory for Preparation and Application of Ordered Structural Materials of Guangdong Province, and Chemistry and Chemical Engineering Laboratory of Guangdong Province, Shantou University, Shantou, Guangdong 515063, P. R. China; orcid.org/0000-0001-5248-5538; Email: jjzhong@ stu.edu.cn

Qing-Xiao Tong – Department of Chemistry, Key Laboratory for Preparation and Application of Ordered Structural Materials of Guangdong Province, and Chemistry and Chemical Engineering Laboratory of Guangdong Province, Shantou University, Shantou, Guangdong 515063, P. R. China; orcid.org/0000-0002-8125-9684; Email: qxtong@stu.edu.cn

Authors

Qian Xiao – Department of Chemistry, Key Laboratory for Preparation and Application of Ordered Structural Materials of Guangdong Province, and Chemistry and Chemical Engineering Laboratory of Guangdong Province, Shantou University, Shantou, Guangdong 515063, P. R. China; School of Chemistry and Environmental Engineering, Hanshan Normal University, Chaozhou, Guangdong 521041, P. R. China

- Hong Zhang Department of Chemistry, Key Laboratory for Preparation and Application of Ordered Structural Materials of Guangdong Province, and Chemistry and Chemical Engineering Laboratory of Guangdong Province, Shantou University, Shantou, Guangdong 515063, P. R. China
- Jing-Hong Li Department of Chemistry, Key Laboratory for Preparation and Application of Ordered Structural Materials of Guangdong Province, and Chemistry and Chemical Engineering Laboratory of Guangdong Province, Shantou University, Shantou, Guangdong 515063, P. R. China
- Jing-Xin Jian Department of Chemistry, Key Laboratory for Preparation and Application of Ordered Structural Materials of Guangdong Province, and Chemistry and Chemical Engineering Laboratory of Guangdong Province, Shantou University, Shantou, Guangdong 515063, P. R. China

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.1c00999

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We gratefully acknowledge the financial support from the National Natural Science Foundation of China (21801163, 51973107), the STU Scientific Research Foundation for Talents (NTF18003), the Chemistry and Chemical Engineering Guangdong Laboratory (1922003), the 2020 Li Ka Shing Foundation Cross-Disciplinary Research Grant (2020LKSFG05A), and the Guangdong Province Universities and Colleges Pearl River Scholar Funded Scheme 2019 (GDUPS2019).

REFERENCES

(1) (a) Jacob, C. A. Scent of Therapy: Pharmacological Implications of Natural Products Containing Redox-Active Sulfur Atoms. *Nat. Prod. Rep.* **2006**, *23*, 851. (b) Clayden, J.; MacLellan, P. Asymmetric Synthesis of Tertiary Thiols and Thioethers. *Beilstein J. Org. Chem.* **2011**, *7*, 582.

(2) (a) Secrist, J. A.; Tiwari, K. N.; Riordan, J. M.; Montgomery, J. A. Synthesis and Biological Activity of 2'-Deoxy-4'-Thio Pyrimidine Nucleosides. *J. Med. Chem.* **1991**, *34*, 2361. (b) Ilardi, E. A.; Vitaku, E.; Njardarson, J. T. Data-Mining for Sulfur and Fluorine: An Evaluation of Pharmaceuticals To Reveal Opportunities for Drug Design and Discovery. *J. Med. Chem.* **2014**, *57*, 2832. (c) Feng, M.; Tang, B.; Liang, S. H.; Jiang, X. Sulfur Containing Scaffolds in Drugs: Synthesis and Application in Medicinal Chemistry. *Curr. Top. Med. Chem.* **2016**, *16*, 1200.

(3) (a) Mishra, A.; Ma, C.-Q.; Bäuerle, P. Functional Oligothiophenes: Molecular Design for Multidimensional Nanoarchitectures and Their Applications. *Chem. Rev.* **2009**, *109*, 1141. (b) Hoyle, C. E.; Lowe, A. B.; Bowman, C. N. Thiol-Click Chemistry: A Multifaceted Toolbox for Small Molecule and Polymer Synthesis. *Chem. Soc. Rev.* **2010**, *39*, 1355. (c) Cinar, M. E.; Ozturk, T. Thienothiophenes, Dithienothiophenes, and Thienoacenes: Syntheses, Oligomers, Polymers, and Properties. *Chem. Rev.* **2015**, *115*, 3036.

(4) (a) Hoyle, C. E.; Bowman, C. N. Thiol-Ene Click Chemistry. Angew. Chem., Int. Ed. 2010, 49, 1540. (b) Sinha, A. K.; Equbal, D. Thiol-Ene Reaction: Synthetic Aspects and Mechanistic Studies of an Anti-Markovnikov-Selective Hydrothiolation of Olefins. Asian J. Org. Chem. 2019, 8, 32.

(5) (a) Kondo, T.; Mitsudo, T.-a. Metal-Catalyzed Carbon-Sulfur Bond Formation. *Chem. Rev.* **2000**, *100*, 3205. (b) Beletskaya, I. P.; Ananikov, V. P. Transition-Metal-Catalyzed C-S, C-Se, and C-Te Bond Formation via Cross-Coupling and Atom-Economic Addition Reactions. Chem. Rev. 2011, 111, 1596. (c) Chauhan, P.; Mahajan, S.; Enders, D. Organocatalytic Carbon-Sulfur Bond-Forming Reactions. Chem. Rev. 2014, 114, 8807. (d) Wang, M.; Jiang, X. Sulfur-Sulfur Bond Construction. Top. Curr. Chem. 2018, 376, 14.

(6) (a) ten Brummelhuis, N.; Diehl, C.; Schlaad, H. Thiol-Ene Modification of 1,2-Polybutadiene Using UV Light or Sunlight. *Macromolecules* **2008**, *41*, 9946. (b) Rissing, C.; Son, D. Y. Thiol-Ene Reaction for the Synthesis of Multifunctional Branched Organosilanes. *Organometallics* **2008**, *27*, 5394.

(7) (a) Ipatieff, V. N.; Pines, H.; Friedman, B. S. Reaction of Aliphatic Olefins with Thiophenol. J. Am. Chem. Soc. **1938**, 60, 2731. (b) Screttas, C. G.; Micha-Screttas, M. Markownikoff Two-Step Hydrolithiation of α -Olefins. Transformation of Secondary and Tertiary Alkyl Phenyl Sulfides to the Relevant Alkyllithium Reagents. J. Org. Chem. **1979**, 44, 713. (c) Belley, M.; Zamboni, R. Addition of Thiols to Styrenes: Formation of Benzylic Thioethers. J. Org. Chem. **1989**, 54, 1230.

(8) (a) Kanagasabapathy, S.; Sudalai, A.; Benicewicz, B. C. Montmorillonite K 10-Catalyzed Regioselective Addition of Thiols and Thiobenzoic Acids Onto Olefins: An Efficient Synthesis of Dithiocarboxylic Esters. *Tetrahedron Lett.* **2001**, *42*, 3791. (b) Mosaferi, E.; Ripsman, D.; Stephan, D. W. The Air-Stable Carbocation Salt [(MeOC₆H₄)CPh₂][BF₄] in Lewis Acid Catalyzed Hydrothiolation of Alkenes. *Chem. Commun.* **2016**, *52*, 8291. (c) Taniguchi, N. Brønsted Acid-Assisted Zinc-Catalyzed Markovnikov-Type Hydrothiolation of Alkenes Using Thiols. *J. Org. Chem.* **2020**, *85*, 6528. (d) Wang, H.; Lu, Q.; Chiang, C. W.; Luo, Y.; Zhou, J.; Wang, G.; Lei, A. Markovnikov-Selective Radical Addition of S-Nucleophiles to Terminal Alkynes through a Photoredox Process. *Angew. Chem., Int. Ed.* **2017**, *56*, 595.

(9) Castarlenas, R.; Di Giuseppe, A.; Pérez-Torrente, J. J.; Oro, L. A. The Emergence of Transition-Metal-Mediated Hydrothiolation of Unsaturated Carbon-Carbon Bonds: A Mechanistic Outlook. *Angew. Chem., Int. Ed.* **2013**, *52*, 211.

(10) Weïwer, M.; Coulombel, L.; Duñach, E. Regioselective Indium(III) Trifluoromethanesulfonate-Catalyzed Hydrothiolation of Non-Activated Olefins. *Chem. Commun.* **2006**, *42*, 332.

(11) Brouwer, C.; Rahaman, R.; He, C. Gold(I)-Mediated Hydrothiolation of Conjugated Olefins. *Synlett* **2007**, 2007, 1785.

(12) Menggenbateer; Narsireddy, M.; Ferrara, G.; Nishina, N.; Jin, T.; Yamamoto, Y. Gold-Catalyzed Regiospecific Intermolecular Hydrothiolation of Allenes. *Tetrahedron Lett.* **2010**, *51*, 4627.

(13) Cabrero-Antonino, J. R.; Leyva-Pérez, A.; Corma, A. Iron-Catalysed Markovnikov Hydrothiolation of Styrenes. *Adv. Synth. Catal.* **2012**, 354, 678.

(14) (a) Tamai, T.; Ogawa, A. Regioselective Hydrothiolation of Alkenes Bearing Heteroatoms with Thiols Catalyzed by Palladium Diacetate. J. Org. Chem. 2014, 79, 5028. (b) Tamai, T.; Fujiwara, K.; Higashimae, S.; Nomoto, A.; Ogawa, A. Gold-Catalyzed Anti-Markovnikov Selective Hydrothiolation of Unactivated Alkenes. Org. Lett. 2016, 18, 2114.

(15) Xi, H.; Ma, E.; Li, Z. Copper-Catalyzed Selective Syntheses of Markovnikov-Type Hydrothiolation Products and Thioacetals by the Reactions of Thiols with Alkenes Bearing Heteroatoms. *Tetrahedron* **2016**, *72*, 4111.

(16) Taniguchi, N. Brønsted Acid-Assisted Zinc-Catalyzed Markovnikov-Type Hydrothiolation of Alkenes Using Thiols. *J. Org. Chem.* **2020**, *85*, 6528.

(17) (a) Zeitler, K. Photoredox Catalysis with Visible Light. Angew. Chem., Int. Ed. 2009, 48, 9785. (b) Yoon, T. P.; Ischay, M. A.; Du, J. Visible Light Photocatalysis as a Greener Approach to Photochemical Synthesis. Nat. Chem. 2010, 2, 527. (c) Xuan, J.; Xiao, W. J. Visible-Light Photoredox Catalysis. Angew. Chem., Int. Ed. 2012, 51, 6828. (d) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis. Chem. Rev. 2013, 113, 5322. (e) Romero, N. A.; Nicewicz, D. A. Organic Photoredox Catalysis. Chem. Rev. 2016, 116, 10075. (f) Staveness, D.; Bosque, I.; Stephenson, C. R. J. Free Radical

Chemistry Enabled by Visible Light-Induced Electron Transfer. Acc. Chem. Res. 2016, 49, 2295. (g) Liu, Q.; Wu, L.-Z. Recent Advances in Visible-Light-Driven Organic Reactions. Natl. Sci. Rev. 2017, 4, 359. (h) Cai, B.-G.; Xuan, J.; Xiao, W.-J. Visible Light-Mediated C-P Bond Formation Reactions. Sci. Bull. 2019, 64, 337. (i) 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. Photoinduced Synthesis of Fluorinated Dibenz[b,e]azepines via Radical Triggered Cyclization. Chem. Commun. 2019, 55, 10848. (j) Zhong, J.-J.; To, W.-P.; Liu, Y.; Lu, W.; Che, C.-M. Efficient Acceptorless Photo-Dehydrogenation of Alcohols and N-Heterocycles with Binuclear Platinum(II) Diphosphite Complexes. Chem. Sci. 2019, 10, 4883.

(18) (a) Li, Y.; Miyazawa, K.; Koike, T.; Akita, M. Alkyl- and Aryl-Thioalkylation of Olefins with Organotrifluoroborates by Photoredox Catalysis. Org. Chem. Front. 2015, 2, 319. (b) Timpa, S. D.; Pell, C. J.; Ozerov, O. V. A Well-Defined (POCOP)Rh Catalyst for the Coupling of Aryl Halides with Thiols. J. Am. Chem. Soc. 2014, 136, 14772. (c) Li, Y.; Xie, W.; Jiang, X. Mechanistic Study of a Photocatalyzed C-S Bond Formation Involving Alkyl/Aryl Thiosulfate. Chem. - Eur. J. 2015, 21, 16059. (d) Xu, J.; Boyer, C. Visible Light Photocatalytic Thiol-Ene Reaction: An Elegant Approach for Fast Polymer Postfunctionalization and Step-Growth Polymerization. Macromolecules 2015, 48, 520. (e) Healy, J.; Rasmussen, T.; Miller, S.; Booth, I. R.; Conway, S. J. The Photochemical Thiol-Ene Reaction as a Versatile Method for the Synthesis of Glutathione S-Conjugates Targeting the Bacterial Potassium Efflux System Kef. Org. Chem. Front. 2016, 3, 439. (f) Zalesskiy, S. S.; Shlapakov, N. S.; Ananikov, V. P. Visible Light Mediated Metal-Free Thiol-Yne Click Reaction. Chem. Sci. 2016, 7, 6740. (g) Wimmer, A.; König, B. Photocatalytic Formation of Carbon-Sulfur Bonds. Beilstein J. Org. Chem. 2018, 14, 54. (h) Zhu, J.; Yang, W.-C.; Wang, X.-D.; Wu, L. Photoredox Catalysis in C-S Bond Construction: Recent Progress in Photo-Catalyzed Formation of Sulfones and Sulfoxides. Adv. Synth. Catal. 2018, 360, 386. (i) Li, Y.; Cai, J.; Hao, M.; Li, Z. Visible Light Initiated Hydrothiolation of Alkenes and Alkynes Over ZnIn₂S₄. Green Chem. 2019, 21, 2345.

(19) (a) Tyson, E. L.; Ament, M. S.; Yoon, T. P. Transition Metal Photoredox Catalysis of Radical Thiol-Ene Reactions. J. Org. Chem. 2013, 78, 2046. (b) Tyson, E. L.; Niemeyer, Z. L.; Yoon, T. P. Redox Mediators in Visible Light Photocatalysis: Photocatalytic Radical Thiol-Ene Additions. J. Org. Chem. 2014, 79, 1427. (c) Keylor, M. H.; Park, J. E.; Wallentin, C.-J.; Stephenson, C. R. J. Photocatalytic Initiation of Thiol-Ene Reactions: Synthesis of Thiomorpholin-3-Ones. Tetrahedron 2014, 70, 4264. (d) Bhat, V. T.; Duspara, P. A.; Seo, S.; Abu Bakar, N. S. B.; Greaney, M. F. Visible Light Promoted Thiol-Ene Reactions Using Titanium Dioxide. Chem. Commun. 2015, 51, 4383. (e) Fadeyi, O. O.; Mousseau, J. J.; Feng, Y.; Allais, C.; Nuhant, P.; Chen, M. Z.; Pierce, B.; Robinson, R. Visible-Light-Driven Photocatalytic Initiation of Radical Thiol-Ene Reactions Using Bismuth Oxide. Org. Lett. 2015, 17, 5756. (f) Zhao, G.; Kaur, S.; Wang, T. Visible-Light-Mediated Thiol-Ene Reactions through Organic Photoredox Catalysis. Org. Lett. 2017, 19, 3291. (g) Kaur, S.; Zhao, G.; Busch, E.; Wang, T. Metal-Free Photocatalytic Thiol-Ene/Thiol-Yne Reactions. Org. Biomol. Chem. 2019, 17, 1955. (h) Limnios, D.; Kokotos, C. G. Photoinitiated Thiol-Ene "Click" Reaction: An Organocatalytic Alternative. Adv. Synth. Catal. 2017, 359, 323.

(20) (a) Chen, B.; Wu, L.-Z.; Tung, C.-H. Photocatalytic Activation of Less Reactive Bonds and Their Functionalization via Hydrogen-Evolution Cross-Couplings. Acc. Chem. Res. 2018, 51, 2512.
(b) Zhong, J.-J.; Meng, Q.-Y.; Chen, B.; Tung, C.-H.; Wu, L.-Z. Visible Light Induced Cross-Coupling Hydrogen Evolution Reactions. Huaxue Xuebao 2017, 75, 34. (c) Zhong, J.-J.; Meng, Q.-Y.; Liu, B.; Li, X.-B.; Gao, X.-W.; Lei, T.; Wu, C.-J.; Li, Z.-J.; Tung, C.-H.; Wu, L.-Z. Cross-Coupling Hydrogen Evolution Reaction in Homogeneous Solution without Noble Metals. Org. Lett. 2014, 16, 1988. (d) Meng, Q.-Y.; Zhong, J.-J.; Liu, Q.; Gao, X.-W.; Zhang, H.-H.; Lei, T.; Li, Z.-J.; Feng, K.; Chen, B.; Tung, C.-H.; Wu, L.-Z. A Cascade Cross-Coupling Hydrogen Evolution Reaction by Visible Light Catalysis. J.

Am. Chem. Soc. 2013, 135, 19052. (e) He, K. H.; Li, Y. Oxidant-Free Dehydrogenative Coupling Reactions via Hydrogen Evolution. ChemSusChem 2014, 7, 2788. (f) Wang, H.; Gao, X.; Lv, Z.; Abdelilah, T.; Lei, A. Recent Advances in Oxidative \mathbb{R}^1 -H/ \mathbb{R}^2 -H Cross-Coupling with Hydrogen Evolution via Photo-/Electrochemistry. Chem. Rev. 2019, 119, 6769. (g) Zhang, H.; Xiao, Q.; Qi, X.-K.; Gao, X.-W.; Tong, Q.-X.; Zhong, J.-J. Selective Photoredox Decarboxylation of α -Ketoacids to Allylic Ketones and 1,4-Dicarbonyl Compounds Dependent on Cobaloxime Catalysis. Chem. Commun. 2020, 56, 12530.

(21) For detailed information, see the SI and CCDC no. 2041016. (22) (a) Zhao, Q.-Q.; Chen, J.; Zhou, X.-S.; Yu, X.-Y.; Chen, J.-R.; Xiao, W.-J. Photogenerated Neutral Nitrogen Radical Catalyzed Bifunctionalization of Alkenes. *Chem. - Eur. J.* **2019**, *25*, 8024. (b) Zhao, Q.-Q.; Li, M.; Xue, X.-S.; Chen, J.-R.; Xiao, W.-J. Visible-Light-Driven Neutral Nitrogen Radical Mediated Intermolecular Styrene Difunctionalization. *Org. Lett.* **2019**, *21*, 3861. (c) Yu, X.-Y.; Zhao, Q.-Q.; Chen, J.; Xiao, W.-J.; Chen, J.-R. Visible-Light-Driven Neutral Nitrogen Radical Mediated Intermolecular Styrene Difunctionalization. *Acc. Chem. Res.* **2020**, *53*, 1066.